Title: Spinal Cord and Dorsal Root Ganglion Stimulation

**Medical Policy**

**Professional**
- Original Effective Date: September 26, 2007
- Revision Date(s): March 28, 2012; April 26, 2013; March 18, 2015; January 1, 2016; July 22, 2016; October 1, 2016; June 9, 2017; August 15, 2017; July 6, 2018
- Current Effective Date: July 6, 2018

**Institutional**
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<table>
<thead>
<tr>
<th>Populations</th>
<th>Interventions</th>
<th>Comparators</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individuals:</td>
<td>Interventions of interest are:</td>
<td>Comparators of interest are:</td>
<td>Relevant outcomes include:</td>
</tr>
<tr>
<td>• With treatment-refractory chronic pain of the trunk or limbs</td>
<td>• Standard spinal cord stimulation</td>
<td>• Medical therapy</td>
<td>• Symptoms</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Surgical therapy</td>
<td>• Functional outcomes</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Quality of life</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Medication use</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Treatment-related morbidity</td>
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<tr>
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<td>• High-frequency spinal cord stimulation</td>
<td>• Standard spinal cord stimulation</td>
<td>• Symptoms</td>
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<td>• Quality of life</td>
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Contains Public Information
### Populations | Interventions | Comparators | Outcomes
---|---|---|---
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: • Medical 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

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**DESCRIPTION**

Spinal cord stimulation (SCS) delivers low-voltage electrical stimulation to the dorsal columns of the spinal cord to block the sensation of pain; this is achieved through a surgically implanted SCS device, which comes equipped with a radiofrequency receiver. The neurostimulator device is also issued with a standard power source (battery) that can also be implanted or worn externally. Other neurostimulators target the dorsal root ganglion.
OBJECTIVE
The objective of this policy 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 (SCS) has been used in a wide variety of chronic refractory pain conditions, including pain associated with cancer, failed back pain syndromes, arachnoiditis, and complex regional pain syndrome (ie, chronic reflex sympathetic dystrophy). There has also been interest in SCS as a treatment of critical limb ischemia, primarily in patients who are poor candidates for revascularization and in patients with refractory chest pain.

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

SCS devices consist of several components: (1) the lead that delivers the electrical stimulation to the spinal cord; (2) an extension wire that conducts the electrical stimulation from the power source to the lead; and (3) a power source that generates the electrical stimulation. 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. The other, a radiofrequency receiver, is implanted, and the power source is worn externally with an antenna over the receiver. Totally implantable systems are most commonly used.

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

Traditional SCS devices use electrical stimulation with a frequency on the order of 100 to 1000 Hz. In 2015, an SCS 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 paresthesias, which are a recognized effect of SCS. In addition, in 2016, FDA
approved a clinician programmer “app” that allows an SCS device to provide stimulation in “bursts” rather than at a constant rate. Burst stimulation is proposed to relieve pain with fewer paresthesias. The burst stimulation device works in conjunction with standard SCS devices. With the newly approved app, stimulation is provided in five 500-Hz burst spikes at a rate of 40 Hz, with a pulse width of 1 ms.

Other neurostimulators target the dorsal root ganglion. Dorsal root ganglia are located between spinal nerves and the spinal cord on the posterior root and are believed to play an important role in neuropathic pain perception. Two systems have received approval or clearance from FDA.

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

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

<table>
<thead>
<tr>
<th>Domain</th>
<th>Outcome Measure</th>
<th>Description</th>
<th>Clinically Meaningful Difference</th>
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</table>
| Pain intensity          | Numeric rating scale                   | Rating of pain intensity on a scale of 0 (no pain) to 10 (pain as bad as you can imagine) or from 0 to 10 cm | • Minimally important: 10%-20% decrease  
• Moderately important: ≥30% decrease  
• Substantial: ≥50% decrease |
|                         | Verbal rating scale                    |                                                                             |                                                                                                  |
|                         | Visual analog scale                    |                                                                             |                                                                                                  |
|                         |                                        |                                                                             |                                                                                                  |
| Physical functioning    | Disease specific                       | Measures of the interference of pain with physical functioning              |                                                                                                |
|                         | Multidimensional Pain Inventory        | • 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 decrease³ |
|                         | Interference Scale                     |                                                                             |                                                                                                  |
|                         | Brief Pain Inventory                   | • 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 decrease³ |
<p>|                         | Interference Scale                     |                                                                             |                                                                                                  |</p>
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<th>Clinically Meaningful Difference</th>
</tr>
</thead>
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|                        | Oswestry Disability Index<sup>6</sup>    | Measures functional impairment due to lower back pain:  
  - 10 sections, self-report  
  - Sections: intensity of pain, lifting, ability to care for oneself, ability to walk, ability to sit, sexual function, ability to stand, social life, sleep quality, and ability to travel  
  - Each section is scored on a 0 to 5 scale with 5 indicating the greatest disability  
  - Total score calculated by taking the mean of the section scores and multiplying by 100 | 10 points<sup>7</sup> |
| General                | 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<sup>8–10</sup> |
| Emotional functioning  | Beck Depression Inventory<sup>11</sup>   | 21 items, self-report  
  - Measures severity of current symptoms of depressive disorders  
  - Scores range from 0 to 63 | ≥5-point decrease<sup>3</sup> |
|                        | Profile of Mood States<sup>12</sup>     | 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<sup>3</sup> |
| 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<sup>3</sup> |

**REGULATORY STATUS**

A large number of neurostimulator devices, some used for spinal cord stimulation (SCS), have been approved by the U.S. Food and Drug Administration (FDA) through the premarket approval (PMA) process. Examples of fully implantable SCS devices approved through the PMA process include the Cordis programmable neurostimulator (Cordis Corp., Downers Grove, IL), approved in 1981; the Itrel® (Medtronic, Minneapolis, MN), approved in 1984; the Genesis and Eon devices (St. Jude Medical) approved in 2001; and the Precision Spinal Cord Stimulator (Advanced Bionics, Switzerland), approved in 2004. FDA product code: LGW.

In May 2015, the Nevro Senza™ Spinal Cord Stimulator (Nevro Corp., Menlo Park, CA), a totally implantable neurostimulator device, was approved by FDA for the following
indications: “chronic intractable pain of the trunk and/or limbs, including unilateral or bilateral pain associated with the following: failed back surgery syndrome (FBSS), intractable low back pain, and leg pain.”\textsuperscript{13} This device uses a higher frequency of electrical stimulation (10 kHz) than standard devices.

