Spinal Cord Stimulation

Policy Number: MM.06.013
Original Effective Date: 04/01/2008
Line(s) of Business: HMO; PPO; QUEST Integration
Current Effective Date: 10/01/2017
Section: Surgery
Place(s) of Service: Outpatient; Inpatient

I. Description

Spinal cord stimulation (SCS) delivers low-voltage electrical stimulation to the dorsal columns of the spinal cord to block the sensation of pain. SCS devices have a radiofrequency receiver that is surgically implanted and a power source (battery) that is either implanted or worn externally.

Treatment-Refractory Chronic Pain
For individuals who have treatment-refractory chronic pain of the trunk or limb who receive standard 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 2 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. The other 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 wireless injectable 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 wireless injectable stimulators had significantly higher rates of treatment success at 3 and 12 months than those receiving standard SCS devices. Both groups experienced paresthesias, so blinding would have been possible. Additional RCTs, especially blinded with a sham-control group as well as an SCS control, are needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

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.

**II. Criteria/Guidelines**
A. Spinal cord stimulation with standard or high-frequency stimulation is covered (subject to Limitations and Administrative Guidelines) for the treatment of severe and chronic pain of the trunk or limbs that is refractory to all other pain therapies.

B. Patient selection focuses on determining whether or not the patient is refractory to other types of treatment. All of the following criteria must be met prior to implantation of a temporary electrode:  
1. The treatment is used only as a last resort; other treatment modalities (pharmacological, surgical, psychological, physical, if applicable) have been tried and failed or are judged to be unsuitable or contraindicated;
2. Pain is neuropathic in nature (i.e., resulting from actual damage to the peripheral nerves). Common indications include, but are not limited to, failed back syndrome, complex regional pain syndrome (i.e., reflex sympathetic dystrophy), arachnoiditis, radiculopathies, phantom limb/stump pain, and peripheral neuropathy;
3. No serious untreated drug habituation exists;
4. All the facilities, equipment, and professional and support personnel required for the proper diagnosis, treatment, and follow-up of the patient are available.

C. In addition to the above criteria, the patient must demonstrate at least 50% pain relief with a temporarily implanted electrode prior to permanent implantation.

**III. Limitations**
A. Spinal cord stimulation is not covered for all other indications including but not limited to treatment of critical limb ischemia to forestall amputation and treatment of refractory angina pectoris, heart failure, and cancer-related pain.

B. Wireless injectable dorsal root ganglion neurostimulation is is not covered for treatment of severe and chronic pain of the trunk or limbs.

**IV. Administrative Guidelines**
A. Precertification is required before implantation of a temporary electrode and before permanent implantation of the stimulator. To precertify, please complete HMSA’s Precertification Request and mail or fax the form, or use iExchange as indicated along with documentation demonstrating that criteria have been met.

1. The following documentation should be included with the precertification request for the implantation of a temporary electrode:
   a. Clinical notes related to the diagnosis and treatment of chronic neuropathic pain of the trunk or limbs.
   b. Documentation of all treatments tried and failed (e.g., medications, surgical notes, physical therapy notes, psychological notes, etc.).
c. Consultation notes from a psychologist and/or psychiatrist.

2. The following must be submitted before the permanent implantation of the stimulator:
   a. The patient’s pain log (e.g., diary) and physician clinical notes documenting a successful one-week trial of a temporarily implanted electrode.

B. Precertification is not required for the replacement, revision, or removal of a permanently implanted spinal neurostimulator pulse generator.

C. Applicable Codes:

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<tr>
<th>CPT Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>63650</td>
<td>Percutaneous implantation of neurostimulator electrode array; epidural</td>
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<tr>
<td>63655</td>
<td>Laminectomy for implantation of neurostimulator electrodes, plate/paddle; epidural</td>
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<tr>
<td>63661</td>
<td>Removal of spinal neurostimulator electrode percutaneous array(s), including fluoroscopy, when performed</td>
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<tr>
<td>63662</td>
<td>Removal of spinal neurostimulator electrode plate/paddle(s) placed via laminotomy or laminectomy, including fluoroscopy, when performed</td>
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<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>
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<tr>
<td>63685</td>
<td>Insertion or replacement of spinal neurostimulator pulse generator or receiver, direct or inductive coupling</td>
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<tr>
<td>63688</td>
<td>Revision or removal of implanted spinal neurostimulator pulse generator or receiver</td>
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<tr>
<td>95970-95973</td>
<td>Neurostimulator programming and analysis code range</td>
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<thead>
<tr>
<th>HCPCS Code</th>
<th>Description</th>
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<tr>
<td>C1820</td>
<td>Generator, neurostimulator (implantable), with rechargeable battery and charging system (to be used for non-high frequency generators)</td>
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<tr>
<td>C1822</td>
<td>Generator, neurostimulator (implantable), high frequency, with rechargeable battery and charging system.</td>
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<td>L8679</td>
<td>Implantable neurostimulator, pulse generator, any type</td>
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<tr>
<td>L8680</td>
<td>Implantable neurostimulator electrode, each</td>
</tr>
<tr>
<td>L8685</td>
<td>Implantable neurostimulator pulse generator, single array, rechargeable, includes extension</td>
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<tr>
<td>L8686</td>
<td>Implantable neurostimulator pulse generator, single array, nonrechargeable, includes extension</td>
</tr>
<tr>
<td>L8687</td>
<td>Implantable neurostimulator pulse generator, dual array, rechargeable, includes extension</td>
</tr>
<tr>
<td>L8688</td>
<td>Implantable neurostimulator pulse generator, dual array, nonrechargeable, includes extension</td>
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### Spinal Cord Stimulation

