Medical Policy

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Title: Spinal Cord and Dorsal Root Ganglion Stimulation

Professional
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Populations	Interventions	Comparators	Outcomes
Individuals: • With treatment-refractory chronic pain of the trunk or limbs	Interventions of interest are: • Standard spinal cord stimulation	Comparators of interest are: • Medical therapy • Surgical therapy	Relevant outcomes include: • Symptoms • Functional outcomes • Quality of life • Medication use • Treatment-related morbidity

Populations	Interventions	Comparators	Outcomes
Individuals: • With treatment-refractory chronic pain of the trunk or limbs	Interventions of interest are: • High-frequency spinal cord stimulation	Comparators of interest are: • Standard spinal cord stimulation • Medical therapy • Surgical therapy	Relevant outcomes include: • Symptoms • Functional outcomes • Quality of life • Medication use • Treatment-related morbidity
Individuals: • With treatment-refractory chronic pain of the trunk or limbs	Interventions of interest are: • Dorsal root ganglion neurostimulation	Comparators of interest are: • Standard spinal cord stimulation • Medical therapy • Surgical therapy	Relevant outcomes include: • Symptoms • Functional outcomes • Quality of life • Medication use • Treatment-related morbidity
Individuals: • With critical limb ischemia	Interventions of interest are: • Spinal cord stimulation	Comparators of interest are: • Medication therapy • Revascularization surgery • Amputation	Relevant outcomes include: • Overall survival • Symptoms • Functional outcomes • Quality of life • Morbid events • Hospitalizations • Treatment-related morbidity
Individuals: • With treatment-refractory angina pectoris	Interventions of interest are: • Spinal cord stimulation	Comparators of interest are: • Medical therapy • Coronary revascularization	Relevant outcomes include: • Overall survival • Symptoms • Functional outcomes • Quality of life • Morbid events • Hospitalizations • Treatment-related morbidity
Individuals: • With heart failure	Interventions of interest are: • Spinal cord stimulation	Comparators of interest are: • Medical therapy • Coronary revascularization	Relevant outcomes include: • Overall survival • Symptoms • Functional outcomes • Quality of life • Morbid events • Hospitalizations • Treatment-related morbidity
Individuals: • With cancer-related pain	Interventions of interest are: • Spinal cord stimulation	Comparators of interest are: • Medical therapy	Relevant outcomes include: • Symptoms • Functional outcomes • Quality of life • Medication use • Treatment-related morbidity

DESCRIPTION

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

OBJECTIVE

The objective of this evidence review is to evaluate the safety and efficacy of spinal cord stimulation for treating patients with treatment-refractory chronic pain of the trunk or limbs, critical limb ischemia, refractory angina, heart failure, and cancer-related pain.

BACKGROUND

Chronic Pain

Spinal cord stimulation 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 spinal cord stimulation as a treatment of critical limb ischemia, primarily in patients who are poor candidates for revascularization and in patients with refractory chest pain.

Spinal Cord Stimulation

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

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

Traditional spinal cord stimulation devices use electrical stimulation with a frequency of 100 to 1000 Hz. In 2015, an spinal cord stimulation device, using a higher frequency (10,000 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 paresthesia's, which are a recognized effect of spinal cord stimulation. In 2016, the FDA approved a clinician programmer application that allows an spinal cord stimulation device to provide stimulation in bursts rather than at a constant rate. Burst stimulation is proposed to relieve pain with fewer paresthesia's. The burst stimulation device works in conjunction with standard spinal cord stimulation devices. With the newly approved app, stimulation is provided in five, 500-Hz burst spikes at a rate of 40 Hz, with a pulse width of 1 ms.

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. 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. Two systems targeting the dorsal root ganglion 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 dorsal root ganglion stimulation.[2,] 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.

REGULATORY STATUS

A large number of neurostimulator devices, some used for spinal cord stimulation, have been approved by the FDA through the premarket approval process under FDA product code: LGW (stimulator, spinal-cord, totally implanted for pain relief). In October 2016, the FDA approved BurstDR™ stimulation (St. Jude Medical), a clinician programmer application that provides intermittent "burst" stimulation for patients with certain St. Jude spinal cord stimulation devices. The following table lists the original premarket approval information for devices with product code LGW.

Table 1. Premarket Approval Information for Devices With Product Code LGW

Device	Manufacturer	Original PMA number	Original approval date
Algovita Spinal Cord Stimulation System	Nuvectra Corporation	P130028	Nov 2015
Nevro Senza Spinal Cord Stimulation (SCS) System	Nevro Corporation	P130022	May 2015
Precision Spinal Cord Stimulation(SCS) System	Boston Scientific Corporation	P030017	Apr 2004
Genesis And Eon Family Neurostimulation (Ipg) Syst.	St. Jude Medical / Abbott Medical	P010032	Nov 2001
Itrel(R) Totally Implantable Spinal Cord Stim. Sys	Medtronic Neuromodulation	P840001	Nov 1984

Device	Manufacturer	Original PMA number	Original approval date
Cordis Programmable Neural Stimulator Models 900a,	Cordis Corporation	P800040	Apr 1981

LGW: U.S. Food and Drug Administration product code; PMA: premarket approval.
In February 2016, the Axium Neurostimulator System (Abbott) was approved by the FDA through the premarket approval process (P150004) with product code PMP (Dorsal Root Ganglion Stimulator For Pain Relief). This implanted device stimulates the dorsal root ganglion. 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 (K180981) 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. FDA product code: GZB (Stimulator, Spinal-Cord, Implanted (Pain Relief))

POLICY

A. Spinal cord stimulation and dorsal root ganglion neurostimulation 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.

B. Spinal cord stimulation and dorsal root ganglion neurostimulation is considered **experimental / 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 treatment of non-neuropathic cancer-related pain.

C. Wireless injectable dorsal root ganglion neurostimulation is considered **experimental / investigational**.

Policy Guidelines

1. Patient selection focuses on determining whether the patient is refractory to other types of treatment. The following considerations shall **ALL** apply:
   a) The treatment is used when reasonable conservative treatment modalities (pharmacological, surgical, psychological, or physical, if applicable) have been tried and failed or are judged to be unsuitable or contraindicated, **AND**
   b) Pain is neuropathic in nature (ie, resulting from actual damage to the peripheral nerves). Common indications include, but are not limited to, failed back syndrome, complex regional pain syndrome (ie, reflex sympathetic dystrophy), arachnoiditis, radiculopathies, phantom limb/stump pain, and peripheral 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), **AND**
   c) No serious untreated drug habituation exists, **AND**
   d) Demonstration of at least 70% pain relief during a typical 5 to 7 day temporary trial electrode array implant prior to permanent implantation, **AND**
   e) All the facilities, equipment, and professional and support personnel required for the proper diagnosis, treatment, and follow-up of the patient are available, **AND**
   f) Psychological evaluation prior to trial implantation has been performed and indicates no contraindications to spinal cord stimulation.

