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REVIEW ARTICLE

Comparison of clinical outcomes associated with spinal cord stimulation (SCS) or conventional medical management (CMM) for chronic pain: a systematic review and meta-analysis

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Abstract

Objective This study aims to evaluate the efficacy and safety of spinal cord stimulation (SCS) compared to conventional medical management (CMM) for patients diagnosed with chronic pain. Furthermore, the study seeks to compare the utilization of analgesics, as well as the long-term outcomes in terms of quality of life and functional capacity.

Data sources We systematically searched Cochrane Library, Web of Science, PubMed, and EMBASE for randomized controlled trials from inception up to February 2022.

Review methods Inclusion and exclusion criteria were set according to the PICOS criteria. We searched for studies in which SCS was compared with CMM alone for chronic pain. Two reviewers independently identified eligible studies and extracted data. Risk of bias assessments were performed according to Cochrane review criteria and Interventional Pain Management Techniques–quality Appraisal of Reliability and Risk of Bias Assessment (IPM-QRB) criteria.

Results The present meta-analysis comprised eight studies and included a total of 893 patients. Our findings demonstrate that spinal cord stimulation (SCS) in combination with conventional medical management (CMM) is associated with a significant reduction in visual analogue scale (VAS) pain intensity ($P=0.0005$) and decreased scores on the McGill Pain Questionnaire (MPQ) ($P<0.0001$). Moreover, SCS plus CMM was found to improve patients' quality of life, as evidenced by improvements in SF-36 scores ($P<0.00001$), EQ-5D utility index ($P=0.008$), and Oswestry Disability Index (ODI) ($P<0.00001$). Based on the results of four high-quality randomized controlled trials (RCTs), the level of evidence supporting the efficacy of SCS for the treatment of painful neuropathy is graded as level I to II. In contrast, there is currently only low-level evidence to support the use of high-frequency stimulation and other chronic pain conditions, which can be attributed to a lack of sufficient randomized controlled trials.

Limitations The principal limitation of our study is the significant heterogeneity observed among the cohorts investigated. The primary source of this heterogeneity is the fact that spinal cord stimulation is indicated for the treatment of multiple chronic pain conditions. Moreover, variations in the stimulation parameters, differences among manufacturers, and the specific surgical implantation settings contribute to the increased heterogeneity observed in our analyses. To address this issue, we conducted a subgroup analysis based on specific situations and performed evidence synthesis to mitigate the potential impact of heterogeneity. These approaches allow for a more precise interpretation of the results and a more accurate evaluation of the quality of the included studies.

Conclusions SCS is an effective treatment to relieve the pain level of chronic pain, decrease analgesic usage, and increase long-term quality of life and functional capacity.

Keywords Spinal cord stimulation · Conventional medical management · Chronic pain · High-frequency stimulation · Failed back surgery syndrome · Painful diabetic neuropathy · Meta-analysis

Introduction

In 1996, the American Pain Society (APS) proposed that pain should be considered the fifth vital signs [1]. The etiology and pathogenesis of chronic pain are complicated, and

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the burden of disability caused by chronic pain is enormous [2]. Because of being under-diagnosed and under-treated, chronic pain affects more than 30% of people worldwide. Spinal cord stimulation (SCS) has been established for chronic pain control for 50 years. In 1965, Melzack et al. [3] proposed the gate control theory, expounding the pain mechanisms of human perception and regulation of pain, providing the earliest theoretical basis for electrical stimulation to inhibit the physiological transmission of pain. In the treatment, placing electrodes in the epidural space of the corresponding spinal cord segment connected to a spinal cord stimulator by delivering the sub-perception electrical signal to alter the pain sensation [4, 5]. After decades of development, SCS has gradually become an important means of clinical treatment to patients who suffer from chronic pain, and the rate of implantation has increased. The application prospect of neuromodulation for chronic pain is evolving rapidly in recent years; in the USA alone, tens of thousands neurostimulators have been implanted annually [6]. Failed back surgery syndrome (FBSS) (also called postoperative persistent syndrome (POPS), post laminectomy or spinal fusion pain), complex regional pain syndrome (CRPS), and diabetic painful neuropathy (DPN), e.g., are applicable to SCS. The FDA first approved SCS in 1989 to relieve chronic pain from nerve damage in the trunk, arms, or legs, now making for 70% of all neuromodulation treatments.

At present, SCS is widely accepted as an effective therapy for reducing painful events and enhancing quality of life. North et al. revealed that SCS can effectively relieve pain for at least three years compared with re-operation [7]. However, conventional medical management (CMM) included a series of rehabilitation and drug treatment is still the first-line therapy for the patients. Despite difficulties with blinding, SCS has been compared with CMM in several randomized controlled trial with varied results [8, 9].

In past decades, several randomized controlled trial settings have proved the relative effectiveness of SCS versus CMM. However, evidence to compare the effect of SCS and CMM in patients with chronic pain has not been established. The purpose of this meta-analysis was to synthesize the evidence to verify the previous hypothesis that SCS combined with CMM is more effective than CMM alone for patients with chronic pain.

Materials and method

Study design and search strategy

Before conducting this review, the protocol has been registered on PROSPERO as CRD42022303605. Systematically searches were performed in the Cochrane library, Medline, PubMed, and Embase for studies that compared SCS with CMM to chronic pain. We searched the keywords "Spinal cord stimulation," "Chronic pain," and "Randomized Controlled Trial," and researched corresponding Medical Subject Headings (MeSH). Combining the keywords with "AND" or "OR" is our search strategy. Supplemental Appendix 1 show more details of the strategy.Initial exclusion based on titles and abstracts was performed independently by two reviewers (M.Z and H.Z.) and further check of full-text papers for eligibility.

