Evidence scan:

Spinal cord stimulators:

Overview of trial study processes

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Requested by:	*Advisory Group on ACC guidance for Spinal Cord Stimulators*
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1 Purpose & background

1.1 Background

Early in 2017 it was identified that an update of ACC's current clinical practice guidelines on neuromodulation treatment with spinal cord stimulators (SCS) was needed. The update of this guidance is planned as a year-long project using standard guideline development methodology. An Expert Advisory Group (EAG) has been formed to review and interpret the evidence so guidance is created with a common understanding. The Expert Advisory Group has asked ACC Research to perform an evidence scan on the trial implantation procedure for clients to support this work.

This report focuses on primary studies that describe trial implantation procedures for SCS. Guidance on trial procedures from key clinical guidelines is also summarized to inform the 2018 update of the ACC neuromodulation treatment with SCS for pain management guideline. It contributed to sections: 4.1.3 Psychological Consideration Factors; 5.3 Psychological assessment and recommendations; and 6.2 The temporary lead trial for SCS parts of the guideline.

1.2 Purpose

The purpose of the evidence scan is to:

1) Provide a summary of the evidence base from primary studies that describes the process for trial implantation of spinal cord stimulators; and

2) Provide a summary of clinical best practice recommendations for trial stimulation of spinal cord stimulators.

2 Methods

The following sources were searched for publications between 2007 to September 2017:

- Medline, Pre-Medline, PubMed
- Embase
- AMED
- Cochrane Library

The search focused on:

- Studies focusing on SCS trials (n = 26 papers)
- Effectiveness, success and failure rates (focusing on permanent implantation, n = 30 papers)
- Adverse events and complications (n = 11 papers)
- Guidelines (n=15 papers)

Inclusion criteria for primary studies:

Study design: randomised control trials, observations studies (retrospective and prospective cohort), case series

Population: Patients with Failed Back Surgery Syndrome (FBSS), Complex Regional Pain Syndrome (CRPS), Neuropathic pain, peripheral neuropathy, chronic back and limb pain, arachnoiditis, peripheral vascular disease, brachial plexus avulsion

Intervention: Studies that described SCS trial implantation procedure, studies using either paddle or percutaneous leads were included

Outcomes: Trial to permanent implantation / conversion rates, explantation rates, adverse events,

Exclusion criteria

Non-English studies, animal studies, opinion pieces or commentaries, literature reviews, studies in people with angina pectoris, cancer related pain or other cohorts that do not fall under the ACC legislation.

Note: *This is an evidence scan not a full review of the literature. Studies were not critically appraised for quality and the findings are based on a general assessment of the evidence base, rather than a full systematic review. The intention of this evidence scan is to provide an overview of what the literature can offer regarding trial implantation procedures for spinal cord stimulation.*

3 Findings

3.1 Overview

The search yielded 67 potentially useful primary studies of which the titles and abstracts were screened. From these n = 18 primary articles were included in this analysis. These articles were focused on research questions around SCS, however the objectives of what was investigated in each article differed. Information extracted from the articles included: patient demographics; primary objective; type of electrode leads used; description of trial procedure as outlined in the methods section of the article; outcome measures; and adverse effects. More detail regarding each of the studies can be found in the Excel spreadsheet that accompanies this summary.

3.1.1 Study designs

The design of included studies was predominantly retrospective analyses of data collected from medical files (n = 6). Two other retrospective analyses used data extracted from pre-existing databases (Truven MarketScan data[1, 2]). Other study designs were: prospective observational studies (n = 2), surveys (n = 2), randomised controlled trial (n = 1); and prospective case studies (n = 5).

3.1.2 Patient cohorts

The mean age range of patients was 49.4 to 60 years, and were roughly 50% female and male. The predominant reason for SCS implantation across studies was chronic pain from Failed-Back Surgery Syndrome (FBSS), followed by Complex Regional Pain Syndrome (CRPS). Other reported conditions were neuropathic pain, peripheral vascular disease, brachial plexus avulsion, arachnoiditis and neuritis/radiculitis. The duration of chronic pain before the trial implantation procedure was only reported in two studies, one reported average duration as 9.1 years[3] the other reported 72.4 months / 6 years[4].

