Real-world outcomes of single-stage spinal cord stimulation in chronic pain patients: A multicentre, European case series

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ARTICLE INFO

ABSTRACT

Background: Spinal cord stimulation (SCS) is effective in treating chronic neuropathic pain. A screening trial is typically conducted prior to implantation to evaluate whether a patient is a good candidate for SCS. However, the need for a screening trial has been debated. We evaluated real-world clinical outcomes in patients who underwent a single-stage procedure to receive SCS therapy (i.e., no screening trial period) (SS-SCS).

Methods: This observational, multicentre, real-world consecutive case series evaluated SS-SCS chronic pain patients. Pain and other functional outcomes were collected as part of standard care by site personnel with no sponsor involvement. Assessments included Numerical rating scale (NRS), Percent Pain Relief (PPR) and EQ-5D-5L (EuroQol 5 Dimensions-5L), recorded prior to SCS and following implantation.

Results: A total of 171 chronic pain patients (mean age: 59.4; 53.2% females) underwent a single-stage procedure (mean last follow-up, 408 days) and were included in the analysis. A 5.0 ± 2.1-point improvement in overall pain was reported at 3 months and sustained until the last follow-up post-implantation (p < 0.0001). At last follow-up, 50.3% (86/171) of patients reported an NRS pain score ≤3. Additionally, quality of life also improved (46.1-point change, from 70.2 to 25) at the last follow-up, based on EQ-5D-5L scores.

Conclusions: In routine clinical practice, SS-SCS can provide significant long-term pain relief and improve quality of life in chronic pain patients. Our results suggest that effective long-term outcomes and success may be achieved without a trial period prior to permanent implantation of an SCS system.

1. Introduction

Spinal cord stimulation (SCS) is an effective treatment in the management of chronic neuropathic pain [1,2]. Typically, patients who have been selected as good candidates are implanted with leads during a first-stage procedure and undergo a temporary trial period to experience SCS therapy using an external test stimulator. Based on the success of their trial period, the neurostimulator is then implanted in a second stage. This practice varies across countries. There is also a wide variability in trial period duration (days to weeks). The utility of a trial period prior to permanent implantation has been debated, particularly with respect to its clinical value (i.e., predictor of SCS success) and its burden on healthcare resources in the treatment of chronic pain [3–5]. In the Trial-Stim study, for example, there were no differences in the primary outcome (mean pain), proportion of pain responders or other secondary outcomes between the trial screening and no trial screening groups, but trial screening was associated with a higher cost [3].

It is important to note that understanding of the utilisation of SCS therapy has evolved since its first introduction. Patient selection for SCS is now better understood and has been refined over time in relation to physical and psychosocial factors [6,7]. Recent multidimensional patient profiling solutions, using digital tools or machine-learning algorithms, have proposed new ways for identifying the best candidates for SCS and for predicting the response of patients' response to therapy [8–11]. A recent European consensus study led to the development of a patient profiling e-health tool, which helps clinicians identify or confirm candidates for SCS therapy. In a retrospective applicability study of 483 patients implanted with an SCS system, 133 patients proceeded to permanent implant without a trial period. Results from this study suggest that patients who were deemed "appropriate" in the patient e-tool profile at baseline tended to have better SCS outcomes, regardless of whether they had a trial or not. This highlights the relevance of patient selection in determining the predictor of success for SCS.

Over the last 15 years, the capabilities of neurostimulators have expanded to enable delivery of multiple stimulation modalities that may differ in their mechanism of action or the sensation they produce in patients (e.g., paraesthesia versus sub-perception) [12–23]. Results from a randomised controlled trial (RCT) demonstrated that a device capable of providing multiple therapies provided superior long-term outcomes when subjects were able to choose the most effective therapy [24]. Combination therapy (simultaneous delivery of modalities) enabled more patients to achieve a successful outcome that monotherapy alone [25]. SCS is no longer a monotherapy where a single waveform is utilised; instead, multiple programming strategies are available to personalise therapy for each patient [26]. Therefore, trial periods that implement a monotherapy may underrepresent the capabilities of SCS therapy and may result in false negatives [5,27], thus failing to appropriately screen SCS responders, especially during a trial of short duration. Furthermore, no difference in long-term pain relief has been observed with acute (i.e. intraoperative) SCS screening compared with prolonged screening [4]. Results from a recent RCT showed no additional benefit in long-term patient outcomes with the use of an externalised trial period [3].