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

RATIONALE

This evidence review has been updated regularly with searches of the PubMed database. The most recent literature update was performed through February 28, 2020.

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 one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. 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.

SPINAL CORD AND DORSAL ROOT GANGLION STIMULATION

Clinical Context and Therapy Purpose

The purpose of spinal cord stimulation and dorsal root ganglion stimulation in patients who have treatment-refractory chronic pain, critical limb ischemia, 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 question addressed in this evidence review is: Does the use of spinal cord stimulation or dorsal root ganglion stimulation improve the net health outcomes of patients with treatment-refractory chronic pain, critical limb ischemia, angina pectoris, heart failure, or cancer-related pain compared with medical and surgical therapies?

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

Patients

There are several populations of interest in this review:

- Patients with treatment-refractory chronic pain of the trunk or limbs
- Patients with critical limb ischemia
- Patients with treatment-refractory angina pectoris
- Patients with heart failure
- Patients with cancer-related pain.

Interventions

The therapies being considered include:

- spinal cord stimulation: spinal cord stimulation uses low-level epidural electrical stimulation of the spinal cord dorsal columns. Their 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.

- 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 paresthesia's compared with standard spinal cord stimulation.
- 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.

Comparators

The standard of care, by population of interest, consists of:

- Patients with treatment-refractory chronic pain of the trunk or limbs: medical therapy or surgical therapy.
- Patients with critical limb ischemia: medical therapy or surgical therapy (revascularization surgery or amputation).
- Patients with treatment-refractory angina pectoris: medical therapy or coronary revascularization.
- Patients with heart failure: medical therapy or coronary revascularization.
- Patients with 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 (see 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%-20% decrease • Moderately important: ≥ 30% decrease

Domain	Outcome Measure	Description	Clinically Meaningful Difference
			• 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 work, activities away from home, and social activities • Items rated on 0- to 6-point scale • Interference subscale score calculated by mean of subscale items	• ≥0.6-point decrease[5,]
•	• 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,	• 10 points[9,]

Domain	Outcome Measure	Description	Clinically Meaningful Difference
		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	
•	*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,]
•	• 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,]

Domain	Outcome Measure	Description	Clinically Meaningful Difference
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,]

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

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

Refractory Chronic Trunk or Limb Pain

Standard Spinal Cord Stimulation

Review of Evidence

Systematic Reviews
Existing RCTs of standard spinal cord stimulation for chronic trunk or limb pain are summarized in the next section. Systematic reviews have assessed the RCTs included in the next section and overlap substantially.

Two systematic reviews have focused on spinal cord stimulation specifically for complex regional pain syndrome. Visnjevac et al (2017) reported on results of a systematic review of RCTs and observational studies of spinal cord stimulation for complex regional pain syndrome.[15,] The Kemler et al (2000) trial was the only RCT included and it is discussed in the following section. The Cochrane overview of systematic reviews by O'Connell et al (2013) also focused on reviews of complex regional pain syndrome.[16,] The overview included reports from the Kemler et al (2000) RCT. Reviewers concluded that there was very low-quality evidence using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) criteria that spinal cord stimulation using physical therapy was effective at reducing pain or improving quality of life in complex regional pain syndrome compared with physical therapy alone for up to 2 years.

Grider et al (2016) reported on results of a systematic review of RCTs of spinal cord stimulation for chronic spinal pain.[17,] Six RCTs meeting selection criteria were identified; 3 RCTs reported on the efficacy of standard spinal cord stimulation, while 3 assessed adaptive stimulation, high-frequency spinal cord stimulation (discussed below), and burst stimulation. Of the 3 RCTs assessing standard spinal cord stimulation, 2 were considered high-quality and 1 moderate-quality based on Cochrane criteria and Interventional Pain Management Techniques-Quality Appraisal of Reliability and Risk of Bias Assessment. Kapural et al (2015) is discussed below in the section on high-frequency spinal cord stimulation. In the North et al (2005) and Kumar et al (2007) RCTs, spinal cord stimulation was associated with higher rates of pain relief than the comparator groups.

Two systematic reviews have focused on spinal cord stimulation for failed back surgery syndrome, defined as persistent pain after spinal surgery and the initial pain may have been secondary to various causes. Kapural et al (2017) reported on a systematic review of prospective studies of spinal cord stimulation for failed back surgery syndrome.[18,] The North et al (2005) and Kumar et al (2007) trials were the only RCTs included and are discussed in the following section. A systematic review of RCTs and observational studies evaluating spinal cord stimulation for failed back surgery syndrome was conducted by Frey et al (2009).[19,] The 2 RCTs by North et al (2005) and Kumar et al (2007) were included. Using the United States Preventive Services Task Force quality ratings, reviewers found level II-1 evidence (from well-designed controlled trials without randomization) or II-2 evidence (from well-designed cohort or case-control analytic studies, preferably from >1 center or research group) for the clinical use of standard spinal cord stimulation on a long-term basis.

Head et al (2019) reported a systematic review of clinical trials of spinal cord stimulation, including standard, high frequency, and burst stimulation, for the treatment of chronic neuropathic low back and leg pain.[20,] For standard spinal cord stimulation, the North et al (2005),[21,] and Kumar et al (2007)[22,] RCTs were included. For high-frequency spinal cord stimulation (discussed in the following section), the Perruchoud et al (2013)[23,], Kapural et al (2015, 2016)[24,], and De Andes et al (2017)[25,] were included.

Also, Simpson et al (2009) reported on a health technology assessment, funded by the National Institute for Health and Care Excellence (NICE), to obtain clinical and cost-effectiveness data for spinal cord stimulation in adults with chronic neuropathic or ischemic pain with inadequate response to other medical or surgical treatments.[26,] The NICE used the assessment as the basis for its guidance on spinal cord stimulation for chronic pain.[27,] Trials for failed back surgery syndrome and complex regional pain syndrome type I (reported by North et al [2005],[21,] Kumar et al [2007],[22,] and Kemler et al [2000, 2004][28,29,]), suggested that spinal cord stimulation was more effective than conventional medical management or reoperation in reducing pain.

