



Topic Exploration Report

Topic explorations are designed to provide a high-level briefing on new topics submitted for consideration by Health Technology Wales. The main objectives of this report are to:

- Determine the quantity of evidence available for a technology of interest.
- Identify any gaps in the evidence.
- Inform decisions on topics that warrant fuller assessment by Health Technology Wales (HTW).

Topic exploration report number:	TER460
Topic:	Spinal cord stimulation for adults with chronic chemotherapy-induced peripheral neuropathy
Summary of findings:	<p>Spinal cord stimulation (SCS) is recommended by National Institute for Health and Care Excellence (NICE) Technology Appraisal 159 (TA159) as a treatment option for adults with chronic pain of neuropathic origin. Although the evidence included in TA159 does not include chemotherapy-induced peripheral neuropathy (CIPN), NICE concluded that the guidance should take into account other chronic pain conditions of neuropathic origin that were not reflected in the clinical trial data.</p> <p>HTW researchers looked for evidence published since NICE TA159, specifically on the use of SCS for chronic CIPN. We identified one systematic review of 15 case studies (16 people) of very low-certainty, which suggested that SCS is associated with a reduction in pain severity from CIPN, but there were mixed findings for changes in neurological function. No comparative data or economic evidence, specifically for CIPN treated with SCS, were identified.</p>

Introduction and aims

Chemotherapy-induced peripheral neuropathy (CIPN) is defined as any injury, inflammation or degeneration of the peripheral nerves because of the administration of a chemotherapeutic agent (Armstrong et al. 2005). Symptoms may include tingling, pins and needles, numbness, pain, muscle weakness, constipation, dizziness, and problems with balance, walking and co-ordination (Macmillan Cancer Support 2020). Early symptoms are often seen in the hands and feet, and in the arms and legs as it progresses (Argyriou et al. 2012). The severity of CIPN is dependent on the type of chemotherapy agent, cumulative dose, and duration of exposure (D'Souza et al. 2022). Symptoms generally improve with discontinuation of the chemotherapy agent over time, although complete recovery to baseline is not always attained. It is estimated that 50% to 90% of patients who receive chemotherapy go on to develop CIPN in the acute setting, and 30% to 40% of patients continue to suffer from CIPN chronically (D'Souza et al. 2022).

People with chronic neuropathic pain are usually managed with conventional medical management, including pharmacological interventions and non-pharmacological interventions (for example, physiotherapy, acupuncture, transcutaneous electrical nerve stimulation and psychological therapies) (NICE 2008).

Spinal cord stimulation (SCS) is a minimally invasive, non-pharmacological treatment for chronic pain that is recommended by the National Institute for Health and Care Excellence (NICE) after conventional medical management has failed (NICE 2008). SCS modifies the perception of neuropathic and ischaemic pain by stimulating the dorsal column of the spinal cord with an electrical pulse (NICE 2008).

Although SCS is recommended by NICE Technology Appraisal 159 (TA159) as a treatment option for adults with chronic pain of neuropathic origin, including CIPN, the evidence included in TA159 does not include CIPN. HTW researchers looked for evidence published since NICE TA159, specifically on the use of SCS for chronic CIPN.

Evidence overview

Guidance

SCS is recommended by NICE TA159 as a treatment option for adults with chronic pain of neuropathic origin who: continue to experience chronic pain (measuring at least 50 millimetres on a one to 100 millimetre visual analogue scale) for at least six months despite appropriate conventional medical management; and who have had a successful trial of stimulation as part of the assessment by a multidisciplinary team experienced in chronic pain assessment and management of people with spinal cord stimulation devices (NICE 2008). Although the evidence included in TA159 does not include CIPN, NICE concluded that the guidance should take into account other chronic pain conditions of neuropathic origin that were not reflected in the clinical trial data.

Additionally, NICE Medical Technologies Guidance 41 (MTG41) recommends that a specific type of SCS device (Senza), which delivers SCS at 10 kilohertz (HF10 therapy), may be considered for patients with neuropathic pain. NICE reported that additional benefits of Senza compared with low-frequency SCS are not certain in some types of neuropathic pain, and concluded that it would be valuable to gather more evidence about the potential role of Senza for neuropathic pain in patients who have not had previous back surgery (NICE 2019).

There is ongoing NICE Medical Technologies Guidance (GID-MT567) for an SCS device (Evoke), which uses feedback-control to manage neuropathic pain, but it is not specific for CIPN. This guidance has

been suspended whilst further intelligence is gathered, although there is a NICE Medtech Innovation Briefing for this device (MIB238).

Secondary evidence

A systematic review by D'Souza et al. (2022) included 15 case studies of 16 participants, reported as being of very low certainty using the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) framework. The systematic review reported that SCS is associated with a reduction in pain severity from CIPN, with pain relief ranging from 50% to 100% between three months and two years. Mixed results were reported regarding temperature and touch sensation in nine participants treated with SCS. Seven participants reported improved mobility and ability to participate in daily activities, with reasons attributed to improved gait, more stability, better flexibility of their legs, less pain when walking, decreased dependence on assistance from others, and improvement of hand function (D'Souza et al. 2022).

Primary evidence

We did not identify any additional individual studies reporting SCS for CIPN.

Economic

No economic evidence was identified for SCS specifically for CIPN.