In February 2016, the Axium Neurostimulator System (Spinal Modulation, Menlo Park, CA) was approved by FDA through the PMA process. 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, Fort Lauderdale, FL) was cleared for marketing by FDA through the 510(k) process for treating chronic, intractable pain of the trunk and/or lower limbs. The Freedom device has implantable or injectable microstimulators that contain electrode(s). The microstimulators with electrodes are powered by a wireless battery pack worn externally. The device can be placed to target the spinal cord (ie, levels T7 to L5) or to target the dorsal root ganglion.

In October 2016, FDA approved BurstDR™ stimulation (St. Jude Medical, Plano, TX), a clinician programmer application that provides intermittent “burst” stimulation for patients with certain St. Jude SCS devices.

**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 with a temporary implanted electrode 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**

The most recent literature search was reviewed through February 5, 2018. Following is a summary of the key literature to date.

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are 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 to 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 a technology, 2 domains are examined: the relevance and the 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.
Refractory Chronic Trunk or Limb Pain
Standard Spinal Cord Stimulation
Systematic Reviews
Existing RCTs of standard spinal cord stimulation (SCS) for chronic trunk or limb pain are summarized in the next section. Five systematic reviews have assessed the RCTs included in the next section and overlap substantially. The North et al (2005)\textsuperscript{14} and Kumar et al (2007)\textsuperscript{15} RCTs are included in 3 systematic reviews; Kemler et al (2000)\textsuperscript{16} is included in 3 reviews, and Kapural et al (2015)\textsuperscript{17} included in one of the systematic reviews.

Two systematic reviews have focused on SCS specifically for complex regional pain syndrome (CRPS). Visnjevac et al (2017) reported on results of a systematic review of RCTs and observational studies of SCS for CRPS.\textsuperscript{18} The Kemler (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 CRPS.\textsuperscript{19} The overview included reports from the Kemler RCT. Reviewers concluded that there was very low quality evidence using GRADE criteria that SCS using physical therapy was effective at reducing pain or improving quality of life in CRPS compared with physical therapy alone for up to 2 years.

Grider et al (2016) reported on results of a systematic review of RCTs of SCS for chronic spinal pain.\textsuperscript{20} Six RCTs meeting selection criteria were identified; 3 RCTs reported on the efficacy of standard SCS, while 3 assessed adaptive stimulation, high-frequency SCS (discussed below), and burst stimulation. Of the 3 RCTs assessing standard SCS, two were considered high quality and one moderate quality based on Cochrane criteria and Interventional Pain Management Techniques–Quality Appraisal of Reliability and Risk of Bias Assessment. Kapural (2015) is discussed below in the section on high-frequency SCS. In the North and Kumar RCTs, SCS was associated with higher rates of pain relief than the comparator groups.

Two systematic reviews have focused on SCS for failed back surgery syndrome (FBSS), 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 SCS for FBSS.\textsuperscript{21} The North and Kumar trials were the only RCTs included and are discussed in the following section. A systematic review of RCTs and observational studies evaluating SCS for FBSS was conducted by Frey et al (2009).\textsuperscript{22} The 2 RCTs by North and Kumar were included. Using U.S 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 SCS on a long-term basis.

Also, Simpson et al (2009) reported on a health technology assessment, funded by the National Institute for Health and Care Excellence, to obtain clinical and cost-effectiveness data for SCS in adults with chronic neuropathic or ischemic pain with inadequate response to other medical or surgical treatments.\textsuperscript{23} The Institute used the assessment as the basis for its guidance on SCS for chronic pain.\textsuperscript{24} Trials for FBSS and CRPS type I (reported by North et al [2005]),\textsuperscript{14} Kumar et al [2007],\textsuperscript{15} and Kemler et al [2000, 2004]\textsuperscript{16,25}, suggested that SCS was more effective than conventional medical management or reoperation in reducing pain.
**Randomized Controlled Trials**

Five RCTs (total N=310 patients; range, 36-100 patients) have evaluated SCS (see Table 2). Patient populations had FBSS, diabetic neuropathy, and CRPS. The comparators were primarily conventional medical management, although 1 RCT compared CSC with reoperation for FBSS, and another compared SCS 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 (VAS) pain score.\textsuperscript{16} Consistent with clinical practice, RCTs included a trial period of SCS, usually a few days to a week. Patients not reporting improvement in pain during the trial period did not continue receiving SCS during the remainder of follow-up. In most RCTs, these patients were included in the intention-to-treat analyses either as failures to respond or using imputation techniques. All RCTs with the responder primary outcomes reported clinically and statistically significant differences in the primary outcomes at 6 months, favoring SCS (SCS range, 39%-63% vs comparator range, 5%-12%). Outcomes measuring the reduction in analgesic use were consistently numerically larger for SCS but not statistically significant in all studies. Four of the 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)\textsuperscript{26} reported a dural puncture headache ending in death. Two studies reported longer term results for both treatment groups. In each, results continued to favor SCS at 2 years, but for one with 5 years of follow-up, results were not statistically significant at 5 years.

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

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

**High-Frequency SCS**

In 2015, an SCS 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 U.S. Food and Drug Administration. Studies that offer direct comparisons between standard SCS and high-frequency SCS (HFSCS) were sought to evaluate the incremental benefit of HFSCS.

**Systematic Reviews**

Bicket et al (2016) published a systematic review of controlled trials on HFSCS.\textsuperscript{27} Reviewers searched for RCTs and controlled nonrandomized studies of adults with pain for at least 3 months who were treated with HFSCS (ie, ≥1000 Hz) and prospectively assessed pain outcomes. Eight studies met these inclusion criteria; 2 RCTs (detailed below) and 6 controlled nonrandomized studies. Both RCTs and 5 of 6 controlled studies addressed low back pain; the remaining controlled study addressed migraine. Reviewers used the Cochrane criteria to rate bias in the RCTs. One trial (Perruchoud et al [2013]\textsuperscript{28}) was not rated as having a high risk of bias in any
domain, and the other (Kapural et al [2015]17) was rated as having a high risk of bias in the domain of performance and detection bias because it was unblinded. Studies were reviewed qualitatively (ie, study findings were not pooled).