Randomized Controlled Trials

Six RCTs (total n=528 patients; range, 36-218 patients) have evaluated spinal cord stimulation (see Table 3). Patient populations had failed back surgery syndrome, diabetic neuropathy, and complex regional pain syndrome. The comparators were primarily conventional medical management, although one 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 absolute change in

visual analog scale 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%-63% vs. comparator range, 5%-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)[30,] 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	*Int*	*Ctrl*	*p*	
North et al (2005)[21,]	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 %	0.04	
				• Stable or decreased opioids	87%	58 %	0.025	
				• No difference in ADLs impairment due to pain	•			

Study	Population	Interventions	N at Baseline and Follow-Up	Results				Complications
Kumar et al (2007, 2008)[22,31,]	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%	<0.001	
				• SF-36, favoring SCS all domains except RP	•		≤0.02	
				• ODI score	45	56	<0.001	
				• Opioid use	56%	70 %	0.21	
				• NSAID use	34%	50 %	0.14	
			n at 24 mo=87	24 mo (SCS vs. CMM)				
				• 50% reduction in leg pain on VAS	37%	2%	0.003	
Kemler et al (2000, 2004, 2008)[28,29,32,]	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)

Study	Population	Interventions	N at Baseline and Follow-Up	Results				Complications
								• 42% reoperation rate by 5 y
•				• Reduction in VAS pain score	2.4	0.2	<0.001	
				• Much improved GPE	39%	6%	0.01	
				• No difference in functional outcomes or HRQOL	•			
				2 y (SCS vs. PT)				
				• Reduction in VAS pain score	2.1	0.0	<0.001	
				• Much improved GPE	43%	6%	0.001	
			n at 5 y=44	5 y (SCS vs. PT)				
				• Reduction in VAS pain score	1.7	1.0	0.25	
Slangen et al (2014)[30,]	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	59%	7%	<0.01	

Study	Population	Interventions	N at Baseline and Follow-Up	Results				Complications
				improved on patient-reported global impression of change)				
				• Reduction in pain medication	32%	0%		
				• No differences in health utility or HRQOL	•			
			n at 24 mo=17[a]	2 y (SCS only)				
				• Success	65%			
				• No improvement in health utility vs. baseline	•			
				• ~5-point improvement in SF-36 PCS score vs. baseline	•			
De Vos et al (2014)[33]; Duarte et al (2016)[34]	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%	<0.001	

Study	Population	Interventions	N at Baseline and Follow-Up	Results				Complications
				• Reduction in analgesic intake (MQS score)	2.9	-0.09	NR	
				• Change in health utility	0.39	0.00	<0.05	
Rigoard P (2019)[35,]	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%	0.04	
				• Change in SF-36 Short Form	7.5	0	<0.001	

ADL: activities of daily living; CMM: conventional medical management; CRPS: complex regional pain syndrome; ctrl: control; FBSS: failed back surgery syndrome; GPE: global perceived effect; HRQOL: health-related quality of life; Int: intervention;
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; RP: role-physical; SAE: serious adverse events;
SCS: spinal cord stimulation; SF-36: 36-Item Short-Form Health Survey; VAS: visual analog scale; RCT: randomized controlled trial.
[a] SCS only.

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 RCTs evaluating patients with refractory pain due to failed back surgery syndrome, complex regional pain syndrome, or diabetic neuropathy. These trials 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 paresthesia's. Given the extensive treatment effects with consistent findings across studies, this evidence suggests that spinal cord stimulation is a reasonable treatment option.

High-Frequency Spinal Cord Stimulation

In 2015, an spinal cord stimulation device, using a higher frequency of electrical stimulation (10 kHz) than predicate devices (which use frequencies on the order of 100-1000 Hz), was approved by the FDA. Studies that offer direct comparisons between standard spinal cord stimulation and high-frequency spinal cord stimulation were sought to evaluate the incremental benefit of high-frequency spinal cord stimulation.

REVIEW OF EVIDENCE

Systematic Reviews

Bicket et al (2016) published a systematic review of controlled trials on high-frequency spinal cord stimulation.[36,] Reviewers searched for RCTs and controlled nonrandomized studies of adults with pain for at least 3 months who were treated with high-frequency spinal cord stimulation (i.e., ≥1000 Hz) and prospectively assessed pain outcomes. Eight studies met these inclusion criteria; 2 RCTs (detailed below) and 6 controlled nonrandomized studies. Both RCTs and 5 of 6 controlled studies addressed low back pain; the remaining controlled study addressed migraine. Reviewers used the Cochrane criteria to rate bias in the RCTs. One trial (Perruchoud et al [2013][23,]) was not rated as having a high-risk of bias in any domain, and the other (Kapural et al [2015][24,]) was rated as having a high-risk of bias in the domain of performance and detection bias because it was unblinded. Studies were reviewed qualitatively (i.e., study findings were not pooled).

Randomized Controlled Trials

Three RCTs identified addressed high-frequency spinal cord stimulation (see Table 4): Perruchoud et al (2013) compared high-frequency spinal cord stimulation (5000 Hz) with sham-control in a crossover design (n=40), while Kapural et al (2015)[24,] (n=198) and De Andres et al (2017)[25,] (n=60) both compared high-frequency spinal cord stimulation (10000 Hz) with standard spinal cord stimulation. The 3 trials had distinct patient populations and designs such that the results could not be synthesized.

The Perruchoud et al (2013) population was distinct from other trials of spinal cord stimulation or high-frequency spinal cord stimulation in that it included patients who had chronic, treatment-refractory back pain previously treated with standard spinal cord stimulation (i.e., patients were not treatment-naive to spinal cord stimulation).[23,] This trial used a 2×2 crossover design with a run-in and washout period consisting of standard spinal cord stimulation. In the trial treatment periods, patients were treated with high-frequency spinal cord stimulation or sham stimulation. After 2 weeks of treatment, outcomes revealed that 42% of patients were responders in the high-frequency group versus 30% in the sham group. The mean benefit averaged over the 2 crossover sequences was 11%, favoring high-frequency spinal cord stimulation (p=0.30). There were no differences between high-frequency spinal cord stimulation and sham for visual analog scale or health utility scores. However, there was a significant period effect: patients were more likely to respond in the first treatment period of the sequence regardless of sequence assignment. It is difficult to compare the Perruchoud et al (2013) findings with other RCTs due to a number of factors: (1) the enrollment population played a role (only people who had chronic pain-despite previous use of standard spinal cord stimulation were able to participate); (2) the treatment period was short at only 2 weeks; (3) there was the period effect (patients tended to report greater pain reduction in the first period regardless of assigned sequence); and (4) the

use of standard spinal cord stimulation during the 2 weeks preceded each treatment period, which led to carryover effects.

Kapural et al (2015, 2016)[24,37,] included 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).

De Andres et al (2017) included adults from a single-center in Spain with failed back surgery syndrome refractory to standard treatment for at least 6 months with a pain intensity score of at least 5 out of 10 of a numeric rating scale.[25,] The comparator was spinal cord stimulation, and the trial was described as blinded but the method of blinding participants was not given. Patients were told that the 2 treatments were "equally effective." Outcome assessors were reportedly blinded although many of the assessments used were patient-reported. Outcomes were reported at 3, 6, and 12 months. The primary outcome was "a reduction of at least 50% in pain intensity in the numeric rating scale score in the 12-month evaluation"; however, analysis of this outcome was not reported in the tables or text. The sample size calculations were unclear. Seventy-eight participants were assessed for eligibility, and 60 were randomized. It is unclear how many of the 18 not randomized were ineligible due to lack of response during the trial spinal cord stimulation period. Of the 60 randomized, 55 were included in the analysis. Although pain ratings improved in both groups, there were no statistically significant differences in change in numeric rating scale or Oswestry Disability Index scores from baseline at any of the follow-up visits between groups. Lead migration during follow-up was similar in both groups. No patients developed an infection at the implant site. Because of poor reporting, this trial is difficult to evaluate.