In addition, the risk of infection is higher with prolonged trial periods (>10 days) [28] and some patients may present with other comorbidities (e.g., diabetes, lymphoproliferative disease) that increases the risk of infection. In such cases, a single-stage procedure for SCS may be considered advantageous [29,30]. From a patient perspective, a single stage SCS procedure is preferred as it would result in less time off work (e.g. in hospital, attending appointments), less caregiver support, avoid

any device-related concerns (e.g. loose wires connected to the external test stimulator that may become unplugged, resulting in loss of therapy) and ultimately reduced health cost [31]. Higher costs and related healthcare resources are incurred with SCS screening [3,32]. Thus, it would be prudent to challenge the need for a systematic externalised screening trial period as a pre-requisite prior to the implantation of an SCS system.

Accordingly, we evaluated the real-world clinical outcomes of patients who underwent a single-stage procedure for SCS (SS-SCS) (i.e., on-table testing prior to immediate implantation, no external temporary trial period) as part of an ongoing case-series. Our hypothesis was that SS-SCS patients would experience effective, long-term pain relief, thus increasing the evidence base for minimising the use of trial screening in SCS.

2. Materials and methods

Real-world data was collected as part of a multicentre, observational, consecutive case series (Clinicaltrials.gov: NCT01550575) for chronic pain patients who had undergone a single-stage procedure for SCS implantation (i.e., no external temporary trial period) in 18 centres across Europe. All patients provided written, informed consent as per local regulatory requirements. The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committees from each site.

2.1. Study participants

All consecutive chronic pain patients aged ≥18 years who had an SS-SCS implantation were included in the data analysis. All participants were deemed eligible to SCS therapy, in compliance with local regulations and device directions for use. Decision for a single-stage procedure was taken by each site based on their clinical judgment, current practice and/or standard of care. There were no exclusion criteria per study protocol.

2.2. Device description

Various SCS systems were utilised, including Spectra WaveWriter, WaveWriter Alpha, Montage, Novi, Precision, Precision Spectra SCS System (Boston Scientific, Valencia, CA, USA). Based on clinician choice, percutaneous or paddle leads were introduced into the epidural space, offering a range of eight to 32 contacts available for therapy programming. Depending on each clinician's decision and regular practice, on-table testing was performed followed by IPG implantation, where the leads were connected during the same procedure. The SCS systems have a wide range of programming capabilities that allow SCS therapy to be tailored to each patient, including multiple, independent current control (MICC) with Illumina 3D™ targeting, combination therapy, multiple sub-perception waveforms (customised Burst, MicroBurst 3D, high rate (up to 1.2 kHz), FAST™ therapy), advanced field shapes (Contour™), and waveform automation.

2.3. Study outcomes

All data were collected by site personnel, as per standard practice and without any sponsor involvement. Demographic information and outcome measures were documented, including pain location, pain severity and improvement following SCS implant. Overall pain scores were documented using a Numerical Rating Scale (NRS) from 0 (no pain)

to 10 (worst pain). NRS scores ≤3 correspond to mild pain, 4–6 to moderate pain, and ≥7 to severe pain [33]. Quality of life was assessed using the EuroQol 5 Dimensions (EQ-5D)-5L questionnaire, using a visual analogue scale (VAS) scored from 0 ('the worst health you could imagine') to 100 ('the best health you could imagine'). Population norms reported in Europe for the EQ-5D-5L VAS are around 70–80 [34–36]. SCS device settings and patients' most preferred SCS waveforms and therapies were also recorded.

2.4. Statistical analysis

A Kolmogorov–Smirnov Test was performed to confirm the normality of the change in NRS score. Score distribution was calculated for the NRS pain scores. A paired *t*-test with two-sided 0.05 significance level was used to calculate whether the mean reduction in baseline pain at 3, 6 and 12 months was greater than 0. Continuous variables are presented as mean ± standard deviation.

3. Results

3.1. Baseline characteristics

A total of 171 patients (91 women, 80 men), with a mean age of 59.4 ± 13.7 years who had undergone SS-SCS were included in the analysis. Patients were implanted with SCS systems between July 2012 and June 2022 and were diagnosed with one or more of the following: failed back surgery syndrome or persistent spinal pain 2 (PSP2) (46.6%), spinal stenosis (10.4%), lumbosacral radiculopathy or PSP1 (8.4%), complex regional pain syndrome (6%), and various other conditions. Pain locations varied among patients, with most of them reporting low back and leg pain (81.9%) followed by pain in the lower limbs (56.7%).

