Proposed LCD - Nerve Stimulators for Chronic Intractable Pain (DL39406)

Links in PDF documents are not guaranteed to work. To follow a web link, please use the MCD Website.

Proposed LCD
Proposed LCDs are works in progress that are available on the Medicare Coverage Database site for public review.
Proposed LCDs are not necessarily a reflection of the current policies or practices of the contractor.

Contractor Information

CONTRACTOR NAME	CONTRACT TYPE	CONTRACT NUMBER	JURISDICTION	STATES
First Coast Service Options, Inc.	A and B MAC	09101 - MAC A	J - N	Florida
First Coast Service Options, Inc.	A and B MAC	09102 - MAC B	J - N	Florida
First Coast Service Options, Inc.	A and B MAC	09201 - MAC A	J - N	Puerto Rico Virgin Islands
First Coast Service Options, Inc.	A and B MAC	09202 - MAC B	J - N	Puerto Rico
First Coast Service Options, Inc.	A and B MAC	09302 - MAC B	J - N	Virgin Islands

Proposed LCD Information

Document Information

Source LCD ID
N/A

Proposed LCD ID
DL39406

Proposed LCD Title
Nerve Stimulators for Chronic Intractable Pain

AMA CPT / ADA CDT / AHA NUBC Copyright Statement

Issue

Issue Description

Multiple reconsideration requests have been received regarding a variety of electrical nerve stimulation services. There have been significant advancements to the field since the publication of the Spinal Cord Stimulators LCD, therefore this LCD intends to address nerve stimulators (both spinal cord and peripheral nerve) in the context of chronic intractable pain in the Medicare population, using current peer-reviewed evidence.

CMS National Coverage Policy

This LCD supplements but does not replace, modify or supersede existing Medicare applicable National Coverage Determinations (NCDs) or payment policy rules and regulations for nerve stimulators. Federal statute and subsequent Medicare regulations regarding provision and payment for medical services are lengthy. They are not repeated in this LCD. Neither Medicare payment policy rules nor this LCD replace, modify or supersede applicable state statutes regarding medical practice or other health practice professions acts, definitions and/or scopes of practice. All providers who report services for Medicare payment must fully understand and follow all existing laws, regulations and rules for Medicare payment for nerve stimulators and must properly submit only valid claims for them. Please review and understand them and apply the medical necessity provisions in the policy within the context of the manual rules. Relevant CMS manual instructions and policies may be found in the following Internet-Only Manuals (IOMs) published on the CMS Web site:

IOM Citations:

- CMS IOM Publication 100-03, *Medicare National Coverage Determinations (NCD) Manual*,
    - Chapter 1, Part 2, Section 160.18 Vagus Nerve Stimulation, Section 160.19 Phrenic Nerve Stimulator, Section 160.24 Deep Brain Stimulation for Essential Tremor and Parkinson’s Disease, Section 160.7 Electrical Nerve Stimulators, Section 160.7.1 Assessing Patient's Suitability for Electrical Nerve Stimulation Therapy, Section 230.18 Sacral Nerve Stimulation for Urinary Incontinence

- CMS IOM Publication 100-08, *Medicare Program Integrity Manual*,
    - Chapter 13, Section 13.5.4 Reasonable and Necessary Provision in LCDs

Social Security Act (Title XVIII) Standard References:

- Title XVIII of the Social Security Act, Section 1862(a)(1)(A) states that no Medicare payment may be made for items or services which are not reasonable and necessary for the diagnosis or treatment of illness or injury.

Coverage Guidance

Coverage Indications, Limitations, and/or Medical Necessity

Compliance with the provisions in this policy may be monitored and addressed through post payment data analysis and subsequent medical review audits.

History/Background and/or General Information

Electrical nerve stimulators such as spinal cord stimulators (SCS) and peripheral nerve stimulators (PNS) are important tools for managing chronic intractable pain. Neuromodulation in the form of SCS and PNS has demonstrated utility in managing chronic pain conditions which have not responded to other treatments.[1] Clinical goals of this therapy include the following: 1) pain relief, 2) improvement to quality of life, and 3) improvement to functional ability.

While there may be other appropriate uses for neuromodulation outside of pain management, the scope of this LCD is implanted SCS and PNS devices for chronic intractable pain in the Medicare population.

Definitions

Pain – As defined by the International Association for the Study of Pain (IASP), pain is "an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage."[2]

Neuropathic Pain – pain which originates from nerve damage or altered nerve function; can be described as a burning, tingling, shooting, or electric sensation[1]

Nociceptive Pain – pain which results from mechanical, chemical, or thermal irritants; can be described as an aching, dull, throbbing, or sharp sensation[1]

Chronic Pain – pain which lasts longer than the usual course of acute injury or illness (generally more than three to six months) and has an effect on wellbeing[1]

Chronic Intractable Pain - does not have a clear definition or diagnostic criteria; however, it is understood that it should meet the definition for *chronic pain* (extending beyond the usual course of acute illness or injury) as well as being *refractory* (having failed multiple evidence-based biomedical therapies used in a clinically appropriate fashion, in the absence of contributing psychiatric or psychosocial factors)[3 (p.1423)]

Spinal Cord Stimulation (SCS) – involves the placement of an electrode(s) in the epidural space of the bony spinal canal, adjacent to the area of pain.[1]

Peripheral Nerve Stimulation (PNS) – involves the placement of an electrode(s) in the direct vicinity of a specific peripheral nerve located outside the brain or spinal cord, thereby directly stimulating the painful peripheral nerve.[1]

Peripheral Nerve Field Stimulation (PNFS) – involves the placement of an electrode(s) in an area of pain outside the brain or spinal cord, thereby indirectly stimulating a painful peripheral nerve.[1]

Tonic – traditional, low-frequency stimulation, which provides continuous stimulation at frequencies between 20-120 Hz. In many cases, this results in patients having the perception of paresthesia (numbness, tingling) in the area where they previously felt pain.[4]

High-Frequency – also called 10 kHz stimulation, this is a newer technology which provides continuous stimulation at frequencies between 500-10,000 Hz. This type of stimulation allows patients to experience pain relief without paresthesia.[4]

Burst – provides high-frequency stimulation in a "burst" pattern, rather than continuously. This type of stimulation attempts to mimic the firing patterns of neurons in the spinal cord (which allow communication between spinal cord and brain).[4]

Covered Indications

A. Spinal Cord Stimulation:

Spinal cord stimulation is considered medically reasonable and necessary for the treatment of chronic intractable pain in patients who meet **ALL** of the following criteria:

1. Pain must have a neuropathic cause,[5] **AND**
2. Pain must be **chronic** and **intractable** resulting in functional deficit measured using a disability scale and/or pain scale*, **AND**
3. The use of a spinal cord stimulator is a late or last resort for pain management, after documented failure to respond to pharmacologic, non-invasive non-pharmacologic management (as tolerated), or targeted interventional pain procedures (e.g., epidural spinal injections), **AND**
4. The device chosen must be **approved by the FDA** for the diagnosis being treated, **AND**
5. Pain is caused by a diagnosis with **evidence of efficacy to support that spinal cord stimulation** is an effective treatment for pain relief. Based on current evidence-based literature, these diagnoses include:
    - Back pain related to failed back surgery syndrome (FBSS) in the absence of neurological progression requiring surgical intervention.[1,3,6]
    - Axial back pain refractory to conventional medical management, with or without radicular pain.[3,7]
    - Complex regional pain syndrome (CPRS) I & II.[3,6]
    - Upper extremity neuropathic pain syndromes, including radiculopathy.[6]
    - Ischemic peripheral neuropathic pain from peripheral artery disease, when the patient cannot undergo revascularization or when revascularization has failed to relieve painful symptoms and the pain has not responded to medical management.[6]
    - Painful diabetic neuropathy refractory to conventional medical management,[8,9,10,11] **AND**
6. Performance and documentation of a successful stimulation trial precedes permanent neurostimulator placement.[12] A successful trial is characterized by:
    - Greater than or equal to 50% reduction in patient pain from baseline, **AND/OR**
    - Substantial objective improvement in functional ability measures (e.g., walking tolerance, performance of ADLs, sleep, etc.) from baseline.[1]
7. All indications in NCD 160.7 Electrical Nerve Stimulators must be met.

*Pain assessment and/or disability assessment must be performed and documented at baseline, at follow-up visits, and after the trial stimulation period using the same validated scale for each assessment.

B. Peripheral Nerve Stimulation:

Peripheral nerve stimulation is considered medically reasonable and necessary for the treatment of chronic intractable pain in patients who meet **ALL** of the following criteria:

1. Pain must have a neuropathic cause,[5] **AND**
2. Pain must be **chronic** and **intractable** resulting in functional deficit measured using a disability scale and/or pain scale*, **AND**
3. The use of a peripheral nerve stimulator is a late or last resort for pain management, after documented failure to respond to pharmacologic, non-invasive non-pharmacologic management (as tolerated), or targeted interventional pain procedures (e.g., epidural spinal injections), **AND**

4. The device chosen has been **approved by the FDA** for the diagnosis being treated, **AND**
5. Pain is caused by a diagnosis with **evidence of efficacy to support peripheral nerve stimulation** is an effective treatment for pain relief. Based on current evidence-based literature, these use cases include:
    1. Occipital nerve, supraorbital nerve, or supratrochlear nerve stimulation for the management of treatment-resistant migraines.[13,14]
    2. Vagus nerve stimulation for the management of treatment-resistant migraines and cluster headaches.[13,14]
    3. Sphenopalatine ganglion stimulation for the treatment of cluster headaches.[13,15]
    4. Medial branch nerve stimulation for the treatment of chronic low back pain, including that related to failed back surgery syndrome (FBSS).[13,15]
    5. Upper and lower extremity nerve stimulation for the treatment of phantom limb (postamputation) syndrome.[15] **AND**
6. Performance and documentation of a successful stimulation trial precedes permanent neurostimulator placement.[12] A successful trial is characterized by:
    - Greater than or equal to 50% reduction in patient pain from baseline **AND/OR**
    - Substantial objective improvement in functional ability measures (e.g., walking tolerance, performance of ADLs, sleep, etc.) from baseline.[1]
7. All indications in NCD 160.7 Electrical Nerve Stimulators must be met.

*Pain assessment and/or disability assessment must be performed and documented at baseline, at follow-up visits, and after the trial stimulation period using the same validated scale for each assessment.

Limitations

Under the following circumstances, the implantation of electrical nerve stimulators (spinal cord or peripheral nerve), or services and supplies related to such implantation, are **considered not medically reasonable and necessary**:

1. Patients with a correctable pathology such as nerve entrapment;[16,17]
2. Patients who have a current substance abuse disorder;[16]
3. Patients with inadequately controlled psychiatric or psychological problems;[16]
4. Patients with significant surgical risks such as systemic infection or coagulopathy;[16,17]
5. Patients cognitively unable to give informed consent and participate in their care (control the device);[16]
6. Patients who are not willing and/or able to follow institutional protocol for follow-up assessments;[16]
7. Patients with a life expectancy less than 12 months;[16(p578)]
8. Patients who had a negative response to a trial, as evidenced by:
    1. Less than 50% reduction in patient pain from baseline, **OR**
    2. No objective improvement in functional deficits;[1]
9. The use of SCS or PNS for any conditions other than those listed in indications, including post-herpetic neuralgia;[15]
10. The implantation of more than one spinal cord stimulator or peripheral nerve stimulator device in the same patient at the same time.[18] SCS and PNS device implantation is limited to once per lifetime per patient, unless the device must be revised or replaced (e.g., due to device malfunction);
11. Peripheral nerve field stimulation (PNFS) for any indication.[15,19]

Note: For additional coverage information regarding electrical nerve stimulators or services and supplies related to such implantation, please refer to NCD 160.7 Electrical Nerve Stimulators.