Table 4. 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)[23,]	Chronic low back pain radiating in 1 or both	• HFSCS • Sham • 2×2 crossover	N=40 n=33	2 wk (HFSCS vs. sham)				One patient had malaise attributed to a

Study	Population	Interventions	N at Baseline and Follow-Up	Results				Complications
	legs; previously treated with SCS	design with conventional SCS before both arms						vasovagal attack
				• Responder (at least minimal improvement on patient-reported global impression of change)	42 %	30 %	0.30	
				• VAS score	4.35	4.26	0.82	
				• Health utility	0.48	0.46	0.78	
Kapural et al (2015, 2016)[24,37,]	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 %	<0.001	
				• ○ Leg pain	83 %	55 %	<0.001	
			n at 12 mo=171	12 mo (HFSCS vs. SCS)				

Study	Population	Interventions	N at Baseline and Follow-Up	Results				Complications
				• Responders ○ Back pain	80 %	50 %	NR	
				• ○ Leg pain	80 %	56 %	NR	
				• Decreased opioid use	36 %	26 %	0.41	
				• Improvement in ODI score	16.5	13.0	NR	
				24 mo (HFSCS vs. SCS)				
				• Responders o Back pain	77 %	49 %	<0.001	
				o Leg pain	73 %	49 %	<0.001	
De Andes et al (2017)[25,]	FBSS	• HFSC • SCS	N=60 n=55 analyzed	12 mo (HFSCS vs. SCS)				
				Responder (≥50% in pain intensity in NRS score at 12 mo)[a]	NR	NR		
				Improvement in NRS score	6.1	5.9	0.56	
				Improvement in ODI score	23.0	22.1	0.96	

Ctrl: control; 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 not reported in the report.

Case Series

Because RCT data are available for high-frequency spinal cord stimulation, 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 high-frequency spinal cord stimulation.[38,] 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 visual analog scale score for pain intensity decreased from 79 to 10 mm ($p<0.001$) and the mean Oswestry Disability Index score decreased from 53 to 20 ($p<0.001$). At baseline, 90% of the patients were using opioids compared with 12% at 36 months.

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

The evidence for high-frequency spinal cord stimulation compared with standard spinal cord stimulation consists of an RCT that randomized 198 patients not previously treated with spinal cord stimulation and reported a clinically and statistically significant benefit associated with high-frequency spinal cord stimulation. The crossover RCT enrolling patients with pain despite previous treatment with spinal cord stimulation reported no difference between high-frequency spinal cord stimulation and sham stimulation. However, interpretation of this trial is limited due to the significant period effect.

Spinal Cord Stimulation With Burst Stimulation (High-Frequency)

In 2016, a supplement to an 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. Studies that offer direct comparisons between standard spinal cord stimulation and burst spinal cord stimulation were sought to permit evaluation of the incremental benefit of burst spinal cord stimulation.

REVIEW OF EVIDENCE

Systematic Reviews

Hou et al (2016) published a systematic review of burst spinal cord stimulation for the treatment of chronic back and limb pain.[39,] 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

Five crossover RCTs with a total of 180 patients (range, 12-100 patients) were identified, 4 of which were conducted in Europe and the other in the United States (see Table 5). The trials by De Ridder et al (2010, 2013)[40,41,] enrolled patients with neuropathic pain, the trial by Schu et al (2014)[42,] enrolled patients with failed back surgery syndrome, Kriek et al (2017)[43,] enrolled patients with complex regional pain syndrome, and Deer et al (2018)[44,] enrolled patients with

chronic intractable pain of the trunk and/or limbs. All trials compared burst stimulation with spinal cord stimulation. Schu et al (2014), De Ridder et al (2013), and Kriek et al (2017) also compared burst with a sham stimulation group. Schu et al (2014) 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 after 12 weeks of stimulation in Deer et al (2018). All trials reported reductions in absolute pain scores (numeric rating scale or visual analog scale). 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 5. 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. The interpretation of 4 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).[44,] 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 visual analog scale 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 visual analog scale score between burst and spinal cord stimulation was -5.1 mm (95% upper confidence interval [CI], -1.14 mm), demonstrating noninferiority ($p<0.001$) and superiority ($p<0.017$). The proportion of patients with a decrease in visual analog scale 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 ($p=0.230$). 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.

Section Summary: Spinal Cord Stimulation With Burst Stimulation for Chronic Trunk or Limb Pain

Spinal cord stimulation with burst stimulation has been evaluated in 5 crossover RCTs. Four 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 visual analog scale 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.

Table 5. Characteristics and Result of RCTs Using Burst Spinal Cord Stimulation

Study	Population	Interventions	N at Baseline and FU	Results				Complications
Parallel								
Van Havenbergh et al (2015)	FBSS and chronic low back or leg pain	• 500-Hz burst • 1000-Hz burst	•					Not reported
3×3 crossover design without washout				Outcome Measure	Burst	SCS	Sham	
Schu et al (2014)[42,]	FBSS	• Burst stimulation • SCS • No stimulation (sham-control)	N=20 n=20	1 wk (burst vs. SCS vs. sham)[a]				No SAEs reported

Study	Population	Interventions	N at Baseline and FU	Results				Complications
				• 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)[40,]	Neuropathic limb pain	• Burst stimulation • SCS • No stimulation (sham-control)	N=15 n=15	1 wk (burst vs. SCS vs. sham)[a]				Not reported
				• Mean improvement in VAS scores ○ Back pain	3.8	2.2	1.4	
				• ○ Limb pain	3.9	3.9	0.9	
2×2 crossover								

Study	Population	Interventions	N at Baseline and FU	Results				Complications
De Ridder et al (2010)[41,]	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 sensory scores	16.7	8.6		
				• Improvement in SF-MPQ affective scores	6.7	4.3		
Deer et al (2018)[44,]	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<0.001			

Study	Population	Interventions	N at Baseline and FU	Results				Complications
				Responder (≥30% improvement in VAS score)	60%	51%		
5×5 crossover								
Kriek et al (2017)[43,]	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	

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.

Dorsal Root Ganglion Neurostimulators for Chronic Trunk or Limb Pain

Studies offering direct comparisons between standard spinal cord stimulation and dorsal root ganglion neurostimulators were sought to evaluate the benefits of spinal cord stimulation.