A mean overall pain of 8.1 ± 1.2 (n = 171) was reported at baseline (pre-implant), indicating that these chronic pain patients were experiencing severe pain. Patient-reported mean low back and leg pain scores were 7.9 ± 1.8 (n = 134) and 8.2 ± 1.3 (n = 141), respectively. The mean EQ-5D-5L score at baseline was 25.0 ± 2.0 (n = 91). Table 1 provides details of baseline and clinical characteristics.

3.2. Clinical outcomes

A mean 5.0 ± 2.1-point improvement (from 8.1 to 3.1; n = 109) in overall pain was reported at 3 months post-implantation and sustained at 12 months (Fig. 1). At last follow-up (mean duration 408 days), the mean overall pain score had improved by 4.6 ± 2.4 points (from 8.1 to 3.5; n = 171; p < 0.0001) (Fig. 2). Similar significant improvements (p < 0.0001) were noted in low back pain and leg pain, with a reduction in pain scores
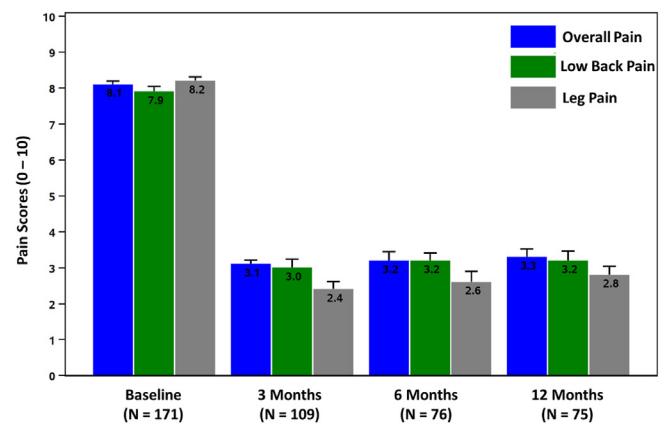

Fig. 1. Overall pain, low back and leg pain scores at baseline and up to 12 months post-implant (mean ± standard error).
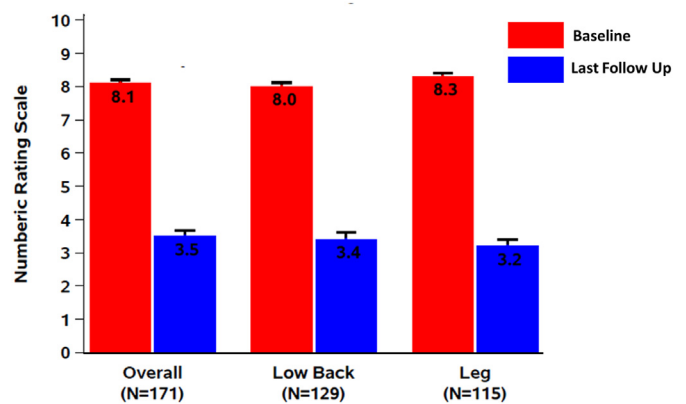

Fig. 2. Overall pain, low back, and leg pain scores at baseline and up to last follow-up (mean = 408 days) (mean ± standard error).

of 4.5 ± 2.5 points (from 8.0 to 3.4; n = 129) and 5.1 ± 2.2 points (from 8.3 to 3.2; n = 115), respectively (Fig. 2). A 2-point improvement in pain scores is considered clinically significant at the last follow-up, the responder rate was 71.3%, with 122/171 patients experiencing ≥50% improvement in pain compared to baseline. An NRS pain score of ≤3 at the last follow-up was reported in 50.3% (86/171) of patients (Fig. 3).

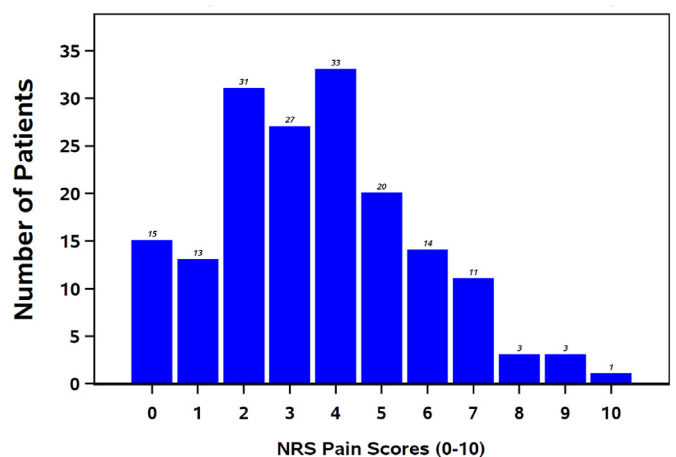A 46.1-point improvement in EQ-5D-5L was noted at the last follow-

Table 1
Patient characteristics (n = 171).