Table 2. Characteristics and Result of RCTs Using Standard SCS

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Interventions</th>
<th>N at Baseline and Follow-Up</th>
<th>Results</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>North et al (2005)14</td>
<td>FBSS</td>
<td>• SCS + CMM • Reoperation + CMM</td>
<td>N=60 N at 6 mo=49</td>
<td>6 months (SCS vs reoperation)</td>
<td>17% device-related complications (infections, hardware technical problems)</td>
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<tr>
<td>Kumar et al (2007, 2008)15,29</td>
<td>FBSS with neuropathic pain</td>
<td>• SCS + CMM • CMM</td>
<td>N=100 N at 6 mo=93</td>
<td>6 months (SCS vs CMM)</td>
<td>32% device-related complications (electrode migration, infection, loss of paresthesia)</td>
</tr>
<tr>
<td>Kemler et al (2000, 2004, 2008)16,25,30</td>
<td>CRPS</td>
<td>• SCS + PT • PT</td>
<td>N=54 N at 6 mo=54</td>
<td>6 months (SCS vs PT)</td>
<td>25% device-related complications (dural puncture, infection, unsatisfactory placement of electrode, defective lead) 42% reoperation rate by 5 y</td>
</tr>
<tr>
<td>Slangen et al (2014)26</td>
<td>Diabetic neuropathy of LEs</td>
<td>• SCS • CMM</td>
<td>N=36 N at 6 mo=36</td>
<td>6 months (SCS vs CMM)</td>
<td>2 SAEs (1 infection, 1 post-dural puncture headache ending in death)</td>
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Outcome Measures | Int | Ctrl | p |
--- | --- | --- | --- |
• Success (50% pain relief and patient satisfaction) | 39% | 12% | 0.04 |
• 50% reduction in VAS leg pain | 48% | 9% | <0.001 |
• SF-36, favoring SCS all domains except RP | 48% | 9% | <0.001 |
• ODI score | 45 | 56 | 0.025 |
• Opioid use | 56% | 70% | 0.21 |
• NSAIDs use | 34% | 50% | 0.14 |
• 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 | 43% | 6% | 0.001 |
• Reduction in VAS pain score | 2.1 | 0.0 | <0.001 |
• Much improved GPE | 43% | 6% | 0.001 |
• Reduction in VAS pain score | 1.7 | 1.0 | 0.25 |
• Success (50% reduction in pain for 4 d or at least much improved on patient-reported global impression of change) | 59% | 7% | <0.01 |
• Reduction in pain medication | 32% | 0% |
• No differences in health utility or HRQOL | 32% | 0% |
Spinal Cord and Dorsal Root Ganglion Stimulation

<table>
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<tr>
<td></td>
<td></td>
<td></td>
<td>N at 24 m/o=17 (SCS only)</td>
<td>2 years (SCS only)</td>
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<td>Success 65%</td>
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<td>No improvement in health utility vs baseline</td>
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<td>+5-point improvement in SF-36 PCS score vs baseline</td>
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Diabetic neuropathy of LEs • SCS • CMM N=60 N at 6 m/o=54 6 months (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         |
|       |               | Reduction in analgesic intake (MQS score) | 2.9 | -0.09 | NR |
|       |               | Change in health utility    | 0.39                         | 0.00                     | <0.05          |

**Randomized Controlled Trials**

Three RCTs identified addressed HFSCS (see Table 3): Perruchoud et al (2013) compared HFSCS (5000 Hz) with sham-control in a crossover design (N=40), while Kapural et al (2015)\textsuperscript{17} (N=198) and De Andres et al (2017)\textsuperscript{33} (N=60) both compared HFSCS (10,000 Hz) with standard SCS. The 3 trials had distinct patient populations and designs such that the results could not be synthesized.

The Perruchoud population was distinct from other trials of SCS or HFSCS in that it included patients who had chronic, treatment-refractory back pain previously treated with standard SCS (ie, patients were not treatment-naive to SCS).\textsuperscript{28} This trial used a 2×2 crossover design with a run-in and washout period consisting of standard SCS. In the trial treatment periods, patients were treated with HFSCS or sham stimulation. After 2 weeks of treatment, outcomes revealed that 42% of patients were responders in the high-frequency group vs 30% in the sham group. The mean benefit averaged over the 2 crossover sequences was 11%, favoring HFSCS (p=0.30). There were no differences between HFSCS and sham for VAS 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 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 SCS—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 SCS during the 2 weeks preceded each treatment period, which led to carryover effects.

Kapural et al (2015, 2016)\textsuperscript{17,34} included patients with chronic leg and back pain who had received conventional medical management but not SCS. Kapural (2015) included an active but unblinded comparator (standard SCS) and included a trial SCS period up to 2 weeks postrandomization after which only responders continued with stimulation. Outcomes were reported after 3, 12, and 24

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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.
months of treatment. The response in the standard SCS group was similar to previous trials of SCS, between 45% and 50% for back pain and 50% to 55% for leg pain at 3, 12, and 24 months. The response was clinically and statistically significantly higher with HFSCS than with SCS for both back (range, ≈75% to 85%) and leg pain (range, ≈70% to 85%) at all time points. A limitation of the Kapural 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 HFSCS and 37% in SCS 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 FBSS 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 (NRS).33 The comparator was SCS, 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 NRS 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 SCS 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 NRS 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>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Interventions</th>
<th>N at Baseline and Follow-Up</th>
<th>Outcome Measure</th>
<th>Results</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perruchoud et al (2013)</td>
<td>Chronic low back pain radiating in 1 or both legs; previously treated with SCS</td>
<td>• HFSCS &lt;br&gt;• Sham &lt;br&gt;• 2×2 crossover design with conventional SCS before both arms</td>
<td>N=40&lt;br&gt;N=33</td>
<td>2 weeks (HFSCS vs sham)</td>
<td></td>
<td>One patient had malaise attributed to a vasovagal attack</td>
</tr>
<tr>
<td>Kapural et al (2015, 2016)</td>
<td>Chronic back and leg pain</td>
<td>• HFSCS &lt;br&gt;• SCS</td>
<td>N=198&lt;br&gt;N=171&lt;br&gt;N=156</td>
<td>3 months (HFSCS vs SCS)</td>
<td></td>
<td>Stimulation discomfort, 0% vs 47% &lt;br&gt;No stimulated-rated SAEs or neurologic deficits</td>
</tr>
</tbody>
</table>

Table 3. Characteristics and Result of RCTs of Using HFSCS
Spinal Cord and Dorsal Root Ganglion Stimulation