Note: For additional information regarding patient selection and suitability for electrical nerve stimulation therapy, please refer to NCD 160.7.1 Assessing Patients Suitability for Electrical Nerve Stimulation Therapy.

Notice: Services performed for any given diagnosis must meet all of the indications and limitations stated in this policy, the general requirements for medical necessity as stated in CMS payment policy manuals, any and all existing CMS national coverage determinations, and all Medicare payment rules.

Provider Qualifications

Patient safety and quality of care mandate that healthcare professionals who perform nerve stimulator trials or permanent implantation are appropriately trained and credentialed by an accredited interventional pain medicine training program or an accredited surgical training program.[16(p574)] At a minimum, training should include patient selection criteria, contraindications to neuromodulation, identification and management of complications, and collaboration with other interdisciplinary professionals.[1(p531)]

Services will be considered medically reasonable and necessary when:

- All aspects of care are within the scope of practice of the provider's professional licensure, and
- Services are performed according to the supervision requirements per state scope of practice laws, and
- All procedures are performed by appropriately trained providers in the appropriate setting.

Summary of Evidence

Introduction

Please refer to the "History/Background and/or General Information" section for general information on nerve stimulators.

This evidence review focuses on nerve stimulators (both spinal cord and peripheral), and whether the evidence currently available is adequate to draw conclusions about improved health outcomes for the Medicare population. Ideal patient outcomes demonstrate equal to or greater than 50% pain reduction, substantially improved functional ability, and improved quality of life.

Internal Technology Assessment

A literature search was conducted via PubMed and Google Scholar using the following key words: nerve stimulators/stimulation; peripheral nerve stimulators/stimulation; dorsal column stimulators/stimulation; spinal cord stimulators/stimulation; pain management; chronic intractable pain; guidelines; society guidelines; clinical practice guidelines; best practice; standard of care; recommendations; regulations. The literature search was filtered to locate full-text articles published within 5-10 years, with preference given to randomized controlled trials (RCTs), prospective trials, and systematic reviews.

In a search for professional society guidelines for spinal cord stimulation or peripheral nerve stimulation, several guidelines are available from the Neuromodulation Appropriateness Consensus Committee (NACC) and/or the International Neuromodulation Society (INS). Additionally, one summary of best practices which references NACC parameters and one practice recommendation from the U.S. Food and Drug Administration (FDA) were located.

Spinal Cord Stimulation (Traditional and High-Frequency)

In a multi-national, multi-center prospective study, Scalone et al[20] assessed health-related quality of life (HRQoL) in patients with FBSS, the relationship between pain, disability, and HRQoL, and how these health outcomes change over a two-year period from a SCS intervention. FBSS can be defined as "chronic low back and/or leg pain persisting

or recurring after one or more lumbar surgeries" and is associated with reduced quality of life and function, in addition to loss of productivity and economic impact. This study uses real-world context in an attempt to establish instruments for use in clinical practice to guide optimal treatment decisions for patients with FBSS.

This study took place across nine specialty centers (six specialized in pain, and three specialized in neurosurgery) across Italy, each having at least five years of experience in using SCS to treat patients with FBSS. Between June 2005 and October 2007, 80 patients met inclusion criteria and agreed to participate. Inclusion criteria required patients to be at least 18 years of age, have FBSS pain radiating to lower limbs for at least six months, rate their pain as greater than 5 on a numeric rating scale (NRS) of 0-10, have failed conservative therapy, and consent to the procedure and study participation. Patients were excluded if they had another pain condition besides FBSS, were unable to manage the neurostimulator, were illiterate or did not speak Italian, or had other contraindications to spinal cord stimulation (such as coagulation problems, psychiatric disorder, or pregnancy).

During the study, each patient underwent a percutaneous lead implantation and were observed during a trial period of 15 days. Patients who responded positively to the trial (defined as at least 50% pain reduction and 80% overlap of paresthesia with painful area) were implanted with a non-rechargeable totally implantable pulse generator and were followed for up to two years. Data, including socio-demographic information, clinical characteristics, pain intensity, physical ability, and HRQoL, was collected using a Case Report Form and a patient diary. Data collection occurred during the pre-SCS period (12 months prior to enrollment), and at every follow-up visit for two years after implantation. Pain intensity was assessed using the NRS. Patients were asked to rate their average and maximum perceived pain using the NRS in the previous 12 months (at enrollment) or in the previous six months (during the follow-up window). Disability was assessed using the Oswestry Disability Questionnaire (ODI), a back pain-specific survey covering several dimensions of functional ability. Patients were asked to rate their severity of limitation for each dimension, according to their current status. HRQoL was assessed using two questionnaires (the Medical Outcome Study Short Form 36, and the EQ-5D) which assess physical and psychological health. A multilevel random intercept regression linear analysis was utilized to estimate the relationships between pain, functional ability, and HRQoL during the observation period.

On average, patients reported high levels of pain perception, low levels of ability function, and low HRQoL at baseline. The mean pain level assessed with the NRS was 7.6, and the maximum was 9.2 at baseline. 65% of patients reported extreme pain or discomfort on the ODI, and overall, the mean ODI score was 61.6. On the EQ-5D HRQol assessment, 41.3% of patients reported extreme problems performing usual activities. It was also identified that study subjects had an impaired HRQoL compared to the general population of the same age, sex, and education level. Using the multilevel regression model, authors identified that patients with higher NRS or ODI scores also had worse HRQoL (the authors determined statistical significance for every parameter).

While other studies and literature reviews have concluded that SCS is a safe and effective treatment for intractable pain conditions, Scalone et al identified that six months after SCS implantation, "an improvement of health was found in every domain of every instrument used."[20(p7)] During the follow-up period, pain and disability scores decreased, while HRQoL increased significantly during the first six months post-implantation, remaining stable after the first six months. This real-world study suggests that pre- and post-implantation assessment of not only pain, but disability and health-related quality of life as well, are relevant for patients being treated with spinal cord stimulation for failed back surgery syndrome.

In their pivotal multicenter, randomized controlled trial (the SENZA-RCT), Kapural et al[7] examined the efficacy and safety of 10-kHz SCS compared to traditional low-frequency SCS systems for the management of back pain. While SCS has been indicated for the management of chronic back pain, the authors identified that traditional low-frequency SCS devices are not always effective for this indication due to challenges associated with obtaining adequate and stable paresthesia coverage in this region. That said, 10-kHz SCS does not produce paresthesia, which eliminates these challenges. The primary endpoint for the study was to identify the percentage of patients who experienced greater than or equal to 50% pain reduction using SCS, without experiencing a neurological deficit. Secondary endpoints included percentage changes from baseline back or leg pain, ODI scores and opioid utilization.

Patients were assessed for eligibility at 10 comprehensive pain centers. Patients were included in the study if they had chronic, intractable pain of the trunk or limbs which was refractory to other treatments and had been present for at least three months, and met the identified criteria for back pain, leg pain, and perceived disability. Patients were excluded if they had active psychiatric disorders, spine instability, prior experience with SCS, or were unable to comply with the study requirements. One hundred ninety-eight patients meeting these inclusion criteria were randomized 1:1 to receive a traditional or high-frequency SCS system. Of those, 171 had successful 14-day trials and proceeded to permanent implant. Study participants had an average of 13.6 years since diagnosis and had a mean age of 54.9. Of the study participants, 86.6% had previous back surgery, and 77.1% were diagnosed with failed back surgery syndrome.

Responders for the study were defined as achieving 50% or greater pain reduction with no neurological deficit. At three months, 84.5% of patients with back pain who received high-frequency SCS devices were treatment responders, compared with 43.8% of patients with traditional SCS devices. For patients with leg pain, 83.1% of patients with high-frequency SCS devices were treatment responders, compared with 55.5% of those with traditional SCS devices. These results were sustained through 12 months; 80% of patients with either back or leg pain who received high-frequency SCS devices were treatment responders at month 12, compared with 50-55% of patients with traditional SCS devices.

The authors reported that level of disability (measured using ODI) improved for both treatment groups; at month 12, of patients in the high-frequency SCS group 62.9% reported minimal or moderate disability, compared with 45.7% of patients in the traditional SCS group. Kapural et al also identified that 35.5% of patients who received high-frequency SCS devices were able to decrease or eliminate opioid medication use after 12 months of therapy, compared with 26.4% of patients who received traditional SCS devices. Furthermore, at 12 months, 62.9% of patients who received high-frequency SCS devices reported minimal or moderate disability, compared with 45.7% of patients who received traditional SCS devices. Both treatment groups reported high satisfaction with their SCS treatment.

The most significant limitation of the SENZA-RCT was the lack of blinding; since traditional SCS produces paresthesia and high-frequency SCS does not, it was impossible to blind patients to their treatment methodology. Furthermore, since investigators had to program the devices, they could not be masked. The study was also industry-funded. Despite these limitations, the authors concluded that high-frequency SCS was superior to traditional SCS over 12 months, for patients with either back or leg pain.

DiBenedetto et al[21] describes a retrospective single-center study which attempts to evaluate both the clinical outcomes and healthcare utilization of patients who received conventional medical management (CMM) in addition to SCS for low back and leg pain at 12-months post-implantation, as compared to a matched sample of patients who received CMM only. This study was performed using data from a single community-based interdisciplinary pain center.

During the identified time-period (December 1, 2014, through December 31, 2017), thirty-two patients had a 10-kHz SCS device placed. Patients included in SCS + CMM group were also required to have been active patients at the clinic for at least one year before and one year after the implantation, and could not have had the device removed during the study. A 2:1 matched sample of patients receiving CMM was also identified; these patients were required to have been active patients at the clinic for at least two years during the same timeframe, and not have a SCS placed. A propensity-score matching approach was utilized, with criteria including age, gender, pain severity at baseline, visit and procedure volume over the prior 12 months, and opioid dose at baseline. The authors felt it was important to use visit volume in the matching criteria because "patients who are in the clinic monthly vs once per year receive a different level of engagement in education and exposure to the clinic's philosophy to prioritize functional outcomes," in addition to the clinical differences associated with frequently seen patients vs infrequently seen patients.

Patients in both study groups were seen and treated for low back pain, with or without lower extremity pain. The authors analyzed both groups' clinical outcomes (identified by self-reported pain severity and progress towards functional goals), and healthcare utilization (identified by opioid dose and visit volume). Pain severity was assessed on two scales: the Functional Pain Scale (FPS) and the NRS. Neither group had a statistically significant change in pain using the FPS. Patients in the SCS + CMM group had a significant reduction in low back pain (42.6%) and lower extremity pain (50.9%), measured by the NRS.

To determine patient functional ability, patients were assessed using several measures, including the pain catastrophizing scale, the World Health Organization Disability Assessment Schedule 2.0 (WHO-DAS 2.0), the Roland-Morris Disability Questionnaire (RMDQ), and the patient health questionnaire (PHQ-9), which is a widely accepted measure of depression severity. There was no significant difference between the two groups' RMDQ scores. Not all patients completed the other functional assessments, therefore there was no statistical significance.