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<tr>
<th>ICD-10-CM Code</th>
<th>Description</th>
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<tr>
<td>G56.40-G56.42</td>
<td>Causalgia of upper limb code range</td>
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<tr>
<td>G57.70-G57.72</td>
<td>Causalgia of lower limb code range</td>
</tr>
<tr>
<td>G89.21-G89.8</td>
<td>Chronic pain, not elsewhere classified, code range</td>
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<tr>
<td>G89.4</td>
<td>Chronic pain syndrome</td>
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<tr>
<td>G90.50-G90.59</td>
<td>Complex regional pain syndrome I (CRPS I), code range</td>
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<tr>
<td>M25.50-M25.579</td>
<td>Pain in joint, code range</td>
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<tr>
<td>M54.10-M54.18</td>
<td>Radiculopathy, code range</td>
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<tr>
<td>M54.30-M54.32</td>
<td>Sciatica, code range</td>
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<tr>
<td>M54.40-M54.42</td>
<td>Lumbago with sciatica, code range</td>
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<tr>
<td>M54.5</td>
<td>Low back pain</td>
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<tr>
<td>M54.6</td>
<td>Pain in thoracic spine</td>
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<tr>
<td>M54.81, M54.89</td>
<td>Other dorsalgia codes</td>
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<tr>
<td>M54.9</td>
<td>Dorsalgia, unspecified</td>
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<tr>
<td>M79.1</td>
<td>Myalgia</td>
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<tr>
<td>M79.60-M79.676</td>
<td>Pain in limb, hand, foot, fingers and toes code range</td>
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<tr>
<td>R52</td>
<td>Pain, unspecified</td>
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<th>ICD-10-PCS Code</th>
<th>Description</th>
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<td>00HU0MZ, 00HU3MZ, 00HU4MZ</td>
<td>Surgical, central nervous system, insertion, spinal canal, neurostimulator lead, code by approach</td>
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<tr>
<td>00HV0MZ, 00HV3MZ, 00HV4MZ</td>
<td>Surgical, central nervous system, insertion, spinal cord, neurostimulator lead, code by approach</td>
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<tr>
<td>00WU0MZ, 00WU3MZ, 00WU4MZ</td>
<td>Surgical, central nervous system, removal, spinal canal, neurostimulator lead, code by approach</td>
</tr>
<tr>
<td>00PV0MZ, 00PV3MZ, 00PV4MZ</td>
<td>Surgical, central nervous system, removal, spinal cord, neurostimulator lead, code by approach</td>
</tr>
<tr>
<td>00WU0MZ, 00WU3MZ, 00WU4MZ</td>
<td>Surgical, central nervous system, revision, spinal canal, neurostimulator lead, code by approach</td>
</tr>
<tr>
<td>00WV0MZ, 00WV3MZ, 00WV4MZ</td>
<td>Surgical, central nervous system, revision, spinal cord, neurostimulator lead, code by approach</td>
</tr>
<tr>
<td>OJH60M6, OJH60M7, OJH60M8, OJH60M9, OJH63M6, OJH63M7, OJH63M8, OJH63M9, OJH70M6, OJH70M7, OJH70M8, OJH70M9, OJH73M6, OJH73M7, OJH73M8, OJH73M9, OJH80M6, OJH80M7, OJH80M8, OJH80M9, OJH83M6, OJH83M7</td>
<td>Surgical, subcutaneous tissue and fascia, insertion, stimulator generator, code by body part, approach, number of arrays and whether rechargeable or not</td>
</tr>
</tbody>
</table>
V. 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, and the Precision Spinal Cord Stimulator (Advanced Bionics, Switzerland), approved in 2004.

