ORIGINAL ARTICLE

# Predictors of Pain Relief Following Spinal Cord Stimulation in Chronic Back and Leg Pain and Failed Back Surgery Syndrome: A Systematic Review and Meta-Regression Analysis

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■ **Abstract:** We sought to assess the extent to which pain relief in chronic back and leg pain (CBLP) following spinal cord stimulation (SCS) is influenced by patient-related factors, including pain location, and technology factors. A number of electronic databases were searched with citation searching of included papers and recent systematic reviews. All study designs were included. The primary outcome was pain relief following SCS, we also sought pain score (pre- and post-SCS). Multiple predictive factors were examined: location of pain, history of back surgery, initial level of pain, litigation/worker's compensation, age, gender, duration of pain, duration of follow-up, publication year, continent of data collection, study design, quality score, method of SCS lead implant, and type of SCS lead. Between-study association in predictive factors and pain relief were assessed by meta-regression. Seventy-four studies ($N$ = 3,025 patients with CBLP) met the inclusion criteria; 63 reported data to allow inclusion in a quantitative analysis. Evidence of substantial statistical heterogeneity ($P < 0.0001$) in level of pain relief following SCS was noted. The mean level of pain relief across studies was 58% (95% CI: 53% to 64%, random effects) at an average follow-up of 24 months. Multivariable meta-regression analysis showed no predictive patient or technology factors. SCS was effective in reducing pain irrespective of the location of CBLP. This review supports SCS as an effective pain relieving treatment for CBLP with predominant leg pain with or without a prior history of back surgery. Randomized controlled trials need to confirm the effectiveness and cost-effectiveness of SCS in the CLBP population with predominant low back pain. ■

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Submitted: April 16, 2013; Revision accepted: May 29, 2013
DOI. 10.1111/papr.12095




**Key Words:** spinal cord stimulation, back pain, systematic review, meta-regression analysis, predictive factors, outcomes

## BACKGROUND

Randomized controlled trials have shown spinal cord stimulation (SCS) to be a clinically effective adjunct to

medical management and an alternative to a further operation in individuals with chronic back and leg pain (CBLP), whom have undergone previous back surgery, so-called "failed back surgery syndrome" (FBSS).[1,2] Through improved pain relief, SCS provides important enhancement to the functionality and health-related quality of life of those with CBLP.[3] The National Institute for Health and Care Excellence (NICE) in the United Kingdom recently reviewed these trials and evidence of cost-effectiveness.[4–6] On the basis of their review, NICE recommended SCS as a treatment for patients suffering from refractory chronic neuropathic pain conditions, including CBLP.[7]

Chronic back and leg pain (CBLP) represents a poorly defined group of pain conditions, ranging from chronic low back (axial) pain to persistent hip, buttock and leg (radicular) pain syndromes, but often consists of a combination of both.[8] CBLP consists of both back and leg pain and is differentiated here from CLBP. Greater success of SCS in treatment of radicular pain has been reported than with axial low back pain;[9,10] however, both randomized controlled trials of SCS in FBSS recruited only those individuals who presented with predominant leg pain, excluding those with a chief complaint of axial pain exceeding radicular pain.[1,2] A meta-analysis of cases series in CBLP noted a substantial level of heterogeneity in the level of pain relief following SCS.[11] Although the authors of this analysis examined a number of predictive factors that may influence the differing degree of pain relief, they did not consider pain location, that is, whether pain was predominantly leg or back in origin. With the continued technological development of SCS (eg, number of electrodes, electrode configurations, programming options), there is a growing interest in understanding how these innovations impact on the level of pain relief experienced by patients with CBLP.[12–14]

The aim of this study was to examine the predictive value of patient-related factors, including leg versus back pain location and whether patients have undergone previous back surgery (FBSS), as well as SCS technology-related factors.

