s22

s22

From: s22 @health.gov.au>
Sent: Tuesday, 13 September 2022 3:57 PM
To: s22 @health.gov.au>
Subject: RE: TGA/TAAD matters [SEC=OFFICIAL]

Hi s22
I have attached the ACMD paper attachments in-confidence.

I'd be very interested in having a look at the TAAD Utilisation review, in confidence.

I'll ask s22 and s22 if they would like to/are available to join the meeting.

Thanks
s22

s22

s22 Devices Post Market Reforms & Reviews Section

Medical Devices and Product Quality Division | Health Products Regulation Group
Medical Devices Surveillance Branch
Australian Government Department of Health and Aged Care
T: 02 6289 s22 M: s22 | E: s22 @health.gov.au

Location: Perth
PO Box 100, Woden ACT 2606, Australia

The Department of Health acknowledges the Traditional Custodians of Australia and their continued connection to land, sea and community. We pay our respects to all Elders past and present.

From: s22 @health.gov.au>
Sent: Tuesday, 13 September 2022 3:23 PM
To: s22 @health.gov.au>
Subject: RE: TGA/TAAD matters [SEC=OFFICIAL]

Sounds good.
I'll send an invite.
Re the ACMD submission, could I also look at Attachments 3 and 4? (I have 1&2: the Cochrane review and the Jones et al article).
I'll send you the TAAD Utilisation review, in confidence, FYI. Just in the interests of improving the TAAD/TGA interface. We elaborated on TGA's feedback on the Jones et al study following a discussion with s22 , alongside an analysis of Casemix and MBS data.
The way we integrate our respective pieces of work to get the best whole-of-system outcome is the next phase of the discussion…
Do you think s22 would like to be invited to this meeting?

From: s22 @health.gov.au>
Sent: Tuesday, 13 September 2022 2:53 PM
To: s22 @health.gov.au>
Subject: RE: TGA/TAAD matters [SEC=OFFICIAL]

Hi s22
Tuesday 18 will work for me – will 10am suit you?
Thanks
s22

s22

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From: s22 @health.gov.au>
Sent: Tuesday, 13 September 2022 2:10 PM
To: s22 @health.gov.au>
Subject: RE: TGA/TAAD matters [SEC=OFFICIAL]

Many thanks s22 .
How about the week after ACMD, week beginning 17 Oct, for a meeting?
Tues – Thurs before 3pm works best for me. Do you have a preferred timeslot?
s22

From: s22 @health.gov.au>
Sent: Tuesday, 13 September 2022 12:49 PM
To: s22 @health.gov.au>
Subject: RE: TGA/TAAD matters [SEC=OFFICIAL]

Hi s22
I'd be happy to meet with you and s22 next month after ACMD and also OK to share, in confidence, the ACMD paper on spinal cord stimulators (attached).
Thanks
s22

s22

s22 Devices Post Market Reforms & Reviews Section

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From: s22 @health.gov.au>
Sent: Tuesday, 13 September 2022 12:01 PM
To: s22 @health.gov.au>
Subject: TGA/TAAD matters [SEC=OFFICIAL]

Hi s22
2 things:

1. It would be great to get you and s22 TAAD's post Market Review Section in a meeting together (plus some others). Could we meet for a TAAD/TGA post market meeting sometime? – maybe next month after ACMD?
2. I asked s22 if I could look (in Confidence) at the ACMD submission around spinal cord stimulators. He seemed fine with this though I understand you have ownership of this one. Are you OK with this?

Hope you are well
s22

s22

s22

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Australian Government
Department of Health

Celebrating 100 YEARS OF HEALTH 1921-2021

SPINAL CORD STIMULATORS

SYSTEMATIC REVIEWS SUMMARIES

1. **A review of spinal cord stimulation systems for chronic pain (Verrills, 2016) AUSTRALIAN STUDY**

TGA Assessor summary:

- The most recent systematic and comprehensive review of the effectiveness of SCS in treating chronic spinal pain demonstrated that there is a significant (Level I–II) evidence for SCS as a treatment for lumbar FBSS, where conventional medical management has failed.
- Furthermore, there is now Level I evidence for high-frequency stimulation but only limited evidence for burst stimulation.
- In another recent and extensive review and meta-analysis of conventional SCS, more than half of all patients experienced significant pain relief. The authors observed that this was maintained for a mean follow-up period of 24 months.
- These reviews above demonstrate that traditional SCS is an effective treatment option for a cohort that is notoriously difficult to treat.
- The literature, when viewed historically, must be tempered by the developments in skills, application, and technological advances.
    - Hence, the traditional SCS papers have often reported successful pain relief as an undifferentiated generic pain that is not specific to the site of the primary or greatest pain (eg, back or leg).
    - This observation is important because conventional SCS therapy has historically been prescribed for limb pain and has had only limited success in managing back pain.
    - Recent studies that have included back pain as the primary source have involved HF10 therapy at 10,000 Hz; this therapy has evolved to better capture significant back, leg, and radicular pain.
- Tolerance to SCS has been observed in patients where pulse amplitude needs to be increased to achieve the same analgesic benefit over time and/or efficacy has been lost.
    - Tolerance cannot be predicted
    - Data pertaining to HF10 SCS have demonstrated no tolerance at this point.
- Despite strict criteria for patient selection, a substantial number of patients fail to achieve optimal pain relief with SCS.
    - A number of factors have been identified as possible indicators for treatment failure including tobacco and drug use, age, and lengthy delay between times of original pain onset to SCS implant.
- DRG SCS has been demonstrated as effective in multiple etiologies, including FBSS, CRPS, and chronic postsurgical pain.
    - A recent study reported 1 year outcomes for DRG with overall pain scores reducing from 77.6 to 33.6 ($P<0.005$)
    - Back pain reduced from 74.5 to 39.7 ($P<0.05$), and leg pain reduced from 74.6 to 28.7 ($P<0.0005$).

  - The most compelling pain reduction happened for foot pain with scores reducing from 81.4 to 22.0 (P<0.05).
  - Approximately 60% of the DRG SCS patients reported >50% improvement in their pain, and the pain localized to the back, legs, and feet was reduced by 42%, 62%, and 80%, respectively.
  - Other outcome parameters including quality of life, mood, and satisfaction were improved and maintained throughout the 12 months.
- The Accurate study is a US pivotal RCT between DRG SCS and traditional SCS Medtronic system
  - The largest RCT in the history of CRPS and causalgia, running from 2013 with primary completion estimated for 2018.
  - The sample size for the study is 152; with 76 randomized to DRG SCS and 76 to the control arm using Medtronic traditional SCS.
  - Superiority was demonstrated in the DRG SCS group with 81% of patients achieving >50% pain reduction and meeting the primary endpoint at the 3-month mark, and 74% maintaining that primary endpoint at 12-month follow-up.
  - The traditional SCS arm demonstrated 56% of patients having >50% pain reduction at 3 months and 53% maintaining this through 12 months.
  - It was noted that 70% of patients achieved >80% pain reduction in the DRG group versus 52% in the Medtronic group.
- The Sunburst study ran from 2013-2016.
  - It is a prospective randomized, non-inferiority controlled trial
  - Patients who required to have pre-existing pain scores >6/10 and a >50% pain reduction in a traditional SCS trial using tonic stimulation.
  - The sample size for the study was 121 with 100 people randomized.
  - Analysis demonstrated superiority for burst stimulation over tonic stimulation
- The Senza RCT is a Level I study design run from 2012-2015
  - This is the first-ever RCT of two SCS therapies with patients randomized to HF10 SCS (Senza System) or traditional SCS commercially available, Precision Plus SCS system
  - 198 patients were randomized with 101 to the HF10 SCS group and 97 to traditional
  - Of these, 90 HF10 SCS patients and 81 traditional SCS patients were subsequently implanted.
  - The primary endpoint of >50% back pain reduction at 3 months was achieved in 80.9% of the HF10 SCS group versus 42.5% of the traditional SCS group This met the criteria; At 12 months, this primary endpoint was met in 78.7% versus 51.3% of the patients.
  - Similarly, the primary endpoint for leg pain reduction was met in 80.0% of the HF10 SCS group versus 49.4% of the traditional SCS group
  - The responder rates for >50% leg pain reduction at 3 months was 83.1% in the HF10 SCS group and 55.0% in the traditional SCS group. The 12-month outcome data for the same groups were 78.7% versus 51.3%
  - This study demonstrated superiority of HF10 SCS to traditional SCS in all primary and secondary endpoints that has led to the labeling of HF10 therapy as superior to traditional low-frequency SCS by the FDA

Economical or cost efficiency

- Cost-efficacy studies show that despite significant initial costs, SCS compared with other conventional treatments available to chronic pain patients results in long-term reductions in health care costs, which offset the high initial treatment costs over time.44

Safety and tolerability

- In the literature, SCS is reported as a safe procedure due to its reversible and minimally invasive characteristics.
- Although catastrophic complications are possible, they are very rare.
- However, the incidence of minor complications of SCS has a higher incidence
- The complications are divided into three main categories: mechanical, biological, and technique-related.
    - Complications of a mechanical origin are more common than those of biological origin.
    - Incidence of minor complications 30-40% (readily reversible and generally resolved).
    - Hardware related complications 24-50%
    - Mechanical complications eg lead fracture or disconnection 5-9%
    - Lead migration 0-27%; migration requiring intervention in <5%
    - Implantable pulse generator failure occurred at a reported frequency of 1.7%
    - These complications are minimised by using the appropriate lead, anchoring and suturing techniques; minimising patient movement in first 3 months to allow scarring to form around leads
- One study demonstrated that lead migration of significance and requiring intervention in both the HF10 and traditional SCS arms occurred <5%. This most likely reflects improvements in both lead design and the anchoring systems used
- Biological complications include infection, allergic reaction, pain at implant site, implantable pulse generator seroma, epidural fibrosis, epidural hematoma, dural puncture, and, rarely, neurological injury.
    - The most common biological complication is infection with a rate between 3% and 8%, and the majority of these are superficial.
    - The occurrence of dural puncture is reported as between 0.3% and 2%.
    - Other adverse biological events such as epidural fibrosis, compressive phenomenon, or spinal cord injury, while serious, are rare.

2. Effectiveness of Spinal Cord Stimulation in Chronic Spinal Pain: A Systematic Review (Grider, 2016)

<u>TGA Assessor summary:</u>

- Summary measures included 50% or more reduction of pain in at least 50% of the patients, or at least a 3-point decrease in pain scores and a relative risk of adverse events including side effects.
- Improvement for less than 12 months is considered as short-term and longer than 12 months is considered as long-term.
- Of the 3 randomized trials evaluating SCS, all of them reported effectiveness for short- and long-term relief

Table 4. Results of published studies of effectiveness of spinal cord stimulation in failed back surgery syndrome.