In May 2015, FDA approved the Nevro Senza™ Spinal Cord Stimulator (Nevro Corp., Menlo Park, CA), a totally implantable neurostimulator device, 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, intractable low back pain, and leg pain.” This device uses a higher frequency of electrical stimulation (10 kHz) than standard devices.

VI. Background

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 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.

SCS devices consist of several components: (1) the lead that delivers the electrical stimulation to the spinal cord; (2) an extension wire that conducts the electrical stimulation from the power source to the lead; and (3) a power source that generates the electricity. The lead may incorporate from 4 to 8 electrodes, with 8 electrodes more commonly used for complex pain patterns. There are 2 basic types of power source. One type, the power source (battery), can be surgically implanted. 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.
Spinal Cord Stimulation

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.

Another variation on SCS is the wireless injectable stimulator. These miniaturized neurostimulators are transforaminally placed at the dorsal root ganglion (DRG) and are used to treat pain. DRG 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.

**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.” This device uses a higher frequency of electrical stimulation (10 kHz) than standard devices.

Two wireless injectable neurostimulators have been approved or cleared by FDA. In February 2016, the Axium Neurostimulator System (Spinal Modulation, Menlo Park, CA) was approved by FDA through the PMA process. The device 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.

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.

**VII. Rationale**

This policy was originally created in 1996 and has been updated regularly with searches of the MEDLINE database. Most recently, the literature was reviewed through February 23, 2017. Following is a summary of the key literature to date.

**Refractory Chronic Trunk or Limb Pain**

**Standard Spinal Cord Stimulation**

**Systematic Reviews**

Existing randomized controlled trials (RCTs) of standard spinal cord stimulation (SCS) for chronic trunk or limb pain are summarized in the next section. Three systematic reviews have assessed the RCTs included in the next section and overlap substantially. The North et al (2005)2 and Kumar et al (2007)3 RCTs are included in all 3 systematic reviews; Kapural et al (2015)4 and Kemler et al (2000)5 are each one of the systematic reviews.

In 2016, Grider et al reported results of a systematic review of RCTs of SCS for chronic spinal pain. 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, 2 were considered high quality and 1 moderate quality based on Cochrane criteria and Interventional Pain Management Techniques—Quality Appraisal of Reliability and Risk of Bias Assessment. Kapural et al (2015) will be 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.

In 2009, a systematic review of RCTs and observational studies of SCS in failed back surgery Syndrome (FBSS; defined as persistent pain after spinal surgery; the initial pain may have been secondary to various causes) was undertaken by Frey et al. 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 clinical use of standard SCS on a long term-basis.

Also in 2009, Simpson et al reported on a health technology assessment, funded by the National Institute for Health and Care Excellence (NICE), to obtain clinical and cost-effectiveness data for SCS in adults with chronic neuropathic or ischemic pain with inadequate response to other medical or surgical treatments. NICE used the assessment as the basis for its guidance on SCS for chronic pain. Trials for FBSS and complex regional pain syndrome (CRPS) type I (reported by North
Spinal Cord Stimulation

et al, Kumar et al, and Kemler et al) suggested that SCS was more effective than CMM or reoperation in reducing pain.

Randomized Controlled Trials
Five RCTs (total N=310 patients; range, 36-100 patients) have evaluated SCS (see Table 1). Patient populations had FBSS, diabetic neuropathy, and CRPS. The comparators were primarily conventional medical management, although 1 RCT compared to reoperation for FBSS, and another compared SCS to 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. 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 reduction in analgesic use were consistently numerically larger for SCS but not statistically significant in all studies. Four of the five studies did not report differences in functional, quality of life, 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)11 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 in the 1 study with 5 years of follow-up, results were not statistically significant at 5 years.