Both groups had daily opioid dose (in morphine milligram equivalent [MME]) assessed three times during the study. For individuals who were prescribed opioid medications, a significant reduction was identified in the SCS + CMM group (mean of 92.2 MME at baseline and 66.0 MME at 12 months post-implant). 71.4% of patients in the SCS + CMM group had dose decreases during the study. Comparatively, only 47.4% of patients in the CMM group had a dose decrease, and 31.6% of patients had a dose increase during the study.

Both the SCS + CMM group and the CMM group had a decrease in office visit volume during the study, but only the CMM group's change was statistically significant (and the authors noted this could have been due to the 2:1 sample). There was no statistically significant difference between the two groups' visit volume, however, there was a significant difference in interventional procedure volume. Interventional procedures for this study included injections (epidural steroid, facet joint, major joint), and radiofrequency ablations. The SCS + CMM group underwent less than half as many interventional procedures during the study period as the CMM group.

Limitations of this study include its retrospective cohort design, subjective patient-reported measures as outcomes, and small sample size. The study was also industry-funded. That said, the retrospective nature of the study also allows it to reflect real-world data and treatment decisions without interference from research objectives. The authors concluded that 10-kHz SCS is associated with positive clinical outcomes and decreased healthcare utilization for the population of patients with low back and lower extremity pain and self-reported disability.

Deer et al[3] conducted a systematic literature review on SCS for pain, on the basis that neurostimulation is a treatment option for chronic refractory pain and while there have been consensus and best practice statements issued, no comprehensive systematic review of the evidence has been published. The intention of this review was to analyze the quality of the available evidence and foundational knowledge about SCS for the treatment of chronic intractable pain.

A comprehensive literature search was conducted, limiting included studies to RCTs which enrolled patients who reported chronic and intractable pain for at least one year, and had a minimum patient follow-up of at least six months. The authors used the following definition for intractable pain: "1) multiple evidence based biomedical therapies used in clinically appropriate and acceptable fashion have failed to reach treatment goals that may include adequate pain reduction and/or improvement in daily functioning or have resulted in intolerable adverse effects, and when 2) psychiatric disorders and psychosocial factors that could influence pain outcomes have been assessed and appropriately addressed."[3(p1423)] Six RCTs that met inclusion criteria were identified.

The authors used several tools for assessing study quality. First, the Cochrane Collaboration's Risk of Bias tool was utilized to assess risk of bias. Next, the Interventional Pain Management Techniques—Quality Appraisal of Reliability and Risk of Bias Assessment (IPM-QRB), developed by the American Society of Interventional Pain Physicians (ASIPP), to assess RCTs, was utilized to evaluate each study. Finally, the US Preventative Services Task Force (USPSTF) hierarchy of studies was utilized to determine a final "grade" for the evidence. Reviewers independently reviewed the literature and assigned grades to the evidence; if a discrepancy resulted in differing quality scores, two

additional reviewers assessed the evidence. In addition to study quality, the authors also utilized a qualitative approach to grade and describe the evidence. For instance, for a study to receive a Level 1 (Strong) rating, the requirements are as follows: "evidence obtained from multiple relevant high-quality randomized controlled trials for effectiveness, or evidence obtained from multiple relevant high-quality observational studies or large case series for assessment of preventative measures, adverse consequences, and effectiveness of other measures."[3(p1425)]

Based on these criteria, the authors provided an analysis of the evidence on axial back and radicular pain and CPRS. Axial back and radicular pain was found to have Level 1 evidence, based on five RCTs focused on treating low back pain (with and without radicular pain) with SCS. The studies were identified to have high-quality design and low to moderate risk of bias. Other key points identified in the review of the literature suggested that for patients with FBSS, SCS may offer more effective pain relief than reoperation or conventional medical management alone. CPRS was also found to have high-quality evidence, however, this was based upon a single randomized trial which focused on treating CPRS with SCS in addition to physical therapy versus physical therapy alone. The evidence for CPRS could not be classified as Level 1 because the Level 1 criteria require at least two trials. The study was found to have low to moderate risk of bias. The authors concluded that while additional research may be needed, pain management using SCS for chronic spine and lower extremity pain and CPRS are both supported by high-quality evidence.

In a multicenter, randomized controlled trial, Slangen et al[8] randomized 36 patients with painful diabetic peripheral neuropathy (PDPN) to receive either best medical treatment (BMT) alone, or BMT in combination with spinal cord stimulation. The intent of this study was to determine if SCS may be an effective modality of pain management for PDPN, which is a common complication of diabetes, but generally not successfully managed by pharmacological therapies.

Patients were screened at two diabetic outpatient clinics and were included in the study if they met the following criteria: age between 18 and 80, diagnosis of moderate to severe PDPN in the lower limbs, insufficient pain relief or unacceptable side effects with pharmacological therapy, pain present for greater than 12 months, and mean pain intensity at least 5 or higher on a numeric rating scale (0-10). Patients were randomized 3:2 (22 patients to the SCS group and 14 patients to the BMT group). Outcome measurements included pain severity and intensity compared to baseline, interference with daily life, health related quality of life, sleep, mood, and medication use. These outcomes were assessed at baseline, three months, and six months.

All patients in the SCS group underwent a two-week trial stimulation, and only those with a successful trial (defined as at least 50% improvement in pain intensity, or a score of 6 or higher on the patient global impression of change scale [indicating pain and sleep were "much improved" or "very much improved"]) were implanted with a SCS. Trial stimulation was successful in 17 patients (77%). At six months, Slangen et al identified that 13 patients (59%) in the SCS group experienced treatment success, compared to one patient (7%) in the BMT group. Mean daytime pain score for the SCS group was reduced by 3.1 points, and nine patients reported greater than or equal to 50% daytime pain relief; comparatively, the BMT group reported no change in pain score or percentage pain relief. Additionally, the authors noted that nine patients in the SCS group were able to reduce or eliminate pharmacological treatments for pain; however, in both the SCS and BMT groups, the majority of patients (12 and 9, respectively) reported no change in medication use.

It should be noted that two patients had serious events (subdural hematoma in one patient, infection of the SCS system in the other). Limitations of the study included the small sample size, lack of blinding, and inability to generalize the outcomes for patients with less pain; as identified by Henson et al[22], this creates an elevated risk of bias. Additionally, the study was industry sponsored. That said, the findings presented demonstrate SCS in combination with BMT as a viable pain management solution for patients with PDPN.

In a multicenter, randomized trial, de Vos et al[9] randomized 60 patients with PDPN to receive either conventional medical therapy alone (control), or in combination with spinal cord stimulation. The intent of this study was to determine the effect of SCS on PDPN. Patients were screened at seven pain clinics and were included in the study if

they met the following criteria: at least 18 years of age, presence of diabetic neuropathic pain, pain present for at least one year, pain determined to be refractory as evidenced by failure of conservative treatments, and average pain score of at least 50 on a visual analogue scale (0-100). Patients were randomized 2:1 (40 patients to the SCS group and 20 patients to the control group). Outcome measurements included pain severity and intensity compared to baseline, interference with daily life, health related quality of life, and medication use. These outcomes were assessed at baseline, three months, and six months after enrollment or initiation of SCS treatment.

All patients in the SCS group underwent a seven-day trial stimulation, and only those with a successful trial (defined as at least 50% improvement in pain intensity) were implanted with a SCS. The short trial period was chosen due to patients with diabetes' susceptibility to infections. Trial stimulation was unsuccessful in three patients, and one additional patient withdrew from the study prior to the six-month mark. In the control group, five patients withdrew from the study. Thirty-six patients in the SCS group and 18 patients in the control group were followed for the complete six-month study window.

At six months, de Vos et al identified that 26 patients (65%) in the SCS group experienced much or very much pain reduction (more than 50%) compared to baseline, compared to three patients (15%) in the control group. Additionally, 35 patients (95%) in the SCS group reported they might or would recommend this treatment modality to other patients with PDPN, while only four patients (20%) of the control group reported the same.

Adverse events related to SCS implantation were as follows: pain due to the implanted pulse generator (two patients), electrode lead migration (one patient), infection (one patient), and coagulopathy (one patient). No serious adverse events were noted. Limitations of the study included the open label design, lack of blinding, and potential bias created by offering patients in the control group a crossover to SCS after six months; as identified by Henson et al[22] this study has an elevated risk of bias. That said, the findings presented demonstrate SCS in combination with conventional medical therapy has the potential to both reduce pain and improve quality of life in patients with PDPN.

The Comparison of 10-kHz SCS Combined with CMM to CMM Alone in the Treatment of Neuropathic Limb Pain (SENZA-PDN) randomized control trial described by Petersen et al[10] aimed to discover whether 10-kHz SCS improved outcomes for patients with PDPN. PDPN usually presents distally and symmetrically and effects activities of daily living, work, sleep, and mental wellbeing due to neuropathic pain in the hands and feet. There are also higher healthcare costs and utilization seen with PDPN; therefore, there is an increasing interest in finding non-medicative options for treatment. One such proposed treatment is high-frequency SCS at 10-kHz. High-frequency SCS at 10-kHz uses a 10,000 Hz waveform to provide pain relief without causing paresthesia. This treatment technique has shown potential for usage in PDPN treatment. This study attempts to extend observations from low-frequency SCS studies and solidify 10-kHz SCS as a treatment option for this patient population.

Patients with PDPN for one year or more refractory to gabapentinoids and at least one other analgesic class, lower limb pain intensity of 5 cm or more on a 10-cm visual analogue scale (VAS), body mass index (calculated as weight in kilograms divided by height in meters squared) of 45 or less, hemoglobin A1c (HbA1c) of 10% or less, daily morphine equivalents of 120 mg or less, and medically appropriate for the procedure were recruited from clinic patient populations and digital advertising. Patients were enrolled from multiple sites across the U.S., including academic centers and community pain clinics, between August 2017 and August 2019 with six-month follow-up and optional crossover at six months.

Screening of 430 patients resulted in 214 who were excluded or declined participation and 216 who were randomized. At six-month follow-up, 187 patients were evaluated. The prespecified primary end point was percentage of participants with 50% pain relief or more on VAS without worsening of baseline neurological deficits at three months. Secondary end points were tested hierarchically, as prespecified in the analysis plan. Measures included pain VAS, neurological examination, health-related quality of life (EuroQol Five-Dimension questionnaire), and HbA1c over six months.

Randomized patients had a mean age of 60.8 years, median duration of diabetes of 10.9 years, and median duration

of peripheral neuropathy of 5.6 years. Seventy-five patients (79%) in the SCS plus CMM group achieved at least 50% pain reduction from baseline, as compared to five patients (5%) in the CMM group. There were two incidences of infection requiring device explant in the SCS plus CMM group. For the 10-kHz SCS plus CMM group, the mean pain VAS score was 7.6 cm at baseline and 1.7 cm at six months, compared to the CMM group mean pain VAS score of 7.0 cm at baseline and 6.9 cm at six months. Investigators observed neurological examination improvements for 52 of 84 in the 10-kHz SCS plus CMM group (62%) and 3 of 92 patients in the CMM group (3%) at six months. Petersen et al concluded that the substantial pain relief and improved health-related quality of life sustained over six months demonstrates 10-kHz SCS can safely and effectively treat patients with refractory PDPN.