Study	Study Characteristics	Methodological Quality Scoring	Patients	Pain Relief		Results	
				≤ 12 mos.	> 12 mos.	Short-term ≤ 12 mos.	Long-term > 12 mos.
Kapural et al (38,39)	RA, AC	Cochrane:8/12 IPM-QRB: 34/48	SCS = 81 HF10 = 90	55% vs. 80%	55% vs. 80%	P	P
North et al (13)	RA, AC	Cochrane: 7/12 IPM-QRB: 31/48	SCS = 29 Reoperation = 31	52% vs. 10%	52% vs. 10%	P	P
Kumar et al (18,86)	RA, AC	Cochrane: 9/12 IPM-QRB: 32/48	Total = 100 CMM = 48 SCS = 52	18% vs. 48%	18% vs. 48%	P	P
Schultz et al (77)	RA, AC	Cochrane: 7/12 IPM-QRB: 20/48	Manual = 40 Adaptive = 36 Total = 76	U	NA	U	NA
Perruchoud et al (78)	RA, AC	Cochrane: 7/12 IPM-QRB: 23/48	Total = 33 Sham vs HFSCS = 20	N	NA	N	NA
Schu et al (79)	RA, AC	Cochrane: 9/12 IPM-QRB: 24/48	20	P (burst)	NA	U	NA

RA = randomized; AC = Active-control; SCS = spinal cord stimulation; CMM = conventional medical management; vs = versus; P = positive; N = negative; NA = Not applicable; U = undetermined; HF10 = 10 kHz high frequency therapy; HFSCS = high frequency spinal cord stimulation

3. *SYSTEMATIC REVIEW OF EFFICACY OF SPINAL CORD STIMULATION FOR MANAGEMENT OF PAIN IN CHRONIC PANCREATITIS (Ratanake)*

Background: Spinal cord stimulation (SCS) is frequently used to manage chronic pain syndrome in patients with chronic pancreatitis (CP). This systematic review aimed to summarise the indications and effectiveness of SCS in the management of pain associated with CP.

Materials and Methods: A systematic review employing Prisma methodology was performed through interrogation of the PubMed, Medline, EMBASE and Cochrane databases.

Results: Seven studies including sixty-six patients met the inclusion criteria. The patient groups included five case series and two observational cohort studies. The pooled mean age of the study group was 44 years and 23% (15/66) had alcohol induced CP. The SCS leads were commonly placed at the level of T5-6 near the anatomic midline of the spine. Patients reported a pooled mean reduction of visual analogue pain scores of 56% and a pooled mean reduction of morphine equivalent opioid use of 70% at the end of follow-up. In contrast to percutaneous leads, surgical leads showed a broader stimulation pattern, lower stimulation requirement and was associated with reportedly better longterm effectiveness.

Conclusion: This systematic review has shown that the use of SCS in patients with chronic pancreatitis may decrease pain, reduce opioid use and improve functional capacity. Further randomised, controlled trials are required to establish efficacy in the application of SCS for visceral abdominal pain from CP.

TGA Assessor summary:

- SCS *may* reduce pain and opiod use
- Further studies required

4. The Effectiveness of Spinal Cord Stimulation for the Treatment of Axial Low Back Pain: A Systematic Review with Narrative Synthesis (Conger, 2020)

TGA Assessor summary:

- The reviewed studies were found to be heterogenous across patient populations, interventions (different SCS technologies), comparators (low-frequency SCS, conventional medical management, various lead configurations), and outcome measurement tools. For these reasons, meta-analysis of comparative measures of effect such as a proportion ratio or proportion difference was not performed.
- This is the first systematic review to examine the effectiveness of different SCS technologies specifically for long-term reduction of axial LBP in patients with or without concomitant leg symptoms.
- Review included 2 RCTs (four publications), 4 nonrandomized comparative studies, and 9 single-group cohort studies.
- Several studies did not use back pain as the primary outcome (many measured overall pain or leg pain) but did report back pain–specific scores.
  Secondary outcomes included medication use (opioid and nonopioid), measures of patient satisfaction, quality of life, and disability.
- Based on low-quality evidence, 10-kHz SCS appears effective beyond six months for axial LBP reduction in patients with predominantly axial spine pain and in those with mixed axial low back and leg pain.
- Improvements in pain relief, functional improvement, patient satisfaction, and reduced opioid use were seen
- Considering the consistently large magnitude and durable pain reductions observed in these studies, further controlled, investigator-initiated studies with long-term follow-up are needed to investigate the relative effectiveness of 10-kHz SCS on axial LBP compared with continued non neuromodulation management and compared with other SCS technologies to determine relative effectiveness.
- Only one study using burst SCS met inclusion criteria for this review.
    - A small, nonrandomized comparative study of 10-kHz SCS and burst modalities showed similar effectiveness between burst and 10-kHz SCS for the treatment of axial LBP, with similar associated improvement in sleep and physical function, however, this study included only 14 patients.
    - Despite its exclusion
- Previous studies indicate that traditional low frequency SCS is less effective for reducing axial LBP as compared with neuropathic leg pain.
- The PROCESS trial (2007) compared traditional low-frequency SCS to CMM and demonstrated a 48% responder rate for leg pain reduction at six months but failed to achieve meaningful axial LBP reduction.

5. Spinal Cord Stimulation vs Conventional Therapies for the Treatment of Chronic Low Back and Leg Pain: A Systematic Review of Health Care Resource Utilization and Outcomes in the Last Decade (Odonker 2019)

TGA Assessor summary:

- 11 studies meeting inclusion criteria were analyzed, representing 31,439 SCS patients and 299,182 CT patients
    - 6 of 11 studies evaluating SCS vs CT
        - SCS was associated with favorable outcomes and found to be more cost-effective than conventional treatment approaches for chronic low back pain
    - The most common indication for SCS was failed back surgery syndrome (FBSS), which was evaluated in 6 of 11 studies.
        - Other indications included complex regional pain syndrome (CRPS), peripheral arterial disease (PAD), refractory angina pectoris (RAP), chronic back and leg pain, chronic axial low back pain, degenerative disc disease,

radiculitis, neuropathic leg and back pain, and chronic benign pain syndrome.

- Cost Analysis
  - In 6 of 11 studies analysing costs, SCS was associated with favourable outcomes in terms of cost-effectiveness and health resource utilization compared with conventional therapy
- Pain Relief
  - Overall, 3 of 11 studies included pain relief outcomes
  - There was a large discrepancy in reported pain relief outcomes depending on the type of study and population evaluated
  - Some studies suggested that success rate (measured by a >50% improvement in leg pain) of SCS vs conventional treatment at 24 months was 16% vs 21%, respectively
  - Compared with conventional treatment, there was a 2.5-fold reduction in pain scores at six months, although no differences in reported pain scores, opioid use, or physical function were found at 24months
  - One study showed that 51% of patients achieved >50% improvement in leg pain intensity.
  - Another found that the probability of achieving >50% pain relief was 9.3% for CT and 58.5% for SCS
  - Studies among workers' compensation patients generally showed less pain relief from SCS compared with conventional treatments.

- Complications
  - Adverse events associated with SCS were reported in 3 of 11 studies
    - When lumbar surgery was compared with SCS, SCS resulted in a lower complication rate of 8.6% compared with 16.52% for lumbar surgery
    - Types of complications included renal, cardiac, neurological, pulmonary, DVT/PE, systemic infection, and pocket site wound infection.
    - The authors concluded that overall costs between SCS and lumbar surgery were similar, but SCS was associated with fewer complications and improved outcomes
  - Complications were noted as a major contributor to overall SCS expense
    - An annual complication rate of 19%/year for SCS þ CT has been reported
- Quality Assessment and Level of Evidence Results of quality assessment and level of evidence, using the GRADE framework
  - 4 of 11 studies (36%) had moderate-quality evidence and
  - 7 of 11 (64%) had low-quality evidence supporting the primary outcome measures of higher costeffectiveness, higher percent reduction in opioid use, shorter hospitalizations, and lower resource utilization with SCS therapy compared with conventional management
- Risk of Bias Analysis
  - There was high publication bias in 7 of 11 studies (64%) and low publication bias in 4 of 11 studies (36%).
  - The majority of studies did not report any blinding of participants, personnel or outcome assessment, and allocation concealment.
  - Only one study was an RCT, but almost all studies (10/11) had complete data and, as far as estimable, little selective reporting bias

6. Spinal cord stimulation for low back pain (Protocol)

STUDY NOT COMPLETED

Description of the intervention

Spinal cord stimulation (SCS) involves implanting an electrical device in the lower back that generates electrical pulses and delivers them to the spinal cord via electrodes (Kemler 2000). Electrodes are positioned in the dorsal epidural space adjacent to the area of the spinal cord thought to be causing the pain.

The 'leads', containing sets of electrodes, can be implanted via laminectomy or percutaneously. Depending on the location and intensity of the person's pain, a clinician may select from a varying number and type of leads (uni-, bi-, or multi-polar), and parameters of stimulation (amplitude, pulse width, electrode selection). The device requires power from a battery pack implanted under the skin or transcutaneously via a radiofrequency transmitter. Parameters of stimulation can be adjusted wirelessly using a remote control (Mailis-Gagnon 2013).

Before a surgeon implants the device, current protocols usually require a screening period. Leads are temporarily placed percutaneously, and the clinician assesses the individual's response to the stimulation while they continue with usual activities. The screening phase lasts from days to weeks. A positive response is often defined as at least 50% pain relief (Kemler 2000). If the screening phase is positive, a surgeon may offer a laminectomy to permanently implant the stimulator and leads. Batteries for the stimulator systems can be rechargeable (stimulator type is known as a 'rechargeable implantable pulse generator (IPG)') or conventional (known as a 'conventional IPG'). Conventional IPGs require repeat surgeries to replace the battery.

How the intervention might work

The mechanism of action of SCS for low back pain is poorly understood. SCS was originally thought to work via the gate-control mechanism (Melzack 1965), that is, stimulation of part of the spinal cord interrupts transmission of pain-related information to the cortex. However, evidence of the eKects of SCS on the relay of pain-related information at the spinal cord in humans is limited (Meyerson 2000). In addition, SCS does not appear to influence pain in response to an experimentally induced noxious stimulus (Meyerson 2000). Other suggested mechanisms have included inhibition of the sympathetic nervous system (sympatholytic effect) (Kemler 2000), and interrupted transmission of pain-related

nerve impulses by the brain (supraspinal inhibition) (Meyerson 2000). It is unclear whether the mechanism of action differs in people with chronic low back pain, compared to those with leg pain, or those diagnosed with FBSS (Meyerson 2000).