DORSAL ROOT GANGLION IMPLANTED DEVICE

REVIEW OF EVIDENCE

Systematic Reviews

Chang Chien et al (2017) published a systematic review on intraspinal stimulation of nondorsal column targets, including neurostimulation of the dorsal root ganglion for chronic pain.[45,] Reviewers included reports published through March 2015. They identified 6 studies of dorsal root ganglion stimulation: 1 conference presentation of the preliminary RCT data from ACCURATE (A Safety and Effectiveness Trial of Spinal Cord Stimulation of the Dorsal Root Ganglion for Chronic Lower Limb Pain) as discussed below, 4 publications describing 3 prospective observational studies, and 1 retrospective chart review. In the 3 prospective observational studies (n=32, 10, and 8), follow-up ranged from 7 days to 12 months. The retrospective study reported on 25 patients with a follow-up to 32 weeks. Meta-analyses could not be conducted with one RCT.

Vuka et al (2019) conducted a systematic review of the use of dorsal root ganglion stimulation for various pain syndromes (for example, complex regional pain syndrome, diabetic and non-diabetic peripheral neuropathy).[46,] The literature search, conducted through September 2018, identified 29 studies for inclusion, 1 RCT, (ACCURATE trial; discussed below) and the remaining were case series or case reports. The median sample size was 6 (range 1 to 152). Most of the studies reported positive results with dorsal root ganglion stimulation. No meta-analyses could be conducted.

Huygen et al (2020) reported a pooled analysis of prospective studies of dorsal root ganglion stimulation for the treatment of chronic pain.[47,] One RCT was included (ACCURATE) which is described in the following section and 6 prospective, single-arm, observational studies were included. The analysis included 217 patients with a permanent implant at 12-month follow-up.

Randomized Controlled Trial

The ACCURATE study (NCT01923285) compared dorsal root ganglion neurostimulation with standard spinal cord stimulation.[48,49,] 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 complex regional pain syndrome 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 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) 50% or greater reduction in visual analog scale score and (2) no stimulation-related neurologic deficits. The noninferiority margin was set at 10%. Results are shown in Table 7. No patients experienced neurologic deficits in either group. Regarding paresthesia's, at 3 months and 12 months, spinal cord stimulation patients were significantly more likely to report paresthesia's in nonpainful areas than dorsal root ganglion patients. At 3 months, 84.7% of dorsal root ganglion patients and 65% of spinal cord stimulation patients reported paresthesia's only in their painful areas; at 12 months, these percentages were 94.5% and 61.2%, respectively. Limitations in study relevance, design, and conduct are shown in Tables 8 and 9.

Mekhail et al (2019) conducted a sub-analysis on the patients receiving dorsal root ganglion neurostimulation in the ACCURATE study, to evaluate the occurrence and risk factors for paresthesia.[50,] 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)[48,]; ACCURATE (NCT01923285)	U.S.	22	2013-2016	• CRPS or causal lower extremities • Chronic pain (6 mo) • Stimulation-naïve • Failed ≥2 pharmacologic treatments	AXIUM Neurostimulator System (n=76)	RestoreUltra and RestoreSensor (n=76)

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

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)[48,]						
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<0.001; superiority p<0.001)	1.1 (0.2 to 2.1) (<0.05 favoring DRG)	NR (0.04 favoring DRG)	2.5 (-0.7 to 5.7)	3.5 (-0.5 to 7.5)	
At 12 months						
n	132	105	NR	105	105	152
DRG	74%	3.9	»18	11.5	6.2	11%
SCS	53%	2.6	»8	8.0	3.6	15%
TE (95% CI) (p)	NR (noninferiority p<0.001; superiority p<0.001)	1.3 (0.2 to 2.3)(<0.05 favoring DRG)	NR (<0.001)	3.5 (-0.1 to 7.1)(0.04 favoring DRG)	2.6 (-1.9 to 7.1)	NR (0.62)

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

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

Study	Population	Intervention	Comparator	Outcomes	Follow-Up
Deer et al (2017)[48,]	None noted				
Key	1.Intended use population unclear 2.Clinical context for treatment is unclear 3.Study population unclear 4.Study population not representative of intended use 5.Study population	1.Not clearly defined 2.Version used unclear 3.Delivery not similar intensity as comparator	1.Not clearly defined 2.Not standard or optimal 3.Delivery not similar intensity as intervention 4.Not delivered effectively	1.Key health outcomes not addressed 2.Physiologic measures, not validated surrogates 3.Not CONSORT reporting of harms 4.Not established and validated measurements 5.Clinically significant difference not prespecified	1.Not sufficient duration for benefits 2.Not sufficient duration for harms

Study	Population	Intervention	Comparator	Outcomes	Follow-Up
	is subpopulation of intended use			6.Clinically significant difference not supported	

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

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)[48,]	None noted	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
Key	1.Participants not randomly allocated 2.Allocation not concealed 3.Allocation concealment unclear 4.Inadequate control for selection bias	1.Not blinded to treatment assignment 2.Not blinded outcome assessment 3.Outcome assessed by treating physician	1.Not registered 2.Evidence of selective reporting 3.Evidence of selective publication	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)	1.Power calculations not reported 2.Power not calculated for primary outcome 3.Power not based on clinically important difference	1.Test is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event 2.Test is not appropriate for multiple observations per patient 3.Confidence intervals and/or p values not reported 4.Comparative treatment effects not calculated

DRG: dorsal root ganglion; RCT: randomized controlled trial; SCS: spinal cord stimulation.

Case Series

The remaining evidence for the use of dorsal root ganglion stimulation for chronic pain consists of case series.[51,52,53,54,55,56,57,58,]

The case series evaluated the Axium dorsal root ganglion neurostimulator or an unnamed dorsal root ganglion stimulator in patients with failed back surgery syndrome, diabetic and non-diabetic

peripheral nerve injury, postsurgical neuropathic pain, groin pain, and complex regional pain syndrome are identified: Liem et al (2015)[52,] and Schu et al (2015).[51,] Liem et al (2015) had a larger sample size (n= 51 vs. n=29) and longer follow-up. Fifty-one patients with chronic pain of the trunk, lower back, or lower limbs who had failed conventional treatment underwent trial stimulation, and 32 underwent permanent implantation. Sample sizes ranged from 10 to 65 patients. One study had a 6-month follow-up,[42,] most studies had 1-year follow-up,[52,53,55,56,57,58,] and the largest study followed half of the patients for 3 years.[54,] For the studies reporting at least 1 year follow-up, the proportion of patients achieving a 50% or greater reduction in overall pain ranged from 49% to 83%. The largest case series, by Morgalla et al (2018), reported that after 3 years of follow-up, the patients continued to experience decreased Beck Depression Inventory scores, decreased Pain Disability Index scores, and 72% achieved a 50% or greater reduction in overall pain.

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.[59,] 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.