Inclusion and exclusion criteria

The inclusion criteria were listed as: (1) patients who suffer from chronic and stubborn back and/or limb pain last over a year; (2) two types of intervention: SCS and SCS plus CMM (the paresthesia-free stimulation paradigm including intensity, frequency, and subdivide modes of SCS were not limited) are included in studies; (3) the studies that have a patient follow-up period of at least 3 months; and (4) the RCTs studies. The exclusion criteria were as follows: (1) neurostimulation intervention other than SCS; (2) others papers including commentaries/editorial, methodological paper, conference proceeding, review, and protocol/design; and (3) study only available as abstract or other insufficient information. Two reviewers discussed any disagreements and, if necessary, consulted with a third reviewer to resolve them.

Data extraction

In a pre-constructed spreadsheet, all relevant information from included studies was extracted and summarized independently by two investigators. The study details were collected, including first author, year of publication, country, study level, sample size, treatment, last follow-up, and outcome measures. Consultation and discussion with the third author to resolve discrepancies when inconsistencies occur. When there were any missing data, attempt to contact corresponding authors to obtain these missing items.

Risk of bias and methodological quality assessment

In order to assess the methodological quality of the included studies, the "Risk of Bias" tool developed by the Cochrane Collaboration was utilized. This tool evaluates studies based on a number of criteria, including single-blind or double-blind design, randomization, selection bias of outcomes, data completeness, and outcome evaluation. The risk of bias for each study was classified as either low, high, or unclear based on these criteria. Additionally, for randomized trials, the Interventional Pain Management Techniques—Quality Appraisal of Reliability and Risk of Bias Assessment (IPM-QRB) tool was used to evaluate the quality and risk of bias

(Supplemental Appendix 1) [10]. Trials with a score less than 16 on the IPM-QRB tool were considered to be of low quality and were subsequently excluded from the analysis. The use of these tools helped to ensure that the included studies were of high methodological quality, which is essential for drawing reliable conclusions from the findings.

Outcome measures

Our primary efficacy outcome was pain relief, quality of life and drug use. For pain assessment, the visual analogue scale (VAS; 0–10 cm) or the numeric rating scale (NRS; 0–10) were used. We standardized the VAS (0–10 cm) and the NRS (0–10), and we converted the VAS by dividing pain scores by 10. Additionally, McGill Pain Questionnaire Short-Form (MPQ) also used to assess pain relief. For quality of life, 36-item Short-Form (SF-36), EuroQol Five Dimensions Questionnaire (EQ-5D), Medication Quantification Scale (MQS) and Oswestry Disability Index (ODI) were used. The use of drug was also evaluated.

Analysis of evidence

The evidence analysis was carried out using the American Society of Interventional Pain Physicians' (ASIPP) best evidence synthesis, which was developed by adapting various criteria [11]. The analysis classified evidence into five levels, ranging from level I (strong evidence) to level V (opinion or consensus-based evidence) (Supplemental Appendix. 2).

Statistical analysis

For continuous outcomes, standardized mean difference (SMD) and 95% confidence interval (CI) were applied to summarize the connection. Statistical heterogeneity was determined using I^2 tests. I^2 values of 25%, 50%, and 75% were qualitatively classified as low, moderate, and high heterogeneity. A random effects model was used when heterogeneity occurred. The primary outcome of the study was the mean change from baseline to follow-up. For VAS and NRS, subgroup analyses were conducted. A P value < 0.05 was considered a significant difference. All meta-analyses were conducted by RevMan (Review Manager, version 5.4.1).

Result

Study identification and inclusion

A total of 280 potentially relevant articles were obtained from three electronic databases. Our search strategy yielded 53 studies, after removal of the duplicate articles. Of these, 13 irrelevant studies and 4 case reports were excluded following abstract review. We then subjected the remaining 36 articles to full-text review. Of these, 9 were excluded due to the inconsistent with theme, 12 were excluded due to the lacking of data accessible, and 7 were not RCTs. Finally, 8 RCTs were included as targets for meta-analysis. The flow diagram of the study selection process is presented in Fig. 1, which strictly followed PRISMA guidelines.

Study characteristics

Characteristics of the included studies are in Table 1. The meta-analysis included 8 RCTs. These studies were conducted in 5 countries (Netherlands, USA, UK, Canada, France) and involved 893 patients. One study restricted the participants to chronic complex regional pain syndrome Type I. Three studies investigated the pain relief effects on participants with painful diabetic neuropathy. Two studies included participants with failed back surgery syndrome. One study was patients with critical limb ischemia. One study was patients with refractory angina. The minimum follow-up time is 6 months, and the longest is 5 years.

Assessment of study quality

The methodological quality of all eligible studies was assessed using the Cochrane Risk of Bias Tool (version 5.1.0) (Fig. 2). Considering the manner in which the whole implantation process conducted, all studies were unblinded to the surgery and commissioning processes. Hence, a blinding trial did not succeed in blinding either participants or personnel. All trials had a high risk of bias in this category. The randomization methods were described in all trials, allocation concealment was reported in 5 studies [14–16, 18, 19]. Three studies' other bias cannot verify because lack of information and hard to judge. The RCTs that met the inclusion criteria underwent a quality assessment using IPM-QRB criteria for randomized trials, which are presented in Table 2.