In a 12-month follow-up study, Petersen et al[11] identified that 10-kHz SCS maintained effectiveness for patients with PDPN. Treatment responders were defined as those with at least 50% pain relief from baseline. At both 6 and 12 months, 86% of patients who had SCS devices implanted (72 of 84) were treatment responders. This study used pain VAS scores to measure results from baseline, month six, and month 12. The mean lower limb pain VAS was 7.6 cm for 10-kHz SCS + CMM patients at baseline, 1.7cm at six months, and maintained at 1.7cm at 12 months. This represents a 77.1% mean pain relief. Lower limb pain VAS for the crossover group (who did not have >50% pain relief with CMM alone and elected to receive a 10-kHz SCS implant after the six-month mark) was 7.2cm at baseline, with no change at six months but improvement after crossover. Those originally assigned to 10-kHz SCS had a mean 70.3% pain relief at 12 months. After 12 months, Petersen et al determined that high-frequency SCS is associated with substantial and durable pain relief for patients with refractory PDPN.

It should be noted that there were also eight procedure related infections during this study, five of which required explant of the device. That said, there were no explants during the study due to loss of efficacy. Additional limitations of both Petersen et al studies included lack of blinding and potential bias, as well as potential placebo effects.

Eckmann et al[18] describe a single case in which a patient was implanted with two separate spinal cord stimulators (one to treat upper extremity pain and one to treat lower extremity pain, with four leads total) for the treatment of whole-body pain associated with small fiber neuropathy. The authors described the patient as a 20-year-old male with neuropathic pain in the legs, hands, arms, trunk, and face for approximately one year. Previous treatments were limited to several classes of medication. After extensive testing for potential etiology by neurology, the patient was referred to a pain clinic, where other treatment options were discussed, but not attempted. Additional pharmacologic treatments were attempted without success. Approximately three years after his initial visit to neurology, the patient agreed to a SCS trial with both cervical and thoracic leads. The authors did not discuss what defined a successful trial, but stated the patient had a "great response."[18(p2)]

At six months post-implant, the patient reported complete resolution of his pain, and was using the stimulation intermittently for pain flares. The authors discuss that SCS has limited indications, and very little literature exists supporting SCS for small fiber neuropathy, however, their case demonstrated its effectiveness for this purpose. Furthermore, the authors identified that the patient studied was only using his SCS intermittently to circumvent pain flares, which is not a typical application. The case study did not include reference to any other studies where patients were implanted with more than one SCS pulse generator, and while the authors stated they were hopeful to illustrate a unique use of multiple spinal cord stimulators, their findings cannot be generalized to other patient populations or other patients with the same diagnosis.

In September 2020, the FDA published a letter to healthcare providers reminding them that conducting a trial stimulation to confirm satisfactory pain relief prior to implanting a spinal cord stimulator is best practice to prevent complications[12]. This letter was published subsequent to the FDA receiving a high number of medical device reports (MDRs) between July 27, 2016, and July 27, 2020, associated with SCS devices for pain management. MDRs could be related to patient problems (serious side effects) or device problems (device failures). During that timeframe, a total of 107,728 MDRs were received by the FDA, including "497 associated with a patient death, 77,937 with patient injury, and 29,294 with device malfunction."[12] The most common patient problem, accounting for approximately 28% of patient-related MDRs, was inadequate pain relief. Because of this unfortunate statistic, the FDA states that "permanent SCS should only be implanted in patients who have undergone and passed a stimulation trial," and

defines a successful trial as a 50% reduction in pain symptoms. This is consistent with other published clinical guidelines and best practice recommendations.

The NACC has published several systematic reviews attempting to evaluate the safety and efficacy of neuromodulation for the treatment of chronic pain,[1,16] in addition to identifying potential complications of neuromodulation.[23,24] "The NACC was formed to evaluate current literature and best practice, to collect expert opinions, and to give guidance to physicians, other health-care providers, and payors on the appropriateness of PNS and SCS for chronic disease and pain."[1(p517)] NACC guidelines are established utilizing a combination of literature review, expert opinion, clinical experience, and individual research by members of the committee, as appropriate. Additionally, guidelines related to the appropriate use of neurostimulation were developed in collaboration with the International Neuromodulation Society (INS), which "determined that there is a need for guidance regarding safety and risk reduction for implantable neurostimulation devices."[16(p572)]

NACC strength of recommendation is intended to rank published works in categories, from the highest level of evidence (RCTs) to the lowest level of evidence (expert committee consensus and opinions). In order to achieve the NACC's highest recommendation (Level IA, strongly recommended), the level of evidence for a SCS indication must be supported by well-designed experimental, clinical, or epidemiological studies. In order to achieve Level IB (recommendable), the level of evidence for a SCS indication must be supported by some studies (experimental, clinical, or epidemiological), as well as having a strong theoretical rationale. The NACC is clear that while RCTs are considered to be the highest level of evidence, it is still important to individualize patient care and use the good clinical judgement of a multidisciplinary team of professionals.[1(p519)]

As other reviews have mentioned, appropriate patient selection is a cornerstone for SCS success. In their summary of NACC recommendations, Sitzman and Provenzano[6] also highlight the importance of a successful multiday trial prior to permanent SCS implantation, using the NACC definition of a successful trial (>50% pain relief and subjective functional improvement). In addition to the successful trial stimulation requirement, NACC recommendations for patient selection include failure of conservative or less invasive treatments for at least three to six months, predominantly neuropathic pain, lack of untreated psychiatric conditions or drug use, life expectancy greater than twelve months, and the ability to cognitively participate in care.[16(p575-578)] The NACC also cautions that PNS "should be reserved for patients in whom the pain distribution is primarily in and in close proximity to a named nerve known to innervate the area of pain."[1(p527)] Likewise, Level IA and IB NACC recommendations for disease-specific indications include FBSS, significant axial low back pain, CPRS type I and II, upper extremity neuropathic pain syndrome, and ischemic peripheral neuropathic pain secondary to peripheral artery disease. Other indications are noted as having lower levels of evidence, or more appropriate to be handled on a case-by-case basis.

Because there is a risk for both patient- and device-related complications secondary to neurostimulator implantation, NACC-recommended standards include assessment for psychiatric comorbidities, preoperative MRI to assess for alternate pathologies causing the pain, health management to promote wound healing and reduce infection risk, assessment for systemic infection or abnormal blood clotting, and preoperative screening for carriers of *Staphylococcus aureus.*[24]

The NACC also provides recommendations for implanters of neuromodulation devices, emphasizing that implanters should be "properly trained and credentialed by either an accredited interventional pain medicine training program or an accredited surgical training program,"[16(p574)] and that such training should include patient selection, contraindications, anatomy, identification and management of complications (both patient- and device-related), and device troubleshooting, in addition to interdisciplinary collaboration.[16(p581)] The NACC cautions that while trial extracranial neurostimulation systems may be implanted in the office setting, providers "must obtain privileges to perform implantation in an accredited hospital setting, properly certified surgical center, or similar facility," [16(p581)] and suggests that any provider who cannot obtain these privileges should not perform implantations. Additionally, the NACC recommends against permanent implantation of any neurostimulation devices in the office setting. As concluded by Sitzman and Provenzano[6], following the NACC guidelines for patient selection, SCS indications, training recommendations, and perioperative standards are necessary to achieve optimal patient safety and patient

outcomes.

Peripheral Nerve Stimulation and Peripheral Nerve Field Stimulation

In a randomized controlled trial of patients implanted with a high-frequency SCS (58 patients) or PNS (11 patients), Finch et al[25] conducted a clinical audit and examined the effect of 10-kHz stimulation on pain using two study protocols (stimulator either on or off for two hours or four hours). Patients and investigators were both blinded to the stimulation settings in both protocols, to limit placebo effects.

All patients included in the study had a successful stimulation trial prior to SCS or PNS electrode placement between January 8, 2013, and February 14, 2014. Electrode placements included the dorsal epidural space, along a branch of the occipital or trigeminal nerve, along a limb nerve, near the S1 nerve root, near the genito-femoral nerve, and near the ileo-inguinal nerve. Diagnoses treated included a variety of neuropathic pain conditions. For 12 months after the SCS or PNS electrode placement, the patients' medical charts were assessed for changes in medication intake, physical impairment, satisfaction with the intervention, and pain relief. Not all patients had pain scores available for the full follow-up period. Decreases in pain were noted in both SCS and PNS groups after 12 months, however the authors noted greater change in pain in the PNS group. Likewise, patients in the PNS group also had more significant decrease in medication use, greater gains in physical ability, and higher satisfaction than patients in the SCS group. This suggests that high-frequency stimulation may be more effective for PNS indications than for SCS indications.

Patients were then randomized into one of two study protocols. Protocol 1 participants arrived at the study with their stimulator switched on; the stimulator was adjusted after two hours, with neither the patient nor the investigator knowing if it was on or off. Protocol 2 participants were instructed to switch their stimulator device off the evening before the trial, so it was off for approximately 12 hours. The stimulator was adjusted, with neither the patient nor the investigator knowing if it was on or off and left in that setting for four hours. In both protocols, patients had quantitative sensory testing (QST, including pressure pain threshold, sharp stimulus sensitivity, light touch, tactile sensitivity, cold, and heat) performed before, during, and after the trial. The second arm of the Protocol 2 trial was completed between 7 and 84 days later (stimulator off if previously on, and on if previously off).

In Protocol 1, pain intensity did not change when the stimulator was turned off, and there was not a significant difference in patient QST scores. The authors identified this could have been related to inadequate time with the device turned off (not enough time for pain to fully return). Likewise, in Protocol 2, pain intensity higher at baseline than in Protocol 1, and there was a reduction in pain ratings with the device turned on. There was not a significant difference in patient QST scores in this protocol either. The authors concluded that PNS at 10-kHz leads to reduced pain intensity when conducted for at least four hours.

Deer et al[13] conducted a systematic literature review on PNS and peripheral nerve field stimulation (PNFS) for pain, on the basis that neurostimulation is a treatment option for chronic refractory pain and while there have been consensus and best practice statements published, no comprehensive systematic review of the evidence has been published. The intention of this review was to analyze the quality of the available evidence and foundational knowledge about PNS for the treatment of chronic intractable pain.

A comprehensive literature search was conducted, limiting included studies to RCTs which enrolled patients with intractable pain and had a minimum patient follow-up of at least two months. The authors used the following definition for intractable pain: "1) multiple evidence based biomedical therapies used in clinically appropriate and acceptable fashion have failed to reach treatment goals that may include adequate pain reduction and/or improvement in daily functioning or have resulted in intolerable adverse effects, and when 2) psychiatric disorders and psychosocial factors that could influence pain outcomes have been assessed and appropriately addressed."[13(p1591)] Fourteen RCTs that met inclusion criteria were identified.

The authors used several tools for assessing study quality. First, the Cochrane Collaboration's Risk of Bias tool was utilized to assess risk of bias. Next, the IPM-QRB developed by the ASIPP to assess RCTs, was utilized to evaluate

each study. Finally, the USPSTF hierarchy of studies was utilized to determine a final "grade" for the evidence. Reviewers independently reviewed the literature and assigned grades to the evidence; if a discrepancy resulted in differing quality scores, two additional reviewers assessed the evidence.