Dorsal Root Ganglion Wireless Injectable Device

No controlled studies were identified. A case series, which included 11 patients, was published by Weiner et al (2016).[60,] 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 visual analog scale scores were 5 or higher in all patients. Seven (63%) of the 11 patients reported good to excellent overall pain relief (visual analog scale score reduction, ≥50%), 2 patients reported fair overall intensity pain relief (25%-50% reduction), and 2 patients reported poor or no overall pain relief (0%-25%). No adverse events were reported.

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

One unblinded RCT and many 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 percentage achieving >50% pain reduction, emotional functioning score, and 36-Item Short Form Health Survey scores. Both groups experienced paresthesia's but patients in the dorsal root ganglion group reported less postural variation in paresthesia and reduced extraneous stimulation in nonpainful 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. Many case series have also been published; all reporting results consistent with the RCT.

The percentages of patients achieving 50% or greater reduction in overall pain ranged from 49% to 83% among the case series. The largest series, which had the longest follow-up of 3 years, reported that 83% of patients at 12 months and 72% of patients at 3 years experienced 50% or greater reduction in overall pain.

Critical Limb Ischemia

Critical limb ischemia is described as pain at rest or the presence of ischemic limb lesions. 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.

An updated Cochrane review by Ubbink and Vermeulen (2013) assessed the use of spinal cord stimulation in peripheral vascular diseases.[61,] Reviewers included RCTs and non-RCTs evaluating the efficacy of spinal cord stimulation in adults with nonreconstructable, 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 was 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 (pooled 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 (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.[62,] The same 5 RCTs identified in the Cochrane review (previously described) were included. Reviewers did not find a statistically significant difference in the rate of amputation in the treatment or the control groups. The relative risk of amputation was 0.79, with a risk difference of -0.07 (p=0.15). Reviewers also conducted additional analyses of data from their 1999 RCT to identify factors associated with better or worse prognoses.[63,] 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 one of the treatments. The review identified 5 RCTs for inclusion.[64,] In the pooled analysis, reviewers found that spinal cord stimulation was associated with reduced risk of amputation (odds ratio, 0.53; 95% CI, 0.36 to 0.79). However, they concluded that the evidence was of "relatively low quality … mainly due to imprecision (i.e., small sample size and wide CIs) and the risk of bias."

Section Summary: Critical Limb Ischemia
Five relatively small RCTs comparing spinal cord stimulation with usual care have assessed patients with critical limb ischemia. In some pooled analyses of these RCTs, spinal cord stimulation did not result in a significantly lower rate of amputation, although one meta-analysis which included a nonrandomized study reported a significant difference. This evidence is not sufficient to determine whether spinal cord stimulation would improve outcomes for patients with critical limb ischemia.

REFRACTORY ANGINA PECTORIS

REVIEW OF EVIDENCE

Systematic Reviews
Several systematic reviews have evaluated spinal cord stimulation for treating angina pectoris. More recently, Pan et al (2017) identified 12 RCTs that evaluated spinal cord stimulation in patients with refractory angina pectoris.[65,] Most studies had small sample sizes (i.e., <50 patients) and together totaled 476 patients. Reviewers did not discuss the control interventions reported in the RCTs. Pooled analyses favored the spinal cord stimulation group in most cases (e.g., for exercise time after the intervention, pain level [visual analog scale 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).[66,] 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 2-3)." 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
Zipes et al (2012) published an industry-sponsored, single-blind, multicenter trial with sites in the United States and Canada.[67,] 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=0.81). The trial sample size was small, and it might have been underpowered for clinically meaningful differences.

A small 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%-80% of the sensory threshold) (n=7), or very low-intensity spinal cord stimulation (n=8).[68,] 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=0.002). Nonsignificant variables included the use of nitroglycerin, quality of life, visual analog scale, Canadian Cardiovascular Society angina class, exercise-induced angina, and scores on 5 subscales of the Seattle Angina Questionnaire.

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
Findings of a small pilot crossover RCT evaluating spinal cord stimulation for heart failure were published by Torre-Amione et al (2014).[69,] 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 one 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.[70,] 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=0.30). 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=0.36). The trial was originally powered based on a planned enrollment of 195 implanted patients but enrollment was stopped early due to enrollment 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
A Cochrane review by Lihua et al (2013) assessed spinal cord stimulation for the treatment of cancer-related pain in adults.[71,] Reviewers did not identify any RCTs evaluating the efficacy of spinal cord stimulation in this population. Four case series using a before-after design (total n=92 patients) were identified. Peng et al (2015) updated this review, finding no new studies meeting inclusion criteria identified.[72,] 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.

Potential Adverse Events
Whereas RCTs are useful for evaluating the efficacy, observational studies can provide data on the likelihood of potential complications. Mekhail et al (2011) retrospectively reviewed 707 patients treated with spinal cord stimulation between 2000 and 2005.[73,] Patients' diagnoses included complex regional pain syndrome (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 a spinal cord stimulation 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 spinal cord stimulation 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.

Lanza et al (2012) reviewed observational studies on spinal cord stimulation in patients with refractory angina pectoris.[74,] They identified 16 studies (total n=1204 patients) but noted that patients might have been included in more than 1 report. The most frequently reported

complications were lead issues (i.e., electrode dislodgement or fracture requiring repositioning) or internal programmable generator failure during substitution. Lead issues were reported by 10 studies (n=450 patients). In these studies, 55 cases of lead or internal programmable generator failure were reported. No fatalities related to spinal cord stimulation treatment were reported.

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 a meaningful 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 3 RCTs. Relevant outcomes are symptoms, functional outcomes, quality of life, medication use, and treatment-related morbidity. One RCT comparing high-frequency with standard spinal cord stimulation in patients who had not previously been treated with spinal cord stimulation found a clinically and statistically significant benefit 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 a meaningful 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 an RCT and many 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 percentage achieving >50% pain reduction, emotional functioning score, and 36-Item Short-Form Health Survey scores. Both groups experienced paresthesia's 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. While most of the case series were small (sample sizes ranged from 10 to 65), all reported results that were consistent with the RCT results. The largest case series had the longest follow-up, reporting continued improvements in pain and psychological scores through 3 years. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Critical Limb Ischemia

For individuals who have critical limb ischemia who receive spinal cord stimulation, the evidence includes several small RCTs. Relevant outcomes are overall survival, symptoms, functional outcomes, quality of life, morbid events, hospitalizations, and treatment-related morbidity. In some pooled analyses of these RCTs, spinal cord stimulation did not result in a significantly lower rate of amputation, although one meta-analysis that included a nonrandomized study reported a significant difference. The evidence is insufficient to determine the effects of the technology on health outcomes.

Treatment-Refractory Angina Pectoris

For individuals who have treatment-refractory angina pectoris 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. 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 the effects of the technology on health outcomes.