Why it is important to do this review

SCS is thought to be helpful for chronic low back pain, sciatica and FBSS. The National Institute for Health and Care Excellence (NICE) recommends SCS for refractory neuropathic pain (NICE 2020). In 2014, the SCS market was estimated to be valued at 1.3 billion US dollars (USD) (PRWeb 2015). In the USA the average cost of implanting a stimulator is USD 30,000, plus USD 10,000 per annum for maintenance care if the person experiences complications. One study estimated that 12% of people who had SCS experienced at least one complication, such as lead migration or wound infection (Shamji 2015).

Evidence on the benefits and harms of SCS compared with placebo or no treatment, is limited. A Cochrane Review of efficacy in chronic pain was withdrawn because it was out of date (Mailis-Gagnon 2013). Grider 2016conducted a systematic review of SCS for low back pain and focused on a wide range of trials, including those that compared SCS with different stimulation regimens and various other control treatments of unknown efficacy. This made the true efficacy of the procedure difficult to determine. Grider 2016 did find three small trials that compared SCS to no treatment or placebo/sham (160 participants in total). The trials had mixed results. One small trial (n = 40) found no effect on pain intensity at four weeks compared with placebo SCS (device switched oK) (Perruchoud 2013). One hallmark 2007 trial by Kumar and colleagues (n =100) investigating SCS as an addition to 'conventional medical management' found a large effect on leg pain at six months (-26.7 (95% CI -40.4 to -13.0) points on a 100-point scale) (Kumar 2007). Because the 'conventional medical management' was not standardised or provided in a controlled way, the comparison was

essentially between SCS and no treatment.
There have been additional trials since the 2016 review. In 2019, Riogard and colleagues reported on the PROMISE trial (Rigoard 2019). Similar to the trial by Kumar and colleagues (Kumar 2007), PROMISE compared SCS plus 'optimal medical management' with 'optimal medical management' alone. The 'optimal medical management' was not standardised or controlled by the investigators and so the comparison was, once again, essentially between SCS and no treatment. At six months, the between-group difference in low back pain was 1.1 (95% CI 0.6 to 1.6) points on a 0 to 10 scale. The large effect on leg pain previously observed by Kumar and colleagues in 2007 was not replicated: at six months the effect was 1.3 (95% CI 0.7 to 1.9) points on 0 to 10 scale. The SCS Frequency Study, a small study (n = 24) that compared SCS treatment at three different frequencies against 'sham' SCS treatment (device is switched on but not delivering any stimulation), found that some SCS regimens were not superior to sham (Al-Kaisy 2018). In the Riogard trial, 18% of participants experienced a stimulator-related adverse event. New trials are also underway (e.g. MODULATE-LBP (Al-Kaisy 2020)) or have overdue results.
To date, the evidence from trials of SCS suggests that, compared with placebo or no treatment, the effects on low back pain and leg pain are uncertain. Another Cochrane Review is underway, examining the effect of SCS on any pain condition (O'Connell 2020). However, those authors have not planned a subgroup analysis focused specifically on people with low back pain. A focused Cochrane Review will help resolve some of the uncertainty regarding efficacy of SCS for people with low back pain, and help clinicians, people with low back pain and policymakers make decisions based on the best available evidence.

TGA Assessor summary:

- This study is under way but not complete
- Study Objectives:
    1. To assess the benefits and harms of spinal cord stimulators for people with low back pain, with or without leg pain.
- Types of outcome measures:

Major outcome measures

a) Outcomes assessing benefits:
    1. Pain intensity: numeric rating scale (NRS), visual analogue scale, pain severity subscale of brief pain inventory
    2. Function: using various scales/scores
    3. Health-related quality of life: using various scales/scores
    4. Global assessment of efficacy: participant-rated improvement measured as per cent improvement or on categorical scale

b) Outcomes assessing harms:
    1. Proportion of withdrawals due to adverse events
    2. Proportion of participants with adverse events: any adverse events reported (e.g. cardiovascular events, worsening of pain, fatigue, etc.)
    3. Proportion of participants with serious adverse events (defined as leading to hospitalisation, disability or death)

Minor outcomes

a) Medication use: number and proportion of participants taking any pain medication, daily dose of opioids as a morphine equivalent dose, or as reported in trials
b) Health care use: number of visits to any healthcare provider for care related to participant's back pain or management of the SCS, or both
c) Work status: number and proportion of participants reported to have returned to work, work absences,or as reported in trials

7. **A Systematic Review of the Cost-Utility of Spinal Cord Stimulation for Persistent Low Back Pain in Patients With Failed Back Surgery Syndrome (McClure 2020)**

TGA Assessor summary:

SCS Technology and Cost-Effectiveness

- The types of delivery system used and the frequency and tonicity of the stimulation provided by the device are under heavy development. The use of a more novel paddle design and configuration has shown superior outcomes compared to traditional electrode size and placement.
- Other technological improvements include the use of SCS devices that provide stimulation at much higher frequencies (10 000 vs. 50-100Hz).
- A recent randomized trial demonstrated that not only do patients prefer the higher frequency SCS devices' lack of paraesthesia compared to traditional stimulation devices, the higher frequency devices also provide superior and more durable pain relief.
- A different stimulation method that also seemingly improves upon traditional stimulation methods provides SCS in a burst pattern rather than tonic stimulation.
- The burst stimulation method is more novel than the high frequency method. As such, studies assessing its efficacy at time points greater than a year remain unpublished.
- Literature that examined the cost-effectiveness of these more novel devices was not found.
- An improvement in SCS cost-effectiveness would result from prolonging the battery life of non-rechargeable devices. As it currently stands, the published literature that compared the cost-effectiveness of non-rechargeable and rechargeable devices showed a slight benefit to rechargeable devices. This is largely due to having fewer replacements over the patient's lifetime and the associated surgical costs.
- The industry standard device longevity for non-rechargeable devices is *4.5 years. If a non-rechargeable device does not require replacement until after 4.5 years from initial implantation, it becomes more economical to utilize compared to the rechargeable models, given the initial device costs are similar. As such, if the cost of non-rechargeable devices could be maintained while simultaneously improving battery life, this would further improve cost-effectiveness of SCS devices.

Improving SCS Cost-Effectiveness With Refined Patient Selection

- An alternative method to improving the cost effectiveness of SCS devices is further refining patient selection.
- Several studies have analysed this; however, most of them utilize rather small sample sizes. Combining the findings from these studies, an ideal responder would not use tobacco, be of normal weight, and be free of psychiatric comorbidities other than anxiety.
- The data surrounding which age group might better respond to SCS for LBP is mixed.
- North et al found that patients who failed SCSdi and crossed over to re-operation failed to achieve adequate pain relief. This cross-over resulted in inferior outcomes for patients of lesser pain-relief achieved and lower patient satisfaction, both coming at higher costs as well; a patient who did not respond to SCS and underwent subsequent re-operation ended up costing more than double the average patient who just had re-operation and over 5 times the amount of a patient just receiving SCSdi.

8. **Systematic Review of Research Methods and Reporting Quality of Randomized Clinical Trials of Spinal Cord Stimulation for Pain (McNicol 2021)**

TGA Assessor summary:

- Review of 46 studies identified deficiencies in both reporting and methodology.

9. The Role of Spinal Cord Stimulation in Reducing Opioid Use in the Setting of Chronic Neuropathic Pain (Smith, 2022)

TGA Assessor summary:

- The 17 studies examined in this review illustrate the ability of SCS to aid in the reduction of opioid use over a wide range of preimplantation doses at 12 months post implantation.
- 6 of the studies included showed 46% to 71.4% of participants were able to reduce their daily opioid dose from 25% to 64% from their preimplantation dose
- Likewise, 7 from 9 studies showed that participants were able to reduce their daily opioid dose from 20% to 48.6% from their preimplantation dose, with one study showing only a 7% dose reduction
- In a systematic review of 5 trials totaling 489 patients, Pollard and colleagues found that SCS patients were more likely to reduce their opioid consumption than patients using medical therapy alone.
- In a large, retrospective study of 5476 patients, Sharan et al found that > 91% of patients kept their implant over all opioid doses at 1 year, with the majority of patients maintaining or decreasing opioid dosage.
- The success of SCS in supporting the reduction in opioid dose is connected with its ability to reduce chronic pain.
- 6 of the 17 studies provided a percentage of patients who were able to discontinue opioid use at 12 months post implantation
    - These percentages varied from 1.5% to 42.8%.
    - In 2 of these studies, a correlation was made between a particular preimplantation opioid dose or dose range and an increased likelihood of discontinuation of opioid use
- Collectively, these studies suggest that a low preimplantation opioid dose may provide patients with the best chance of eliminating opioid use post-SCS implantation.
- Of note, in addition to increasing the possibility of opioid discontinuation, reduction in preimplantation opioid dose may also increase the effectiveness of SCS pain reduction.
- Preimplantation opioid use has been consistently shown to reduce the likelihood of pain remission after SCS.
- The precise reason for this diminution in effectiveness is unknown.
- Studies have shown:
    - At 1 and 2-year follow-up after SCS implantation, system explant was significantly associated with opioid use
    - Others have demonstrated that patients who do not use opioids before SCS implantation experience superior outcomes as compared with those patients who used opioids before surgery.
- SCS is an effective treatment for many types of chronic pain, with significant advantages over medical management alone in both pain relief and side effect profile.
- SCS can also lead to reduction or elimination of chronic opioid use.
- Current research supports the conclusion that SCS should not be reserved as a therapeutic of last resort, rather it should be considered earlier in the therapeutic process.
- Recent studies have demonstrated that longer pain-to-SCS time has been shown to correspond to a decreased efficacy of SCS, and increasing pain-to-SCS time is also associated with significant increases in health care resource utilization.
- Current studies demonstrate that SCS is most effective when used in patients who are not chronic opioid users before implantation.