Sex (females), n (%)	91 (53.2)
Age, mean (SD) [a]	59.4 (13.7)
Pain location (may have multiple locations), n (%)	
Low back and legs	140 (81.9)
Lower limbs	97 (56.7)
Upper limbs	12 (7.0)
Head/neck	11 (6.4)
Key diagnosis for receiving SCS (may have multiple diagnosis), n (%)	
Failed back surgery syndrome (persistent spinal pain 2)	116 (46.6)
Spinal stenosis	26 (10.4)
Lumbosacral radiculopathy (persistent spinal pain 1)	21 (8.4)
Complex regional pain syndrome	15 (6.0)
Baseline overall pain score (NRS), mean (SD)	8.1 (1.2)
EQ-5D 5L, mean (SD)	25.0 (19.3) [b]

[a] n = 147.
[b] n = 91. NRS, numerical rating scale (from 0 to 10); SD, standard deviation.

Fig. 3. Distribution of overall pain scores at last follow-up (mean = 408 days). 50.3% (86 of 171 patients) reported a pain score ≤3.
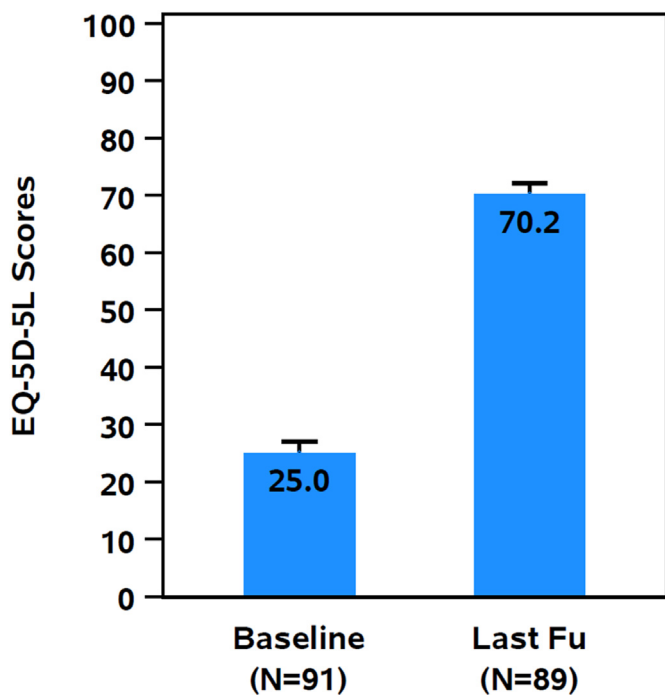
Fig. 4. Mean quality of life at last follow-up (mean = 408 days), assessed using the EQ-5D-5L (0 = 'the worst health you could imagine' to 100 = 'the best health you could imagine'). A 46.1-point improvement in EQ-5D-5L was noted.

up (from 25 to 70.2; n = 83), demonstrating improved quality of life in patients with data available (Fig. 4).

3.3. SCS therapy and programming

All commercially approved leads were available for use in this real-world cohort. Lead information was available for 160 patients (274 total leads).