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Interventions</th>
<th>N at Baseline and Follow-Up</th>
<th>Results</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>N at 12 mo=171</td>
<td>o Back pain</td>
<td>83%</td>
<td>55%</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>12 months (HFSCS vs SCS)</td>
<td>o Leg pain</td>
<td>80%</td>
<td>50%</td>
<td>NR</td>
<td></td>
</tr>
</tbody>
</table>

- Responders
  - o Back pain
    - 80%
  - o Leg pain
    - 80%
  - Decreased opioid use
    - 36%
  - Improvement in ODI score
    - 16.5

24 months (HFSCS vs SCS)
- Responders
  - o Back pain
    - 77%
  - o Leg pain
    - 73%

De Andes et al (2017) FBSS • HFSCS • SCS N=60 N=55 analyzed 12 mo (HFSCS vs SCS)
- Responded (≥50% in pain intensity in NRS score at 12 mo)a
  - NR
- Improvement in NRS score
  - 6.1
- Improvement in ODI score
  - 23.0

HFCS: high-frequency spinal cord stimulation; NR: not reported; ODI: Oswestry Disability Index; SAE: serious adverse events; SCS: spinal cord stimulation; VAS: visual analog scale.

a Despite the responder criteria being stated to be on the primary outcome, the results for not reported in the report.

Case Series
Because RCT data are available for HFSCS, case series are discussed if they add information not available from the RCTs (eg, longer follow-up, data on an important subgroup).

Al-Kaisy et al (2017) reported 36-month results for 20 patients with chronic low back pain without previous spinal surgery who were treated with 10-kHz HFSCS. Seventeen patients completed the 36-month follow-up; 1 patient died (unrelated to study treatment), 1 patient was explanted due to lack of efficacy, and 1 patient had new leg pain. Among patients analyzed, the mean VAS score for pain intensity decreased from 79 to 10 mm (p<0.001) and the mean 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 SCS for Chronic Trunk or Limb Pain
The evidence for HFSCS compared with standard SCS consists of an RCT that randomized 198 patients not previously treated with SCS and reported a clinically and statistically significant benefit associated with HFSCS. The crossover RCT enrolling patients with pain despite previous treatment with SCS reported no difference between HFSCS and sham stimulation. However, interpretation of this trial is limited due to the significant period effect.

SCS with Burst Stimulation
In 2016, a supplement to an SCS device (in the form of a clinician programmer application), which allows for the provision of burst stimulation, was approved by the Food and Drug Administration. Studies that offer direct comparisons between standard SCS and burst SCS were sought to permit evaluation of the incremental benefit of burst SCS.
**Systematic Reviews**

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

**Randomized Controlled Trials**

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 4). The trials by De Ridder et al (2010, 2013)37,38 enrolled patients with neuropathic pain, the trial by Schu et al (2014)39 enrolled patients with FBSS, Kriek et al (2017)40 enrolled patients with CRPS, and Deer et al (2018)41 enrolled patients with chronic intractable pain of the trunk and/or limbs. All trials compared burst stimulation with SCS. Schu (2014), De Ridder (2013), and Kriek (2017) also compared burst with a sham stimulation group. Schu (2014) included patients receiving standard SCS while De Ridder (2010, 2013) and Deer (2018) included patients not previously treated with SCS. It was not clear in Kriek (2017) whether patients had previously received SCS. Results were reported for 1 week of stimulation in Schu (2014) and De Ridder (2013), and after two, 1-hour sessions of SCS or burst in De Ridder (2010), after 2 weeks of stimulation in Kriek (2017), and after 12 weeks of stimulation in Deer (2018). All trials reported reductions in absolute pain scores (NRS or VAS). Schu (2014) and De Ridder (2013) did not account for their crossover designs in data analyses, so analyses and p values are incorrect and not reported in Table 3. De Ridder (2010) did not provide between-group comparisons. Kriek reported only per-protocol analyses. Four trials reported numerically larger reductions in pain scores with burst than with SCS; Kriek (2017) did not report less pain for SCS at any frequency compared with burst. In Kriek (2017), 48% of patients preferred the 40-Hz SCS compared with 21%, 14%, 14%, and 3% that preferred 500-Hz SCS, 1200-Hz SCS, and burst and sham, respectively. The interpretation of the four 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).41 SUNBURST was a 12-week, multicenter, randomized, unblinded, crossover, noninferiority trial evaluating traditional SCS or burst stimulation in 100 patients with chronic pain of the trunk and/or limbs enrolled between January 2014 and May 2015. Patients were SCS-naive and completed a trial stimulation period. Forty-five patients were randomized to SCS then burst, and the remaining 55 were randomized to burst then SCS. At the end of the second crossover period, patients were allowed to choose the stimulation mode they preferred and were followed for 1 year. Patients’ mean age was 59 years; 60% of patients were women; and 42% of patients had FBSS while 37% had radiculopathies. The primary outcome was the difference in mean VAS score, with a noninferiority margin of 7.5 mm. Analyses were intention-to-treat with missing values imputed using the hot deck method. Also, outcomes were imputed for patients who underwent invasive procedures for pain or had
medication increases. The estimated difference in the overall VAS score between burst and SCS 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 VAS score of 30% or more was 60% (60/100) during burst stimulation and 51% (51/100) during SCS. The proportion of patients whose global impression was minimally improved, moderately improved, or very much improved was approximately 74% in both groups. There were no significant differences in Beck Depression Inventory scores (p=0.230). Patients were asked to rate their satisfaction levels for both periods: 78% were satisfied with both SCS and burst, 4% were dissatisfied with both SCS and burst, 7% were satisfied with SCS but not burst, and 10% were satisfied with burst but not SCS. However, more patients (70.8%) reported preferring burst stimulation over SCS 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: SCS With Burst Stimulation for Chronic Trunk or Limb Pain

SCS 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 SCS or burst stimulation in 100 patients with chronic pain of the trunk and/or limbs. The burst was noninferior to SCS for overall VAS score (at 12 weeks). The proportion of patients whose global impression was improved (minimally, moderately, or very much improved) was approximately 74% in both groups. Seventy-eight percent of patients reported being satisfied with both SCS and burst at the end of the 24-week crossover portion of the trial, while 7% were satisfied with SCS but not burst and 10% were satisfied with burst but not SCS. However, more patients (70.8%) reported preferring burst stimulation over SCS stimulation after the 24-week crossover.