3.2 Trial procedure description

Table 1 gives an outline of the common factors described in the trial procedure in the methods section of the studies. The trial procedure was mostly described within a hospital setting, however seven studies described it as an outpatient procedure where once the patient was able they could return home for the duration of the trial.

It is important to note that the included studies did not focus on efficacy of different trial procedures.

Table 1 below describes the components of the trial procedures as described within the methodology of the articles, but the articles themselves did not justify their reasoning for their trial implantation procedure. Some variance was attributed to individual patient factors like deformed anatomy (scoliosis), further detail can be found in Table 1 and the accompanying excel spreadsheet.

Table 1. Main components of trial implant procedure described in study methodologies

Variable	Finding
Lead type	**Percutaneous:** Most electrode leads reported for trial implants and described as inserted under imaging (n = 10 articles – refer to excel spreadsheet). One study described 83% of centres used percutaneous[5] another that 71.4% were percutaneous and 3.8% paddle[1]. **Paddle:** Paddles (tripolar and bipolar) electrode arrays were described specifically for trial procedures in two articles[6, 7]. However studies did mention them as an option for permanent procedure[8], or for consideration in the trial procedure if percutaneous leads not appropriate (e.g. in event of spinal scoliosis, percutaneous lead migration during outpatient trial period, warfarin therapy, previous spinal cord tumour resection)[7]. **Other:** Descriptions of other electrode lead types, configurations and models included in the studies were: octrodes / octads / octapolar, quadripolar, Pisces Quad leads, Verify lead, Resume lead and Sigma monopolar electrodes. The three main lead manufacturers reported were: Medtronic, St Jude and Boston Scientific. Other manufacturers mentioned were Pisces and Sigma.
Setting	**Hospital:** patient stays for the duration of the trial period[4]. **Outpatient:** Seven studies mentioned trial implants as an outpatient procedure where patients were discharged home after being deemed stable after implantation with an external pulse generator[1, 5, 6, 8-12]. The rest of the articles did not mention if the trial period was conducted in or out of a hospital setting.
Trial duration *(internally implanted leads, to external pulse generator)*	Varied across studies: From 24 – 48 or up to 72 hours[6], 3/5 – 7 days[1, 4, 5, 7, 10], 7 days[3, 11, 13], 3 – 15 days[12],1 – 3 weeks[14-16] and 15 – 21 days[17]. Most studies reported trial durations that averaged around 3 – 7 days (n = 11 studies).
Measure of successful trial : *On the table*	- Patient feedback regarding coverage / overlap of painful area with paraesthesia [3, 4, 6, 12] - Patient reported a pleasant paraesthesia covering at least 50% of the painful area[11]
Measure of successful trial: *After x days with*	- Three consecutive 'yes' answers to moving to permanent implant[12] (if patients reached 28 days without a clear decision trial was deemed a failure) - VAS scores[3, 12]

external pulse generator	- Functional scores: Oswestry[3], 2 points or greater improvement on Roland-Morris Disability Questionnaire[18] - Quality of life scores (SF-36, EQ-5D)[17] - Hamilton's scale for depression[17] - >50% pain relief without adverse effects[1, 3, 4, 7, 8, 10, 14, 18] - Less than daily opioid medication use[18] - Patient may not have achieved >50% relief, but reported efficacy was more satisfactory after permanent implantation and functional improvement with SCS therapy[16]
Unsuccessful trial	In one study 44 patients (of n = 122; 65.9%) failed the trial due to unacceptable pain relief in spite of sufficient paraesthesia, other reasons included insufficient paraesthesia or painful or unpleasant sensation or unable to tolerate the procedure (n = 1) [2].
Permanent implant on same day	Two studies discussed proceeding to a permanent implantation on the same day as the on the table trial[9, 11]. The process in one study was that after a successful trial (pleasant paraesthesia covering 50% of the painful area, the p leads were fixed and the IPG implanted[11]. Post operatively the patient remained in hospital for 24 hours then discharged on antibiotics. They were followed up 7 days later. If on the table trial unsuccessful leads removed on same day. Trial included 80 patients (46 FBSS, 34 CRPS).

3.3 Conversion rates

From these studies conversion rates of patients with trial implants opting for a permanent implant ranged from 62 – 82% [1, 9, 17], however if conversion rates are of further interest to the group a separate focused literature search is needed.