In addition to study quality, the authors also utilized a qualitative approach to grade and describe the evidence. For instance, for a study to receive a Level 1 (Strong) rating, the requirements are as follows: "evidence obtained from multiple relevant high-quality randomized controlled trials for effectiveness, or evidence obtained from multiple relevant high-quality observational studies or large case series for assessment of preventative measures, adverse consequences, and effectiveness of other measures."[13(p1593)]

Based on these criteria, the authors provided an analysis of the evidence on several chronic pain conditions, with level of evidence being based upon specific indications. Level 1 evidence (four high-quality RCTs and one moderate-quality RCT) was available to support occipital nerve stimulation for the treatment of migraines. Level 1 evidence (three high-quality RCTs) was available to support PNS for the treatment of chronic low back pain. Level 2 evidence (one RCT each) was available to support sphenopalatine ganglion stimulation for cluster headaches, PNS for poststroke shoulder pain, and PNS for neuropathic pain of the extremities and trunk. Level 3 evidence (two low-quality RCTs and one moderate-quality RCT) was available to support peripheral tibial nerve stimulation for chronic pelvic pain.

The authors noted that while there are other diagnoses which may benefit from PNS, there is currently insufficient literature to support these indications. Furthermore, while the authors mentioned three studies investigating PNFS for chronic low back pain, two studies had significant weaknesses limiting their generalizability, and one was terminated early due to slow recruitment.

Zhou et al[14] conducted a systematic review of the literature in order to assess the clinical evidence for PNS in treating chronic and intractable headaches. Headaches are one of the most common medical complaints worldwide, causing a significant burden on the healthcare system. As the authors identified, PNS and PNFS have recently emerged as a potential treatment option for individuals with chronic and intractable headaches. While there are few specific guidelines regarding the use of PNS, it is generally indicated for "chronic neuropathic pain disorders originating from specific peripheral nerves," which "should logically follow that of a specific nerve distribution."[14(p2)] Via a comprehensive search of the literature, the authors identified RCTs and observational studies on occipital nerve stimulation (ONS), supraorbital nerve stimulation (SNS), infraorbital nerve stimulation (INS), transcutaneous SNS (tSNS), supratrochlear nerve stimulation (STN), vagus nerve stimulation (VNS), and noninvasive VNS (nVNS). The intent of this review was to summarize and synthesize the evidence on the subject. In order to be high-quality, an indication was required to be supported primarily by RCTs, and in order to be moderate quality, an indication could be supported by a mix of observational studies and RCTs.

ONS yielded the highest number of studies (24 observational studies, and 7 RCTs). The largest RCT reviewed examined 157 patients at 12-week and 52-week follow-ups, concluding that patients who received ONS reported less headache days and migraine-related disability. Despite that, patients did not have greater than 50% reduction in pain scores. Other studies had similar findings; in a single-center RCT, Mekhail et al[26] found patients who received ONS reported 8.51 fewer headache days per month than control groups. Zhou et al concluded for ONS, there was high-quality evidence supporting chronic migraines as an indication. Likewise, the authors also concluded there was high quality evidence supportive of tSNS for episodic and acute migraines, as well as nVNS for cluster headaches. Moderate quality evidence was identified for tSNS for chronic migraines, STN for chronic migraines, and nVNS for both chronic migraines and episodic migraines. All other indications were identified as having low quality evidence. Zhou et al concluded that PNS offers promising treatments for intractable headaches, but additional research is needed in order to use PNS for indications beyond those identified above.

Xu et al[15] conducted a systematic review of the literature in order to assess the clinical evidence for PNS in treating acute and chronic pain. The intention of this review was to synthesize evidence from RCTs and observational studies, in order to determine what indications have high-level supporting evidence.

A comprehensive search of the literature was performed, using several databases, with preference given to prospective RCTs and meta-analysis. Two hundred twenty-seven studies met inclusion criteria and were analyzed. The authors synthesized studies focused on PNS for headaches, limb pain (including CPRS and postamputation pain), torso pain (including postherpetic neuralgia), and lower back pain, in addition to PNFS.

Study quality was assessed using several tools, including the Cochrane Collaboration's Risk of Bias tool, the American Society of Interventional Pain Physicians' IPM-QRB, and the USPSTF hierarchy of studies. Reviewers independently reviewed the literature and assigned grades to the evidence; if a discrepancy resulted in differing quality scores, a third reviewer assessed the evidence in order to establish a consensus. In addition to study quality, the authors also utilized a qualitative approach to grade and describe the evidence, using levels 1 through 5. For instance, for a study to receive a Level 1 (Strong) rating, the requirements are as follows: "evidence obtained from multiple relevant high-quality randomized controlled trials."[15(p26)]

For headaches, Xu et al reviewed studies on both migraines and cluster headaches. Several studies on migraines (Mekhail et al[26], Saper et al[27], Serra and Marchioretto[28]) trialed occipital nerve stimulation for chronic pain associated with migraines and determined that PNS of the occipital nerves reduced both pain and disability. Only one RCT[29] studied sphenopalatine ganglion (SPG) stimulation for chronic cluster headaches and determined it to be a safe and effective modality. The authors summarized that there is Level 1 evidence supporting PNS for migraines, and Level 2 evidence supporting PNS for cluster headaches, indicating PNS should be a treatment option when these conditions are nonresponsive to more conservative measures.

For limb pain, Xu et al reviewed studies on peripheral neuropathic pain, CPRS, postamputation pain, and shoulder pain. Most RCTs focused on peripheral neuropathic pain included etiologies secondary to traumatic injury. The authors summarized that there is Level 2 evidence (only one high-quality study) supporting PNS for peripheral neuropathic pain secondary to trauma or surgery (all other evidence is case reports), indicating PNS could be considered for peripheral neuropathic pain when it is nonresponsive to more conservative measures. Studies focused on CPRS were limited to case series or reports; however, both studies reviewed (Hassenbusch et al[30] and Cooney[31]) identified that PNS is likely to be more effective in cases where patient symptoms are isolated to one major peripheral nerve. Xu et al concluded that there is Level 4 evidence for PNS as it pertains to CPRS treatment. For postamputation pain, studies reviewed included both traditional PNS modalities and high-frequency stimulation modalities. The authors identified that while there are a few high-quality studies supporting PNS for postamputation pain, they all had small sample sizes, therefore the evidence could not be rated higher than Level 2. However, the authors indicated that due to the difficulty with treating postamputation pain, PNS should be considered. For shoulder pain, the authors reviewed one small RCT and one case study, mostly focused on hemiplegic shoulder pain secondary to stroke. Both studies demonstrated improvement to pain and quality of life after PNS implantation; therefore, the evidence was scored as Level 2. Xu et al identified that further research is needed on the subject of PNS for limb pain, as the literature on many of these indications was limited by study design or sample size.

For torso pain, Xu et al reviewed studies on thoracic postherpetic neuralgia, and inguinal/genital/pelvic pain. In both cases, there was a scarcity of published evidence and limited high-quality studies supportive of PNS for these indications, so the authors were unable to provide a rating of the evidence.

Finally, the authors reviewed several studies focused on PNS for the management of chronic lower back pain, including that related to FBSS. The studies analyzed (Eldabe et al[19], Cohen et al[32]) demonstrated clinically significant pain reduction as compared to conservative medical management. While the evidence reviewed for this indication was scored as Level 2 and Level 3, the authors noted that further high-quality research is necessary to support this indication.

Xu et al also reviewed several studies on PNFS, for indications including craniofacial pain, back pain, and other neuropathic pain conditions. The evidence for PNFS in craniofacial pain was limited to Level 3; a high revision rate was also noted for this use, indicating there are associated hardware and/or technical issues. Likewise, the evidence

for PNFS in back pain was not provided an evidence level, as it included conflicting results, small sample sizes, and significant limitations. The largest of these studies was Eldabe et al[19], with a sample size of 116 patients from 21 different medical centers. The results from this indicate PNFS in addition to medical management is more effective than medical management alone; however, this study was terminated early due to recruitment difficulty. Xu et al identified that other neuropathic pain conditions were studied in a small prospective case series, but the evidence for these conditions was not rated; therefore, further studies are necessary to elucidate the evidence for PNFS.

In a prospective multicenter RCT, Eldabe et al[19] randomized patients with FBSS 1:1 to either receive optimized medical management (OMM) alone, or in combination with peripheral nerve field stimulation, which they refer to as subcutaneous nerve stimulation (SQS). The primary outcome of this study was to determine the percentage of patients in the study who had greater than or equal to 50% reduction in pain from baseline at nine months, as measured by VAS. The authors also wanted to assess the mean change in back pain intensity from baseline to either six or nine months in both cohorts.

Patients were screened at 25 sites across Europe, Israel, and Australia, and were eligible to be included in the study if they were diagnosed with FBSS which was intractable and persistent for six months following their most recent back surgery, had no further therapeutic surgical options, and were an appropriate candidate for implantation. Patients were excluded if they had previously been treated with an implanted device for pain management, had evidence of a disruptive psychiatric disorder, had a prior spinal fusion at more than three levels, or had another chronic pain condition besides their FBSS. A total of 116 patients were randomized (56 to SQS + OMM, and 60 to OMM alone).

For patients randomized to the SQS+ OMM cohort, a trial stimulation period was conducted. A successful trial was defined as greater than 30% pain reduction along with improved function, quality of life, or reduction in pain medications. Fifty-two patients had a trial stimulation, of which 46 (90.2%) were successful. One patient withdrew from the study after the trial, so a total of 45 patients successfully received permanent SQS implants.

For the primary outcome, 33.9% of patients in the SQS + OMM cohort had a greater than or equal to 50% reduction in back pain at the nine-month mark, compared to 1.7% of patients in the OMM cohort. This was consistent at the six-month assessment as well. Mean baseline VAS scores were 68.8 in the SQS + OMM cohort and 70.2 in the OMM cohort. In the SQS + OMM cohort, mean VAS was reduced to 38.4 at six months, and 36.9 at the nine-month mark. Comparatively, in the OMM cohort, mean VAS was 69.8 at month six, and 67.5 at month nine. Patients in the OMM cohort had the opportunity to crossover after the nine-month visit.

The authors noted 193 events throughout the study period (178 adverse events, and seven strictly device-related issues). The most common adverse event was back or extremity pain. There were four infections, three lead fractures, and two lead dislocations noted.

A significant limitation of this study was its early termination due to challenges with enrollment. Originally, the study intended to obtain 314 participants, and follow them for 36 months. While the primary and secondary endpoints of the study were met, this early termination creates bias because the opportunity to follow up at six and nine months was not available to all patients. Lack of blinding is another limitation. Ultimately the authors concluded that while SQS + OMM is clinically more effective at relieving pain than OMM alone, the long-term effectiveness of this treatment has yet to be determined.

Analysis of Evidence (Rationale for Determination)

Neuromodulation in the form of SCS and PNS is an important tool in the treatment algorithm for chronic and intractable pain, refractory to treatments such as medications, physical therapy, psychological therapy, nerve blocks, corticosteroid injections, or facet joint injections. Nerve stimulation is, however, a challenging subject due to variability in the literature and lack of well-defined diagnostic criteria and indications for use.