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 (n=66) did not find significant differences between groups but might have been underpowered to do so. The evidence is insufficient to determine the effects of the technology on 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 the effects of the technology on health outcomes.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

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.[75,] 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 complex regional pain syndrome (Table 10). 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 10. International Association for the Study of Pain Recommendations for Spinal Cord Stimulation

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

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

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.[76,] 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".

Earlier evidence-based guidelines from the Society (2007) found the evidence for spinal cord stimulation in failed back surgery syndrome and complex regional pain syndrome strong for short-term relief and moderate for long-term relief.[77,] Reported complications with spinal cord stimulation ranged from infection, hematoma, nerve damage, lack of appropriate paresthesia coverage, paralysis, nerve injury, to death.

American Society of Anesthesiologists

In 2011, the American Society of Anesthesiologists' Task Force and the American Society of Regional Anesthesia and Pain Management updated and published guidelines for chronic pain management.[78,] The guideline concluded that spinal cord stimulation "may be used in the multimodal treatment of persistant radicular pain in patients who have not responded to other therapies" and that spinal cord stimulation "may also be considered for other selected patients (e.g., complex regional pain syndrome, peripheral neuropathic pain, peripheral vascular disease, and postherpetic neurolgia."

International Neuromodulation Society

The International Neuromodulation Society 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.[79,] 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 10 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 11. 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, the National Institute for Health and Care Excellence (NICE) issued guidance on spinal cord stimulation for chronic pain of neuropathic or ischemic origin.[27,] 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 0-100 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.

Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this review are listed in Table 12.

Table 12. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT02112474	The Pain Suppressive Effect of Alternative Spinal Cord Stimulation Frequencies	30	Mar 2019
NCT02514590[a]	Wireless High-Frequency Spinal Cord Stimulation for Chronic Pain	80	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
NCT02514590[a]	Multi-center, Prospective, Randomized, Controlled Clinical Trial of Wireless High-Frequency Spinal Cord Stimulation to Demonstrate Non-Inferiority in the Treatment of Chronic Pain as Compared to Traditional Stimulation	80	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
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 (Tsunami)	38	Aug 2020
NCT03014583	Study Comparing Conventional, Burst and High Frequency (HF) Spinal Cord Stimulation (SCS) in Refractory Failed Back Surgery Syndrome (FBSS) Patients After a 32-contact Surgical Lead Implantation (MULTIWAVE)	28	Jul 2021
NCT03228420	A Post-Market, Multicenter, Prospective, Randomized Clinical Trial Comparing 10 kHz Spinal Cord Stimulation (HF10™ Therapy) Combined With Conventional Medical Management to Conventional Medical Management Alone in the Treatment of Chronic, Intractable, Neuropathic Limb Pain	360	Jul 2022
NCT03957395	Comparison of Effectiveness of Tonic, High Frequency and Burst Spinal Cord Stimulation in Chronic Pain Syndromes: a Double-blind, Randomized, Cross-over, Placebo-Controlled Trial	50	Dec 2022
NCT03681262	Comparing Long-Term Effectiveness of High Frequency and Burst Spinal Cord Stimulation Comparing Long-Term Effectiveness of High Frequency and Burst Spinal Cord Stimulation	160	Dec 2024

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

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. 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.

CPT/HCPCS

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/transmitter (eg, contact group[s], interleaving, amplitude, pulse width, frequency [Hz], on/off cycling, burst, magnet mode, dose lockout, patient selectable parameters, responsive neurostimulation, detection algorithms, closed loop parameters, and passive parameters) by physician or other qualified health care professional; with brain, cranial nerve, spinal cord, peripheral nerve, or sacral nerve, neurostimulator pulse generator/transmitter, without reprogramming
95971	Electronic analysis of implanted neurostimulator pulse generator/transmitter (eg, contact group[s], interleaving, amplitude, pulse width, frequency [Hz], on/off cycling, burst, magnet mode, dose lockout, patient selectable parameters, responsive neurostimulation, detection algorithms, closed loop parameters, and passive parameters) by physician or other qualified health care professional; with simple spinal cord or peripheral nerve (eg, sacral nerve) neurostimulator pulse generator/transmitter programming by physician or other qualified health care professional
95972	Electronic analysis of implanted neurostimulator pulse generator/transmitter (eg, contact group[s], interleaving, amplitude, pulse width, frequency [Hz], on/off cycling, burst, magnet mode, dose lockout, patient selectable parameters, responsive neurostimulation, detection algorithms, closed loop parameters, and passive parameters) by physician or other qualified health care professional; with complex spinal cord or peripheral nerve (eg, sacral nerve) neurostimulator pulse generator/transmitter programming by physician or other qualified health care professional
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
L8681	Patient programmer (external) for use with implantable programmable neurostimulator pulse generator, replacement only
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

- In 2016, a HCPCS "C" code was issued for high-frequency neurostimulator generator: C1822.
- The Centers for Medicare & Medicaid Services has issued instructions that the existing implantable neurostimulator code C1820 should only be used for stimulators that are not high frequency.

ICD-10 Diagnoses

G56.41	Causalgia of right upper limb
G56.42	Causalgia of left upper limb
G56.43	Causalgia of bilateral upper limbs
G57.71	Causalgia of right lower limb
G57.72	Causalgia of left lower limb
G57.73	Causalgia of bilateral lower limbs
G89.21	Chronic pain due to trauma
G89.22	Chronic post-thoracotomy pain
G89.28	Other chronic postprocedural pain
G89.29	Other chronic pain
G89.3	Neoplasm related pain (acute) (chronic)
G89.4	Chronic pain syndrome
G90.511	Complex regional pain syndrome I of right upper limb
G90.512	Complex regional pain syndrome I of left upper limb
G90.513	Complex regional pain syndrome I of upper limb, bilateral
G90.521	Complex regional pain syndrome I of right lower limb
G90.522	Complex regional pain syndrome I of left lower limb
G90.523	Complex regional pain syndrome I of lower limb, bilateral
G90.59	Complex regional pain syndrome I of other specified site
M50.11	Cervical disc disorder with radiculopathy, occipito-atlanto-axial region