Section Summary: Standard Spinal Cord Stimulation for Chronic Trunk or Limb Pain
The evidence on the efficacy of standard SCS for treatment of chronic limb or trunk pain consists of 5 RCTs (range, 36-100 patients) with refractory pain due to FBSS, CRPS, or diabetic neuropathy. These trials were heterogenous in terms of patient populations and participants were unblinded (no trials used sham surgeries or devices) but they consistently reported improvements in pain with clinically and statistically significant effect sizes and reductions in medication use for at least 6 months. Even with a sham surgery or device, blinded outcomes assessment may not be feasible for SCS, because active SCS stimulation is associated with paresthesias. Given the large treatment effects with consistent findings across studies, this evidence suggests that SCS is a reasonable treatment option.
<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>
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<tbody>
<tr>
<td>North et al</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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<td>Success (50% pain relief and patient satisfaction) 39% 12% 0.04</td>
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<td>Stable or decreased opioids 87% 58% 0.025</td>
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<tr>
<td>Kumar et al</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>
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<td>50% reduction in VAS leg pain 48% 9% &lt;0.001</td>
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<td>SF-36, favoring SCS all domains except RP 48% 48% 0.02</td>
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<td>ODI score 45 56 &lt;0.001</td>
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<td>Opioid use 56% 70% 0.21</td>
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<td>NSAIDs use 34% 50% 0.14</td>
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<td>N at 24 mo=87</td>
<td>24 months (SCS vs CMM)</td>
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<td>50% reduction in leg pain on VAS 37% 2% 0.003</td>
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<tr>
<td>Kemler et al</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)</td>
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<tr>
<td></td>
<td>CRPS</td>
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<td>Reduction in VAS pain score 2.4 0.2 &lt;0.001</td>
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<td>Much improved GPE 39% 6% 0.01</td>
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<td>No difference in functional outcomes or HRQOL 2 years (SCS vs PT)</td>
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<td>Reduction in VAS pain score 2.1 0.0 &lt;0.001</td>
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<td>Much improved GPE 43% 6% 0.001</td>
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<td>N at 5 y=44</td>
<td>5 years (SCS vs PT)</td>
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<td>Reduction in VAS pain score 1.7 1.0 0.25</td>
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<tr>
<td>Stangen et al</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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<td></td>
<td>Success (50% reduction in pain for 4 d or at least 59% 7% &lt;0.01)</td>
<td></td>
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<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>much improved on patient-reported global impression of change)</td>
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<td></td>
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<td></td>
<td></td>
<td>• Reduction in pain medication 32% 0%</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• No differences in health utility or HRQOL</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>N at 24 mo=17 (SCS only)</td>
<td>2 years (SCS only)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Success 65%</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• No improvement in health utility vs baseline</td>
<td></td>
</tr>
<tr>
<td>De Vos et al (2014)</td>
<td>Diabetic neuropathy of LEs</td>
<td>SCS CMM</td>
<td>N=60 N at 6 mo=54</td>
<td>6 months (SCS vs CMM)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• 50% reduction in pain 62.5% 5% &lt;0.001</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Reduction in analgesic intake (MQS score) 2.9 -0.09 NR</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Change in health utility 0.39 0.00 &lt;0.05</td>
<td></td>
</tr>
</tbody>
</table>

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.
High-Frequency Spinal Cord Stimulation

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 FDA. Studies that offer direct comparisons between standard SCS and high-frequency SCS (HFSCS) were sought to evaluate the incremental benefit of HFSCS.

Systematic Reviews

In 2016, Bicket et al published a systematic review of controlled trials on HFSCS. Reviewers searched for RCTs and controlled nonrandomized studies in 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 (discussed in detail 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 risk of bias tool to rate bias in the RCTs. One trial (Perruchoud et al, 2013) was not rated as having a high-risk of bias in any domain and the other (Kapural et al, 2015) was rated as having a high risk of bias in the domain of performance and detection bias because it was unblinded. Studies were reviewed qualitatively (ie, study findings were not pooled).

Randomized Controlled Trials

Two RCTs identified addressed HFSCS (see Table 2): Perruchoud et al (2013) compared high-frequency stimulation (5000 Hz) with sham control in a crossover design (N=40) and Kapural et al (2015) compared HFSCS (10,000 Hz) with standard SCS (N=198). The 2 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-naïve to SCS). Perruchoud et al 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. Outcomes were reported after 2 weeks of treatment. Forty-two percent were responders in the high-frequency group versus 30% in the sham group. The mean benefit averaged over the 2 crossover sequences was 11% favoring 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 to other RCTs due to the enrolled population (only people who had chronic pain despite previous use of standard SCS), the short treatment period (2 weeks), the period effect (patients tended to report greater pain reduction in first period regardless of assigned sequence), and the use of standard SCS during the 2 weeks preceding each treatment period, which could lead to carryover effects.

Outcomes were reported after 3, 12, and 24 months of treatment. 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. 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 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 versus 37% in SCS for back pain and 74% versus 46% for leg pain (calculated, data not shown).