## METHODS

This review was carried out and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[15]

### Literature Searches

Studies were initially identified from a previous systematic review undertaken by some of the authors (RST, RJT).[11] This list of studies was updated by searching the following electronic databases from the end date of the previous review (ie, January 2002) up to June 2012: MEDLINE (Ovid), MEDLINE InProcess (Ovid), EMBASE (Ovid), Cochrane Library (Cochrane Central Register of Controlled Trials [CENTRAL], Databases of Abstracts of Reviews of Effects [DARE], Health Technology Assessment [HTA] database, NHS Economic Evaluation Database [NHSEED]; Wiley). The search strategy was developed to maximize sensitivity of article identification and was not restricted by language, or any other limits (see Appendix S1). Current controlled trials registers (metaRegister of Controlled Trials ISRCTN database, metaRegister of Controlled Trials, UK Clinical Research Network Portal, World Health Organisation International Clinical Trials Research Portal and ClinicalTrials.gov) were searched for information on current or recently completed studies. Citation lists of included papers and recent systematic reviews were checked for additional references.[16–18] Issues of the journal "*Neuromodulation*" were hand searched up to September 2012. Two reviewers (RST and RJT) independently scanned all the titles and abstracts and identified potentially relevant articles to be retrieved. Where there was uncertainty, full-text copies of papers were obtained.

### Inclusion and Exclusion Criteria

Studies were considered eligible if they fulfilled the following criteria:

- Population—adults with CBLP, who present with predominant leg pain, predominant back pain, or mixed leg and back pain, irrespective of whether they have undergone prior back surgery or not.
- Intervention—SCS.
- Comparator—none or any comparative therapy.
- Outcomes—our primary outcome was the proportion of patients achieving pain relief. Pain outcome reported as a continuous score was a secondary outcome.

Studies were excluded on the basis of: combining SCS with other interventional procedures, such as intrathecal drug delivery or other types of neurostimulation, reporting of only technical outcomes (ie, device settings

or stimulation protocols or parasthesia coverage) and no pain-related outcomes, mixed case series (ie, recruit patients from a number of indication groups) where only aggregated results were reported, single case reports or case reports, studies published as abstracts only; and non-English language publications.

### Data Extraction

The following categories of information were extracted from included studies: study population baseline characteristics (eg, age, gender, duration and location of pain); (2) SCS intervention (ie, use of test screen, type of internal implant generator, lead and placement method, stimulation parameters); study characteristics (eg, study design, country of publication, length of follow-up); and outcome results. Where studies assessed outcomes at more than one follow-up, we extracted the latest follow-up.

### Study Quality Assessment

In accord with a previous systematic review,[11] the following five factors were considered in the assessment of study quality: (1) prospective study design; (2) consecutive patient sampling; (3) explicit statement of patient inclusion/exclusion criteria; (4) losses to follow-up; and (5) blinded/independent assessment of outcome. Data extraction and quality assessment were undertaken by a single reviewer (RJT) using a standardized form and verified by a second reviewer (RST). Any disagreements were resolved by consensus.

### Data Synthesis and Analysis

Quantitative data analysis focused on the primary outcome, that is, the proportion of patients experiencing pain relief following SCS. In the case of controlled studies, only the SCS arm was used. For each study, pain relief was expressed as a percentage and the 95% confidence interval calculated (based on an exact binomial distribution). Results were pooled across studies using meta-analysis methods using the inverse variance approach.[19,20]

Heterogeneity among studies was first explored qualitatively (by comparison of the characteristics of included studies) and quantitatively (using the $\chi^2$ test of heterogeneity and $I^2$ statistic). Given that both the level of clinical and statistical heterogeneity were seen (ie, $\chi^2$ test of heterogeneity $< 0.05$ and $I^2$ statistic $> 50\%$), the DerSimonian Laird random-effects method was used to pool studies.[21,22] Rather than simply calculate a single overall pooled estimate of the effectiveness of SCS, the primary aim of analysis was to explore heterogeneity and assess the patient and technology-related factors that were associated with SCS pain relief. The funnel plot was examined and Egger et al.'s test calculated to examine the likely presence of publication bias and small-study effect.[23]