There was some variance in when the permanent procedure occurred. One study reported that 41.4% of permanent procedures were performed within 3 months of the percutaneous trial, with 7.38% performed 90 days after trial[2].

3.4 Adverse events

Adverse events fitted into two main categories: technical or hardware related, and clinical / biological, which related to factors to do with the surgery or body reaction to the implant. These are reported in Table 2 below.

There are two important points that should be noted when considering the data:

1. A separate search was not completed for adverse events for SCS, rather it is reported here the common adverse events reported in the 18 articles originally selected for the primary research question regarding trial procedures.
2. For similar reasons outlined in (1) we cannot determine if adverse events are related to a specific type of electrode as information from this group of studies will be biased towards percutaneous leads as the trial procedures predominantly report using percutaneous leads.

If further information on adverse events related to lead type is required for the update of the ACC SCS Guidelines a separate structured search would need to be performed. This was not deemed necessary for the 2018 update. Some further description of adverse events reported across studies can be found in the excel spreadsheet that accompanies this document.

Table 2. Adverse events reported in included articles

Technical / Hardware	Clinical / Biological
• Cable fractures • Lead fractures • Battery depletion • Lead dislocation	• Infection • Abscess around internally implanted pulse generator (IPG) • Subcutaneous hematoma • Cerebrospinal Fluid lead • Decreased efficacy • Lead migration

3.5 Clinical guidelines

Fifteen clinical guidelines were reviewed for guidance related to the recommended characteristics of the trial stimulation procedure for SCS. Five guidelines[19,20,21,22,23] included specific recommendations for the trial procedure and these are outlined in Appendix A.

3.5.1 Overview of recommendations

- There is some variability in the recommendations; however, most include a statement around the necessity of a trial with leads connected to a temporary external stimulator. In all cases further information was provided regarding patient selection criteria in order to be eligible for the trial. As the focus of this scan is the characteristics of the trial stimulation, these have not been extracted from the guidelines.
- Most guidelines do not specifically recommend one type of lead (percutaneous or surgical plate/paddle) for the trial stimulation period. One guideline[20] indicated a preference for the use of temporary percutaneous electrodes for the trial stimulation as a first option; however, this appears to be based on individual patient and clinical factors rather than the comparative performance of either type of electrode. Pros and cons of percutaneous and paddle electrodes were outlined in this guideline and these are summarised in Table 3.
- Trial length is not specified in many of the guidelines but where it is described, recommendations range from 3 days to 2 weeks. The setting for the trial (hospital inpatient or outpatient) was mostly not specified.
- Generally trial success was primarily based on adequate pain relief; additionally, stable or improved functional ability and medication, acceptability of the paraesthesia sensation, and patient satisfaction were also considered important.
- Two guidelines acknowledge limitations in the predictive ability of the trial stimulation results[20, 21]. One suggests there may be value in some cases of an on-table trial followed by immediate implantation with a permanent device if the on-table trial is successful (British Pain Society, 2009). The other (North et al, 2007) notes that while the level of paraesthesia coverage and pain relief can be assessed within a short time of activating the trial stimulation, other characteristics of a successful trial need additional time for assessment, for example, functional ability and medication use, the acceptability of the paraesthesia sensation and use of the device. They therefore recommend a period of 3 – 7 days trial, preferably with domestic use of the trial stimulator included in that period.

Table 3. Pros and cons of percutaneous and paddle trial electrodes identified in North et al (2007)[20]

Percutaneous electrodes	Surgical plate/Paddle electrodes
• Easy access to multiple spinal levels to facilitate mapping of paraesthesia/pain overlap • Relatively inexpensive, insertion and removal is comparatively easy • Opportunity to improve the screening results with the new permanent electrode • Possibility that the permanent implanted electrode will not reproduce the pain/paraesthesia overlap identified through the trial • Higher risk of lead migration	• Required for patients where the epidural space cannot be accessed satisfactorily • Increases incisional pain and potential for infection • Increased screening procedure costs (due to the use of an operating room) but overall reduced cost of hardware • Less risk of lead migration

4 Other points for discussion

- The focus of the search for this document was details around trial implantations for SCS. If further information is required for this guidance on adverse events and conversion rates, a separate literature search is required; this is briefly mentioned in this document as reported from the studies included for the primary research question.