FINAL COMMENTS

- The SCS systems are used in quite complex chronic pain scenarios
- It appears that these systems have undergone design changes and improvements over the years, with newer version addressing past issues and concerns
- The high complication rates are acknowledged but the causes of these appear to be multi-factorial in nature e.g Patient selection is crucial; the version of the device used etc
- Non-inferiority studies have shown that new iterations of SCS systems are superior to the older ones
- Although the cost-effectiveness analyses are based predominantly on overseas data, we would expect a similar outcome here
- Further data can be requested from manufacturers to determine if there is any areas of concern for the TGA regarding the numbers and types of complications being encountered in Australia. A comparison can then be made on whether this is consistent with the international experience.
    - It would be helpful is data could be provided for the following: patient demographics; therapy type eg burst/high/low frequency therapy; duration of treatment; numbers of patients who had resolution of symptoms and subsequent removal of SCS; what patients are told to do routinely following surgery; how frequent follow-up reviews are
    - Depending on the data we receive, I anticipate that we would need to also review the IFU/PIL and technique guides to ensure that risks are discussed and mitigated where possible

Spinal Cord Stimulators

Literature Summary

Brief summary:

These devices appear to be a last resort for many cases – the patient populations in the studies usually specified that patients had to be refractory to one or more medications.

The Cochrane review of Dec 2021 is an excellent synopsis of SCS risk.

They found that SCS is associated with complications including infection, electrode lead failure/migration and a need for reoperation/re-implantation. The level of certainty regarding the size of those risks is very low. The authors found very low-certainty evidence that SCS may not provide clinically important benefits on pain intensity compared to placebo stimulation. At six months follow-up their estimates suggest a 4% risk of infection, a 4% risk of lead failure/ displacement and an 11% risk of requiring reoperation/reimplantation. The authors found reports of some serious adverse events as a result of the intervention. These included autonomic neuropathy, prolonged hospitalisation, prolonged monoparesis, pulmonary oedema, wound infection, device extrusion and one death resulting from subdural haematoma.

It appears from initial analysis that the serious complications of neurological adverse events e.g. paralysis, spinal cord hematoma, dural puncture are rare. But lead migration is quite common and does require a surgical procedure to correct. Similarly, in the publication of concern by the group of PhD authors, found that as a proportion of the 'device failure' adverse events, lead migration/fracture was 35%. Rates of explantation vary from study to study. The Cochrane review identified an n=44 study that found 94% of patients had the device explanted at 5 year follow up.

There's a fair few trials on the SENZA device, which I think is 330704 on the ARTG (see below summary table)

Also for the Evoke model (ARTG 336330) (see below summary table)

There's a French registry study including a number of Medtronic models – only 2 years follow up though, funded by Medtronic.

Just looking through the ARTG list of spinal cord stimulators, a lot of devices have been approved recently -2021 and 2020. None have conditions of inclusion on them (suggesting that PMCFs were not underway at the time of approval). Being Class III or AIMD, these devices would have undergone a Clinical review in App Audits and any devices with poor evidence or safety concerns would be questioned. It is possible that older devices are contributing more to the hardware complications reported in the TGA adverse event publication, and whether possibly designs have improved in recent times, however the signal exists.

Article/Authors/Year	Study type/ patients/ sample size/device used	Results	Conclusions	Level of evidence (NHMRC Hierarchy) + Clinical Assessment (benefit/risk/uncertainty)
Spinal Cord Stimulators: An Analysis of the Adverse Events Reported to the Australian Therapeutic Goods Administration Jones et al 2022	Retrospective review of adverse event reports submitted to the TGA between 2012 and 2019 Parallel collection of implantation and explantation numbers of spinal cord stimulators for the same years, using a national health database	520 AE's between 2012-2019 • 484 (93%) rated as serious using NHMRC criteria ○ 73.1% single surgical intervention ○ 10.3% Other ○ 4% Single surgical intervention + IV antibiotics ○ 3.1% multiple surgical interventions ○ 2.5% Single surgical intervention and PO Abx ○ 2.3% admitted to hospital for medical management CTCAE coding • 1% resulted in death • 13% life threatening • 79% severe • 3% moderate • 3% mild 26,786 implanted and 10,702 removed. 4 in every 10 being removed. Most common events: • Device malfunction n=296/56.5% ○ Failures of device N=247/47.1% ○ Migration of the electrical lead/fracture n=87 (35%) ○ Faulty device n=42/17% ○ Poor positioning n=23/9% ○ Unspecified issue with a lead n=19/8% • Pain n=110/21% • Infection/inflammatory reaction n=55/10.5% • Haemorrhage/hematoma n=7/1.3% • Headache n=6/1.1% • Puncture/laceration n=5/1%	Authors conclude: Spinal cord stimulators have the potential for serious harm and each year in Australia, many are removed. In view of the low certainty evidence of their long-term safety and effectiveness, our results raise questions about their role in providing long-term management of intractable pain. Raises the need for a registry to obtain long-term safety and efficacy data	**Level IV – retrospective review** One author has affiliation with Media outlet SMH Limitations • AE data likely underreported – true number likely to be significantly higher than that reported to TGA, therefore likely a significant signal • No info on what the indication was for insertion OR removal • No stratification of adverse events and implantations per device type (multiple SCS on ARTG…) • No information on the timing of the AE in relation to the event • Inability to actually calculate adverse event rates for each device type from this publication • 'Device malfunction/faulty device' needs further explanation

Cochrane Review December 2021 Implanted spinal neuromodulation interventions for chronic pain in adults.	Systematic review 15 published studies in this review that randomised 908 participants. All the included evidence in this review relates to spinal cord stimulation(SCS). Adults ≥ 18 with non-cancer and non-ischaemic pain of longer than three months duration, due to a variety of causes including nerve disease, chronic low back pain, chronic neck pain and complex regional pain syndrome	**Active stimulation v placebo** **Pain intensity** 6 studies (N = 164) demonstrated a small effect in favour of SCS at short-term follow-up. The point estimate falls below our predetermined threshold for a clinically important effect (≥10 points). No studies reported the proportion of participants experiencing 30% or 50% pain relief for this comparison. **SCS + other intervention versus other intervention alone** **Pain Intensity** **Mean difference** 3 studies (N = 303) demonstrated a potentially clinically important mean difference in favour of SCS of -37.41 at short term, and medium-term follow-up and no clear evidence for an effect of SCS at long-term follow-up **Proportion of participants reporting ≥50% pain relief** An effect was found in favour of SCS at short-term (2 studies, N = 249, RR 15.90, 95% CI 6.70 to 37.74, I2 0% ; risk difference (RD) 0.65 (95% CI 0.57 to 0.74, very low certainty), medium term (5 studies, N = 597, RR 7.08, 95 %CI 3.40 to 14.71, I2 = 43%; RD 0.43, 95% CI 0.14 to 0.73, low-certainty evidence), and long term (1 study, N = 87, RR 15.15, 95% CI 2.11 to 108.91 ; RD 0.35, 95% CI 0.2 to 0.49, very low certainty) follow-up. **Adverse events** At medium-term follow-up, the incidence of lead failure/displacement (3 studies N = 330) ranged from 0.9 to 14% (RD 0.04, 95% CI -0.04 to 0.11, I2 64%, very low certainty). The incidence of infection (4 studies, N = 548) ranged from 3 to 7% (RD 0.04, 95%CI 0.01, 0.07, I2 0%, very low certainty). The incidence of reoperation/reimplantation (4 studies, N =5 48) ranged from 2% to 31% (RD 0.11, 95% CI 0.02 to 0.21, I2 86%, very low certainty). One study (N = 44) reported a 55% incidence of lead failure/displacement (RD 0.55, 95% CI 0.35, 0 to 75, very low certainty), and a 94% incidence of reoperation/reimplantation	SCS is associated with a reasonably common incidence of procedure and device-related complications including infection, lead failure or displacement, and the need for further surgical procedures. For example, at six months follow-up our estimates suggest a 4% risk of infection, a 4% risk of lead failure/ displacement and an 11% risk of requiring reoperation/reimplantation.	Level I – systematic review of RCTs The authors found very low-certainty evidence that SCS may not provide clinically important benefits on pain intensity compared to placebo stimulation. SCS is associated with complications including infection, electrode lead failure/migration and a need for reoperation/re-implantation. The level of certainty regarding the size of those risks is very low. Benefits may not outweigh risks to patients but based on low-certainty evidence. Short term follow up in most studies so unknown long term performance (pain relief) and potential for increased risk of side effects

		(RD 0.94, 95% CI 0.80 to 1.07, very low certainty) at five-year follow-up. The authors found reports of some serious adverse events as a result of the intervention. These included autonomic neuropathy, prolonged hospitalisation, prolonged monoparesis, pulmonary oedema, wound infection, device extrusion and one death resulting from subdural haematoma.		
A review of spinal cord stimulation systems for chronic pain (Verrills, 2016)	Narrative review of spinal cord stimulation systems for chronic pain	Mechanical complications include lead fracture or disconnection, which has a reported incidence of between 5% and 9%; lead migration has a reported incidence between 0% and 27%; implantable pulse generator failure occurred at a reported frequency of 1.7%. The most common biological complication is infection with a rate between 3% and 8%, and the majority of these are superficial The occurrence of dural puncture is reported as between 0.3% and 2%. Other adverse biological events such as epidural fibrosis, compressive phenomenon, or spinal cord injury, while serious, are rare.	Significant evidence exists for traditional SCS as a safe, clinical, and cost-effective treatment for many chronic pain conditions. Indeed, the field is rapidly evolving, and there is now Level I evidence for newer techniques including HF10 SCS and DRG SCS, which demonstrate dramatic improvements in overall efficacy in reducing pain in specific conditions, including failed back surgery, back pain, neuropathic leg pain, CRPS, and causalgia.	N/A narrative review Conflicts: Paul Verrills is a consultant to NEVRO Corp and St Jude Medical Advisory and peer to peer teaching. Comments: • Incidence of minor complications 30-40% (readily reversible and generally resolved). • Hardware related complications 24-50% • Mechanical complications eg lead fracture or disconnection 5-9% • Lead migration 0-27%; migration requiring intervention in <5% These complications are minimised by using the appropriate lead, anchoring and suturing techniques; minimising patient movement in first 3 months to allow scarring to form around leads
Effectiveness of Spinal Cord Stimulation in Chronic Spinal Pain: A Systematic Review (Grider, 2016)	To assess the role and effectiveness of spinal cord stimulation (SCS) in chronic spinal pain.	Results showed 6 RCTs with 3 efficacy trials and 3 stimulation trials. There were also 2 cost effectiveness studies available. Based on a best evidence synthesis with 3 high quality RCTs, the evidence of efficacy for SCS in lumbar FBSS is Level I to II. The evidence for high frequency stimulation based on one high quality RCT is Level II to III.	There is significant (Level I to II) evidence of the efficacy of spinal cord stimulation in lumbar FBSS; whereas, there is moderate (Level II to III) evidence for high frequency stimulation; there is limited evidence for adaptive stimulation and burst stimulation.	Level I – systematic review of RCTs Conflicts: multiple: Grider – Medtronic and Intralink Spinal; Vallego – Cephalon/Teva, Nevro; Christo – Medtronic and Boston Scientific There is level 1 evidence for efficacy of SCS in lumbar FBSS (failed back surgery syndrome)