**Section Summary: High-Frequency Spinal Cord Stimulation for Chronic Trunk or Limb Pain**
The evidence for HFSCS compared to standard SCS consists of 1 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 on this trial is limited due to the significant period effect.
### Table 2: Characteristics and Result of RCTs of Using HFSCS

<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>Perruchoud et al (2013)&lt;sup&gt;17&lt;/sup&gt;</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;• 2x2 crossover design with conventional SCS before both arms</td>
<td>N=40&lt;br&gt;N=33</td>
<td>2 weeks (HFCS vs sham)&lt;br&gt;<strong>• Responder (at least minimal improvement on patient reported global impression of change):</strong> 42% 30% 0.30&lt;br&gt;<strong>• VAS score:</strong> 4.35 4.26 0.82</td>
<td>One patient had malaise attributed to a vasovagal attack</td>
</tr>
<tr>
<td>Kapural et al (2015, 2016)&lt;sup&gt;18&lt;/sup&gt;</td>
<td>Chronic back and leg pain</td>
<td>• HFCS&lt;br&gt;• SCS</td>
<td>N=198&lt;br&gt;N at 3 mo=171&lt;br&gt;N at 24 mo=156</td>
<td>3 months (HFCS vs SCS)&lt;br&gt;<strong>• Responder (≥50% back pain reduction with no stimulation-related neurologic deficit):</strong>&lt;br&gt;○ Back pain 85% 44% &lt;0.001&lt;br&gt;○ Leg pain 83% 55% &lt;0.001&lt;br&gt;<strong>• Health utility:</strong> 0.48 0.46 0.78&lt;br&gt;<strong>• Stimulation discomfort:</strong> 0% vs 47%&lt;br&gt;<strong>• No stimulated-rated SAEs or neurologic deficits</strong>&lt;br&gt;<strong>• Decreased opioid use:</strong> 36% 26% 0.41&lt;br&gt;<strong>• Improvement in ODI score:</strong> 16.5 13.0 NR</td>
<td>&lt;br&gt;12 months (HFCS vs SCS)&lt;br&gt;<strong>• Responders:</strong>&lt;br&gt;○ Back pain 80% 50% NR&lt;br&gt;○ Leg pain 80% 56% NR&lt;br&gt;<strong>• Decreased opioid use:</strong> 36% 26% 0.41&lt;br&gt;<strong>• Improvement in ODI score:</strong> 16.5 13.0 NR</td>
</tr>
</tbody>
</table>

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

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

In 2016, Hou et al published a systematic review of burst SCS for 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. In addition, 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 Association of Neurology (AAN) criteria, reviewers originally rated 4 studies as class III and 1 study as class IV. However, given the small sample sizes and short-term duration of the 4 studies, they 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**

There are 3 crossover RCTs with a total of 47 patients (range, 12-20 patients), all conducted in Europe (see Table 3). The trials by De Ridder et al (2010, 2013) enrolled patients with neuropathic pain and the trial by Schu (2014) enrolled patients with FBSS. All trials compared burst stimulation to SCS. Schu (2014) and De Ridder (2013) also compared Burst to a sham stimulation group. Schu (2014) included patients receiving standard SCS; De Ridder (2010, 2013) included patients not previously treated with 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). All trials reported reductions in absolute pain scores (numeric rating scale or visual analog scale). Schu (2014) and De Ridder (2013) did not account for the crossover design in their data analyses so analyses and p values are incorrect and not reported in Table 3. De Ridder (2010) did not provide between-group comparisons. All trials reported numerically larger reductions in pain scores with burst than with SCS. Trial interpretation was limited by small sample sizes, short follow-up, and incorrect or missing statistical analyses.
## Table 3: Characteristics and Result of RCTs Using Burst SCS

<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>×3 crossover design without washout</td>
<td></td>
<td></td>
<td></td>
<td>1 week (burst vs SCS vs sham)(^a)</td>
<td></td>
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</tr>
</tbody>
</table>
| Schu et al (2014) | FBSS receiving standard SCS | • Burst stimulation  
• SCS  
• No stimulation (sham control) | N=20  
N=20 | | | | | | |
| | | | | • Mean NRS pain intensity scores, favoring burst | 4.7 | 7.1 | 8.3 |
| | | | | • Mean SF-MPQ pain quality scores, favoring burst | 19.5 | 28.6 | 33.5 |
| | | | | • Mean ODI scores, favoring burst | 19.8 | 24.6 | 29.5 |
| De Ridder et al (2013) | Neuropathic limb pain | • Burst stimulation  
• SCS  
• No stimulation (sham control) | N=15  
N=15 | 1 week (burst vs SCS vs sham)\(^a\) | | | | | | Not reported |
| | | | | • Mean improvement in VAS scores  
 o Back pain | 3.8 | 2.2 | 1.4 |
| | | | | o Limb pain | 3.9 | 3.9 | 0.9 |
| 2×2 crossover | | | | Two 1-h sessions (burst vs SCS)\(^b\) | | | | | | Not reported |
| De Ridder et al (2010) | Neuropathic pain | • Burst stimulation  
• SCS | N=12  
N=unclear | | | | | | |
| | | | | • Mean improvement in VAS scores  
 o Axial pain | 5.3 | 1.8 |
| | | | | o Limb pain | 7.3 | 4.4 |
| | | | | • Improvement in SF-MPQ sensory scores | 16.7 | 8.6 | | | |
| | | | | • Improvement in SF-MPQ affective scores | 6.7 | 4.3 | | | |

