Washington State Health Care Authority

FINAL Key Questions

Spinal Cord Stimulation

Background

Chronic pain is a leading cause of disability and is an immense public health challenge. Pain is chronic when it occurs for extended periods (usually defined as >3 months), and can affect other aspects of an individual's health and function, including physical, emotional, social, and mental, often leading to a loss in quality of life[1-6]. Treatment of chronic pain aims to improve function and quality of life in addition to pain relief. Primary treatments include disease and injury-specific treatments such as nerve root decompression or reoperation, and other therapies such as pharmaceuticals, physical therapy, behavioral and psychological therapies, and neurostimulation therapies such as transcutaneous nerve electrical stimulation (TENS). Spinal cord stimulation (SCS) may be considered for moderate or severe pain that does not respond to standard therapies. A 2020 U.S. Food and Drug Administration (FDA) communication estimated that 50,000 SCS devices are implanted annually.[7]

SCS was developed in the 1960's based on the Melzack and Wall's gate-control theory and has been used to treat a number of chronic pain issues.[8,9] Mechanisms of pain relief using SCS are not completely understood, although current theories suggest stimulation occurs through a pulse delivering a specific current to dorsal fibers which interfere with or suppress the transmission of pain signals between nerves and the brain.[10-12] Originally, pain relief through parameter changes were completely dependent on user input. Open loop and closed loop systems have been described. *Open loop* (OL) systems ignore external stimuli, such as movement of the spinal cord, heart rate, and respiration.[13,14] In contrast, *closed loop* (CL) systems automatically adapt and modify stimulator settings in response to patient position and activity in real time, maintaining stimulation within an individualized therapeutic range.[13,14] Further details on the mechanism of SCS systems have been described in great detail elsewhere.[11,12,15]

SCS systems involve percutaneous implantation of electrode leads into the epidural space until they reach the dorsal column of the spinal cord. Currently, 16 FDA approved SCS devices are available. Approved musculoskeletal indications generally include Failed Back Surgery Syndrome (FBSS), Complex regional pain syndrome (CRPS) Types I and II, intractable low back pain and leg pain. Other indications include epidural fibrosis, degenerative disc disease, and arachnoiditis. Some SCS devices are approved for treatment of diabetic neuropathy. In 2016 the FDA gave premarket approval (PMA) to the first generation of devices implanted onto the dorsal root ganglion (DRG) of the posterior root to treat CRPS type I or type II, reflex sympathetic dystrophy and causalgia.[16-18] Compared with SCS devices, in which leads are implanted into the epidural space, DRG leads enter the epidural space, exit the neuroforamina, and stimulate the adjacent DRG, potentially providing more focused pain relief through specific targeting, as well as decreased paresthesia.[11,19]

The pulse frequency used in SCS, measured in hertz (Hz), can be adjusted to meet the needs of individual pain thresholds.[11,12] Traditional SCS systems are considered "low-frequency", typically defined as 30 Hz to 200 Hz, but may be as low as 10 Hz or high as 1200 Hz.[12] Low-frequency SCS is often associated with paresthesia, a feeling of tingling or buzzing that is perceived differently depending on the individual, which may or may not bring discomfort. "High frequency" (also referred to as "paresthesia free") SCS systems, often defined as greater than 200 Hz, produce stimulations that are

typically unperceivable by patients, and may be preferred.[20] Currently, the highest frequency available is 10,000 Hz. Additionally, in 2016 the FDA approved a clinician application for SCS systems that provide stimulation in "bursts" rather than constant rates (referred to as tonic stimulation or burst stimulation), which may provide greater relief at lower frequencies.[21-24]

Topic Background

A Health Technology Assessment (HTA) on SCS was performed in 2010 and reviewed by the Washington Health Technology Assessment Program (HTAP). The prior report focused on evidence for the effectiveness of and complications for traditional SCS (dorsal column) in patients with chronic neuropathic pain. Signal updates were performed in 2014, 2016, and 2018, all of which concluded that there was not substantial, high-quality new evidence comparing SCS with medical or surgical interventions that did not involve neuromodulation (e.g., SCS, DRG stimulators, peripheral nerve neuromodulation) to trigger an updated report. The HTAP is interested in re-evaluation of spinal cord stimulation as additional evidence on technical advances related to use of SCSs, including use of high frequency and burst stimulation, may be available. Dorsal root ganglion stimulators will not be included in this review, given differences in lead placement compared with traditional SCS. This is consistent with the scope of the prior report. The proposed assessment update will be restricted to devices approved by the FDA for management of the FDA-approved conditions related to neuropathic and non-neuropathic musculoskeletal pain as described in the PICOTS (Table 1). Comments from the public posting of the KQ and PICOTS and consultation with the HTAP were considered for finalization of the Key Questions and scope.