Eight- or 16-contact percutaneous leads were used in 87% of patients (148/171), while 16-contact or 32-contact paddle leads were implanted in 7.6% of patients (13/171). Two leads were implanted in 57.3% of these patients (n = 99), while a single lead was used in 32.1% of patients (n = 55). Three or four leads were used in three patients each (n = 6).
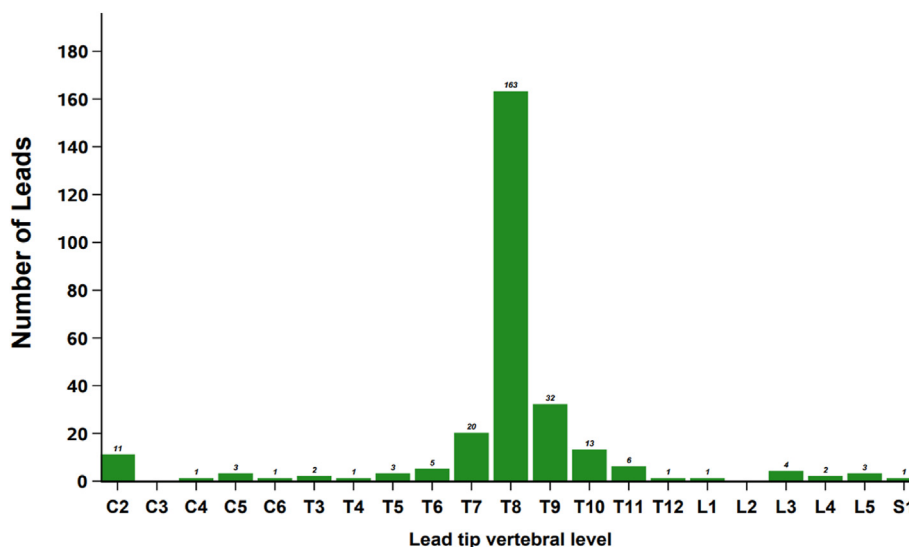
Table 2
Patients' preferred programs/waveforms at last follow-up (408 days; n = 171).

Preferred program/waveform, n (%) [a]	
Combination therapy	59 (35)
Standard rate with MICC (tonic)	31 (18)
Sub-perception with Burst or Microburst 3D	29 (16)
Sub-perception with FAST therapy	27 (15)
Sub-perception with high rate (up to 1.2 kHz) or Contour	26 (15)
Other	7 (4)

[a] Note that some patients may have preferred multiple waveforms. MICC, multiple independent current control.

Information related to number of leads implanted was not provided in 11 patients.

Of these, 59.4% (163 leads) were placed with the lead tip at T8 level and 11.7% (N = 32) were at T9 level (Fig. 5). In 62.6% of cases (171/273 leads), epidural leads were positioned midline, while 31.1% (85/273) were paramedial. Various neurostimulation therapies were used by patients over time. At the last follow-up (mean duration 408 days, i.e., 1.1 years), the most preferred programs were sub-perception waveforms (48%), followed by combination therapy (34%) and standard rate therapy (18%) (Table 2).

4. Discussion

The clinical value of an SCS trial stimulation period before SCS implantation has come under some scrutiny in recent years [3–5,9]. Trials may not reflect the potential for pain relief [3] and also place a burden on healthcare resources and on patients [32,37]. A single-stage SCS procedure, where patients are tested on-table prior to immediate implantation, could help to alleviate not only the strain on healthcare systems [32], but may also be a preferred option for chronic pain patients [31]. However, as widely now reported, there do exist significant advantages as well as possible limitations of a single-stage SCS procedure when compared to "dual"-staged procedures (Table 3).

Recently, RCT-derived evidence has demonstrated no significant difference in pain relief between patients who underwent SCS with no trial screening period compared to those who underwent one [3,38]. For example, in both assessed groups in the TRIAL-STIM RCT, the NRS pain score decreased by > 3.0 points at 6 months compared to baseline, and ~40% of patients in both groups similarly achieved ≥50% pain relief. Furthermore, long-term follow-up analyses at 36-months recapitulated these results per determination of no significant differences in pain relief

Fig. 5. Distribution of lead location (lead tip shown) among n = 171 patients. Information related to 11 patients was not provided.

Table 3
Reported Advantages ("Pros") and Disadvantages ("Cons) of Single vs Dual Staged SCS Procedure(s).

	Pros (i.e., reported advantages)	Cons (i.e. reported disadvantages
Dual-Stage SCS (i.e., screening trial followed by permanent implantation)	• Allows patients to experience SCS before permanent implant procedure [3,31] • Ease of removal of SCS device apparatus and equipment during trial if deemed necessary [31] • Provides for a baseline from which to evaluate magnitude of achievable pain relief response [39] • Can facilitate more careful selection of SCS device and/or neurostimulative modality or programming approach for use in a future permanent implantation [31]	• Screening trials may not be accurately predictive of long-term SCS outcomes and may under-represent the capabilities of SCS resulting in false negatives and/or inappropriate screening out of potential responders [37,40] • Increased risk of infection [3,28,39] • Duplicative procedures requiring added consumption of healthcare resources [6, 32] • Requires an increased number of appointments and time away from employment, and in some patients imposes additional travel obligation [31]
Single-Stage SCS (i.e., no screening trial; "on-table" testing followed by permanent implant)	• Decreased infection risk [3,28,39] • Less consumption of healthcare resources [6, 32] • Lower number of appointments needed thereby less travel and "time off" required [31] • Only 1 time period of hospital admission and/or recovery needed [31]	• Does not allow patients a "preview" of SCS therapy prior to undergoing procedure [3] • Proceeding straight to permanent SCS implant may be difficult for some patients [31]