		Based on a lack of high quality studies demonstrating the efficacy of adaptive stimulation or burst stimulation, evidence is limited for these 2 modalities.	Limitations: The limitations of this systematic review continue to require future studies illustrating effectiveness and also the superiority of high frequency stimulation and potentially burst stimulation.	Did not consider adverse events
SYSTEMATIC REVIEW OF EFFICACY OF SPINAL CORD STIMULATION FOR MANAGEMENT OF PAIN IN CHRONIC PANCREATITIS (Ratanake)	Only abstract available This systematic review aimed to summarise the indications and effectiveness of SCS in the management of pain associated with chronic pancreatitis.	7 studies including 66 patients met the inclusion criteria. The patient groups included five case series and two observational cohort studies. The pooled mean age of the study group was 44 years and 23% (15/66) had alcohol induced CP. The SCS leads were commonly placed at the level of T5-6 near the anatomic midline of the spine. Patients reported a pooled mean reduction of visual analogue pain scores of 56% and a pooled mean reduction of morphine equivalent opioid use of 70% at the end of follow-up. In contrast to percutaneous leads, surgical leads showed a broader stimulation pattern, lower stimulation requirement and was associated with reportedly better longterm effectiveness.	This systematic review has shown that the use of SCS in patients with chronic pancreatitis may decrease pain, reduce opioid use and improve functional capacity. Further randomised, controlled trials are required to establish efficacy in the application of SCS for visceral abdominal pain from CP.	Level IV – systematic review of observational studies TGA Assessor summary: SCS may reduce pain and opiod use Further studies required No information on adverse events/safety Low quality evidence Small numbers of patients, compatible with the atypical indication (chronic pancreatitis)
The Effectiveness of Spinal Cord Stimulation for the Treatment of Axial Low Back Pain: A Systematic Review with Narrative Synthesis (Conger, 2020)	Systematic review. Patients: aged 18 with axial LBP with or without accompanying leg pain. Intervention: Traditional low-frequency, burst, or high-frequency SCS. Comparison. Sham, active standard of care treatment, or none. Outcomes: The primary outcome was 50% pain improvement, and the secondary outcome was functional improvement	Randomized or nonrandomized comparative studies and nonrandomized studies without internal controls were included. 17 publications included. For high-frequency SCS, the only level 1 study showed that 79% (95% confidence interval ¼ 70–87%) of patients reported 50% pain improvement. For low-frequency SCS, the only level 1 study reported no categorical data for axial LBP-specific outcomes; axial LBP improved by a mean 14mm on the visual analog scale at six months.	According to GRADE, there is low-quality evidence that high-frequency SCS compared with low-frequency SCS is effective in patients with axial LBP with concomitant leg pain. There is very low-quality evidence for low-frequency SCS for the treatment of axial LBP in patients with concomitant leg pain. There is insufficient evidence addressing the effectiveness of burst SCS to apply a GRADE rating.	Level I – systematic review including RCTs TGA Assessor summary: • Only low quality evidence of effectiveness of high frequency vs low frequency SCS for LBP with leg pain • Only low quality evidence for low frequency SCS for back pain with leg pain • No information on adverse events/safety No funding sources Conflicts of interest: Zachary L. McCormick, MD, serves on the Board of Directors of the

	measured six or more months after treatment intervention.			Spine Intervention Society. Mark A. Mahan, MD, is a consultant for Joimax and Axogen.
Spinal Cord Stimulation vs Conventional Therapies for the Treatment of Chronic Low Back and Leg Pain: A Systematic Review of Health Care Resource Utilization and Outcomes in the Last Decade (Odonker 2019)	The purpose of this review is to critically appraise the literature for evidence supporting the health care resource utilization and cost-effectiveness of spinal cord stimulation (SCS) compared with conventional therapies (CTs) for chronic low back and leg pain.	11 studies met inclusion criteria, representing 31,439 SCS patients and 299,182 CT patients. In 8/11 studies, SCS was associated with favorable outcomes and found to be more cost-effective than CT for chronic low back pain. Compared with CT, SCS resulted in shorter hospital stays and lower complication rates and health care costs at 90 days. SCS was associated with significant improvement in health-related quality of life, health status, and quality-adjusted life-years. Adverse events associated with SCS were reported in 3/11 studies When lumbar surgery (N=16,060) was compared with SCS (N=395), SCS resulted in a lower complication rate of 8.6% compared with 16.52% for lumbar surgery Another study looking at 196 SCS cases reported hardware malfunction in 45 patients, infection in 10 patients, and subcutaneous hematoma in eight patients An annual complication rate of 19%/year for SCS + CT has been reported and corroborates prior reports citing an 18%/year complication rate after SCS implantation	For the treatment of chronic low back and leg pain, the majority of studies are of fair quality, with level 3 or 4 evidence in support of SCS as potentially more cost-effective than CT, with less resource expenditure but higher complication rates. SCS therapy may yet play a role in mitigating the financial burden associated with chronic low back and leg pain.	Level I – systematic review of RCTs, and other studies TGA Assessor summary: • Mainly Level 3 or 4 evidence showing evidence which supports cost-effectiveness of SCS in chronic lower back pain and leg pain • Higher complication rates with SCS noted • No conflicts, no funding sources to declare
A Systematic Review of the Cost-Utility of Spinal Cord Stimulation for Persistent Low Back Pain in Patients With Failed Back Surgery Syndrome (McClure 2020)	A systematic review was conducted inclusive of all publications in the Medline database and Cochrane CENTRAL trials register within the last 10 years (English language only) assessing the cost-effectiveness of Spinal Cord Stimulator device implantation (SCSdi) in patients	The majority of reviewed publications that analyzed cost-effectiveness of SCSdi compared to conventional medical management (CMM) or re-operation in patients with failed back surgery syndrome (FBSS) showed an overall increase in direct medical costs; these increased costs were found in nearly all cases to be offset by significant improvements in patient quality of life.	The data suggest that SCSdi provides both superior outcomes and a lower incremental cost: effectiveness ratio (ICER) compared to CMM and/or re-operation in patients with FBSS. These findings are in spite of the fact that the majority of studies reviewed were agnostic to the type of device or innervation utilized in SCSdi. Newer devices utilizing burst or higher	Level IV – systematic review of observational studies Comments: significant funding received by one author in personal fees from various medical device companies Only provides cost effectiveness information, nothing on adverse events or performance

	with previous lumbar fusion surgery.	The cost required to achieve these increases in quality adjusted life years (QALY) falls well below $25 000/QALY, a conservative estimate of willingness to pay.	frequency stimulation have demonstrated their superiority over traditional SCSdi via randomized clinical trials and may provide lower ICERs.	The data suggest that SCSdi provides both superior outcomes and a lower incremental cost: effectiveness ratio compared to conventional medical management or re-operation in patients with failed back surgery syndrome
Systematic Review of Research Methods and Reporting Quality of Randomized Clinical Trials of Spinal Cord Stimulation for Pain (McNicol 2021)	Relevant articles were identified by searching the following databases through December 31, 2018: MEDLINE, Embase, WikiStim, The Cochrane Database of Systematic Reviews, and The Cochrane Central Register of Controlled Trials. 46 studies were included. 87% of articles identified a pain related primary outcome. Secondary outcomes included physical functioning, health-related quality of life, and reductions in opioid use. 19 of the 46 studies prespecified adverse events as an outcome, with 4 assessing them as a primary outcome.	11 studies stated that they blinded participants. Of these, only 5 were assessed as being adequately blinded. The number of participants enrolled was generally low (median 38) and study durations were short (median 12 weeks), particularly in studies of angina. 15 studies employed an intention-to-treat analysis, of which only seven specified a method to accommodate missing data. Review of these studies identified deficiencies in both reporting and methodology. The review's findings suggest areas for improving the design of future studies and increasing transparency of reporting.	Useful reporting recommendations for RCTs of SCS for pain For example: These should include: • Study methodology: • Clinical eligibility criteria • Duration of washout in cross-over trials • Extent and methodology of blinding • Methods of randomization and its concealment • Role of screening phase in enrollment of participants • Initial settings and adjustment parameters for SCS units • Allowance of concurrent treatments • Methods to ensure balanced expectation of benefit of both researchers and patients (equipoise) between groups, and also balance of nonintervention treatment between groups (eg, programming time, psychological support, physical activity, rescue meds, etc.)	Level I – systematic review of RCTs TGA Assessor summary: Review of 46 studies identified deficiencies in both reporting and methodology. Significant conflicts of interest and funding sources declared Nothing specific for SCS but it does include a very useful table for criteria to assess in reading RCTs of SCS for pain. (page 12/16)
Treatment-Limiting Complications of Percutaneous Spinal	The study aims to evaluate the long-term implant survival and complications of spinal cord	345 patients were considered candidates for dorsal column stimulation and underwent a trial.	SCS is an effective treatment for chronic noncancer pain. It is a minimally	Level IV TGA Assessor summary:

Cord Stimulator Implants: A Review of Eight Years of Experience From an Academic Center Database (Hayek, 2015)	stimulation (SCS) leading to surgical revision or explant in patients treated for chronic noncancer pain. Retrospective study of all patients who underwent a percutaneous SCS trial followed by implant in an academic pain medicine division by 4 practitioners from 2007-2013 with follow up data through 2014	234 patients were implanted with an implant-to-trial ratio of 67–86% across various chronic pain entities (postlaminectomy syndrome, complex regional pain syndrome, small-fiber peripheral neuropathy, abdominal/pelvic pain, nonsurgical candidates with lumbosacral neuropathy, and neuropathic pain not otherwise specified), with the exception of nonsurgical candidates with lumbosacral neuropathy who had an implant ratio of 43%. The complication rate was 34.6%, with the hardware related being the most common reason, comprising 74.1% of all complications. The revision and explant rates were 23.9% each. The most common reason for explant was loss of therapeutic effect (41.1%).	invasive procedure, safe, and with good long-term outcomes. However, the surgical revision and explant rates are relatively high. As the use of SCS continues to grow, research into the causes of and risk factors for SCS-related complications is paramount to decrease complication rates in the future.	SCS is an effective treatment for chronic noncancer pain. It has good long-term outcomes. The surgical revision and explant rates are relatively high. Dr. Salim Hayek is a paid consultant for Boston Scientific and owns stock option with Neuros Medical
The Role of Spinal Cord Stimulation in Reducing Opioid Use in the Setting of Chronic Neuropathic Pain (Smith, 2022)	Systematic review of literature from PubMed, Web of Science, and Ovid Medline search of “opioid” and “pain” and “spinal cord stimulator.” Inclusion criteria included original research providing data on SCS preimplantation opioid dosing and 12 months postimplantation opioid dosing or that correlated specific preimplantation opioid dose or opioid dose cutoff with significantly increased likelihood of opioid use discontinuation at 12 months postimplantation.	Systematic review of the literature yielded 17 studies providing data on pre-SCS and post-SCS implantation dose and 4 providing data on the preimplantation opioid dose that significantly increased likelihood of opioid use discontinuation at 12 months postimplantation. Data from included studies indicated that SCS is an effective tool in reducing opioid dose from preimplantation levels at 12 months postimplantation. Data preliminarily supports the assertion that initiation of SCS at a preimplantation opioid dose of ≤ 20 to ≤ 42.5 morphine milligram equivalents increases the likelihood of postimplantation elimination of opioid use.	SCS is an effective treatment for many types of chronic pain and can reduce or eliminate chronic opioid use. Preimplantation opioid dose may impact discontinuation of opioid use postimplantation and the effectiveness of SCS in the relief of chronic pain. More research is needed to support and strengthen clinical recommendations for initiation of SCS use at lower daily opioid dose.	Level III-IV – systematic review of observational studies TGA Assessor summary: SCS is an effective treatment for many types of chronic pain and can reduce or eliminate chronic opioid use. No information on adverse events
Efficacy and Safety of 10 kHz Spinal Cord Stimulation for the Treatment of Chronic Pain: A Systematic Review and Narrative	In total, 16 articles were eligible for inclusion; 15 reported effectiveness outcomes and 11 presented safety outcomes.	Mean pain relief was >50% in most studies, regardless of follow-up duration. Responder rates ranged from 67–100% at ≤12 months follow-up, and from 46–76% thereafter. 32–71% of patients decreased opioid or nonopioid analgesia intake. Safety:	Complication incidence rates were consistent with other published SCS literature. Findings suggest 10 kHz SCS provides safe and durable pain relief in pragmatic populations of chronic pain patients. Furthermore, it may decrease opioid requirements, highlighting the	Level IV - Systematic review of retrospective case series Only reviewed PubMed Low bar for included studies “if the clinical outcome or safety data were collected retrospectively from at least three human

Synthesis of Real-World Retrospective Studies 2021	Patients: heterogenous group. various conditions Device: Senza® 10 kHz SCS system (Nevro Corp., Redwood City, CA, USA)	• Lead migration: 0-7.1% for leads in thoracic region and 4.3-18.2% for leads in cervical area • Infection: 0-13% • Pain over site of implantable pulse generator: 0-27.3% • Insufficient pain relief/nonresponders/treatment failure: 0-15.8% • Lead fracture: 0-2.6% • Neurological injury: neuro deficit not reported by any study. • System explantation: 3.7 – 5%	key role 10 kHz SCS can play in the medium-term management of chronic pain.	subjects implanted with a Senza® 10 kHz SCS system. The minimum follow-up period was 3 months." Low quality evidence for safety and effectiveness
Effect of High-frequency (10-kHz) Spinal Cord Stimulation in Patients With Painful Diabetic Neuropathy 2021	N=216 prospective, multicentre, open-label, randomised controlled trial comparing 10kHz spinal cord stimulation with the SENZA-PDN to medical management in painful diabetic neuropathy Patients with PDN for >1 year refractory to gapapentinoids and at least 1 other analgesic class SENZA-PDN 6-month follow up and optional crossover at 6 months	The prespecified primary end point was percentage of participants with 50% pain relief or more on VAS without worsening of baseline neurological deficits at 3 months. The primary end point assessed in the intention-to-treat population was met by 5 of 94 patients in the CMM group (5%) and 75 of 95 patients in the 10-kHz SCS plus CMM group (79%; difference, 73.6%; 95% CI, 64.2-83.0; P < .001). There were no study-related AEs reported for the CMM group 18 AEs reported among 14 patients in the 10-kHz SCS plus CMM group: • 3 study-related AEs for infection, 2 for wound dehiscence, and 1 for impaired healing among 5 of 90 patients (6%). • Of 90 total implanted patients, 2 (2%) required explant. • There were no stimulation-related neurological deficits in the 10-kHz SCS plus CMM group.	Patients with painful diabetic neuropathy with inadequate pain relief despite best available medical treatments should be considered for 10-kHz spinal cord stimulation. Substantial pain relief and improved health-related quality of life sustained over 6 months demonstrates 10-kHz SCS can safely and effectively treat patients with refractory PDN.	Level II - RCT Short follow-up – 6 months only
Complications of Spinal Cord Stimulation and Peripheral Nerve Stimulation Techniques: A Review of the Literature 2016	A review of the major recent publications in the literature on the subjects of spinal cord, occipital, sacral and peripheral nerve field stimulation Multiple databases searched but no information on the number of studies included	The incidence of complications reported varies from 30% to 40% of patients affected by one or more complications. Incidence of complications varied depending on the study: Lead migration: mean 15.49%, range 2.1-27% Lead fracture and malfunction: mean 6.37%, range 0-10.2% Implant-related pain: mean 6.15%, range 0.9-12% Infection: mean 4.89%, range 2.5-10% Battery failure: range 1.7-10.2%	Spinal cord and peripheral neurostimulation techniques are safe and reversible therapies. Hardware-related complications are more commonly observed than biological complications. Serious adverse events such as neurological damage are rare. The rate of development of complications is governed by factors	N/A – narrative review This publication was cited in the 2022 TGA adverse events data analysis No conflicts, no funding sources

		Device removal: 0-47% Dural puncture: 0-0.3% Neurological injury: major neurological deficit 0.25%, 0.14% limited motor deficit, 0.013% autonomic changes, 0.1% sensory deficit in a sample of 44,587 cases Factors affecting the rate of occurrence of complications: • Location of the lead • Epidural vs extra-spinal position of the lead • Relative novelty of a technique and operating surgeon's experience • Hardware appropriateness for the procedure • Reporting of complications	such as the lead position in the spine or periphery, the experience of the surgeon and the availability of custom-made equipment for the technique.	
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 2015	N=198 subjects with both back and leg pain Multicenter, randomized, controlled, pivotal trial Comparing high frequency (HF) SCS to conventional SCS An investigational HF10 therapy system (Senza® System; Nevro Corp., USA)	Responders (the primary outcome) were defined as having 50% or greater back pain reduction with no stimulation-related neurological deficit. At 3 months, 84.5% of implanted HF10 therapy subjects were responders for back pain and 83.1% for leg pain, and 43.8% of traditional SCS subjects were responders for back pain and 55.5% for leg pain ($P < 0.001$ for both back and leg pain comparisons). The relative ratio for responders was 1.9 (95% CI, 1.4 to 2.5) for back pain and 1.5 (95% CI, 1.2 to 1.9) for leg pain. The superiority of HF10 therapy over traditional SCS for leg and back pain was sustained through 12 months ($P < 0.001$). HF10 therapy subjects did not experience paresthesias. No stimulation-related neurological deficits in either treatment group. The most common study-related AEs were implant site pain (in 11.9% of HF10 therapy subjects and 10.3% of traditional SCS subjects) and uncomfortable paresthesia (in 0.0% of HF10 therapy subjects and 11.3% of traditional SCS subjects). Lead migration resulting in surgical revision occurred in 3.0% of HF10 therapy subjects and 5.2% of traditional SCS subjects	The study is the first pivotal study in the history of SCS to provide comparative safety and effectiveness data between two SCS systems, providing long-term outcomes for both back and leg pain.	Level II – RCT Benefit for high frequency SCS over conventional SCS Limitations: Multiple conflicts of interest declared by authors Confounding effect of analgesics allowed during the trial Investigators and subjects were not masked to the assigned treatment group Short follow-up 12 months

Pain Relief and Safety Outcomes with Cervical 10 kHz Spinal Cord Stimulation: Systematic Literature Review and Meta-analysis 2021	Systematic literature search including studies reporting outcomes for cervical 10 kHz SCS 15 studies included: 8 retrospective observational studies, 4 prospective single-arm studies, 2 case reports, and 1 post-hoc sub-analysis that combined the data from two of the prospective observational studies Patient population: upper limb and/or neck pain, neuropathic limb pain, headache/migraine, CRPS. Senza® SCS system	Primary outcome measures: magnitude of change in pain from baseline to follow-up, the proportion of subjects achieving a 50% reduction in pain, and adverse events related to the device or procedure. **Performance**: The proportion of patients who achieved ≥ 50% pain reduction was 83% (95% CI 77–89%) in both the FE and RE models. The proportion of patients who reduced/eliminated their opioid consumption was 39% (95% CI 31–46%) in the FE model and 39% (95% CI 31–48%) in the RE model. **Safety**: Pain or discomfort with the implant: 2-27% of patients Lead migration: incidence 0-14% Surgical revision rates: 0-29% Explantation: 0-13% Neurological/paraesthesia: 0% of patients in included studies	Findings suggest 10 kHz SCS is a promising, safe, minimally invasive alternative for managing chronic upper limb and neck pain.	Level III – systematic review of observational studies **Limitations** - Funded by Nevro Corp - Limited by low quality of included evidence – no RCTs - Heterogenous patient indications
Timing and prevalence of revision and removal surgeries after spinal cord stimulator implantation Negoita, 2018	N=100 retrospective chart review of chronic pain patients presenting with SCS related encounters Johns Hopkins hospital 2011-2018	Out of 100 patients who had SCS implants, we found that 34% of patients underwent revision surgery and 53% of patients had their implant removed. Of the patients who required revision surgeries, the majority (56%) eventually opted for removal of their SCS system. The median time to the first revision surgery was 16 months post implantation and the median time to removal was 39 months post implantation.	Our findings demonstrate that most SCS systems are removed within a few years post implantation, highlighting the clinical need for a more complete understanding of SCS technology in order to refine patient selection criteria.	Level IV Conflicts: WSA is a consultant for Globus Medical and is on the Advisory Board of Longeviti, LLC Funding: PQD was supported by NIH Medical Scientist Training Program Training Grant T32GM007205 Post-implantation surgeries can either be revisions due to device-related complications, which are quite frequent for SCS or complete removal of the SCS system
Progressive Paraplegia from Spinal Cord Stimulator Lead Fibrotic Encapsulation	Case report n=1 Discusses the first reported case of SCS electrode fibrotic encapsulation	61-yr-old man presented with progressive bilateral lower extremity weakness resulting in complete paraplegia, T4YT10 bilateral radicular pain, and bladder and bowel incontinence for 12 mos	SCS implantation is generally a safe procedure, but rare severe late neurologic complications occur, in this case 10 yrs after SCS implantation, and are reported.	N/A case report