Ctrl: control; FBSS: failed back surgery syndrome; NRS: numeric rating scale; ODI: Oswestry Disability Index; SAE: serious adverse events; SCS: spinal cord stimulation; SF-MPQ, Short-Form McGill Pain Questionnaire; VAS: visual analog scale.

\(^a\) Analyses do not appear to properly take into account the crossover design therefore p values are not reported here.

\(^b\) Statistical treatment comparisons not provided.
**Wireless Injectable Neurostimulators**

Wireless injectable neurostimulators have been cleared or approved by FDA. Studies that offer direct comparisons between standard SCS and wireless injectable dorsal root ganglion (DRG) neurostimulators were sought to allow an evaluation of the incremental benefit of SCS.

**Randomized Controlled Trial**

One RCT, the ACCURATE study, compared wireless injectable neurostimulators and standard SCS. The trial, published by Deer et al in 2017, was a multicenter unblinded noninferiority trial. Eligibility criteria 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 to standard SCS. They 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. Implanted patients were followed for 12 months, with assessments at 3, 6, 9, and 12 months postimplant.

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. Twelve-month data were available for 105 patients (55 patients in the DRG group, 50 in the SCS group). The primary outcome was a composite measure of treatment success. Success was defined as: (1) 50% or greater reduction in VAS score from baseline to the end of the trial phase; (2) VAS scores at 3 months that was reduced by 50% or more from baseline; and (3) no stimulation-related neurologic deficits during the study. The noninferiority margin was set at 10%; the trial was designed such that, if the noninferiority end point was met, a superiority analysis was also performed. Treatment success at 3 month was achieved by 55 (81.2%) of 69 patients in the DRG arm and by 39 (55.7%) of 70 in the SCS arm. The noninferiority margin was met, and DRG was found to be statistically superior to SCS (p<0.001). At the 12-month follow-up, the primary end point was achieved by 49 (74.2%) of 66 in the DRG group and by 35 (53%) of 66 in the SCS group; and, again, DRG was considered noninferior and superior to SCS (p<0.001). In terms of paresthesias, at 3 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. Twenty-one serious adverse events occurred in 19 patients (8 in the DRG group, 11 in the SCS group; between-group difference, p=NS). Limitations of this trial were that its unblinded design and industry sponsorship, which could have biased outcome assessment and reporting.

**Case Series**

Several case series evaluating wireless injectable neurostimulators in patients with pain have been published. Two used the Axium device (Liem et al [2015], n=51; Schu et al [2015], n=29) and 1 used the Freedom SCS device (Weiner et al [2016], n=11). Liem et al published the series with the longest 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.

**Section Summary: Wireless Injectable Neurostimulators for Chronic Trunk or Limb Pain**

One unblinded RCT and several case series have evaluated wireless neurostimulators in patients with chronic trunk and/or limb pain. The RCT (N=152) found that patients receiving wireless injectable stimulators had significantly higher rates of treatment success at 3 and 12 months than those receiving standard SCS devices. Both groups experienced paresthesias, so blinding would have been possible. Several case series have also been published. The largest series (N=32) with the longest follow-up found that 60% of patients had 50% or greater reduction in overall pain at 12 months. Additional RCTs, especially blinded and with a sham-control group as well as an SCS control, are needed.

**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.

A systematic review from the Cochrane group on the use of SCS in peripheral vascular diseases was updated in 2013. The review 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 5 were single-country studies. SCS was compared with other nonsurgical interventions. One study was nonrandomized and none were blinded.

In a pooled analysis of data from all 6 studies, there was a significantly higher rate of limb survival in the SCS group than in the control group at 12 months (pooled risk difference [RD], -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 (number needed to treat, 9; 95% CI, 5 to 50). However, when the nonrandomized study was excluded, the difference in the rate of amputation no longer differed significantly between groups (RD = -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 studies, 31 (15%) of 210 patients had a change in stimulation requiring intervention, 8 (4%) experienced end of battery life, 6 (3%) infections required device removal.