Ongoing

We identified one ongoing meta-analysis investigating CIPN for SCS, due to be completed in May 2023, and an additional American observational study of 20 people with CIPN treated with SCS, due to be completed in April 2024.

Areas of uncertainty

Although SCS for CIPN is included in NICE recommendations, no evidence specifically for CIPN is included in the guidance. Only a small number of case studies of very low certainty were identified since publication of NICE guidance. No comparative data or economic evidence specific to CIPN were identified.

Literature search results

Health technology assessments and guidance

Health Technology Assessment of Scheduled Procedures (2013). Spinal Cord Stimulation for chronic pain: https://www.hiqa.ie/sites/default/files/2017-01/Spinal_cord_stimulation_2013.pdf

No specific mention of CIPN

Macmillan Cancer Support. Peripheral neuropathy (2020): <https://www.macmillan.org.uk/cancer-information-and-support/impacts-of-cancer/peripheral-neuropathy>

No specific mention of SCS

NICE Technology Appraisal (TA159) (2008 [reviewed 2014]). Spinal cord stimulation for chronic pain of neuropathic or ischaemic origin: <https://www.nice.org.uk/guidance/ta159>

No specific mention of CIPN

NICE Medical Technologies Guidance (MTG41) (2019). Senza spinal cord stimulation system for delivering HF10 therapy to treat chronic neuropathic pain: <https://www.nice.org.uk/guidance/mtg41>

NICE started a review of this guidance in April 2022

No specific mention of CIPN

NICE Medtech Innovation Briefing (MIB305) (2022). Differential target multiplexed spinal cord stimulation for chronic lower back pain and leg pain: <https://www.nice.org.uk/advice/mib305>

No specific mention of CIPN

NICE Medtech Innovation Briefing (MIB238) (2020). Evoke Spinal Cord Stimulator for managing chronic neuropathic or ischaemic pain: <https://www.nice.org.uk/advice/mib238>

No specific mention of CIPN

NICE Shared Learning (2020). Spinal cord stimulator implantation: Improving theatre efficiency: <https://www.nice.org.uk/sharedlearning/scsi>

Leeds Teaching Hospitals NHS Trust

No specific mention of CIPN

Simpson E L, Duenas A, Holmes M W, Papaioannou D, Chilcott J (2009). Spinal cord stimulation for chronic pain of neuropathic or ischaemic origin: systematic review and economic evaluation. *Health Technol Assess*;13(17):

<https://doi.org/10.3310/hta13170>

No specific mention of CIPN

Evidence reviews and economic evaluations

D'Souza, R.S., Her, Y.F., Jin, M.Y., Morsi, M. and Abd-Elsayed, A., 2022. Neuromodulation therapy for chemotherapy-induced peripheral neuropathy: a systematic review. *Biomedicines*, 10(8), p.1909:

<https://doi.org/10.3390/biomedicines10081909>

Ongoing research

NICE Medical Technologies Guidance (GID-MT567). Evoke Spinal Cord Stimulator for managing chronic neuropathic or ischaemic pain: <https://www.nice.org.uk/guidance/indevelopment/gid-mt567>

Expected publication date: Suspended. Topic is paused whilst further topic intelligence is gathered

reed Yaras, Oliver Acosta. Efficacy and Safety of Spinal Cord Stimulation for the Treatment of Chemotherapy Induced Peripheral Neuropathy: A Systematic Review and Meta-Analysis. PROSPERO 2023 CRD42023392707 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42023392707

Expected completion: May 2023

Assessing effect of spinal cord stimulation on pain and quality of life in patients with chemotherapy-induced peripheral neuropathy: <https://clinicaltrials.gov/ct2/show/NCT05411523>

Observational study of 20 participants in USA

Expected completion: April 2024

Additional references used in TER

Argyriou, A.A., Bruna, J., Marmioli, P. and Cavaletti, G., 2012. Chemotherapy-induced peripheral neurotoxicity (CIPN): an update. *Critical reviews in oncology/hematology*, 82(1), pp.51-77:
<https://doi.org/10.1016/j.critrevonc.2011.04.012>

Armstrong, T., Almadrones, L. and Gilbert, M.R., 2005, March. Chemotherapy-induced peripheral neuropathy. In *Oncology nursing forum* (Vol. 32, No. 2)

Date of search:	March 2023
Concepts used:	Spinal cord stimulation/stimulator (SCS), chemotherapy-induced peripheral neuropathy (CIPN)

Proposed research question and evidence selection criteria (if selected)

Proposed research question	What is the clinical and cost effectiveness of spinal cord stimulation for chronic chemotherapy-induced peripheral neuropathy, compared to standard of care?
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	Included	Excluded
Population	Adults with chronic chemotherapy-induced peripheral neuropathy after standard treatments have failed	Acute chemotherapy-induced peripheral neuropathy
Intervention	Spinal cord stimulation (SCS)	
Comparison/ comparators	Conventional medical management: <ul style="list-style-type: none"> • Pharmacological interventions (e.g. NSAIDs, tricyclic antidepressants, anticonvulsants, analgesics and opioids) • Non-pharmacological interventions (e.g. physiotherapy, acupuncture, transcutaneous electrical nerve stimulation and psychological therapies) 	
Outcomes	<ul style="list-style-type: none"> • Pain • Neuropathy and neurological deficits • Need for further treatment (e.g. opioid medication and hospital visits) • Quality of life (including mobility) Patient satisfaction	
Study design	All	