A "between-study" analysis used meta-regression to examine the influence of the following prespecified study level factors: initial level of pain (mean pain score) type of CBLP (predominant back pain vs. predominant leg pain vs. mixed leg and back pain; CBLP with history of back pain surgery vs. CBLP with no history of back pain surgery); age (mean); gender (% male); duration of pain (mean); duration of follow-up (mean); litigation/worker's compensation; year of publication; continent of data collection (North America vs. Europe vs. other); study setting (single vs. multicenter); SCS intervention (surgical vs. percutaneous leads, quadripolar vs. octapolar vs.16-contacts); study design (RCT or non-RCT vs. case series); and quality score. These factors were assessed in both a univariable and multivariable model with *P* value adjustment for multiple testing.[24]

Studies reporting continuous pain scores (either as visual analog scale [VAS] or numerical rating scale [NRS]) were separately pooled using meta-analysis as pre- and post-SCS change scores. In accord with recommended methods for pooling pain outcomes, where necessary, pain scores were transformed, so all studies were expressed on a 0–10 scale.[11,25,26] Where not reported, standard deviation for change was calculated using pre- and post-SCS standard deviations (assuming a within-study correlation coefficient of 0.9).[20]

A number of studies reported the association between patient-related and technology-related factors and SCS pain relief. The results of these "within-study" analyses were tabulated and reported descriptively. All quantitative analyses were performed using STATA v.11.1 (Stata Corp., College Station, TX, U.S.A.).

## RESULTS

### Identification and Selection of Studies

Our previous systematic review included a total of 78 studies of which 21 studies were judged not to meet the revised inclusion criteria of this present review.[11] The

main reasons for exclusion were non-English language and abstract only publications.

The electronic searches for this updated review yielded a total of 992 titles, of which 18 new studies were included. Therefore, a total of 74 studies (77 publications) were included, of which 68 were case series, four were RCTs, and two were comparative studies using a nonrandomized design. The selection process is summarized in Figure 1 (citations of studies included and excluded on the basis of full paper review are listed in Appendix S2). The characteristics of the included studies are summarized in Table 1.

### Study Quality

Details of study methodology were generally poorly reported, therefore, limiting our ability to assess study quality (see Table 2). Only four studies fulfilled all five criteria, that is, used a prospective design, recruited consecutive or all eligible patients, provided an explicit description of inclusion and exclusion criteria, blinded outcome assessment or used a third party assessor, and reported a loss to follow of 20% or less [lvi, xxxviii, lxix, lxx]. The overall quality of studies was in general relatively poor with a median quality score of 2 out of a potential maximum score of 5. There was evidence of an increase in quality score over time (ie, median quality score of studies published in 1980–1989: 1 vs.1990–1999: 2 vs. 2000 or later: 3).

### Level of Pain Relief with SCS

A total of 63 studies reported the proportions of individuals with CBLP patients experiencing pain relief following SCS. Only four studies reported percentage pain relief in the leg or back or both [ii, lxv, lxvii, lxx]. The majority of studies (59/63), therefore, assessed and reported generic pain relief, that is, undifferentiated by back or leg location. For the purpose of our between-study analysis, the results of all 63 studies were pooled.

There was evidence of substantial statistical heterogeneity in the level of pain relief at longest follow-up across studies ($\chi^2$ statistic: 402.91, $P < 0.0001$, $I^2$