Effects of SCS on pain relief

The most commonly used pain intensity measurement scales in the included randomized controlled trials (RCTs) were the numeric rating scale (NRS) and the visual analog scale (VAS), both of which are valid and reliable instruments for measuring pain intensity. It is noteworthy that these two scales have been found to be strongly correlated in previous studies [20–22]. The NRS scale is a commonly used tool in clinical settings due to its ease of use for pain quantification. On the other hand, the VAS requires the patient to mark a horizontal line with a length of 100 mm to represent their pain level (Fig. 1). In this meta-analysis, we combined the results obtained from the NRS and VAS scales to evaluate

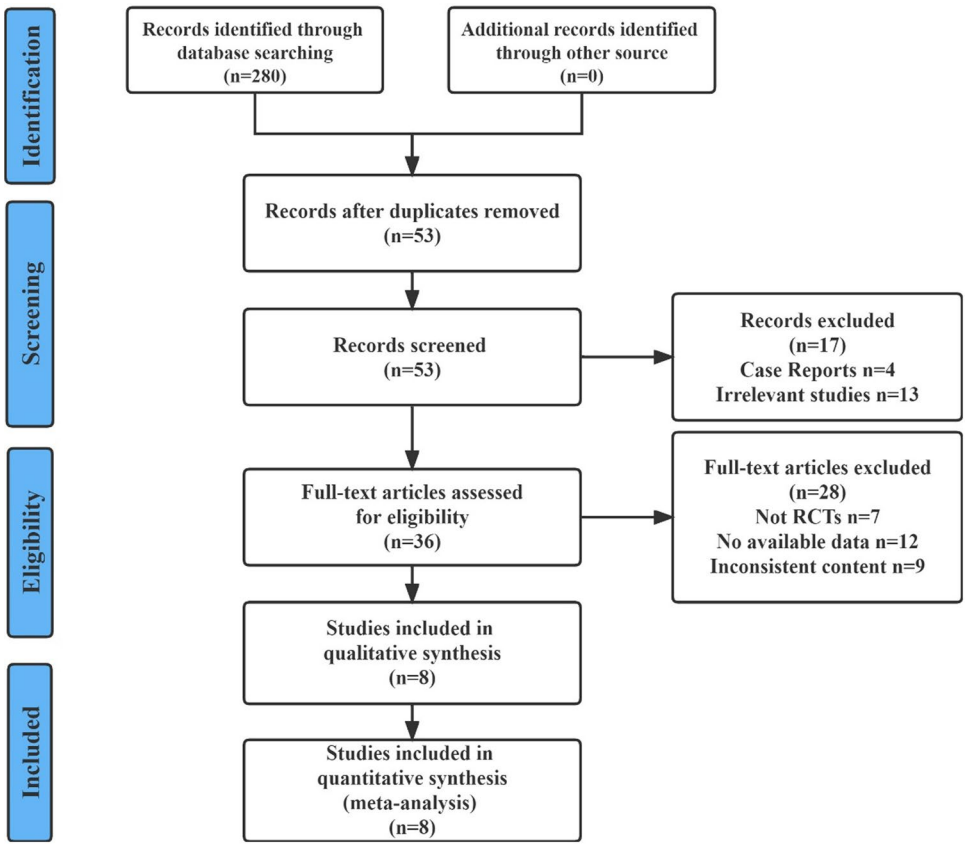


Fig. 1 Flowchart of eligible study selection

the effect of SCS plus CMM on pain severity. Our results showed a statistically significant reduction in pain intensity (Fig. 3a), although with high heterogeneity ($P = 0.0005$; $I2 = 95\%$) based on the heterogeneity test. The McGill Pain Questionnaire (MPQ) is a multidimensional pain assessment tool that has been widely used in pain assessment for musculoskeletal conditions [23]. In Fig. 3d, a statistically significant effect on the MPQ pain scale was observed, albeit with high heterogeneity ($P < 0000.1$, $I2 = 99\%$). These findings indicate a strong analgesic effect of SCS plus CMM on pain intensity. Furthermore, we conducted subgroup analyses to evaluate the effect of SCS plus CMM in different chronic pain conditions, including diabetic pain and other types of pain. The results showed a similar trend in pain relief in both subgroups. We also analyzed the baseline demographic characteristics (Supplemental Appendix 3) of each control group and categorized them into short-course and long-course subgroups based on the duration of the disease course for pain relief subgroup analysis.

Effects of SCS on quality of life

The Medical Outcomes Study 36-item Short-Form (SF-36) health survey is a widely used generic questionnaire that assesses an individual's physical and mental health and has been adopted as a reliable tool for evaluating health-related quality of life (HRQoL), addressing the methodological limitations of earlier studies [24]. Four studies reported improvements in SF-36 scores, indicating successful clinical outcomes. As depicted in Fig. 4a, summary results showed a significant improvement in SF-36 scores in the SCS group ($P < 0.00001$, $I2 = 0\%$, 95CI% = 0.54–0.98). The EQ-5D is a widely used generic measure of health status, incorporating descriptive and visual analog scales to evaluate health in five dimensions, namely mobility, self-care, usual activities, pain/discomfort, and anxiety/depression [25, 26]. Our findings showed a significant increase in EQ-5D utility index ($P = 0.008$, $I2 = 98\%$) for SCS treatment compared to CMM. The Oswestry Disability Index (ODI) is a critical metric used to assess an individual's permanent functional disability, and is widely adopted by researchers and disability patients [27, 28]. ODI was evaluated and reported as an outcome measure in two of the studies included in our analysis, with the combined results demonstrating a decrease in ODI scores following SCS treatment.

Effects of SCS on medication use

The Medication Quantification Scale (MQS) is a tool that can serve both clinical and research purposes. Its development dates back to 1992 [29], and it has undergone revisions in 1998 [30] and 2005 [31], with a specific focus on meeting