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Interventions</th>
<th>N at Baseline and Follow-Up</th>
<th>Outcome Measure</th>
<th>Burst</th>
<th>SCS</th>
<th>Ctrl</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>3x3 crossover design without washout</td>
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<tr>
<td>Schu et al (2014)19</td>
<td>FBSS receiving standard SCS</td>
<td>Burst stimulation, SCS, No stimulation (sham control)</td>
<td>N=20 N=20</td>
<td>1 week (burst vs SCS vs sham)</td>
<td>4.7 7.1 8.3</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>De Ridder et al (2013)18</td>
<td>Neuropathic limb pain</td>
<td>Burst stimulation, SCS, No stimulation (sham control)</td>
<td>N=15 N=15</td>
<td>1 week (burst vs SCS vs sham)</td>
<td>Not reported</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Population</td>
<td>Interventions</td>
<td>N at Baseline and Follow-Up</td>
<td>Results</td>
<td>Complications</td>
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<td><strong>2 x 2 crossover</strong></td>
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<td></td>
</tr>
<tr>
<td>De Ridder et al (2010)</td>
<td>Neuropathic pain</td>
<td>Burst stimulation; SCS</td>
<td>N=12; N=unclear</td>
<td>Two 1-h sessions (burst vs SCS)&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Not reported</td>
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<td></td>
<td></td>
<td>• Mean improvement in VAS scores</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>o Axial pain</td>
<td>5.3; 1.8</td>
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<td></td>
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<td></td>
<td></td>
<td>o Limb pain</td>
<td>7.3; 4.4</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Improvement in SF-MPQ sensory scores</td>
<td>16.7; 8.6</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Improvement in SF-MPQ affective scores</td>
<td>6.7; 4.3</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Deer et al (2018)</td>
<td>Chronic intractable pain of the trunk and/or limbs</td>
<td>Burst stimulation; SCS</td>
<td>N=100</td>
<td>12 week (burst vs SCS)</td>
<td>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</td>
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<td></td>
<td></td>
<td>Mean VAS scores at end of period, favoring burst</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Diff=-5.1 mm (noninferiority p&lt;0.01)</td>
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</tr>
<tr>
<td><strong>5 x 5 crossover</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Kriek et al (2017)</td>
<td>CRPS</td>
<td>Burst stimulation; SCS 40 Hz; SCS 500 Hz; SCS 1200 Hz; No stimulation (sham-control)</td>
<td>N=33; N=29</td>
<td>2 wk (burst vs SCS at 40, 500, and 1200 Hz vs sham)</td>
<td>No SAEs reported; 3 electrodes became dislodged; 2 patients reported itching</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Mean VAS scores at end of period</td>
<td>48; 40&lt;sup&gt;c&lt;/sup&gt;; 64</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Mean global perceived effect (7-point scale where 7 [very satisfied] to 1 [not at all satisfied])</td>
<td>4.7; 5.3&lt;sup&gt;c&lt;/sup&gt;; 3.5</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Ctrl: control; FBSS: failed back surgery syndrome; NRAS: 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.

<sup>2</sup>Analyses do not appear to properly take into account the crossover design, therefore p values are not reported here.

<sup>3</sup>Statistical treatment comparisons are not provided.

<sup>4</sup>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 SCS and dorsal root ganglion (DRG) neurostimulators were sought to evaluate the benefits of SCS.
**DRG Implanted Device**

**Systematic Reviews:** Chang Chien et al (2017) published a systematic review on intraspinal stimulation of nondorsal column targets, including neurostimulation of the DRG for chronic pain. Reviewers included reports published through March 2015. They identified 6 studies of DRG stimulation: 1 conference presentation of the preliminary RCT data from the ACCURATE trial (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.

**Randomized Controlled Trial:** The ACCURATE study (NCT01923285) compared DRG neurostimulation with standard SCS. As reported by Deer et al (2017), eligibility criteria for this multicenter unblinded noninferiority trial included chronic (≥6 months) intractable (failed ≥2 drugs from different classes) neuropathic pain of the lower limbs associated with a diagnosis of CRPS or causalgia and no previous neurostimulation. Patients were randomized to DRG stimulation with the Axium device or standard SCS. Patients first underwent a temporary trial of stimulation lasting 3 to 30 days, depending on the protocol at each site. Patients who had 50% or greater reduction in lower limb pain after the temporary trial were eligible for permanent stimulation. Those who failed temporary stimulation exited the trial but were included in the analysis as treatment failures. Trial characteristics are shown in Table 5.

A total of 152 patients were randomized, and 115 (n=61 DRG, n=54 SCS) had a successful temporary trial and continued to permanent implantation. The primary outcome was a composite measure of treatment success. Success was defined as: (1) 50% or greater reduction in VAS score and (2) no stimulation-related neurologic deficits. The noninferiority margin was set at 10%. Results are shown in Table 6. No patients experienced neurologic deficits in either group. Regarding paresthesias, at 3 months and 12 months, SCS patients were significantly more likely to report paresthesias in nonpainful areas than DRG patients. At 3 months, 84.7% of DRG patients and 65% of SCS patients reported paresthesias only in their painful areas; at 12 months, these percentages were 94.5% and 61.2%, respectively. Gaps in study relevance, design, and conduct are shown in Tables 7 and 8.

**Table 5. RCT Characteristics of DRG Implanted Devices**

<table>
<thead>
<tr>
<th>Study</th>
<th>Countries</th>
<th>Sites</th>
<th>Dates</th>
<th>Participants</th>
<th>Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deer et al (2017)43; ACCURATE (NCT01923285)</td>
<td>U.S.</td>
<td>22</td>
<td>2013-2016</td>
<td>CRPS or causal lower extremities</td>
<td>AXIUM Neurostimulator System (n=76)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Chronic pain (≥6 mo)</td>
<td>RestoreUltra and RestoreSensor (n=76)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Stimulation-naive</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Failed ≥2 pharmacologic treatments</td>
<td></td>
</tr>
</tbody>
</table>

CRPS: complex regional pain syndrome; DRG: dorsal root ganglion; SCS: spinal cord stimulation.