and/or likelihood of explant between patients who underwent a trial versus those who did not [38]. Our real-world, multicentre study described here was designed to obtain outcomes in a cohort of SCS patients implanted with no screening trial period, as typically done per the standard of care in each centre. In so doing, there was no direct involvement of the sponsor as it pertains to the collection of data at each of the participating study sites.

Results from this observational case-series demonstrate significant improvement in overall pain, low back, and leg pain over 408 days (last follow-up). Patients reported severe pain prior to SCS implant and experienced a highly significant 5.0-point improvement from baseline that was noted 3 months after implantation and sustained for up to 12 months. At the last follow-up, more than half of SS-SCS patients reported a pain score ≤3. The reduction in pain relief was accompanied by a significant improvement in quality of life. The EQ-5D-5L VAS, which was low at baseline (25 points), increased to a mean value of 70.2 points after SS-SCS at the last follow-up, indicating that the patients' quality of life had reached population norms for healthy people in Europe [34–36]. Additionally, the real-world evidence obtained in this study demonstrates that SCS implantation can be performed in a single-stage procedure while maintaining long-term pain relief and quality of life. These findings, combined with observations from earlier studies [3,4], suggest that critical analysis and/or revision of established clinical practice guidelines for SCS should be considered to reflect individual patient needs and the selection process for SCS therapy. Presently however, mandatory requirements in some European countries (e.g., France, Netherlands, and Belgium) enforce the undertaking of an SCS trial to ensure insurance reimbursement. While in other counties, though not

obligatory, initial assessment of all candidates for SCS within the context of a screening trial is still commonly preferred among implanting providers. Yet, the growing compendium of publicly reported clinical and health economic evidence, of which this current analysis now contributes, increasingly supports the implementation of a single-stage SCS procedure in appropriately selected patients [3,31,32,37–40]. Accordingly, there is now a drive to individualize the diagnosis and treatment of chronic pain patients such that personalised (sometimes referred to as "patient-centered") care is emphasized [41]. Thus, we assert that rather than making screening trials compulsory (as in specific countries), offering patients for whom SCS therapy is highly recommended [8], a single-stage implantation procedure (per the standard discussion of potential risks and benefits), may in fact represent a more "patient-centered" approach that is of greater preference and ultimate benefit to those seeking to more effectively manage their chronic pain. This approach though should not impede the ability to impose a compulsory screening trial when the conditions of select patients are clearly more challenging, making it therefore more difficult to anticipate the benefits of SCS.

This study does have limitations. Comparison with a matched control group from the same case-series would have been beneficial to corroborate whether the real-life clinical improvements in SS-SCS patients were at least as good as in those who first underwent trial screening. The number of patients fluctuated over the 12-month period of the analysis, but this reflects clinical practice, where for various reasons patients are often unable to make a follow-up appointment. It might also have been of value to analyse other outcomes (e.g., patient satisfaction) to indirectly compare with results from controlled clinical trials in patients who underwent trial screening for SCS. However, such outcomes are not often recorded as standard in clinical practice. In addition, the retrospective nature of our design might be associated with the risk of selection bias that is inherent in retrospective studies. However, we included all patients who underwent SS-SCS, without any exclusion criteria.

5. Conclusions

Our real-world evidence demonstrates that a single-stage implantation procedure for SCS, without a trial screening period, not only provides long-term pain relief and improves quality of life in patients with chronic pain, but also avoids delay in patient care and could reduce overall healthcare-related costs. Careful patient selection and the use of contemporary platforms that are safe and can readily adapt to the patient's dynamic pain situation of the patient will alleviate suffering, pain and associated functional impairments. A more flexible policy based on individual patient needs and preferences is needed.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Pasquale De Negri reports administrative support, statistical analysis, and writing assistance were provided by Boston Scientific Neuromodulation. Pasquale De Negri reports a relationship with Boston Scientific Neuromodulation that includes: non-financial support. This study was sponsored by Boston Scientific, and personnel from the Clinical Research Department within Boston Scientific's Division of Neuromodulation were involved in the study design (RJ), analysis (RJ, YP), interpretation of the

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