Table 1 Characteristics of included studies

Study	Country	Type of study	Subjects	Treatment	Level	Stimulation device/ parameter	Setting	Source of funding	Adverse events	Last follow-up	Outcomes
Kemler et al. [12]	Netherlands	RCT	54 patients with chronic complex regional pain syndrome Type I	Spinal cord stimulation and Physical Therapy(PT)	Level of the nerve roots innervating the painful area	Not mentioned	Single Center	Not mentioned	a: 17 b: 11 c: 8 d: 6 e: 3 f: 1	60 months	①②④⑤⑧
de Vos et al [13]	Netherlands	RCT	60 patients with Painful diabetic neuropathy	spinal cord stimulation and conventional pain treatments	Between T9 and T12	Electrode lead (Octrode or S8 Lamitrode) Pulse generator (EonC, Eon, Eon Mini)/ Cyclic stimulation	Multicenter	St. Jude Medical	a: 2 d: 2 f: 1	6 months	①②④⑨
Rigoard et al. [14]	France	RCT	278 patients with Failed back surgery syndrome	Spinal cord stimulation with optimal medical management	Painful site	Multicolumn surgical lead (Specify 5–6-5,Medtronic) Neurostimulator (Models 37,701, 37,702, 37,712 etc. Medtronic)	Multicenter	Medtronic Inc	d: 1 g: 8	24 months	③④⑥⑩
Kumar et al [15]	Canada	RCT	100 Patients with neuropathic pain secondary to failed back surgery syndrome	Spinal cord stimulation with conventional medical management	Painful site	Neurostimulation system (Synergy^{Tm} system, Medtronic) Mean settings were an amplitude of 3.7 V, a pulse width of 350 μs and a rate of 49 HZ	Multicenter	Medtronic Inc	a: 1 b: 10 c: 4 d: 1 g: 7	12 months	①⑥⑩
Petersen et al. [16]	United state	RCT	216 patients with refractory painful diabetic neuropathy	10-kHz spinal cord stimulation and conventional medical management	T8 to T11	Bipole, 10-kHz frequency, 30-μs width, amplitude range of 0.5 to 3.5 mA (Nevro Corp)	Multicenter	Nevro Corp	e: 2 g: 2	6 months	①②④⑪

Table 1 (continued)

Study	Country	Type of study	Subjects	Treatment	Level	Stimulation device/parameter	Setting	Source of funding	Adverse events	Last follow-up	Outcomes
Slangen et al. [17]	Netherlands	RCT	36 patients painful diabetic peripheral neuropathy	Spinal cord stimulation with best medical treatment	Lumbar Level	Octapolar lead (Medtonic) Programmable stimulator (Synergy Versitrel or Prime Advanced; Medtronic)	Two-center	Medtronic	h: 1 g: 1	6 months	③④⑥⑫⑬, MOS
Spincemaille et al. [18]	Netherlands	RCT	120 patients with patients with critical Limb ischemia	Spinal cord stimulation with medical treatment	Not mentioned	Stimulation system(Itreal II, Quad lead, Medtronic)	Multicenter	Sickness Funds Council(Health Insurance Executive Board)	b: 11 f: 1 g: 3	18 months	①②④⑦⑨⑭
Eldabe et al. [19]	United kingdom	RCT	29 patients with refractory angina	Spinal cord stimulation with usual care	Thoracic Level	Not mentioned	Single Center	Medtronic and Boston scientific	g: 2	42 months	④⑮

a: Pulse generator replacement; b: Repositioning of lead; c: Pulse generator pocket revision; d: Replacement lead; e: Explanation of system; f: Reimplantation of system; g: Implant site infection; h: Dural puncture

①: Visual analog scale (VAS) ②: McGill pain questionnaire (MPQ) ③: Numerical rating scale (NRS) ④: EuroQol five dimensions questionnaire (EQ-5D) ⑤: Health-related quality of life (HRQoL) ⑥: 36-item short-form (SF-36) ⑦: Nottingham health profile (NHP) ⑧: Self-rating depression scale ⑨: Medication quantification scale (MQS) ⑩: Oswestry disability index (ODI) ⑪: Douleur neuropathique (DN4) ⑫: Pain severity index (PSI) and the pain interference index (PII) ⑬: Patient global impression of change (PGIC) ⑭: Sickness impact profile ⑮: Seattle angina questionnaire (SAQ)

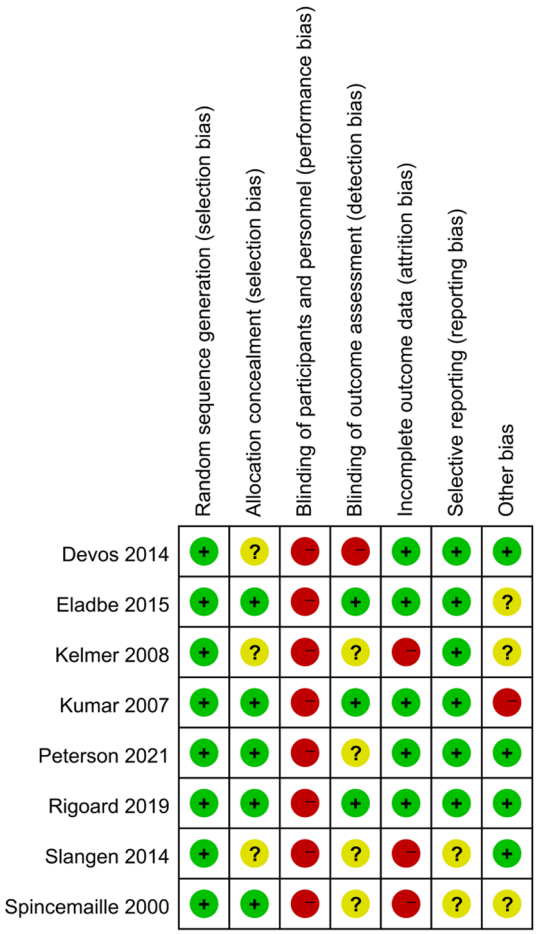


Fig. 2 Risk of bias summary: (+) indicates a low risk of bias, (?) means an unclear risk and (–) means a high risk of bias

the needs of individuals experiencing chronic nonmalignant pain. The MQS evaluates each medication by assigning a score based on its dose and a consensus-based detriment weight for its pharmacologic class. The cumulative score provides an MQS score, which serves as a useful metric for evaluating medication usage within any pain medication regimen. The MQS's conceptual principle is to provide a score for each medication based on the product of the detriment weight and the relative daily dosage of each pharmacologic class (see Supplemental Appendix 4). The detriment weight reflects the potential harmful effects of long-term medication use, while the dosage level is based on the manufacturer's recommendations. When a patient is prescribed multiple medications, the total MQS score is calculated as the sum of the MQS scores of all the medications that the patient is taking. This approach ensures that the potential risks and benefits of all the medications are accounted for in the overall assessment of the patient's medication regimen. Two trials reported a significant reduction in the mean medication dose as measured by the MQS. Applying random effects analysis and calculating the standardized weighted difference for these two trials ($P < 0.00001$, $I2 = 0\%$), it was observed that the SCS group was able to reduce the MQS score compared to the CMM group, as shown in Fig. 5.