**Table 6. RCT Results of DRG Implanted Devices**

<table>
<thead>
<tr>
<th>Study</th>
<th>≥50% Reduction in VAS Scores for Pain</th>
<th>Physical Functioning</th>
<th>Emotional Functioning</th>
<th>Quality of Life</th>
<th>Safety</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean BPI Interference</td>
<td>POMS Total Score</td>
<td>SF-36 PCS</td>
<td>SF-36 MCS</td>
<td>SAEs</td>
</tr>
<tr>
<td>Deer et al (2017)43 At 3 months</td>
<td>139</td>
<td>113</td>
<td>NR</td>
<td>113</td>
<td>113</td>
</tr>
<tr>
<td>DRG</td>
<td>81%</td>
<td>4.2</td>
<td>NR</td>
<td>11.8</td>
<td>8.3</td>
</tr>
</tbody>
</table>
## Table 7. Relevance Gaps for RCTs of DRG Implanted Devices

<table>
<thead>
<tr>
<th>Study</th>
<th>Population Representation</th>
<th>Intervention Delivery</th>
<th>Comparator Delivery</th>
<th>Outcomes</th>
<th>Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deer et al (2017)</td>
<td>None noted</td>
<td>None noted</td>
<td>None noted</td>
<td>None noted</td>
<td>None noted</td>
</tr>
</tbody>
</table>

**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 is subpopulation of intended use

**BPI:** Brief Pain Inventory; CI: confidence interval; DRG: dorsal root ganglion; MCSI: Mental Component Summary; NR: not reported; NRS: numeric rating scale; 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 Design and Conduct Gaps for RCTs of DRG Implanted Devices

<table>
<thead>
<tr>
<th>Study</th>
<th>Allocation Representation</th>
<th>Blinding</th>
<th>Selective Reporting</th>
<th>Follow-Up</th>
<th>Power Calculation</th>
<th>Statistical Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deer et al (2017)</td>
<td>None noted</td>
<td>1. Participants and study staff not blinded. Outcomes mostly patient reported which could lead to bias. However, an active control (SCS) was used.</td>
<td>None noted</td>
<td>None noted</td>
<td>None noted</td>
<td>4. Treatment effects not reported for some outcomes but p values reported</td>
</tr>
</tbody>
</table>

**Key**

1. Participant allocated (a) not randomly allocated; (b) allocation not concealed
2. Allocation was not concealed
3. Allocation concealment unclear
4. Inadequate control for selection
5. Outcome reported by treating physician
6. Evidence of selective reporting
7. Evidence of selective analysis
8. High number of crossovers
9. Inadequate handling of missing data
10. High loss to follow-up or missing data
11. Not blinded to treatment assignment
12. Not blinded to selective reporting
13. Not blinded to outcome assessment
14. Not registered
15. Low quality of evidence
16. Power not calculated for primary outcome
17. Power not based on clinically important difference
18. Test is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event
19. Test is not appropriate for multiple observations per patient
20. Confidence intervals and/or p values not reported
21. Comparative treatment effects not calculated

DRG: dorsal root ganglion; RCT: randomized controlled trial.
bias analysis (per protocol for noninferiority trials)

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

**Case Series:** Two case series with more than 10 participants evaluating the Axium DRG neurostimulator in patients with chronic trunk and/or limb pain were identified: Liem et al (2015) and Schu et al (2015). 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. From baseline to the 12-month follow-up, the mean VAS score decreased from 77.6 mm (n=32) to 33.6 mm (n=25; p<0.001). Sixty percent of patients achieved a 50% or greater reduction in overall pain.

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

**Section Summary: Dorsal Root Ganglion Neurostimulators for Chronic Trunk or Limb Pain**
One unblinded RCT and several case series have evaluated DRG neurostimulators in patients with chronic trunk and/or limb pain. The RCT (N=152) found that patients receiving DRG neurostimulation had significantly higher rates of treatment success at 3 and 12 months than those receiving standard SCS devices. Both groups experienced paresthesias but patients in the DRG group reported less postural variation in paresthesia and reduced extraneous stimulation in nonpainful areas. Patients in the DRG group also reported more improvement in interference with physical functioning and mood states. Rates of serious adverse events were similar. Several case series have also been published. The largest series, which had the longest follow-up, found that 60% of patients had 50% or greater reduction in overall pain at 12 months. While outcomes have been favorable, additional RCTs are needed to provide greater certainty in the treatment benefit.

**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. SCS has been investigated in this subset of patients as a technique to relieve pain and decrease the incidence of amputation.

An updated Cochrane by Ubbink and Vermeulen (2013) assessed the use of SCS in peripheral vascular diseases. Reviewers included RCTs and non-RCTs evaluating the efficacy of SCS in adults with nonreconstructable chronic critical leg ischemia. Six trials were identified; all were conducted in Europe and five were single-country studies. SCS was compared with other nonsurgical interventions. One study was not randomized, and none was blinded. In a pooled
analysis of data from all 6 studies, there was a significantly higher rate of limb survival in the SCS group than in the control group at 12 months (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 SCS patients required significantly fewer analgesics, and more patients reached Fontaine stage II (intermittent claudication) than in the control group. There was no difference in ulcer healing (but only 2 studies were included in this analysis). In the 6 trials, 31 (15%) of 210 patients had a change in stimulation requiring intervention, 8 (4%) experienced the end of battery life, and 6 (3%) infections required device removal.

Previously, Klomp et al (2009) published a meta-analysis of RCTs that used SCS to treat patients with critical limb ischemia. 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. They found that patients with ischemic skin lesions had a higher risk of amputation than patients with other risk factors. There were no significant interactions between this and any other prognostic factor. The analyses did not identify subgroups of patients who might benefit from SCS.

A systematic review of non-revascularization-based treatments by Abu Dabrh et al (2015), including SCS, for patients with critical limb ischemia also included 5 RCTs. In the pooled analysis, reviewers found that SCS 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 (ie, small sample size and wide CIs) and the risk of bias.”

Section Summary: Critical Limb Ischemia
Five relatively small RCTs comparing SCS with usual care have assessed patients with critical limb ischemia. In some pooled analyses of these RCTs, SCS did not result in a significantly lower rate of amputation, although 1 systematic review and meta-analysis reported a significant difference. This evidence is not sufficient to determine whether SCS would improve outcomes for patients with critical limb ischemia.

Refractory Angina Pectoris
Systematic Reviews
Several systematic reviews have evaluated SCS for treating angina pectoris. More recently, Pan et al (2017) identified 12 RCTs that evaluated SCS in patients with refractory angina pectoris. Most studies had small sample sizes (ie, <50 patients) and together totaled 476 patients. Reviewers did not discuss the control interventions reported in the RCTs. Pooled analyses favored the SCS group in most cases (eg, for exercise time after the intervention, pain level [VAS score], angina frequency), but there were not significant differences between intervention and control groups for physical limitation or angina stability.