Previously, in 2009, Klomp et al published a meta-analysis that selected RCTs on SCS in patients with critical limb ischemia. The same 5 RCTs identified in the Cochrane review, previously described, were included. The authors did not find a statistically significant difference in the rate of amputation in the treatment or the control groups. There was a relative risk of amputation of 0.79 and a risk difference of -0.07 (p=0.15). The authors also conducted additional analyses of data from their 1999 RCT to identify factors associated with a better or worse prognosis. 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 or any other prognostic factor. The analyses did not identify subgroups of patients who might benefit from SCS.

A 2015 systematic review of nonrevascularization-based treatments, including SCS, for patients with critical limb ischemia also included 5 RCTs. In pooled analysis, the authors found that SCS was associated with reduced risk of amputation (odds ratio [OR], 0.53; 95% CI, 0.36 to 0.79). However, the reviewers concluded that there was “relatively low quality of the evidence mainly due to imprecision (ie, small sample size and wide CIs) and the risk of bias.”

**Section Summary: Critical Limb Ischemia**

A number of relatively small RCTs of SCS versus usual care have been completed on 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 did report a significant difference. This evidence is not sufficient to conclude that SCS improves outcomes for patients with critical limb ischemia.

**Refractory Angina Pectoris**

**Systematic Reviews**

Several systematic reviews of the literature have evaluated SCS for treating angina pectoris. Most recently, in 2016, Pan et al 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 report the control interventions reported in the RCTs. Pooled analyses favored the SCS group in most cases (eg, for exercise time after intervention, pain level [VAS score], angina frequency), but there was not a significant difference between intervention and control groups on physical limitation and angina stability.

In 2015, another systematic review was published by Tsigaridas et al. SCS for refractory angina, 7 of which compared SCS to low or no stimulation and 2 of which compared SCS to alternative medical or surgical therapy for angina. Reviewers found that most RCTs were small and variable in quality based on assessment with the modified Jadad score. 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 to 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**

In 2012, Zipes et al published an industry-sponsored, single-blind, multicenter trial with sites in the United States and Canada.33 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 in the trial. Of these, 71 (60%) patients 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 (MACE), 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 MACE 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 2011 RCT from Italy by Lanza et al 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).34 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 after 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 were 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 use of nitroglycerin, QOL (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 was no significant benefit 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 in 2014 by Torre-Amione et al. 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 treatment and 3 months of inactive (off position) treatment in random order. There was a 1-month washout period between treatments. The primary outcome was a composite of death, hospitalization for worsening heart failure, and symptomatic bradyarrhythmia or tachyarrhythmia requiring high-voltage therapy. Four patients experienced at least 1 of the events in the composite end point. The events occurred in 2 patients while the device was turned on and 2 while it was turned off. One patient died about 2 months after implantation while the device
was turned off. The SCS devices did not interfere with the functioning of implantable cardioverter defibrillators.

In 2016, Zipes et al reported the results of the DEFEAT-HF trial, a prospective, multicenter, single-blind RCT trial comparing SCS with active stimulation to sham control in patients with New York Heart Association functional class III heart failure with a left ventricular ejection fraction of 35% or less. Sixty-six patients were implanted with an SCS and randomized in a 3:2 manner to SCS ON (n=42) or SCS OFF (sham; n=24). For the study’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 QOL 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 months of follow-up, there were no significant echocardiographic treatment effects in the overall patient population in echocardiographic parameters (p=0.36). The study 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 may 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 patients) 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 patients) was sham controlled; it did not find significant differences between groups, but might have been underpowered.

**Cancer-Related Pain**
In 2013, a Cochrane review (Lihua et al) assessed SCS for treatment of cancer-related pain in adults. The authors 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. The Cochrane review was updated in 2015 (Peng et al), with no new studies meeting inclusion criteria identified. Peng et al 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 treatment of cancer-related pain.

**Potential Adverse Effects**
Whereas RCTs are useful for evaluating efficacy, observational studies can provide data on the likelihood of potential complications. In 2011, Mekhail et al published a retrospective review of 707 patients treated with SCS between 2000 and 2005. 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%]). There was a mean follow-up of 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 cases, 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 in recent years 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 documented abscesses. There was no significant difference in the infection rate by diagnosis. All cases of infection were managed by device removal.