Final Key Questions and Scope

Key Questions (KQ)
When used in adult patients who have failed other treatment options for pain related to failed back surgery syndrome, chronic back pain, complex regional pain syndrome, or peripheral neuropathy (phantom limb or stump pain, diabetic neuropathy or postherpetic neuralgia):

Key Question 1:
What is the evidence of short and long-term effectiveness of spinal cord stimulation compared with medical and/or surgical treatment (appropriate to condition) that does not include neuromodulation devices?

Key Question 2:
What is the evidence of the safety of spinal cord stimulation compared with medical and/or surgical treatment (appropriate to condition) that does not include neuromodulation devices?

Key Question 3:
What is the evidence that spinal cord stimulation has differential efficacy or safety issues in sub-populations of interest?

Key Question 4:
What is the evidence of cost-effectiveness of spinal cord stimulators compared with other medical or surgical options that do not include neuromodulation?

Table 1. Draft PICOTS Scope

Study Component	Inclusion	Exclusion

Participants	Adults with one of the following: • chronic low back pain, failed back surgery syndrome (low back pain and persistent, significant radicular pain following surgery), complex regional pain syndrome, peripheral neuropathy (phantom limb or stump pain, diabetic neuropathy or postherpetic neuralgia) Special populations/factors of interest: Sex, age, psychological or psychosocial co-morbidities, diagnosis or pain type, provider type, setting or other provider characteristics, health care system type, including worker's compensation, Medicaid, state, employees	• Children, patients <18 years old • Patients with prior use of SCS • Patients who are pregnant • All other pain conditions (e.g., cancer pain, chronic refractory anginal pain, heart failure, critical limb ischemia, peripheral vascular pain, pain at end of life, MS, fibromyalgia, headache, trigeminal neuralgia, chronic pancreatitis, chronic pelvic pain, chronic abdominal pain, post-stroke pain • Studies in which < 75% of patients have chronic musculoskeletal or neuropathic pain or other included pain conditions
Intervention	FDA-approved spinal cord stimulation (permanently implanted pulse generator systems and radiofrequency receiver systems)	• Temporarily implanted spinal cord stimulation devices • Neurostimulation of other parts of the nervous system (e.g., peripheral nerves, deep brain), dorsal root ganglion stimulation • Transcutaneous electrical nerve stimulation (TENs) • Non-FDA approved devices (unless final, phase III trial) • Intrathecal pumps
Comparators	Medical and/or surgical treatment (appropriate to condition) that does not include comparison of SCS methods/devices or other neuromodulation devices	• Comparisons of SCS devices • Comparison of SCS combined with other interventions vs. the other intervention alone • Comparisons of different types/modalities of SCS (e.g., comparisons of low versus high frequency, burst vs. tonic, etc.)
Outcomes	**Primary Outcomes (SOE)** • Function • Pain • Opioid use • **Complications** and adverse effects (e.g., procedural complications and technical failures, harms, infection, revision, removal, painful paresthesia or loss of paresthesia, mortality, serious adverse events) **Secondary outcomes (No SOE)**	• Non-clinical outcomes • Non-validated measures • Intermediate outcomes • Return to work

	• Health-related quality of life (HR-QoL) • Anxiety and depression • Patient satisfaction • Global perceived effect (GPE)/global impression of change	
Setting	Any	
Study design	• RCTs will be the primary focus; prospective high quality comparative nonrandomized studies of intervention (NRSI) with concurrent controls that control for confounding will be considered if RCTs are not available; question 3 is limited to RCTs • NRSIs including case series designed to evaluate harms with at least 5 years follow-up, or which report on rare harms for question 2 will be considered. • Formal cost-effectiveness analyses assessing initial placement and replacement will be considered for question 4	• Case reports • Case series (for KQ1, 3, 4) • Case series not designed to evaluate harms, those with < 5 years follow-up for question 2 unless they report on rare harms outcomes • Non-clinical studies (e.g., animal studies) • Studies with N < 10 patients total or < 10 per group • Studies not reporting on primary outcomes or harms
Publication	• Studies published in English in peer reviewed journals, published HTAs or publicly available FDA reports • Full formal economic analyses (e.g., cost-utility analyses) published in English in an HTA, or in a peer-reviewed journal published after those represented in previous HTAs	• Abstracts, editorials, letters, books, conference proceedings • Studies without abstracts available online • Duplicate publications of the same study which do not report on different outcomes • Single reports from multicenter trials • Studies reporting on the technical • aspects spinal cord stimulation • White papers • Narrative reviews • Articles identified as preliminary reports when results are published in later versions/publications • Other types of economic evaluations (e.g., costing studies, cost-minimization analyses, cost-benefit analyses)

DRGS = Dorsal Root Ganglion Stimulation; FDA = Food and Drug Administration; GPE = Global perceived effect; HFSCS = High-frequency spinal cord stimulation; HR-QoL = Health-related quality of life; HTA = Health Technology Assessment; MS = multiple sclerosis; NRSI = Non-randomized studies of interventions; RCT = Randomized Control Trial; SCS = Spinal cord stimulator; SOE = Strength of Evidence; TENS = Transcutaneous electrical nerve stimulation.

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