Chronic and intractable pain can stem from various etiologies and can therefore be difficult to treat. Because chronic pain conditions are often associated with reduced functional ability, reduced health-related quality of life, and increased healthcare utilization, there exists the need to identify treatment modalities with evidence of efficacy for this purpose. There is not a widely accepted definition of chronic intractable pain; however, it would be expected that a majority of patients were being treated in the biopsychosocial model of chronic pain through a multidisciplinary team approach, nerve stimulation is a late or last resort in the algorithm of pain management, and that prior to a nerve stimulation trial, several pharmacologic, non-invasive non-pharmacologic, or targeted interventional pain procedures have been trialed and determined to be unsuccessful or unsuitable. Several studies on SCS for pain management have also utilized presence of pain for a minimum of one year as inclusion criteria. This is also consistent with NCD 106.7 Electrical Nerve Stimulators, which states that these devices be a "late or last resort" for patients with chronic intractable pain.

For some conditions, SCS and PNS have published high-quality peer-reviewed literature supporting their uses for pain reduction. For other conditions, there is a scarcity of high-quality evidence supporting the effectiveness of neuromodulation. Therefore, in order to improve health outcomes and limit the use of treatments that are unlikely to be effective, it is necessary to identify best practices for the use of SCS and PNS devices, including patient selection, disease-specific indications, limitations and contraindications, management of complications, and implanter training.

Coverage of items and services in the Medicare program is based on reasonable and necessary services. The decision to trial neurostimulation via SCS or PNS should be reserved for circumstances when the treating provider has evaluated the patient and 1) identified that the patient's chronic and intractable pain has failed to respond to pharmacologic, non-invasive non-pharmacologic management, or targeted interventional pain procedures, 2) determined that the pain has a neuropathic cause and no correctable pathology, 3) determined that the cause of the pain is a diagnosis with evidence of efficacy supporting SCS or PNS as an appropriate treatment, 4) chosen a device which has been approved by the FDA for the diagnosis being treated, and 5) determined that the patient has no other contraindications to neurostimulator placement (including but not limited to: a substance use disorder, inadequately controlled psychiatric or psychological problems, or cognitive deficits limiting the ability to provide informed consent or control the device). Because implantation of a neurostimulator does have inherent risks (including but not limited to infection, lead fracture or failure, spinal cord injury, nerve injury, or dural puncture), proper patient selection is critical for risk mitigation.

Appropriate patients should always undergo a successful trial stimulation period prior to neurostimulator implantation. While some studies have defined trial success differently, published guidelines from the NACC and/or the INS define a successful trial as greater than or equal to 50% reduction in patient's pain from baseline in combination with objective improvement in functional deficits (e.g., walking tolerance, performance of ADLs, sleep, quality of life, etc.). The importance of a trial stimulation is corroborated by an FDA letter to providers, encouraging the use of a trial stimulation in order to prevent patient- and device-related complications. The FDA noted that between July 27, 2016, and July 27, 2020, they received 107,728 MDRs related to spinal cord stimulator complications including device malfunction, patient injury, and patient death. The most common MDR was related to inadequate pain relief, supporting the need for proper patient selection and a successful trial stimulation.

Published literature generally agrees that SCS and PNS are best suited for patients with chronic and intractable neuropathic pain conditions and that a neurostimulation trial may be appropriate after more conservative measures fail. The strongest available data related to spinal cord stimulation is supportive of FBSS and CPRS as indications. In a multi-center, multi-national prospective study, Scalone et al identified that SCS was associated with an improvement in pain, perceived disability, and health-related quality of life for patients with FBSS. In a systematic review of the literature, Deer et al, using the USPSTF hierarchy of studies, determined there was Level 1 evidence supporting SCS for axial back and radicular pain. Deer et al's review also suggested SCS may offer more effective pain relief for individuals with FBSS than reoperation. Deer et al also identified Level 2 evidence for CPRS, based upon a single high-quality study. Another systematic review included upper extremity neuropathic pain syndromes and ischemic peripheral neuropathic pain from peripheral artery disease as NACC-recommended indications when conservative treatments fail to provide relief of pain. There is currently a lack of high-quality peer-reviewed evidence

available to support other indications.

Spinal cord stimulation for the management of painful PDPN is a challenging area. Two reconsideration requests were received on this topic, with a total of 27 pieces of literature submitted. All 27 articles relevant to these reconsideration requests were reviewed during the development of this LCD. There have been several well-designed RCTs on tonic and high-frequency SCS for PDPN, including the SENZA-PDN study. These RCTs support that tonic and high-frequency SCS are both effective for the management of pain associated with PDPN. Much of the recently published literature provides follow-up to these RCTs, and conclude the same results, supporting longer-term efficacy. It should be noted, however, that almost all of the literature on SCS for PDPN was industry-sponsored, which is an area of bias. Despite that, because of the challenges associated with managing PDPN, results from the RCTs reviewed support it as an indication for SCS, when other appropriate patient selection criteria are met.

The strongest available data related to peripheral nerve stimulation is supportive of cranial nerve stimulation for migraines and cluster headaches, medial branch nerve stimulation for chronic low back pain, and upper and lower extremity nerve stimulation for phantom limb (postamputation) syndrome. In a systematic review of the literature, Deer et al determined, based on the USPSTF hierarchy of studies, that there was Level 1 evidence supportive of PNS for migraines and chronic low back pain. Level 2 evidence was identified to support sphenopalatine ganglion stimulation for cluster headaches, PNS for hemiplegic shoulder pain, and PNS for neuropathic pain of the extremities and trunk. These indications each only had one RCT demonstrating safety and efficacy. Two other systematic reviews (Xu et al and Zhou et al) focused on PNS for chronic and intractable headaches, identifying high-quality or Level 1 evidence supporting migraines and cluster headaches. Xu et al also identified phantom limb (postamputation) syndrome as having Level 2 evidence; however, because this is a difficult condition to treat, they recommended PNS be included in the treatment algorithm. The authors of all three systematic reviews concluded that there may be other diagnoses which could benefit from PNS, however, there is currently insufficient published evidence supportive of these indications.

Additionally, Eckmann et al described a single case in which a patient was implanted with two separate spinal cord stimulators for the treatment of whole-body pain associated with small fiber neuropathy. The case study did not include reference to any other studies where patients were implanted with more than one SCS pulse generator. There is currently insufficient published evidence supportive of the use of multiple spinal cord stimulators in the same patient.

While the literature is not complete in terms of efficacy and patient selection for SCS and PNS, these devices offer the potential to avoid more invasive procedures or repeat surgery. They also may reduce opioid use, justifying maintaining SCS and PNS as a treatment option in the management of certain neuropathic conditions in properly selected patients despite these limitations. However, as neuromodulation technology advances, new modalities of stimulation are becoming more popular. That said, the amount of high-quality peer reviewed literature available for tonic (low frequency) stimulation in the last several years is limited, as most recent research is focused on high frequency, burst, and DRG stimulation modalities. Several studies comparing tonic stimulation to high frequency stimulation (Kapural et al[7]), and tonic stimulation to burst stimulation (Demartini et al[33]) support the safety and efficacy of these modalities for appropriately selected patients. Part of determining if SCS or PNS is an appropriate treatment should include selection of the most suitable stimulation modality for the patient’s diagnosis.

Additionally, alternatives to traditional PNS have been proposed, including PNFS. There is insufficient evidence in the published medical literature to determine the safety and efficacy of these emerging alternative modalities or approaches for the treatment of chronic intractable pain. While there have been several studies examining PNFS for chronic low back pain, they have mostly involved small sample sizes with limited generalizability. In a systematic review, Xu et al could not provide a level of evidence for PNFS because studies contained conflicting results, small sample sizes, and significant limitations. Eldabe et al, the largest of these studies, had a sample size of 116 patients and was terminated early due to recruitment difficulty, creating bias as some patients in the study were unable to complete the required follow-up visits. Therefore, further high-quality prospective studies are needed to support PNFS for chronic intractable pain management.

Finally, because there is a non-negligible risk of complications associated with neurostimulator implantation, it is critically important that the provider trialing or implanting SCS or PNS devices is well-trained on patient selection, contraindications, anatomy, identification and management of complications, device troubleshooting, and interdisciplinary collaboration. The NACC recommends that implanters be "properly trained and credentialed by either an accredited interventional pain medicine training program or an accredited surgical training program," [16(p574)] and cautions providers to only perform implantation of neurostimulators in ASC or hospital settings.

In summary, neuromodulation via SCS or PNS has the potential to improve patient outcomes by helping to manage chronic and intractable pain which has otherwise failed to respond to treatment. As outlined in this LCD, careful observation of appropriate indications, patient selection, and provider training are necessary in order to achieve the highest quality patient outcomes.

Proposed Process Information

Synopsis of Changes

CHANGES	FIELDS CHANGED
Not Applicable	N/A

Associated Information

Please refer to the related Draft Local Coverage Article: Billing and Coding: Nerve Stimulators for Chronic Intractable Pain (DA59190) for documentation requirements, utilization parameters and all coding information as applicable.

Sources of Information

Contractor Medical Directors

Commercial Payer Policies

Other Contractor Policies

Bibliography

This bibliography presents those sources that were obtained during the development of this policy. The Contractor is not responsible for the continuing viability of Website addresses listed below.

1. Deer TR, Mekhail N, Provenzano D, et al. The appropriate use of neurostimulation of the spinal cord and peripheral nervous system for the treatment of chronic pain and ischemic diseases: the Neuromodulation Appropriateness Consensus Committee. *Neuromodulation*. 2014;17(6):515-550. doi:10.1111/ner.12208.
2. International Association for the Study of Pain. IASP Announces Revised Definition of Pain. https://www.iasp-pain.org/publications/iasp-news/iasp-announces-revised-definition-of-pain/?msclkid=b4c0a94ed12c11ecb12c0b8c2f0cbd77&adlt=strict. Published July 16 2020. Accessed May 18 2022.
3. Deer TR, Grider JS, Lamer TJ, et al. A systematic literature review of spine neurostimulation therapies for the