Levels of evidence

Based on the available evidence, the use of spinal cord stimulation (SCS) in patients with painful diabetic neuropathy is classified as level I to II, as supported by four high-quality randomized controlled trials conducted by Devos et al., Petersen, Slangen, and Spincemaille et al., respectively. Conversely, for 10-kHz high-frequency pattern stimulation in the same patient population, the evidence level is categorized as level III, as demonstrated by a single relevant high-quality randomized controlled trial conducted by Slangen et al.

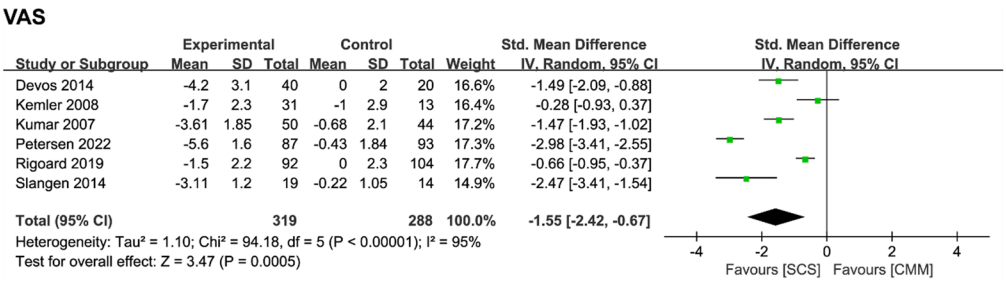
For failed back surgery syndrome (FBSS), the evidence level is classified as level I to II, as evidenced by two relevant high-quality randomized controlled trials with a significant sample size and long follow-up time, as demonstrated by Rigord and Kumar et al. However, for chronic complex regional pain caused by limb ischemia or angina pectoris, the evidence level is categorized as level III, based on two moderate or low-quality randomized controlled trial studies conducted by Kemler and Eldabe et al. A significant limitation of these studies is the relatively small sample size.

Adverse events

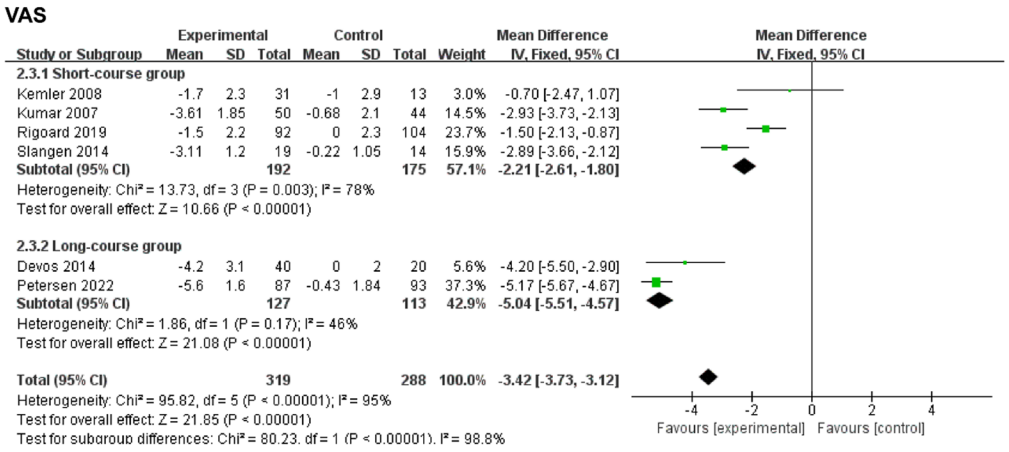
In seven of the eight trials analyzed, adverse events associated with SCS were reported. The most commonly reported adverse event was implantation-related infection, while electrode lead migration was another frequently encountered issue, which often necessitated surgical intervention for its resolution. Notably, Slangen reported two serious adverse events, one involving postdural puncture headache following dural puncture, complicated by a deadly subdural hematoma three days later, and the other involving an infection six weeks after SCS implantation, requiring explantation of the device. In the CMM group, Kumar reported that 25 (52%) patients experienced various non-spinal cord stimulator-related events, mostly comprising drug adverse events and the development of new illnesses, injuries, or conditions.

Discussion

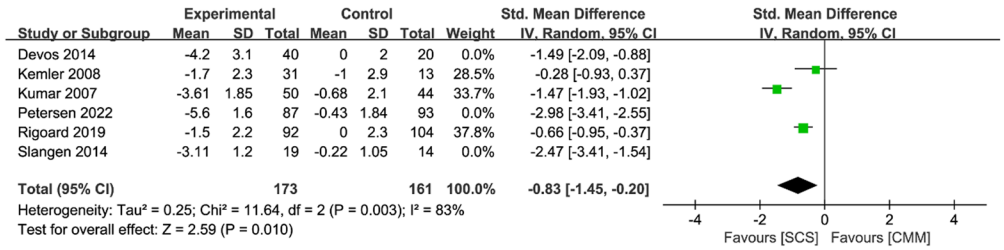
Over the last two decades, several neurostimulation devices have emerged as potential treatment options for chronic pain. These devices offer novel approaches for delivering electrical stimulation to provide pain relief, and many studies have reported promising therapeutic efficacy with optimized parameters. Recently, the European Academy of Neurology