Benfield, 2016	in the thoracic spine occurring 10 yrs after SCS placement causing progressive paraplegia, thoracic radiculopathy, and neurogenic bladder and bowel in the United States.	The computed tomographic myelogram indicated increased dorsal epidural soft tissue around SCS leads at approximately T7Y9 spinal cord level, consistent with focal fibrosis and granulation tissue with an interval increase in spinal canal stenosis. Neurosurgery performed posterior decompressive T7Y9 laminectomies with removal of SCS electrodes and battery. The 3.6 x 3 x 1.1 cm piece of tissue encapsulating the SCS electrodes was soft tissue with acute and chronic inflammation with unremarkable bone and cartilage He is now a home ambulator with a walker but still requires occasional assistance with transfers and use of a manual or power wheelchair in the community and occasionally within his home. There was resolution of his bowel incontinence but no change in his neurogenic bladder, which required a Foley catheter.	Patients with SCS presenting with loss of pain relief and/or worsening neuromuscular examination need to be urgently evaluated for late complications regarding SCS implantation causing cord compression and spinal stenosis at the level of the SCS electrode.	
Infection Rate of Spinal Cord Stimulators After a Screening Trial Period. A 53-Month Third Party Follow-up Rudiger, 2010	Retrospective chart review of 84 patients with SCS implantations between 2004 to 2008 with a trial period lasting 1-3 weeks United Kingdom	During the trial one infection (1.2%) occurred with removal of the SCS leads. Three infections (3.6%) occurred after the second stage and were successfully treated with antibiotics. No full implant was explanted due to infection. The more skilled/experienced operator had a lower infection rate (1.8%) than the less skilled/experienced (13%).	Our infection rate (4.8%) compared favorably with our previous survey (7.5%). The reduced number of SCS infections is likely to be due to: strict asepsis, double layer hydrocolloid dressing during the trial, prophylactic antibiotics, operator experience, and patient education. Two-stage procedures with extended trials do not seem to increase the incidence of SCS infections.	Level IV No funding or conflicts Statistics from article: Serious complications associated with SCS implants, e.g., epidural hematoma (0–0.3%), cerebrospinal fluid leak (0.3–0.5%), permanent neurological harm (paralysis = 0.03%) and death, are rare More commonly lead migration (7–21.5%) or damage (6–9%), malfunction of the equipment or failure (4.5–10%), and insufficient pain relief during a trial period (17–25%) occur (3,7–10). The rate of infections associated with the implantation of an SCS is quoted as 2.5–12%

				SCS device-related infections could lead to neurological harm due to epidural abscesses or meningitis (<1%).
Epidural Hematomas After Removal of Percutaneous Spinal Cord Stimulator Trial Leads Giberson, 2014	2 case reports of spinal epidural hematoma formation Patient 1: chronic pain of right lower extremity Patient 2: chronic severe low back pain	Two patients developed spinal epidural hematomas shortly after removal of their percutaneous trial leads and required multilevel laminectomies for evacuation of the hematoma. Patient 1 reported taking aspirin the morning that his leads were pulled, whereas patient 2 had not taken aspirin in the 7 days before commencing his trial. There were 2 days between identification and evacuation of patient 1's hematoma, and he did not fully recover from the injury to his spinal cord. Patient 2 underwent surgery immediately with complete resolution of his symptoms	American Society of Regional Anesthesia and Pain Medicine guidelines state that nonsteroidal anti-inflammatory drugs do not significantly increase the risk for epidural hematoma with neuraxial anesthesia and, therefore, there is no need to discontinue these drugs before epidural or spinal anesthesia. We suggest that these guidelines may not be appropriate for neuromodulatory techniques that likely subject the surrounding vasculature to more trauma than neuraxial anesthesia.	N/A case reports Authors recommend discontinuing NSAIDs, particularly aspirin, prior to SCS implantation Statistics from article: The actual incidence of hematomas is unknown, but it is believed to be a rare complication, occurring in approximately 0.2% to 0.3% of cases. 5 case reports of epidural hematomas associated with SCS have been published
Successful removal of permanent spinal cord stimulators in patients with complex regional pain syndrome after complete relief of pain Lee, 2019	10-year retrospective study was performed on patients who had received the permanent implantation of an SCS and had removed it 6 months after discontinuation of stimulation, while halting all medications for neuropathic pain. Age, sex, duration of implantation, site and type of CRPS, and their return to work were compared between the removal and non-removal groups.	Five (12.5%, M/F = 4/1) of 40 patients (M/F = 33/7) successfully removed the permanent implant. The mean age was younger in the removal group (27.2 ± 6.4 vs. 43.5 ± 10.7 years, P < 0.01). The mean duration of implantation in the removal group was 34.4 ± 18.2 months. Two of 15 patients (13.3%) and 3 of 25 patients (12%) who had upper and lower extremity pain, respectively, had removed the implant. The implants could be removed in 5 of 27 patients (18.5%) with CRPS type 1. All 5 patients (100%) who removed their SCS returned to work, while only 5 of 35 (14.3%) in the non-removal group did.	Even though this study had limited data, younger patients with CRPS type 1 could remove their SCSs within a 5-year period and return to work with complete pain relief	Level IV – retrospective chart review Comments: No conflicts/funding A minority of patients with CRPS have had the SCS removed, with complete resolution of pain and been able to return to work
Improving care of chronic pain patients with spinal cord	We reviewed literature evidence in PubMed on pain relief and opioid reduction	Evidence found for the ability of an SCS to reduce opioid usage	Both conventional and 10 kHz SCS are associated with improving clinical outcomes while also reducing	N/A – literature review, narrative review

stimulator therapy amidst the opioid epidemic Gupta, 2020	following spinal cord stimulation (SCS) treatment.	Multiple studies, including RCTs, prospective non randomised and retrospective, cited that demonstrate patient reduction in opioid usage, across a variety of conditions (back, leg, upper limb and neck pain)	opioid use and that 10 kHz SCS may be comparatively safer with no uncomfortable paresthesia.	Advantage of 10kHz SCS is that no paraesthesia is triggered Conflicts: Gupta – funds and serving on scientific advisory boards Statistics from article: Conventional, low frequency SCS, typically delivered at frequencies ranging from 40 to 60 Hz, has been shown to provide effective pain relief in approximately 50% of patients in RCTs High-frequency SCS delivered at 10 kHz has demonstrated superiority in magnitude of pain relief and number of responders as compared with low-frequency SCS in an RCT
Awake vs. Asleep Placement of Spinal Cord Stimulators: A Cohort Analysis of Complications Associated With Placement Falowski, 2010	A retrospective review was performed of 387 SCS surgeries among 259 patients which included 167 new stimulator implantation to determine whether first time awake surgery for placement of spinal cord stimulators is preferable to non-awake placement.	The incidence of device failure for patients implanted using neurophysiologically guided placement under general anesthesia was one-half that for patients implanted awake (14.94% vs. 29.7%). The incidence of device failure for patients implanted under general anesthesia was one half that for patients implanted awake (14.94% vs. 29.7%, $p < 0.03$). The rate of infection was analyzed. There was not a statistically significant differencewhen comparing awake (4.48%) to non-awake (5.7%) placement for rate of infection and therefore the occurrence of infection is not explained by whether wake-up was used at the first surgery	Non-awake surgery is associated with fewer failure rates and therefore fewer re-operations, making it a viable alternative. Any benefits of awake implantation should carefully be considered in the future	Level IV No conflicts
Association Between Pain Scores and Successful Spinal Cord Stimulator Implantation	Retrospective review of 88 patients with SCS trials Examined association between post-SCS pain scores and	Of the total cohort, 79% had successful permanent SCS implantation.	Low pain scores after SCS trial are predictive of successful SCS implants with high sensitivity.	Level IV No funding

Orhurhu, 2019	successful permanent SCS implants	Post-SCS trial pain scores less than or equal to 4.9 had greater than 50% probability of a successful permanent SCS implant (97.14% sensitivity, 44.44% specificity, ROC = 0.71). Post-SCS trial pain scores between 4 and 7 were associated with a significantly higher probability of a successful SCS implant among patients without spine surgery compared with those with a history of spine surgery. Compared with males, females with pain scores between 5 and 7 had a higher probability of a successful SCS implant.	Males and surgical patients with higher pain scores had a lower probability of successful SCS implant than their counterparts. Larger studies are needed to further elucidate this relationship	
High-Frequency Spinal Cord Stimulation at 10 kHz for the Treatment of Complex Regional Pain Syndrome: A Case Series of Patients With or Without Previous Spinal Cord Stimulator Implantation Gill, 2019	Retrospective case series n=13 Patients with Complex Regional Pain Syndrome (CRPS) High Frequency (10kHz) SCS Senza System, Nevro Corp., Redwood City, CA, U.S.A	Thirteen patients were trialed, 12 of whom went on to receive a permanent implant. Of the patients receiving permanent implants, the responder rate (50% pain relief) was 67% (95% confidence interval [CI] 0.34 to 0.90), with an average follow-up period of 12.1 +/- 4.6 months. Of the 5 patients who had sympathetically independent pain, 3 were responders, and of the 7 patients who had sympathetically mediated pain, 5 were responders. There were no adverse events.	This small case series suggests that HF10-SCS may be a viable option for patients with CRPS who have chronic intractable pain, including those who had suboptimal results from traditional SCS	Level IV Suggestion of benefit for patients with CRPS Lack of functional assessment Conflicts of interest: Dr. Simopoulos has served as a consultant for Boston Scientific, St. Jude Medical, and Nevro Corp., and for fellow workshops. Dr. Gill has a research grant from Nevro Corp. for programming optimization
Drivers and Risk Factors of Unplanned 30-Day Readmission Following Spinal Cord Stimulator Implantation Elsamadicy, 2017	The aim of this study was to determine drivers of 30-day unplanned readmission following SCS implantation. Retrospective chart review n=1521 patients who underwent SCS implantation	The primary outcome of interest was the rate of unplanned 30-day readmissions and associated driving factors. A multivariate analysis was used to determine independent predictors of unplanned 30-day readmission after SCS implantation. We identified 1521 patients who underwent SCS implantation, with 113 (7.4%) experiencing an unplanned readmission within 30 days. Baseline patient demographics, comorbidities, and hospital characteristics were similar between both cohorts. The 3 main drivers for 30-day readmission after SCS implantation include: 1) infection (not related to SCS device), 2) infection due to device (limited to only hardware infection) 3) mechanical complication of SCS device.	Our study suggests that infectious and mechanical complications are the primary drivers of unplanned 30-day readmission after SCS implantation, with obesity as an independent predictor of unplanned readmission. Given the technological advancements in SCS, repeated studies are necessary to identify factors associated with unplanned 30-day readmission rates after SCS implantation to improve patient outcomes and reduce associated costs	Level IV Mechanical complications of SCS device found to be a main driver for 30-day readmission Conflict of Interest: Shivanand Lad, MD, PhD, has received fees for serving as a speaker and consultant for Medtronic Inc., Boston Scientific, and St. Jude Medical. He serves as the Director of the Duke Neuro-outcomes Center, which has received research funding from NIH KM1 CA 156687, Medtronic Inc. and St. Jude Medical