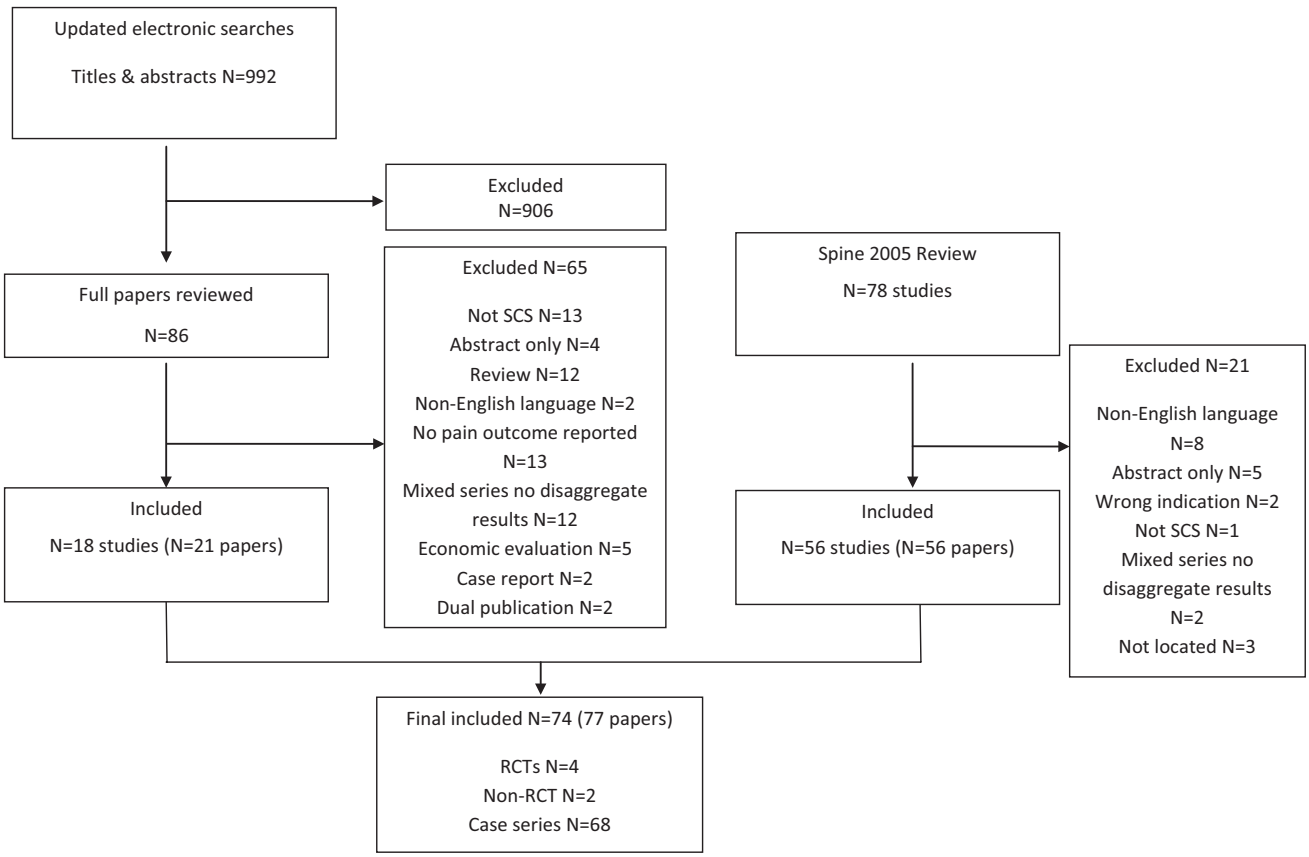



**Figure 1.** Summary of study selection.

**Table 1. Selected Characteristics of the Included Studies (*n* = 74)**

| Characteristic* | Number of Studies (%) or Median (range)† |
|---|---|
| Sample size | 29 (1–196) |
| Publication date | |
| 1980–1989 | 26 (35%) |
| 1990–1999 | 24 (32%) |
| 2000–2009 | 17 (23%) |
| 2010-present | 7 (9%) |
| Study location | |
| North America | 35 (47%) |
| Europe | 36 (49%) |
| Other | 3 (4%) |
| Setting | |
| Single centre | 58 (78%) |
| Multi centre | 16 (22%) |
| Mean age (*n* = 59) | 50 (43–70) |
| Gender (% male; *n* = 53) | 52 (27–86) |
| Previous back operation (% patients; *n* = 64) | 100 (0–100) |
| Duration of pain before SCS (months; *n* = 40) | 85 (6–180) |
| Pain score before SCS (0–10 scale; *n* = 25) | 7.8 (2.7–8.4) |
| Location of CBLP | |
| Predominantly back | 4 (5%) |
| Predominantly leg | 9 (12%) |
| Mix of back and leg | 22 (20%) |
| Not reported | 39 (53%) |
| Workers compensation/insurance | |
| In all or a proportion of patients | 8 (12%) |
| Not reported | 66 (89%) |
| SCS lead placement | |
| Percutaneous lead only | 23 (31%) |
| Surgical lead only | 19 (25%) |
| Both percutaneous & surgical | 13 (17%) |
| Lead | |
| Not reported | 20 (27%) |
| Duration of follow-up (months; *N* = 66) | 24 (1–65) |
| Outcomes reported | |
| Pain relief | 63 |
| Pain score | 12‡ |
| All SCS-related complications | 7 |
| Complications requiring intervention | 13 |