VAS
Experimental
Control
Std. Mean Difference
Std. Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI
IV, Random, 95% CI
Devos 2014 -4.2 3.1 40 0 2 20 16.6% -1.49 [-2.09, -0.88]
Kemler 2008 -1.7 2.3 31 -1 2.9 13 16.4% -0.28 [-0.93, 0.37]
Kumar 2007 -3.61 1.85 50 -0.68 2.1 44 17.2% -1.47 [-1.93, -1.02]
Petersen 2022 -5.6 1.6 87 -0.43 1.84 93 17.3% -2.98 [-3.41, -2.55]
Rigoard 2019 -1.5 2.2 92 0 2.3 104 17.7% -0.66 [-0.95, -0.37]
Slangen 2014 -3.11 1.2 19 -0.22 1.05 14 14.9% -2.47 [-3.41, -1.54]
Total (95% CI) 319 288 100.0% -1.55 [-2.42, -0.67]
Heterogeneity: Tau² = 1.10; Chi² = 94.18, df = 5 (P < 0.00001); I² = 95%
Test for overall effect: Z = 3.47 (P = 0.0005)
-4 -2 0 2 4
Favours [SCS] Favours [CMM]

(a)


VAS
Experimental
Control
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Fixed, 95% CI
IV, Fixed, 95% CI
2.3.1 Short-course group
Kemler 2008 -1.7 2.3 31 -1 2.9 13 3.0% -0.70 [-2.47, 1.07]
Kumar 2007 -3.61 1.85 50 -0.68 2.1 44 14.5% -2.93 [-3.73, -2.13]
Rigoard 2019 -1.5 2.2 92 0 2.3 104 23.7% -1.50 [-2.13, -0.87]
Slangen 2014 -3.11 1.2 19 -0.22 1.05 14 15.9% -2.89 [-3.66, -2.12]
Subtotal (95% CI) 192 175 57.1% -2.21 [-2.61, -1.80]
Heterogeneity: Chi² = 13.73, df = 3 (P = 0.003); I² = 78%
Test for overall effect: Z = 10.66 (P < 0.00001)
2.3.2 Long-course group
Devos 2014 -4.2 3.1 40 0 2 20 5.6% -4.20 [-5.50, -2.90]
Petersen 2022 -5.6 1.6 87 -0.43 1.84 93 37.3% -5.17 [-5.67, -4.67]
Subtotal (95% CI) 127 113 42.9% -5.04 [-5.51, -4.57]
Heterogeneity: Chi² = 1.86, df = 1 (P = 0.17); I² = 46%
Test for overall effect: Z = 21.08 (P < 0.00001)
Total (95% CI) 319 288 100.0% -3.42 [-3.73, -3.12]
Heterogeneity: Chi² = 95.82, df = 5 (P < 0.00001); I² = 95%
Test for overall effect: Z = 21.85 (P < 0.00001)
Test for subgroup differences: Chi² = 80.23, df = 1 (P < 0.00001), I² = 98.8%
-4 -2 0 2 4
Favours [experimental] Favours [control]

(b)


VAS: diabetic neuropathic pain
Experimental
Control
Std. Mean Difference
Std. Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI
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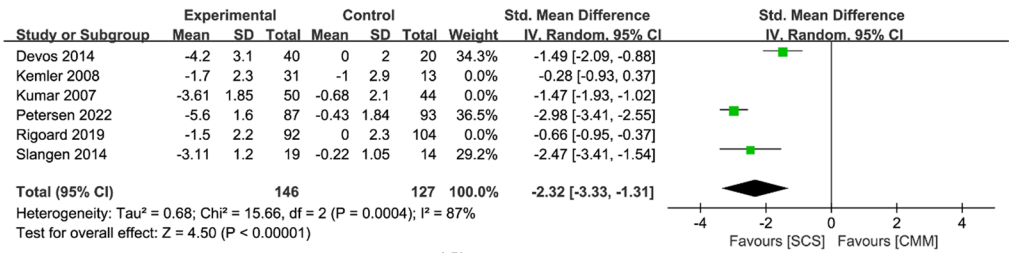
Kumar 2007 -3.61 1.85 50 -0.68 2.1 44 33.7% -1.47 [-1.93, -1.02]
Petersen 2022 -5.6 1.6 87 -0.43 1.84 93 0.0% -2.98 [-3.41, -2.55]
Rigoard 2019 -1.5 2.2 92 0 2.3 104 37.8% -0.66 [-0.95, -0.37]
Slangen 2014 -3.11 1.2 19 -0.22 1.05 14 0.0% -2.47 [-3.41, -1.54]
Total (95% CI) 173 161 100.0% -0.83 [-1.45, -0.20]
Heterogeneity: Tau² = 0.25; Chi² = 11.64, df = 2 (P = 0.003); I² = 83%
Test for overall effect: Z = 2.59 (P = 0.010)
-4 -2 0 2 4
Favours [SCS] Favours [CMM]

(c)


VAS: non-diabetic neuropathic pain
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Std. Mean Difference
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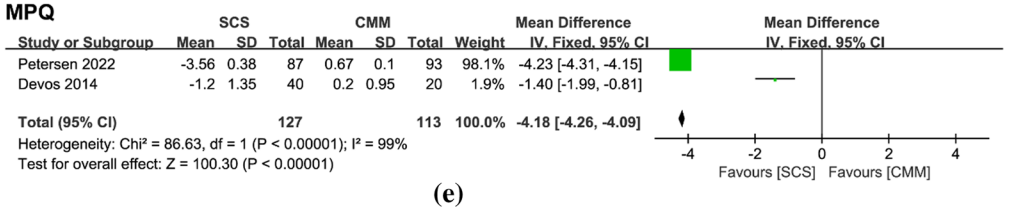
Slangen 2014 -3.11 1.2 19 -0.22 1.05 14 29.2% -2.47 [-3.41, -1.54]
Total (95% CI) 146 127 100.0% -2.32 [-3.33, -1.31]
Heterogeneity: Tau² = 0.68; Chi² = 15.66, df = 2 (P = 0.0004); I² = 87%
Test for overall effect: Z = 4.50 (P < 0.00001)
-4 -2 0 2 4
Favours [SCS] Favours [CMM]