- Reasons for failure of trial stimulation in patients who are otherwise good candidates are poorly understood and could be related to underlying physiology or anatomy[14].

- Most studies showed no significant influence on outcome of trial attributable to gender or age.

- Although implantation of SCS with percutaneous leads is less invasive, there may be advantages to paddle SCS leads (e.g. minimized lead migration and positional effects, they may also provide more consistent coverage)[4].

- There was no specific recommendation to use percutaneous or paddle electrodes for trial stimulation in the included guidelines, however overall there appeared to be a preference for temporary percutaneous electrodes as a first option, unless individual patient and clinical characteristics indicated paddle electrodes should be used.

5 References

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5.1 Appendix A: Summary of clinical guideline recommendations for trial stimulation

Recommendation	General trial guidance	Type of trial	Trial length and setting	Definition of successful trial	Evidence
ANZCA FPM guidance[19]	All patients The screening trial provides important information that will influence the choice of lead and stimulator to be implanted and the optimum stimulator configuration.	External stimulator device temporarily connected to implanted leads	7 – 10 days Setting not specified	Patient-reported pain relief of at least 50% during appropriate (provocative) physical activity Stable or reduced analgesic consumption and improved daily activity, social function and sleep may also be considered as factors indicating benefit.	Evidence-informed position statement
Neuromodulation Therapy Access Coalition (North et al 2007)[20]	For screening trials either a temporary, percutaneous electrode placed with fluoroscopy guidance, or a surgical plate/paddle electrode with a temporary percutaneous extension cable can be used. The choice is determined by individual patient factors and individual clinical factors.	Percutaneous catheter electrode suggested as the first option; surgical plate/paddle electrode as the second option.	3 – 8 days Setting not specified On-table trials followed immediately by implantation of a permanent SCS device are discussed but not considered best practice in most cases	A successful screening trial results in at least 50% patient-reported pain relief despite appropriate provocative physical activity, with stable or reduced analgesic consumption and patient satisfaction	Evidence cited for each recommendation, however it is not clear whether this was identified through a systematic search and appraisal of the literature. Guideline development methodology (AGREE tool) was used to guide the process of developing the recommendations.
British Pain Society (2009)[21] Spinal cord stimulation for the management of pain: recommendations for best clinical practice: Consensus document produced in consultation with	It is common practice to connect electrodes temporarily to external stimulating devices before proceeding to insertion of IPG. This enables a trial period when pain relief, improvement of function, and reduction in medication can be assessed. If trial successful proceed to insertion. Additional comment in the BPS guideline: 8.8 Although a period of trial stimulation has	Surgical or percutaneous electrodes - with a table of recommendations specific to surgically implanted electrodes	No information provided	All patients being considered for SCS must be assessed with regard to physical, psychological, and social functioning.	Primarily based on a systematic review by National Institute of Clinical Excellence (2008)[23]

Society of British Neurological Surgeons	considerable intuitive appeal, the predictive value of a period of trial stimulation is uncertain, and it is well-accepted practice to insert electrodes without trial stimulation. [This doesn't match NICE (2008) recommendation]				
South African Spine Society, Neurological Society of South Africa, South African Society of Anesthesiologists[22]	Electrodes inserted percutaneously or surgically implanted are both described	Electrodes connected temporarily to an external stimulating device	No information	Pain relief, improvement in function, and reduction in medication may be assessed	Based on the British Pain Society guidance and NICE (2008) systematic review
National Institute of Clinical Evidence (2008)[23]	Discussed the benefits and limitations of a trial stimulation and considered, on balance, that permanent implantation should only follow after a successful trial stimulation	Electrodes connected with leads to a temporary external device	No information	Pain relief and tolerability	Systematic review and clinical expertise
Australasian Neurostimulation Working Group guidance[24]	Successful trial screening for duration up to 2 weeks. Too short a trial may mislead success and too long adds potential complications.	External stimulator device	Up to 2 weeks Outpatient setting	Agreed therapy goals e.g. pain relief of at least 50% with appropriate physical activity, improvement in function and/or reduction in medication use	Supported by a grant from Medtronic Australasia