treatment of pain [published correction appears in Pain Med. 2021 Feb 4;22(1):236]. *Pain Med*. 2020;21(7):1421-1432. doi:10.1093/pm/pnz353.
4. Carayannopoulos, A. Review of Advances in Spinal Cord Stimulation Waveform Technology. ASRA Pain Medicine. https://www.asra.com/guidelines-articles/original-articles/article-item/asra-news/2018/07/24/review-of-advances-in-spinal-cord-stimulation-waveform-technology-a-neuromodulation-special-interest-group-article?msclkid=42e54202d15611ec9807d6cca0778d1d&adlt=strict. Published July 24 2018. Accessed May 18 2022.
5. Dones I, Levi V. Spinal cord stimulation for neuropathic pain: Current trends and future applications. *Brain Sci*. 2018;8(8):138. doi:10.3390/brainsci8080138.
6. Sitzman BT, Provenzano DA. Best practices in spinal cord stimulation. *Spine*. 2017;42 Suppl 14:S67-S71. doi:10.1097/BRS.0000000000002220.
7. Kapural L, Yu C, Doust MW, et al. Novel 10-kHz high-frequency therapy (HF10 therapy) is superior to traditional low-frequency spinal cord stimulation for the treatment of chronic back and leg pain: The SENZA-RCT randomized controlled trial. *Anesthesiology*. 2015;123(4):851-860. doi:10.1097/ALN.0000000000000774.
8. Slangen R, Schaper NC, Faber CG, et al. Spinal cord stimulation and pain relief in painful diabetic peripheral neuropathy: a prospective two-center randomized controlled trial. *Diabetes Care*. 2014 Nov;37(11):3016-24. doi: 10.2337/dc14-0684.
9. de Vos CC, Meier K, Zaalberg PB, et al. Spinal cord stimulation in patients with painful diabetic neuropathy: a multicentre randomized clinical trial. *Pain*. 2014 Nov;155(11):2426-31. doi: 10.1016/j.pain.2014.08.031.
10. Petersen EA, Stauss TG, Scowcroft JA, et al. Effect of high-frequency (10-kHz) spinal cord stimulation in patients with painful diabetic neuropathy: A randomized clinical trial. *JAMA Neurol*. 2021;78(6):687-698. doi:10.1001/jamaneurol.2021.0538.
11. Petersen EA, Stauss TG, Scowcroft JA, et al. Durability of high-frequency 10-khz spinal cord stimulation for patients with painful diabetic neuropathy refractory to conventional treatments: 12-month results from a randomized controlled trial. *Diabetes Care*. 2022;45(1):e3-e6. doi:10.2337/dc21-1813.
12. U.S Food and Drug Administration. Conduct a Trial Stimulation Period Before Implanting a Spinal Cord Stimulator (SCS) – Letter to Health Care Providers. https://www.fda.gov/medical-devices/letters-health-care-providers/conduct-trial-stimulation-period-implanting-spinal-cord-stimulator-scs-letter-health-care-providers?adlt=strict. Published Sept 3 2020. Accessed May 18 2022.
13. Deer TR, Esposito MF, McRoberts WP, et al. A systematic literature review of peripheral nerve stimulation therapies for the treatment of pain. *Pain Med*. 2020;21(8):1590-1603. doi:10.1093/pm/pnaa030.
14. Zhou S, Hussain N, Abd-Elsayed A, et al. Peripheral nerve stimulation for treatment of headaches: An evidence-based review. *Biomedicines*. 2021;9(11):1588. Published Oct 31 2021. doi:10.3390/biomedicines9111588.
15. Xu J, Sun Z, Wu J, et al. Peripheral nerve stimulation in pain management: A systematic review. *Pain Physician* . 2021;24(2):E131-E152. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8897810/. Published March 5 2022. Accessed May 27 2022.
16. Deer TR, Mekhail N, Provenzano D, et al. The appropriate use of neurostimulation: Avoidance and treatment of complications of neurostimulation therapies for the treatment of chronic pain. Neuromodulation Appropriateness Consensus Committee. *Neuromodulation*. 2014;17(6):571-598. doi:10.1111/ner.12206.
17. Nayak R, Banik RK. Current Innovations in Peripheral Nerve Stimulation. *Pain Res Treat*. 2018;2018:9091216. Published 2018 Sep 13. doi:10.1155/2018/9091216.
18. Eckmann M, Papanastassiou A, Awad M. A unique case for spinal cord stimulation: successful treatment of small fiber neuropathy pain using multiple spinal cord stimulators. *Case Rep Med*. 2017;2017:6969285. doi:10.1155/2017/6969285.
19. Eldabe SS., Taylor RS., Goossens S, Bouche B, Gultuna I, Green C, Tinsley J, Luyet PP, Buchser E. A randomized controlled trial of subcutaneous nerve stimulation for back pain due to failed back surgery syndrome: The SubQStim study. *Neuromodulation.* 2018;22:519-528. doi:10.1111/ner.12784.
20. Scalone, L, Zucco, F, Lavano, A, et al. Benefits in pain perception, ability function and health-related quality of life in patients with failed back surgery syndrome undergoing spinal cord stimulation in a clinical practice setting. *Health Qual Life Outcomes.* 2018;*16*(68). https://doi.org/10.1186/s12955-018-0887-x.
21. DiBenedetto DJ, Wawrzyniak KM, Schatman ME, Kulich RJ, Finkelman M. 10 kHz spinal cord stimulation: a

retrospective analysis of real-world data from a community-based, interdisciplinary pain facility [published correction appears in J Pain Res. 2019 Jan 31;12:543-544]. *J Pain Res*. 2018;11:2929-2941. doi:10.2147/JPR.S188795.
22. Henson JV, Varhabhatla NC, Bebic Z, Kaye AD, Yong RJ, Urman RD, Merkow JS. Spinal cord stimulation for painful diabetic peripheral neuropathy: A systematic review. *Pain Ther*. 2021 Dec;10(2):895-908. doi: 10.1007/s40122-021-00282-9.
23. Deer TR, Krames E, Mekhail N, Pope J, Leong M, Stanton-Hicks M, Golovac S, Kapural L, Alo K, Anderson J, Foreman RD, Caraway D, Narouze S, Linderoth B, Buvanendran A, Feler C, Poree L, Lynch P, McJunkin T, Swing T, Staats P, Liem L, Williams K. The appropriate use of neurostimulation: new and evolving neurostimulation therapies and applicable treatment for chronic pain and selected disease states. *Neuromodulation.* 2014;17:599-615. doi:10.1111/ner.12204.
24. Deer TR, Provenzano DA, Hanes M, Pope JE, Thomson SJ, Russo MA, McJunkin T, Saulino M, Raso LJ, Lad SP, Narouze S, Falowski SM, Levy RM, Baranidharan G, Golovac S, Demesmin D, Witt WO, Simpson B, Krames E, Mekhail N. The Neurostimulation Appropriateness Consensus Committee (NACC) recommendations for infection prevention and management. *Neuromodulation.* 2017;20:31-50. doi:10.1111/ner.12565.
25. Finch P, Price L, Drummond P. High-frequency (10 khz) electrical stimulation of peripheral nerves for treating chronic pain: A double-blind trial of presence vs absence of stimulation. *Neuromodulation*. 2019;22(5):529-536. doi:10.1111/ner.12877.
26. Mekhail, NA, Estemalik, E, Azer, G, Davis, K, Tepper, SJ. Safety and efficacy of occipital nerves stimulation for the treatment of chronic migraines: Randomized, double-blind, controlled single-center experience. *Pain Pr*. 2016;17:669-677. doi:10.1111/papr.12504.
27. Saper JR, Dodick DW, Silberstein SD, et al. Occipital nerve stimulation for the treatment of intractable chronic migraine headache: ONSTIM feasibility study. *Cephalalgia.* 2011;31:271-285. doi:10.1177/0333102410381142.
28. Serra G, Marchioretto F. Occipital nerve stimulation for chronic migraine: A randomized trial. *Pain Physician.* 2012;15:245-253. https://pubmed.ncbi.nlm.nih.gov/22622909/. Published May-June 2012. Accessed May 27 2022.
29. Schoenen J, Jensen RH, Lanteri-Minet M, et al. Stimulation of the sphenopalatine ganglion (SPG) for cluster headache treatment. Pathway CH-1: A randomized, sham-controlled study. *Cephalalgia.* 2013;33:816-830. doi:10.1177/0333102412473667.
30. Hassenbusch SJ, Stanton-Hicks M, Schoppa D, et al. Long-term results of peripheral nerve stimulation for reflex sympathetic dystrophy. *J Neurosurg.* 1996;84:415-423. doi:10.3171/jns.1996.84.3.0415.
31. Cooney WP. Electrical stimulation and the treatment of complex regional pain syndromes of the upper extremity. *Hand Clin.* 1997;13:519-526. https://doi.org/10.1016/S0749-0712(21)00109-8.
32. Cohen S, Gilmore C, Kapural L, et al. Percutaneous peripheral nerve stimulation for pain reduction and improvements in functional outcomes in chronic low back pain. *Mil Med.* 2019;184:537-541. doi:10.1093/milmed/usz353.
33. Demartini L, Terranova G, Innamorato MA, et al. Comparison of tonic vs. burst spinal cord stimulation during trial period. *Neuromodulation*. 2019;22(3):327-332. doi:10.1111/ner.12867.
34. A Mailis, P Taenzer. Evidence-based guideline for neuropathic pain interventional treatments: Spinal cord stimulation, intravenous infusions, epidural injections and nerve blocks. *Pain Res Manage.* 2012;17(3):150-158. doi:10.1155/2012/794325.
35. Aman MM, Mahmoud A, Deer T, et al. The American Society of Pain and Neuroscience (ASPN) best practices and guidelines for the interventional management of cancer-associated pain. *J Pain Res*. 2021;14:2139-2164. doi:10.2147/JPR.S315585.
36. Baranidharan G, Feltbower R, Bretherton B, Crowther T, Cooper L, Castino P, Radford H. One-year results of prospective research study using 10 khz spinal cord stimulation in persistent nonoperated low back pain of neuropathic origin: Maiden back study. *Neuromodulation.* 2021;24:479-487. doi:10.1111/ner.13345.
37. Camporeze B, Simm RF, Estevão IA, Junior LRM, Aguiar, PHP de, Carrondo-Cottin S. Spinal cord stimulation in the treatment of neuropathic pain: Current perspectives of indications, cost-effectiveness, complications and results. *Journal of Health Sciences.* 2017;7(2):68-79. https://doi.org/10.17532/jhsci.2017.399.
38. Campos WK, Linhares MN, Sarda J, et al. Determinants for meaningful clinical improvement of pain and health-