(d)


MPQ
SCS
CMM
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Fixed, 95% CI
IV, Fixed, 95% CI
Petersen 2022 -3.56 0.38 87 0.67 0.1 93 98.1% -4.23 [-4.31, -4.15]
Devos 2014 -1.2 1.35 40 0.2 0.95 20 1.9% -1.40 [-1.99, -0.81]
Total (95% CI) 127 113 100.0% -4.18 [-4.26, -4.09]
Heterogeneity: Chi² = 86.63, df = 1 (P < 0.00001); I² = 99%
Test for overall effect: Z = 100.30 (P < 0.00001)
-4 -2 0 2 4
Favours [SCS] Favours [CMM]

(e)

◂**Fig. 3** Meta-analysis of pain intensity comparing SCS with CMM. **a** visual analogue scale (VAS) change. **b** visual analogue scale (VAS) change in different course group. **c** VAS changes in patients with diabetic neuropathic pain. **d** VAS changes in patients with non-diabetic neuropathic pain. **e** MPQ pain scale change

guidelines have recommended spinal cord stimulation (SCS) as a treatment for chronic low back pain [32]. Chronic pain can result in reduced productivity, increased medical-care expenses, and decreased quality of life. SCS can help reduce pain, improve sensory and motor functions, and ultimately improve patients' quality of life. In patients with failed back surgery syndrome (FBSS), SCS has demonstrated superior efficacy compared with conventional medical management (CMM) and can lead to long-term medical cost savings. These findings suggest that SCS has excellent potential for long-term therapeutic applications. However, there are contrasting conclusions in the literature. For instance, a study by Hara et al. [33] found no significant difference between burst SCS and sham SCS in the Oswestry Disability Index

Table 2 Methodological quality assessment of randomized trials of spinal cord stimulation utilizing IPM-QRB criteria

		Kemler et al.	de Vos et al.	Rigoard et al.	Kumar et al.	Petersen et al.	Slangen et al.	Spincemaille et al.	Eldabe et al.
I. Trial design and guidance reporting									
1	Consort or spirit	2	2	3	2	3	2	2	3
Design factors									
2	Type and design of trial	2	2	2	2	3	3	2	2
3	Setting/physician	1	1	1	2	2	2	2	2
4	Imaging	0	0	2	3	1	0	1	3
5	Sample size	1	1	3	2	3	1	3	1
6	Statistical methodology	1	1	1	1	1	1	1	1
Patient factors									
7	Inclusiveness of population	2	2	2	2	2	2	2	2
8	Duration of pain	2	2	2	2	2	2	2	2
9	Previous treatments	2	2	2	2	1	2	2	2
10	Duration of follow-up with appropriate interventions	3	3	3	2	1	1	2	3
Outcomes									
11	Outcomes assessment criteria for significant improvement	2	4	2	2	2	2	2	2
12	Analysis of all randomized participants in the groups	1	1	2	2	2	2	2	2
13	Description of drop out rate	1	1	1	2	1	1	1	1
14	Similarity of groups at baseline for important prog- nostic indicators	1	2	2	2	2	2	2	2
15	Role of co-interventions	1	1	1	1	1	1	1	1
Randomization									
16	Method of randomization	2	2	2	2	2	2	2	2
Allocation concealment									
17	Concealed treatment allocation	0	0	0	2	2	2	2	2
Blinding									
18	Patient blinding	0	0	0	0	0	0	0	0
19	Care provider blinding	0	1	0	0	0	0	0	0
20	Outcome assessor blinding	0	0	0	0	0	0	1	1
Conflicts of interest									
21	Funding and sponsorship	0	2	– 3	– 3	– 3	– 3	2	– 3
22	Conflicts of interest	3	3	2	2	1	2	2	1
Total		27	32	30	32	29	27	35	32