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

Randomized Controlled Trials
Zipes et al (2012) published an industry-sponsored, single-blind, multicenter trial with sites in the United States and Canada. This trial was terminated early because interim analysis by the data and safety monitoring board found the treatment futility. A total of 118 patients with severe angina, despite maximal medical treatment, were enrolled. Of the 118 patients, 71 (60%) underwent SCS implantation with the Intrel III neurostimulator (Medtronic). The remaining 47 patients did not meet eligibility criteria postenrollment or had other issues (eg, 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: SCS with standard stimulation (n=10), SCS with low-level stimulation (75%-80% of the sensory threshold) (n=7), or very low intensity SCS (n=8). Thus, patients in groups 2 and 3 were unable to feel sensation during stimulation. After a protocol adjustment at 1 month, patients in the very low intensity group were re-randomized to one of the other groups of which there were 13 patients in the standard stimulation group and 12 patients in the low-level stimulation group. At the 3-month follow-up (2 months after re-randomization), there were statistically significant between-group differences in 1 of 12 outcome variables. There was a median of 22 angina episodes in the standard stimulation group and 10 in the low-level stimulation group (p=0.002). Nonsignificant variables included the use of nitroglycerin, quality of life, VAS, 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 SCS as a treatment for refractory angina. While some studies have reported benefit, 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 SCS for heart failure were published by Torre-Amione et al (2014). Eligibility included symptomatic heart failure despite optimal medical
therapy, left ventricular ejection fraction less than 30%, hospitalization or need for intravenous inotropic support in the past year, and inability to walk more than 450 meters on a 6-minute walk test. All patients had an implanted heart device. Nine patients underwent SCS implantation and received 3 months of active and 3 months of inactive (off position) treatment, in random order. There was a 1-month washout period between treatments. The primary outcome was a composite of death, hospitalization for worsening heart failure, and symptomatic bradyarrhythmia or tachyarrhythmia requiring high-voltage therapy. Four patients experienced at least one of the events in the composite end point. The events occurred in 2 patients while the device was turned on and in two while it was turned off. One patient died about 2 months after implantation with the device turned off. The SCS devices did not interfere with the functioning of implantable cardioverter defibrillators.

Zipes et al (2016) reported on the results of the DEFEAT-HF study, a prospective, multicenter, single-blind RCT comparing SCS using active stimulation with sham-control in patients who had New York Heart Association functional class III heart failure and a left ventricular ejection fraction of 35% or less. Sixty-six patients were implanted with an SCS and randomized 3:2 to SCS on (n=42) or SCS off (sham; n=24). For the trial’s primary end point (change in left ventricular end systolic volume index from baseline to 6 months), there was no significant difference between groups (p=0.30). Other end points 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 SCS 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 SCS for heart failure.

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

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

Section Summary: Cancer-Related Pain
A Cochrane review did not identify any RCTs evaluating SCS for the treatment of cancer-related pain.
**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 SCS between 2000 and 2005.60 Patients’ diagnoses included CRPS (n=345 [49%]), FBSS (n=235 [33%]), peripheral vascular disease (n=20 [3%]), visceral pain in the chest, abdomen, or pelvis (n=37 [5%]), and peripheral neuropathy (n=70 [10%]). Mean follow-up across studies was 3 years (range, 3 months to 7 years). A total of 527 (36%) of the 707 patients eventually underwent permanent implantation of an SCS device. Hardware-related complications included lead migration in 119 (23%) of 527 patients, lead connection failure in 50 (9.5%) patients, and lead break in 33 (6%) patients. Revisions or replacements corrected the hardware problems. The authors noted that rates of hardware failure have decreased due to advances in SCS technology. Documented infection occurred in 32 (6%) of 527 patients with implants; there were 22 cases of deep infection, and 18 patients had abscesses. There was no significant difference in the infection rate by diagnosis. All cases of infection were managed by device removal.

Lanza et al (2012) reviewed observational studies on SCS in patients with refractory angina pectoris.61 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 (ie, electrode dislodgement or fracture requiring repositioning) or internal programmable generator failure during substitution. Lead issues were reported by 10 studies (n=450 patients). In these studies, 55 cases of lead or internal programmable generator failure were reported. No fatalities related to SCS treatment were reported.

**SUMMARY OF EVIDENCE**

**Treatment-Refractory Chronic Pain**

For individuals who have treatment-refractory chronic pain of the trunk or limb who receive standard spinal cord stimulation (SCS), the evidence includes systematic reviews and randomized controlled trials (RCTs). Relevant outcomes are symptoms, functional outcomes, quality of life, medication use, and treatment-related morbidity. Available RCTs are mixed in terms of the underlying diagnoses in select patient populations. However, those including patients with underlying neuropathic pain processes have shown a significant benefit with SCS. Systematic reviews have supported the use of SCS to treat refractory trunk or limb pain, and patients who have failed all other treatment modalities have few options. The evidence is sufficient to determine that the technology results in 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 SCS, 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 to standard SCS in patients who had not previously been treated with SCS found a clinically and statistically significant benefit associated with high-frequency SCS. Another RCT in patients who had chronic pain despite previous treatment with standard SCS found no benefit for those receiving high-frequency stimulation compared with sham control; however, it is difficult to compare these findings to other trials of SCS due to the different patient populations, short treatment periods, and the crossover period effect. The evidence is sufficient to determine that the technology results in 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 1 RCT and case series. Relevant outcomes are symptoms, functional outcomes, quality of life, medication use, and treatment-related morbidity. One unblinded RCT found that patients receiving DRG neurostimulation had significantly higher rates of treatment success at 3 and 12 months than those receiving standard SCS devices. Both groups experienced paresthesias, but patients in the DRG group reported less postural variation in paresthesia and reduced extraneous stimulation in nonpainful areas. Patients in the DRG group also reported more reduction in interference with physical functioning and mood states. Rates of serious adverse events were similar. Given that DRG neurostimulation targets a different portion of the sensory pathway and anatomic location than standard SCS, replication is needed in a confirmatory RCT.