M50.121	Cervical disc disorder at C4-C5 level with radiculopathy
M50.122	Cervical disc disorder at C5-C6 level with radiculopathy
M50.123	Cervical disc disorder at C6-C7 level with radiculopathy
M50.13	Cervical disc disorder with radiculopathy, cervicothoracic region
M51.14	Intervertebral disc disorders with radiculopathy, thoracic region
M51.15	Intervertebral disc disorders with radiculopathy, thoracolumbar region
M51.16	Intervertebral disc disorders with radiculopathy, lumbar region
M51.17	Intervertebral disc disorders with radiculopathy, lumbosacral region
M53.81	Other specified dorsopathies, occipito-atlanto-axial region
M53.82	Other specified dorsopathies, cervical region
M53.83	Other specified dorsopathies, cervicothoracic region
M54.11	Radiculopathy, occipito-atlanto-axial region
M54.12	Radiculopathy, cervical region
M54.13	Radiculopathy, cervicothoracic region
M54.14	Radiculopathy, thoracic region
M54.15	Radiculopathy, thoracolumbar region
M54.16	Radiculopathy, lumbar region
M54.17	Radiculopathy, lumbosacral region
M54.18	Radiculopathy, sacral and sacrococcygeal region
M54.31	Sciatica, right side
M54.32	Sciatica, left side
M54.41	Lumbago with sciatica, right side
M54.42	Lumbago with sciatica, left side
M54.6	Pain in thoracic spine
M54.81	Occipital neuralgia
M79.2	Neuralgia and neuritis, unspecified
M79.601	Pain in right arm
M79.602	Pain in left arm
M79.604	Pain in right leg
M79.605	Pain in left leg
M79.622	Pain in left upper arm
M79.631	Pain in right forearm
M79.632	Pain in left forearm
M79.641	Pain in right hand
M79.642	Pain in left hand
M79.644	Pain in right finger(s)
M79.645	Pain in left finger(s)
M79.651	Pain in right thigh
M79.652	Pain in left thigh
M79.661	Pain in right lower leg
M79.662	Pain in left lower leg
M79.671	Pain in right foot
M79.672	Pain in left foot
M79.674	Pain in right toe(s)
M79.675	Pain in left toe(s)

REVISIONS

03-28-2012	Policy added to the bcbsks.com web site.
04-26-2013	Updated Rationale section.
	Updated Reference section.
	Added ICD-10 Diagnosis Codes *(Effective October 1, 2014)*
03-18-2015	Description section updated
	In Policy section: ▪ In Item A removed "all" and added "reasonable" to read "Spinal cord 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 reasonable pain therapies, when performed according to policy guidelines." ▪ In Item B added "primary", "improve perfusion to", and "non-neuropathic" to read "Spinal cord stimulation is considered experimental / investigational in all other situations including but not limited to primary treatment of critical limb ischemia as a technique to improve perfusion to forestall amputation, treatment for refractory angina pectoris and treatment of non-neuropathic cancer-related pain." In Policy Guidelines: ▪ In Item 1 removed "only as a last resort, other" and "surgical" and added "when reasonable conservative" to read "The treatment is used when reasonable conservative treatment modalities (pharmacological, psychological, or physical, if applicable)…" ▪ In Item 2 removed "i.e., resulting from actual damage to the peripheral nerves" to read "Pain is neuropathic in nature. Common indications include,…" ▪ In Item 4 removed "50%" and "with a temporarily implanted electrode precedes" and added "70%" and "during a typical 5 to 7 day temporary trial electrode array implant prior to" to read "Demonstration of at least 70% pain relief during a typical 5 to 7 day temporary trial electrode array implant prior to permanent implantation" ▪ In Item 6 added "Prior to trial implantation" and "no contraindications to" to read "Psychological evaluation prior to trial implantation has been performed and indicates no contraindications to spinal cord stimulation."
	Rationale section updated
	In Coding section: ▪ Revised CPT code: 95972 *(Effective January 1, 2015)* ▪ Removed ICD-10 Diagnoses: G56.40, G57.70, G90.50, G90.519, G90.529, M50.10, M54.10, M54.30, M54.40, M79.603, M79.606, M79.609, M79.621, M79.629, M79.639, M79.643, M79.646, M79.659, M79.669, M79.673, M79.676
	References updated
01-01-2016	In Coding section: ▪ Revised nomenclature to CPT code 95972. ▪ Removed CPT code 95973.
07-22-2016	Updated Description section.
	In Policy section: ▪ In Item A, added "with standard (non-high-frequency) stimulation" and "all" and removed "reasonable" to read "Spinal cord stimulation with standard (non-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." ▪ In Item B, added "and", "of", and "heart failure" and removed "primary", "as a technique to improve perfusion", and "for", to read "Spinal cord stimulation is considered experimental / investigational in all other situations, including, but not limited to, treatment of refractory angina pectoris, heart failure, and treatment of non-neuropathic cancer-related pain." ▪ Added Item C, "High-frequency spinal cord stimulation is experimental / investigational for the treatment of severe and chronic pain of the trunk or limbs."

	Updated Rationale section.
	Updated References section.
10-01-2016	In Coding section: ▪ Added ICD-10 codes effective 10-01-2016: G56.43, G57.73, M50.121, M50.122, M50.123 ▪ Termed ICD-10 code effective 09-30-2016: M50.12
06-09-2017	Updated Description section.
	In Policy section: ▪ In Item A, added "or" and removed "(non-" and ")" to read, "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." ▪ Removed previous Item C, "High-frequency spinal cord stimulation is experimental / investigational for the treatment of severe and chronic pain of the trunk or limbs." ▪ Added new Item C, "Wireless injectable dorsal root ganglion neurostimulation is experimental / investigational for treatment of severe and chronic pain of the trunk or limbs."
	Updated Rationale section.
	Updated References section.
08-15-2017	Title of policy changed from "Spinal Cord Stimulation."
	Updated Description section.
	In Policy section: ▪ In Item C, added "considered" and removed "Wireless injectable" to read, "Dorsal root ganglion neurostimulation is considered experimental / investigational for treatment of severe and chronic pain of the trunk or limbs." ▪ Updated Policy Guidelines.
	Updated Rationale section.
07-06-2018	Published to the bcbsks.com website on June 6, 2018, with an effective date of July 6, 2018.
	In Policy section: ▪ In Item A, added "and dorsal root ganglion neurostimulation" to read, "Spinal cord stimulation and dorsal root ganglion neurostimulation 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." ▪ In Item B, added "and dorsal root ganglion neurostimulation" to read, "Spinal cord stimulation and dorsal root ganglion neurostimulation is considered experimental / 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 treatment of non-neuropathic cancer-related pain. ▪ In Item C, added "wireless injectable" and removed "for treatment of severe and chronic pain of the trunk or limbs" to read, "Wireless injectable dorsal root ganglion neurostimulation is considered experimental / investigational."
	Updated Rationale section.
	In Coding section: ▪ Added HCPCS codes: C1767, C1778, C1787, C1820, C1822, C1883, C1897, L8679. ▪ Removed ICD-9 codes.
	Updated References section.
01-01-2019	In Coding section: ▪ Revised nomenclature to CPT codes: 95970, 95971, 95972.
05-21-2019	Updated Description section.
	Updated Rationale section.

	Updated References section.
08-28-2019	In Policy section: ▪ In Policy Guidelines Item 1 d, added "during a typical 5 to 7 day temporary trial electrode array implant" and removed "with a temporary implanted electrode" to read, "Demonstration of at least 70% pain relief during a typical 5 to 7 day temporary trial electrode array implant prior to permanent implantation".
	Updated References section.
04-16-2021	Updated Description section
	Updated Rationale section
	Updated references

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