		Obesity was found to be an independent predictor of 30-day readmission		
Treatment of Neuropathic Pain and Functional Limitations Associated With Multiple Sclerosis Using an MRI-Compatible Spinal Cord Stimulator: A Case Report With Two Year Follow-Up and Literature Review Provenzano, 2016	To report a case with two years follow-up of neuropathic pain and functional limitations associated with MS effectively treated with an MRI conditional spinal cord stimulator (SCS) system that allowed for spinal imaging. To present a comprehensive literature review of spinal cord stimulator utilization in the treatment of multiple sclerosis Device: Medtronic SureScan MRI conditional SCS system	N=1 case report, patient with MS implanted with SCS after a successful trial At 24 months follow-up, the patient has had a 77% reduction in pain and a 99% reduction in opioid use. He had improvement in reported tactile sensation, spasticity levels, and ambulation. Post-SCS implant, MRI images at 18 months follow-up provided the ability to review the spinal cord with minimal artifact. No new MS documented plaques occurred during this time period. A literature review demonstrated 33 published reports including a total of 496 trialed and 744 implanted patients. Only 3 of the reports occurred after the year 2000	We report the successful treatment of MS-associated pain and functional limitations with an MRI conditional spinal cord stimulator system. The ability to obtain post-implant MRI imaging of not only the brain but also the spinal cord in MS patients allows for the continued need to document and follow disease progression, especially with the advancements in pharmacological therapy.	N/A – case report and narrative literature review SCS use in MS has been limited as MS patients require regular MRI's and SCS devices not always compatible with MRI Conflict of Interest: Dr. Provenzano is a consultant for Halyard Health, Medtronic, St. Jude Medical, and Trevena. Dr. Scott received research grants and honoraria for speaking from Teve Neuroscience, Biogen-Idec, Novartis, and Genzyme
The Parturient With Implanted Spinal Cord Stimulator Management and Review of the Literature Young, 2015	Retrospective review of 7 patients who had an SCS implanted before becoming pregnant Patient indication for SCS = CRPS	Data on these patients before, during, and after labor were collected through chart review and patient interview. Onset of labor varied among the 7 patients (2 preterm and 5 term). Mode of anesthesia for delivery included 4 neuraxial anesthetics, with 3 successfully obtaining an adequate level of anesthesia for delivery. Four general anesthetics were administered for cesarean delivery, one of which included a failed attempt at neuraxial anesthesia. All infants were born healthy. One women developed foot drop post partum	Definitive conclusions cannot be drawn from this small cohort. We believe that management of a parturient with an implanted SCS requires careful planning between all peripartum physicians	Level IV Conflicts/funding not declared

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On another note....where is the TGA review of spinal cord stimulators at?

s22 30/01/2023, 12:41 PM

still going - no news yet unfortunately

You 30/01/2023, 12:42 PM

Thanks. Will you do a final report when its done? Or is it more about findings for individual devices and the actions that follow, documented on the PMR database?

(this is partly about my TAAD colleagues trying to understand the TGA PMR process)

s22 30/01/2023, 12:42 PM

we will have findings for individual devices and can let you know those as they occur

You 14/12/2023, 3:43 PM

Hi s22, just wondering if there are any updates re the TGA PMR of spinal cord stimulators??

s22 14/12/2023, 3:44 PM

Hi s22 unfortunately nothing we can share yet

s22 [redacted]

From: s22 [redacted] @health.gov.au>
Sent: Friday, November 24, 2023 6:46 AM
To: s22 [redacted] @health.gov.au>; s22 [redacted] @health.gov.au>
Subject: RE: Spinal cord stimulators [SEC=OFFICIAL]

Great, thanks s22 [redacted]

From: s22 [redacted] @health.gov.au>
Sent: Friday, 24 November 2023 6:36 AM
To: s22 [redacted] @health.gov.au>; s22 [redacted] s22 [redacted] @health.gov.au>
Subject: RE: Spinal cord stimulators [SEC=OFFICIAL]

Thanks s22 [redacted]

Once the post market team have finalized their regulatory decisions I'm sure we will inform TAAD given that was one of the stimulators for the review.

s22 [redacted]

s22 [redacted]
s22 [redacted]
Director Clinical Surveillance Section
Health Products and Regulation Group
Department of Health and Aged Care
On 24 November 2023 at 4:33:34 am AEST, s22 [redacted] s22 [redacted] @health.gov.au> wrote:

> Thanks s22 [redacted]
> Yes, a check in re PMRs would be great.
> Would be especially good to know if any devices have been taken off the ARTG.
> s22 [redacted]
>
> ---
>
> **From:** s22 [redacted] @health.gov.au>
> **Sent:** Thursday, 23 November 2023 11:19 PM
> **To:** s22 [redacted] @health.gov.au>
> **Cc:** s22 [redacted] @health.gov.au>; s22 [redacted] s22 [redacted] @health.gov.au>
> **Subject:** Spinal cord stimulators [SEC=OFFICIAL]
>
> Hi s22 [redacted]

s22 gave an interesting presentation on the reimbursement side of the medical device journey at the DCES planning day this week.

One of their projects on the horizon is a review of spinal cord stimulators.

This might be a great opportunity for collaboration given the thorough post market review conducted by the TGA this year.

Kind regards,
s22

s22
s22
Medical Devices Clinical Section
Medical Devices Authorisation Branch

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Please note, my work days are Monday (0915-1445), Tuesday (0915-1445), Wednesday (0915-1445), Thursday (0915-1445), Friday (0915-1215).

[SEC=OFFICIAL]

s22 [redacted]

From: s22 [redacted] @health.gov.au>
Sent: Monday, October 24, 2022 4:17 PM
To: s22 [redacted] @health.gov.au>
Subject: (In Confidence) FW: Neurostimulation devices in pain management - new clinical literature [SEC=OFFICIAL]

From: s47F [redacted] @pha.org.au>
Sent: Thursday, 20 October 2022 11:42 AM
To: s22 [redacted] @health.gov.au>
Cc: FLYNN, Elizabeth s22 [redacted] @health.gov.au>
Subject: FW: Neurostimulation devices in pain management - new clinical literature

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s22 [redacted]

In the context of the post listing review (soon to be?) underway, I thought I should draw your attention to some new literature on neurostimulators, at:

https://jamanetwork.com/journals/jama/article-abstract/2797419

This is claimed to be the first robust placebo-controlled trial and it shows quite clearly that the procedure is ineffective (although some of the clinicians have added caveats – see below).

s47F [redacted],

Thanks

s4 [redacted]

From: s47F
Sent: Thursday, 20 October 2022 5:26 AM
To: s47F
Cc: s47F @safetyandquality.gov.au>; DUFFY, Tracey s22 @health.gov.au>; s47F ; s47F ; s47F @pha.org.au>; s47F s22 @health.gov.au>; s47F s47F ; s47F s47F s47F s47F ; s47F ; s47F s47F >; s47F
Subject: Re: Neurostimulation devices in pain management - Notes from the meeting of May 25th, 2022 - not for distribution beyond attendees [SEC=OFFICIAL]

Dear s47F ,

There is also the 2021 Cochrane review of spinal neuromoduluation for chronic pain suggesting lack of efficacy and s47F . It is not looking good on the efficacy front.

Regards

s47F

s47F

From: s47F
Date: Wednesday, 19 October 2022 at 9:47 pm
To: s47F
Cc: s47F @safetyandquality.gov.au>, "DUFFY, Tracey" s22 @health.gov.au>, s47F s47F s47F @pha.org.au" s47F @pha.org.au>, s47F s22 @health.gov.au>, s47F s47F s47F , s47F s47F s47F s47F s47F

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s47F

Subject: Re: Neurostimulation devices in pain management - Notes from the meeting of May 25th, 2022 - not for distribution beyond attendees [SEC=OFFICIAL]

s47F

I think this is a trial of one particular subtype of stimulation pattern ie burst stimulation, for one particular indication. I think it would be premature to dismiss the entire field of neuromodulation based on one study for one possible indication however well done the study.

s47F

Sent from my iPhone

On 19 Oct 2022, at 7:40 pm, s47F wrote:

Dear all,

Things have been very quiet since our meeting, but I thought I should refer you to this spinal cord stimulator trial published today in JAMA which is very relevant to our previous discussions on safety.

https://jamanetwork.com/journals/jama/article-abstract/2797419

It is the first robust placebo-controlled trial and it shows quite clearly that the procedure is ineffective. It would be challenging to justify the risk of harms given the clear lack of benefit.

It would be good to hear what ever happened to this review. Perhaps it needs to be reinvigorated.

Regards

s47F

s47F

From: s47F @safetyandquality.gov.au>
Date: Friday, 8 July 2022 at 2:23 pm
To: "DUFFY, Tracey" s22 @health.gov.au>, s47F , s47F , s47F , s47F @pha.org.au" s47F @pha.org.au>, s47F s47F , s47F s22 @health.gov.au>, s47F , s47F , s47F , s47F s47F , s47F s47F " s47F , s47F
Cc: s47F s47F

Subject: Neurostimulation devices in pain management - Notes from the meeting of May 25th, 2022 - not for distribution beyond attendees [SEC=OFFICIAL]

Good afternoon,

Please find attached the notes from the Neurostimulation devices in pain management meeting held in May and two presentations from that meeting.- thank you for your participation.

If you have any enquiries in regard to the meeting please get in touch.

Thank you

s47F
s47F
s47F
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The Australian Commission on Safety and Quality in Health Care acknowledges the traditional owners of country throughout Australia, and their continuing connection to land, sea and community. We pay our respects to them and their cultures, and to elders both past and present.

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