related quality of life after spinal cord stimulation for chronic intractable pain. *Neuromodulation.* 2019;22(3):280-289. doi:10.1111/ner.12891.
39. Chen JL, Hesseltine AW, Nashi SE, et al. A real-world analysis of high-frequency 10 khz spinal cord stimulation for the treatment of painful diabetic peripheral neuropathy. *J Diabetes Sci Technol.* 2022;16(2):282-288. doi:10.1177/19322968211060316.
40. Chiarotto A, Maxwell LJ, Terwee CB, Wells GA, Tugwell P, Ostelo RW. Roland-Morris Disability Questionnaire and Oswestry Disability Index: Which has better measurement properties for measuring physical functioning in nonspecific low back pain? Systematic review and meta-analysis. *Phys Ther.* 2016;96(10):1620-1637. doi:10.2522/ptj.20150420.
41. Ciaramitaro P, Cruccu G, de Tommaso M, et al. A Delphi consensus statement of the Neuropathic Pain Special Interest Group of the Italian Neurological Society on pharmacoresistant neuropathic pain. *Neurol Sci.* 2019;40(7):1425-1431. doi:10.1007/s10072-019-03870-y.
42. D'Souza RS, Langford B, Dombovy-Johnson M, et al. Neuromodulation interventions for the treatment of painful diabetic neuropathy: A systematic review. *Curr Pain Headache Rep.* 2022;26(5):365-377. doi:10.1007/s11916-022-01035-9.
43. Daousi C, Benbow SJ, MacFarlane IA. Electrical spinal cord stimulation in the long-term treatment of chronic painful diabetic neuropathy. *Diabet Med.* 2005;22(4):393-398. doi:10.1111/j.1464-5491.2004.01410.x.
44. de Vos CC, Rajan V, Steenbergen W, van der Aa HE, Buschman HP. Effect and safety of spinal cord stimulation for treatment of chronic pain caused by diabetic neuropathy. *J Diabetes Complications*. 2009;23(1):40-45. doi:10.1016/j.jdiacomp.2007.08.002.
45. Deer TR, Gilmore CA, Desai MJ, et al. Percutaneous peripheral nerve stimulation of the medial branch nerves for the treatment of chronic axial back pain in patients after radiofrequency ablation [published correction appears in Pain Med. 2021 May 06]. *Pain Med.* 2021;22(3):548-560. doi:10.1093/pm/pnaa432.
46. Deer TR, Hunter CW, Mehta P, et al. A systematic literature review of dorsal root ganglion neurostimulation for the treatment of pain. *Pain Medicine*. 2020;21(8):1581-1589. doi:10.1093/pm/pnaa005.
47. Deer TR, Jain S, Hunter C, Chakravarthy K. Neurostimulation for intractable chronic pain. *Brain Sci*. 2019;9(2):23. doi:10.3390/brainsci9020023.
48. Dombovy-Johnson ML, Hagedorn JM, Wilson RE, Canzanello NC, Pingree MJ, Watson JC. Spinal cord stimulation for neuropathic pain treatment in brachial plexus avulsions: A literature review and report of two cases. *Neuromodulation.* 2020;23:704-712. doi:10.1111/ner.13128.
49. Dombovy-Johnson ML, Hunt CL, Morrow MM, Lamer TJ, Pittelkow TP. Current evidence lacking to guide clinical practice for spinal cord stimulation in the treatment of neuropathic pain in spinal cord injury: A review of the literature and a proposal for future study. *Pain Pract.* 2020;20(3):325-335. doi:10.1111/papr.12855.
50. Duarte RV, Andronis L, Lenders MW, de Vos CC. Quality of life increases in patients with painful diabetic neuropathy following treatment with spinal cord stimulation. *Qual Life Res*. 2016 Jul;25(7):1771-7. doi:10.1007/s11136-015-1211-4.
51. Duarte RV, Nevitt S, Maden M, Meier K, Taylor RS, Eldabe S, de Vos CC. Spinal cord stimulation for the management of painful diabetic neuropathy: A systematic review and meta-analysis of individual patient and aggregate data. *Pain*. 2021 Nov 1;162(11):2635-2643.doi: 10.1097/j.pain.0000000000002262.
52. Galan V, Scowcroft J, Chang P, et al. 10-kHz spinal cord stimulation treatment for painful diabetic neuropathy: Results from post-hoc analysis of the SENZA-PPN study. *Pain Manag*. 2020 Sep;10(5):291-300. doi: 10.2217/pmt-2020-0033.
53. Grider JS, Manchikanti L, Carayannopoulos A, et al. Effectiveness of spinal cord stimulation in chronic spinal pain: A systematic review. *Pain Physician*. 2016;19(1):E33-E54. https://pubmed.ncbi.nlm.nih.gov/26752493/. Published Jan 2016. Accessed May 27 2022.
54. Gridley L, van den Dolder PA. The Percentage Improvement in Pain Scale as a measure of physiotherapy treatment effects. *Aust J Physiother*. 2001;47(2):133-138. doi:10.1016/s0004-9514(14)60304-4.
55. Hagedorn JM, Deer TR, Canzanello NC, et al. Differences in calculated percentage improvement versus patient-reported percentage improvement in pain scores: A review of spinal cord stimulation trials. *Reg Anesth Pain Med*. 2021;46(4):293-297. doi:10.1136/rapm-2020-102238.
56. Hale J, Bailey-Classen A, Cheng J. Spinal cord stimulation for refractory angina pectoris. *Pain Med*. 2020;21(1):198-200. doi:10.1093/pm/pnz301.

57. Huang Q, Duan W, Sivanesan E, et al. Spinal cord stimulation for pain treatment after spinal cord injury. *Neurosci Bull*. 2019;35(3):527-539. doi:10.1007/s12264-018-0320-9.
58. Johnston SS, Udall M, Alvir J, McMorrow D, Fowler R, Mullins D. Characteristics, treatment, and health care expenditures of Medicare supplemental-insured patients with painful diabetic peripheral neuropathy, post-herpetic neuralgia, or fibromyalgia. *Pain Med*. 2014 Apr;15(4):562-76. doi:10.1111/pme.12328.
59. Labaran L, Jain N, Puvanesarajah V, Jain A, Buchholz AL, Hassanzadeh H. A retrospective database review of the indications, complications, and incidence of subsequent spine surgery in 12,297 spinal cord stimulator patients. *Neuromodulation*. 2020;23:634–638. doi:10.1111/ner.12952.
60. Lee S, Abd-Elsayed A. Some non-FDA approved uses for neuromodulation: A review of the evidence. *Pain Pract* . 2016;16(7):935-947. doi:10.1111/papr.12405.
61. Mehra M, Merchant S, Gupta S, Potluri RC. Diabetic peripheral neuropathy: Resource utilization and burden of illness. *J Med Econ*. 2014 Sep;17(9):637-45. doi:10.3111/13696998.2014.928639.
62. Mekhail NA, Argoff CE, Taylor RS, et al. High-frequency spinal cord stimulation at 10 kHz for the treatment of painful diabetic neuropathy: Design of a multicenter, randomized controlled trial (SENZA-PDN). *Trials*. 2020;21(1):87. doi:10.1186/s13063-019-4007-y.
63. North R, Shipley J, Prager J, et al. Practice parameters for the use of spinal cord stimulation in the treatment of chronic neuropathic pain. *Pain Med*. 2007;8 Suppl 4:S200-S275. doi:10.1111/j.1526-4637.2007.00388.x.
64. Ooi YC, Falowski S, Wang D, Jallo J, Ho RT, Sharan A. Simultaneous use of neurostimulators in patients with a preexisting cardiovascular implantable electronic device. *Neuromodulation*. 2011;14(1):20-26. doi:10.1111/j.1525-1403.2010.00314.x.
65. Piedade GS, Vesper J, Slotty PJ. Synergetic efficacy of simultaneous DRG- and traditional spinal cord stimulation. *Acta Neurochir*. 2020;162(2):257-260. doi:10.1007/s00701-019-04166-y.
66. Pluijms WA, Slangen R, Bakkers M, et al. Pain relief and quality-of-life improvement after spinal cord stimulation in painful diabetic polyneuropathy: A pilot study. *Br J Anaesth*. 2012;109(4):623-629. doi:10.1093/bja/aes251.
67. Pluijms WA, Slangen R, van Kleef M, Joosten EA, Reulen JP. Increased contact heat evoked potential stimulation latencies in responders to spinal cord stimulation for painful diabetic polyneuropathy. *Neuromodulation*. 2015 Feb;18(2):126-32. doi:10.1111/ner.12188.
68. Raghu ALB, Parker T, Aziz TZ, Green AL, Hadjipavlou G, Rea R, FitzGerald JJ. Invasive electrical neuromodulation for the treatment of painful diabetic neuropathy: Systematic review and meta-analysis. *Neuromodulation*. 2021 Jan;24(1):13-21. doi:10.1111/ner.13216.
69. Raut R, Shams S, Rasheed M, Niaz A, Mehdi W, Chaurasia B. Spinal cord stimulation in the treatment of phantom limb pain: A case report and review of literature. *Neurol India.* 2021;69:157-60. doi:10.4103/0028-3886.310092.
70. Sadosky A, Mardekian J, Parsons B, Hopps M, Bienen EJ, Markman J. Healthcare utilization and costs in diabetes relative to the clinical spectrum of painful diabetic peripheral neuropathy. *J Diabetes Complications*. 2015 Mar;29(2):212-7. doi:10.1016/j.jdiacomp.2014.10.013.
71. Sanders RA, Moeschler SM, Gazelka HM, et al. Patient outcomes and spinal cord stimulation: A retrospective case series evaluating patient satisfaction, pain scores, and opioid requirements. *Pain Pract*. 2016;16(7):899-904. doi:10.1111/papr.12340.
72. Slangen R, Pluijms WA, Faber CG, Dirksen CD, Kessels AG, van Kleef M. Sustained effect of spinal cord stimulation on pain and quality of life in painful diabetic peripheral neuropathy. *Br J Anaesth*. 2013;111(6):1030-1031. doi:10.1093/bja/aet397.
73. Strand NH, Burkey AR. Neuromodulation in the treatment of painful diabetic neuropathy: A review of evidence for spinal cord stimulation. *J Diabetes Sci Technol*. 2022;16(2):332-340. doi:10.1177/19322968211060075.
74. Tate JL, Stauss T, Li S, Rotte A, Subbaroyan J. A prospective, multi-center, clinical trial of a 10-khz spinal cord stimulation system in the treatment of chronic pelvic pain. *Pain Pract*. 2021;21(1):45-53. doi:10.1111/papr.12932.
75. van Beek M, Geurts JW, Slangen R, et al. Severity of neuropathy is associated with long-term spinal cord stimulation outcome in painful diabetic peripheral neuropathy: Five-year follow-up of a prospective two-center clinical trial. *Diabetes Care*. 2018 Jan;41(1):32-38. doi:10.2337/dc17-0983.
76. van Beek M, Slangen R, Schaper NC, et al. Sustained treatment effect of spinal cord stimulation in painful

diabetic peripheral neuropathy: 24-month follow-up of a prospective two-center randomized controlled trial. *Diabetes Care.* 2015 Sep;38(9):e132-4. doi: 10.2337/dc15-0740.
77. Verrills P, Vivian D, Mitchell B, Barnard A. Peripheral nerve field stimulation for chronic pain: 100 cases and review of the literature. *Pain Med*. 2011;12(9):1395-1405. doi:10.1111/j.1526-4637.2011.01201.x.
78. Warner NS, Schaefer KK, Eldrige JS, et al. Peripheral nerve stimulation and clinical outcomes: A retrospective case series. *Pain Pract*. 2021;21(4):411-418. doi:10.1111/papr.12968.
79. Wilson RD, Knutson JS, Bennett ME, Chae J. The effect of peripheral nerve stimulation on shoulder biomechanics: A randomized controlled trial in comparison to physical therapy. *Am J Phys Med Rehabil*. 2017;96(3):191-198. doi:10.1097/PHM.0000000000000677.
80. Yagihashi S, Mizukami H, Sugimoto K. Mechanism of diabetic neuropathy: Where are we now and where to go? *J Diabetes Investig*. 2011;2(1):18-32. doi:10.1111/j.2040-1124.2010.00070.x.

Open Meetings

MEETING DATE	MEETING STATES	MEETING INFORMATION
08/25/2022	Florida Puerto Rico Virgin Islands	**The open meeting is for MAC JN.** **Location of Meeting:** Teleconference/Webinar only **Time of Meeting:** 1pm ET **Link to JN website:** https://medicare.fcso.com/Open_Public_Meeting/0458851.asp

Contractor Advisory Committee (CAC) Meetings

N/A

MAC Meeting Information URLs

N/A

Proposed LCD Posting Date

08/11/2022

Comment Period Start Date

08/11/2022

Comment Period End Date

09/24/2022

Reason for Proposed LCD

- Other

Requestor Information

Requestor Name	Requestor Letter
Medtronic Neuromodulation Group	View Letter
Nevro Corporation	View Letter

Contact for Comments on Proposed LCD

Medical Affairs
2020 Technology Parkway
Suite 100
Mechanicsburg, PA 17050
ProposedLCDComments@fcso.com

Associated Documents

Attachments

N/A

Related Local Coverage Documents

Articles

DA59190 - Billing and Coding: Nerve Stimulators for Chronic Intractable Pain

Related National Coverage Documents

NCDs

160.7.1 - Assessing Patient's Suitability for Electrical Nerve Stimulation Therapy
160.24 - Deep Brain Stimulation for Essential Tremor and Parkinson’s Disease
160.7 - Electrical Nerve Stimulators
160.19 - Phrenic Nerve Stimulator
230.18 - Sacral Nerve Stimulation For Urinary Incontinence
160.18 - Vagus Nerve Stimulation (VNS)

Keywords

N/A