In 2012, Lanza et al reviewed observational studies on SCS in patients with refractory angina pectoris. The authors identified 16 studies (total N=1204 patients; although they noted that patients may have been included in >1 report). The most frequently reported complications were lead issues (i.e., electrode dislodgement or fracture requiring repositioning) or internal programmable generator (IPG) failure during substitution. Lead issues were reported by 10 studies (total N=450 patients). In these studies, 55 cases of lead or IPG 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 2 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. The other 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 wireless injectable 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 wireless injectable stimulators had significantly higher rates of treatment success at 3 and 12 months than those receiving standard SCS devices. Both groups experienced paresthesias, so blinding would have been possible. Additional RCTs, especially blinded with a sham-control group as well as an SCS control, are needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

**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**

**European Academy of Neurology**
In 2016, the European Academy of Neurology (EAN) published guidelines on neuromodulation in management of chronic pain. These guidelines updated the 2007 the European Federation of Neurological Societies (EFNS) recommendations. For neuropathic pain and complex regional pain
syndrome (CRPS), the quality of evidence and effect size were rated as “low” and tolerability/safety was rated as “moderate”. EAN issued a “weak” recommendation for use of spinal cord stimulation (SCS) added to conventional medical management in CRPS, chronic back and leg pain, and painful diabetic neuropathy, and as an alternative to reoperation in postsurgical chronic back and leg pain.

**International Association for the Study of Pain**
In 2013, the neuropathic pain special interest group of the International Association for the Study of Pain published recommendations on management of neuropathic pain. The interest group issued 2 recommendations on 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 (FBSS) and for complex regional pain syndrome (CRPS).

**Canadian Pain Society**
In 2012, a special interest group of the Canadian Pain Society published a guideline on interventions for neuropathic pain. The guideline stated that clinicians should consider offering a trial of SCS to patients with FBSS and CRPS who are not surgical candidates and who have failed conservative evidence-based treatments (recommendation based on good evidence with moderate certainty, grade B strength of recommendation). The guideline also stated that clinicians should consider offering a trial of SCS to patients with traumatic neuropathy and brachial plexopathy who are not surgical candidates and have failed conservative evidence-based treatments (recommendation based on fair evidence with moderate certainty, grade C strength of recommendation).

**American Society of Interventional Pain Physicians**
In 2013, the American Society of Interventional Pain Physicians (ASIPP) updated its evidence-based guidelines for interventional techniques in the management of chronic spinal pain. The guidelines included the statement that there is fair evidence in support of SCS in managing patients with FBSS.

An earlier evidence-based guideline from ASIPP found the evidence for SCS in FBSS and CRPS 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 Clinical Excellence**
In October 2008, the National Institute for Health and Clinical Excellence issued a guideline on SCS for chronic pain of neuropathic or ischemic origin. The guideline stated that SCS is recommended 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.

**European Federation of Neurological Societies**
In 2007, a task force from the European Federation of Neurological Societies (EFNS) systematically reviewed the evidence and made recommendations on the use of neurostimulation therapy, including SCS, for neuropathic pain. The review identified RCTs of SCS for complex regional pain syndrome and FBSS, and concluded “We found level B evidence for the effectiveness of SCS in FBSS and CRPS I.”

**Medicare National Coverage**

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

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

**Ongoing and Upublished Clinical Trials**

Some currently unpublished trials that might influence this review are listed in Table 4.

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
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<tr>
<td>Ongoing</td>
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<td>NCT01697358</td>
<td>Prospective, Randomized Study of Multicolumn Implantable Lead Stimulation for Predominant Low Back Pain</td>
<td>300</td>
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<tr>
<td>NCT02112474</td>
<td>The Pain Suppressive Effect of Alternative Spinal Cord Stimulation Frequencies</td>
<td>30</td>
<td>Nov 2016 (ongoing)</td>
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<tr>
<td>NCT02514590*</td>
<td>Wireless High Frequency Spinal Cord Stimulation for Chronic Pain</td>
<td>80</td>
<td>Aug 2017</td>
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<tr>
<td>NCT02902796</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>
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<tr>
<td>NCT02093793*</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>
</tbody>
</table>

NCT: national clinical trial

* Denotes industry-sponsored or cosponsored trial.
VII. Important Reminder

The purpose of this Medical Policy is to provide a guide to coverage. This Medical Policy is not intended to dictate to providers how to practice medicine. Nothing in this Medical Policy is intended to discourage or prohibit providing other medical advice or treatment deemed appropriate by the treating physician.

Benefit determinations are subject to applicable member contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

This Medical Policy has been developed through consideration of the medical necessity criteria under Hawaii’s Patients’ Bill of Rights and Responsibilities Act (Hawaii Revised Statutes §432E-1.4), generally accepted standards of medical practice and review of medical literature and government approval status. HMSA has determined that services not covered under this Medical Policy will not be medically necessary under Hawaii law in most cases. If a treating physician disagrees with HMSA’s determination as to medical necessity in a given case, the physician may request that HMSA reconsider the application of the medical necessity criteria to the case at issue in light of any supporting documentation.

VIII. References