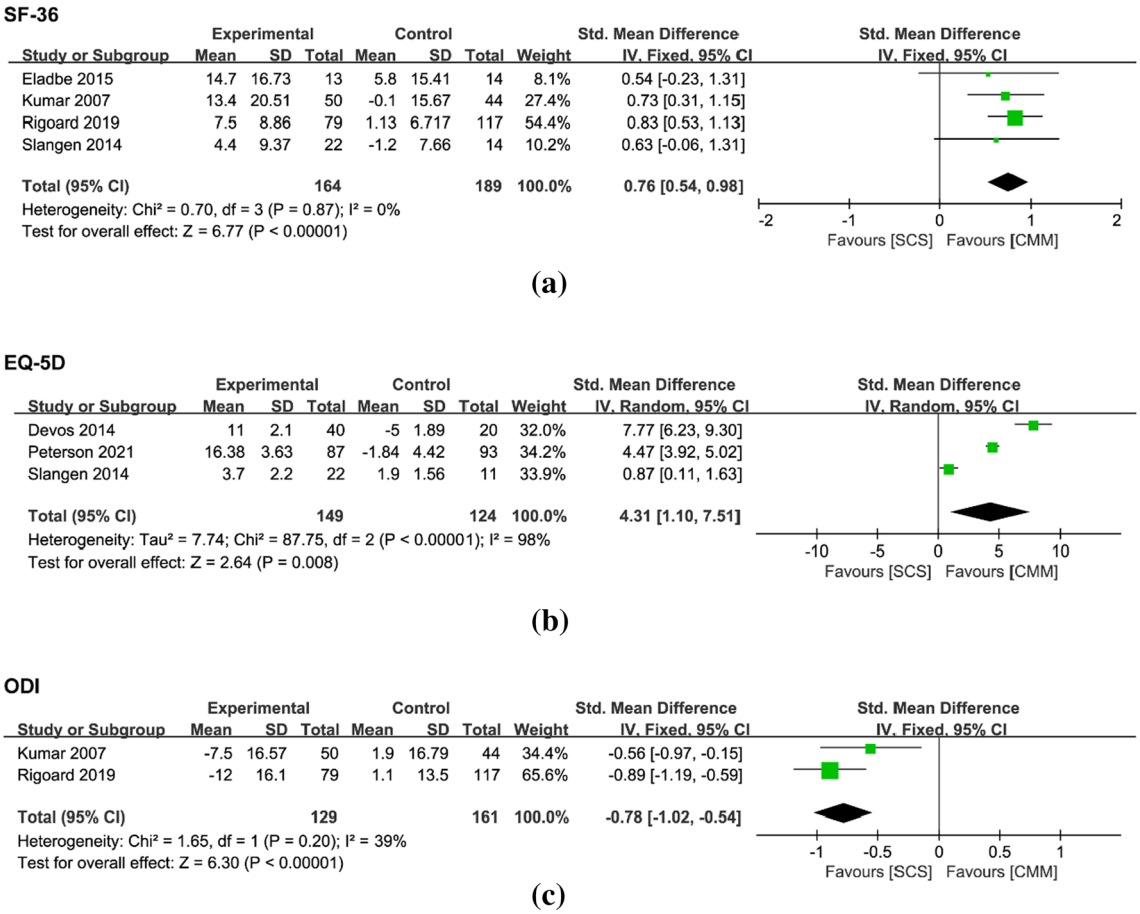


Fig. 4 Meta-analysis of quailty of life comparing SCS with CMM. **a** SF-36. **b** EQ-5D. **c** ODI

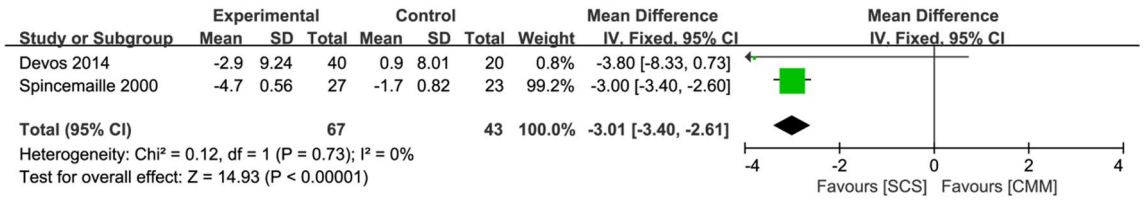


Fig. 5 Meta-analysis of drug use comparing SCS with CMM

(ODI) score in patients with chronic radicular pain after lumbar spine surgery. The authors revealed that there was no difference between burst SCS and sham SCS in ODI score. The choice of the SCS waveform is unusual in the study, and negative results could result from inadequate patient selection [34–36]. Furthermore, the application of only one stimulation modality is not representative of the multimodal SCS systems. These findings suggest that programming and outcomes should be based on an optimal combination that generates the effective dose to reach the critical neural targets and obtain the desired pain-relieving effect.

Functional magnetic resonance imaging (fMRI) studies have shown that SCS can activate the medial primary sensorimotor cortex while decreasing activation in the bilateral primary motor cortices [37]. These findings suggest that SCS impacts neuropathic pain processing based on animal models-based research, with released neurochemicals such as serotonin, noradrenaline, and dopamine that act as antagonists to gamma-aminobutyric acid (GABA) [38].

CMM consists of multiple first-line treatment modalities, including self-care, opioid and non-opioid analgesics, psychological treatments, integrative therapies, and procedures. Although some patients have reported encouraging

results in remission or achieving almost complete pain relief with SCS, clear evidence is still lacking. Our meta-analysis included eight studies with 893 patients and prognostic outcomes. To our knowledge, no previous systematic review of CMM-controlled trials of SCS for chronic pain has been conducted. Our analysis suggests that SCS could be seen as a productive treatment to relieve pain intensity. Additionally, the results showed statistically significant differences in the McGill Pain Questionnaire (MPQ), SF-36, and EQ-5D utility index, all showing beneficial effects of SCS compared with CMM on pain management.

Studies have shown that long-term exposure to opioids can lead to misuse, abuse, diversion, addiction, and overdose, which are serious issues among chronic pain patients, with addiction rates of up to more than 25% of the population studied. The MPQ showed medication dose reduction in the SCS group, suggesting that SCS may reduce the risk of drug abuse [39].

The protocol for this review was registered with PROSPERO and is available online with ID: CRD42022303605. The process of this research, including selection, appraisal, and data extraction of studies, was performed following best practice recommendations and guidance. The revised Cochrane tool for judging the risk of bias was used to assess bias. The results of the comprehensive meta-analysis revealed more evidence on the efficacy of SCS in improving health-related quality of life (HRQoL) and in diminishing pain interference.

Although this study provides more evidence on the efficacy of SCS in pain management, there are still limitations that need to be mentioned. One limitation of our study is that blinding was not possible due to the nature of the stimulation intervention. In addition, the trials included in our meta-analysis utilized conventional SCS to treat chronic pain without accounting for variations in parameter combinations or implantation devices. To further investigate the efficacy of SCS in treating chronic pain, future clinical trials should examine the effectiveness of higher frequencies (> 500 Hz; most often 10 kHz) or lower frequency (40 Hz) stimulation methods compared to CMM. Furthermore, the dorsal root ganglion (DRG) stimulation has received increasing attention as a new therapeutic approach for facilitating pain management and warrants further investigation.

Conclusions

To summarize, our analysis suggests that SCS can significantly alleviate chronic pain, reduce analgesic consumption, and improve long-term survival and quality of life. Nevertheless, larger sample sizes and more rigorous optimization of stimulation parameters are necessary to confirm these results and determine the most effective treatment strategies.

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Declarations

Conflict of interest The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent Informed consent is not required for this meta-analysis.

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