Critical Limb Ischemia
For individuals who have critical limb ischemia who receive SCS, the evidence includes RCTs. Relevant outcomes are overall survival, symptoms, functional outcomes, quality of life, morbid events, hospitalizations, and treatment-related morbidity. In some pooled analyses of these RCTs, SCS did not result in a significantly lower rate of amputation, although 1 systematic review and meta-analysis did report 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 SCS, 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 SCS as a treatment for refractory angina. While some have reported benefit, most have not. In 2 more recent RCTs, there was no significant benefit on 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 SCS, the evidence includes RCTs. Relevant outcomes are overall survival, symptoms, functional outcomes, quality of life, morbid events, hospitalizations, and treatment-related morbidity. One small pilot crossover study (N=9) 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 may 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 SCS, the evidence includes no RCTs. Relevant outcomes are symptoms, functional outcomes, quality of life, medication use, and treatment-related morbidity. No RCTs evaluating SCS in this population were identified. The evidence is insufficient to determine the effects of the technology on health outcomes.

**PRACTICE GUIDELINES AND POSITION STATEMENTS**

**International Association for the Study of Pain**
The International Association for the Study of Pain (2013) published recommendations on the management of neuropathic pain. The Association issued 2 recommendations on spinal cord stimulation (SCS); both were considered weak due to the amount and consistency of the
evidence. The recommendations supported the use of SCS for failed back surgery syndrome and complex regional pain syndrome.

**American Society of Interventional Pain Physicians**
The American Society of Interventional Pain Physicians (2013) updated its evidence-based guidelines on interventional techniques for the management of chronic spinal pain. The guidelines included a statement that there is fair evidence in support of SCS in managing patients with failed back surgery syndrome.

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

**National Institute for Health and Care Excellence**
The National Institute for Health and Care Excellence (2008) issued guidance on SCS for chronic pain of neuropathic or ischemic origin. The Institute recommended SCS as a treatment option for adults with chronic pain of neuropathic origin (measuring at least 50 mm on a 0-100 mm visual analog scale) that continues for at least 6 months despite appropriate conventional medical management, and who have had a successful trial of stimulation as part of an assessment by a specialist team.

**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 9.

**Table 9. Summary of Key Trials**

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ongoing</td>
<td>Wireless High Frequency Spinal Cord Stimulation for Chronic Pain</td>
<td>80</td>
<td>Mar 2018</td>
</tr>
<tr>
<td>NCT02514590a</td>
<td>Comparison of 1000 Hertz (Hz), Burst, and Standard Spinal Cord Stimulation in Chronic Pain Relief</td>
<td>22</td>
<td>Dec 2017</td>
</tr>
<tr>
<td>NCT02093793a</td>
<td>A Randomized Controlled Study to Evaluate the Safety and Effectiveness of the Precision Spinal Cord Stimulator System Adapted for High-Rate Spinal Cord Stimulation</td>
<td>406</td>
<td>Apr 2019</td>
</tr>
<tr>
<td>NCT03014583</td>
<td>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)</td>
<td>28</td>
<td>Jul 2019</td>
</tr>
<tr>
<td>NCT03318172</td>
<td>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</td>
<td>100</td>
<td>Jul 2019</td>
</tr>
<tr>
<td>NCT03228420</td>
<td>A Post-Market, Multicenter, Prospective, Randomized Clinical Trial Comparing 10 kHz Spinal Cord Stimulation (HF10™ Therapy) Combined With Conventional Medical Management to</td>
<td>360</td>
<td>Aug 2020</td>
</tr>
</tbody>
</table>
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

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>63650</td>
<td>Percutaneous implantation of neurostimulator electrode array, epidural</td>
</tr>
<tr>
<td>63655</td>
<td>Laminectomy for implantation of neurostimulator electrodes, plate/paddle, epidural</td>
</tr>
<tr>
<td>63661</td>
<td>Removal of spinal neurostimulator electrode percutaneous array(s), including fluoroscopy, when performed</td>
</tr>
<tr>
<td>63662</td>
<td>Removal of spinal neurostimulator electrode plate/paddle(s) placed via laminotomy or laminectomy, including fluoroscopy, when performed</td>
</tr>
<tr>
<td>63663</td>
<td>Revision including replacement, when performed, of spinal neurostimulator electrode percutaneous array(s), including fluoroscopy, when performed</td>
</tr>
<tr>
<td>63664</td>
<td>Revision including replacement, when performed, of spinal neurostimulator electrode plate/paddle(s) placed via laminotomy or laminectomy, including fluoroscopy, when performed</td>
</tr>
<tr>
<td>63685</td>
<td>Insertion or replacement of spinal neurostimulator pulse generator or receiver, direct or inductive coupling</td>
</tr>
<tr>
<td>63688</td>
<td>Revision or removal of implanted spinal neurostimulator pulse generator or receiver</td>
</tr>
<tr>
<td>95970</td>
<td>Electronic analysis of implanted neurostimulator pulse generator system (e.g., rate, pulse amplitude, pulse duration, configuration of wave form, battery status, electrode selectability, output modulation, cycling, impedance and patient compliance measurements); simple or complex brain, spinal cord, or peripheral (i.e., cranial nerve, peripheral nerve, sacral nerve, neuromuscular) neurostimulator pulse generator/transmitter, without reprogramming</td>
</tr>
<tr>
<td>95971</td>
<td>Electronic analysis of implanted neurostimulator pulse generator system (e.g., rate, pulse amplitude, pulse duration, configuration of wave form, battery status, electrode selectability, output modulation, cycling, impedance and patient compliance measurements); simple spinal cord, or peripheral (i.e., peripheral nerve, sacral nerve, neuromuscular) neurostimulator pulse generator/transmitter, with intraoperative or subsequent programming</td>
</tr>
</tbody>
</table>

NCT: national clinical trial.

\(^a\) Denotes industry-sponsored or cosponsored trial.
Electronic analysis of implanted neurostimulator pulse generator system (eg, rate, pulse amplitude, pulse duration, configuration of wave form, battery status, electrode selectability, output modulation, cycling, impedance and patient compliance measurements); complex spinal cord, or peripheral (ie, peripheral nerve, sacral nerve, neuromuscular) (except cranial nerve) neurostimulator pulse generator/transmitter, with intraoperative or subsequent programming

- 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” 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
Added 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.

REFERENCES


**Other References**


2. Blue Cross and Blue Shield of Kansas Anesthesiology Liaison Committee, Consent Ballot, November 2014.