*$N$ = 74 unless otherwise stated.
†Median and range of study means.
‡Report appropriate data to allow meta-analysis.

**Table 2. Quality of Included Studies (*n* = 74)**

| Criteria | Frequency of Studies (%) | | |
|---|---|---|---|
| | Yes | No | Not Reported |
| Design: Prospective design | 20 (27%) | 20 (27%) | 34 (46%) |
| Population selection: All eligible or consecutive patients | 19 (25%) | 0 | 54 (75%) |
| Population description: Explicit inclusion/exclusion criteria* | 34 (45%) | 40 (55%) | NA |
| Outcome assessment: Blinded or independent | 14 (19%) | 2 (3%) | 58 (78%) |
| Attrition: ≤ 20% drop out/loss to follow-up | 47 (63%) | 8 (5%) | 23 (32%) |
| Quality score† | | | |
| Median (range) | 2 (0–5) | | |

*Defined as sufficient detail to be able to differentiate whether included patients with CBLP had predominantly leg pain, predominantly back pain, or a mix of leg and back pain.
†Number of quality criteria met (0–5).
CBLP, chronic back and leg pain; NA, not applicable.

statistic: 85%). Overall, 58% (95% confidence interval (CI): 53% to 64%, random effects) of patients with CBLP achieved pain relief (see Figure 2). Studies used a range of definitions of pain relief that included objective cut-offs (eg, ≥ 50% reduction in pain) and subjective cut-offs (eg, "satisfactory", "good" or "excellent" pain relief). However, the level of pain relief with SCS appeared consistent when limited to those 32 studies that used an objective definition (53%, 95% CI: 47% to 59%, random effects).

There was evidence of small-study bias and potential publication bias as evidenced by funnel plot asymmetry (see Figure S1) and a significant Egger test ($P = 0.003$).

Eleven studies (12 comparisons) reported pain score before and after SCS data appropriately to allow meta-analysis [ii, lvii, lviii, lix, lx, lxi, lxv, lxix, xliii, lxxv, lxxvii]. There was evidence of significant statistical heterogeneity ($\chi^2$ statistic: 237.8, $P < 0.0001$, $I^2$ statistic: 95%) across studies. The mean reduction in pain score (on 0–10 scale) with SCS across studies was −3.3 (95% CI: −3.9 to −2.7, random effects; see Figure 3). There were insufficient studies to examine the association between patient and device-related factors and the change in pain score with SCS.

### Meta-Regression and Stratified Meta-analysis

In univariable meta-regression analysis, the only study level factor to be associated with level of SCS pain relief was the mean duration of pain ($P = 0.011$; see Table 3). An increasing mean duration of pain across studies was associated with a reduction in the level of SCS pain relief —each 12-month increase in the duration of pain reduced the level of pain relief by ~2.0% (see Figure 4).

Figure 5 shows a meta-analysis stratified by the location of CBLP pain. There appeared a higher level of pain relief with studies in individuals with predominantly back pain compared with studies in those with predominantly leg pain (see Figure 5). However, the number of studies contributing data to this analysis was small [ii, xvi, lxx], and no significant statistical association with pain relief and the location of CBLP was seen in either univariable or multivariable meta-regression. In multivariable analysis, no study- or patient- or technology-related characteristics were seen to be significant predictors of pain relief following SCS (see Table 3).

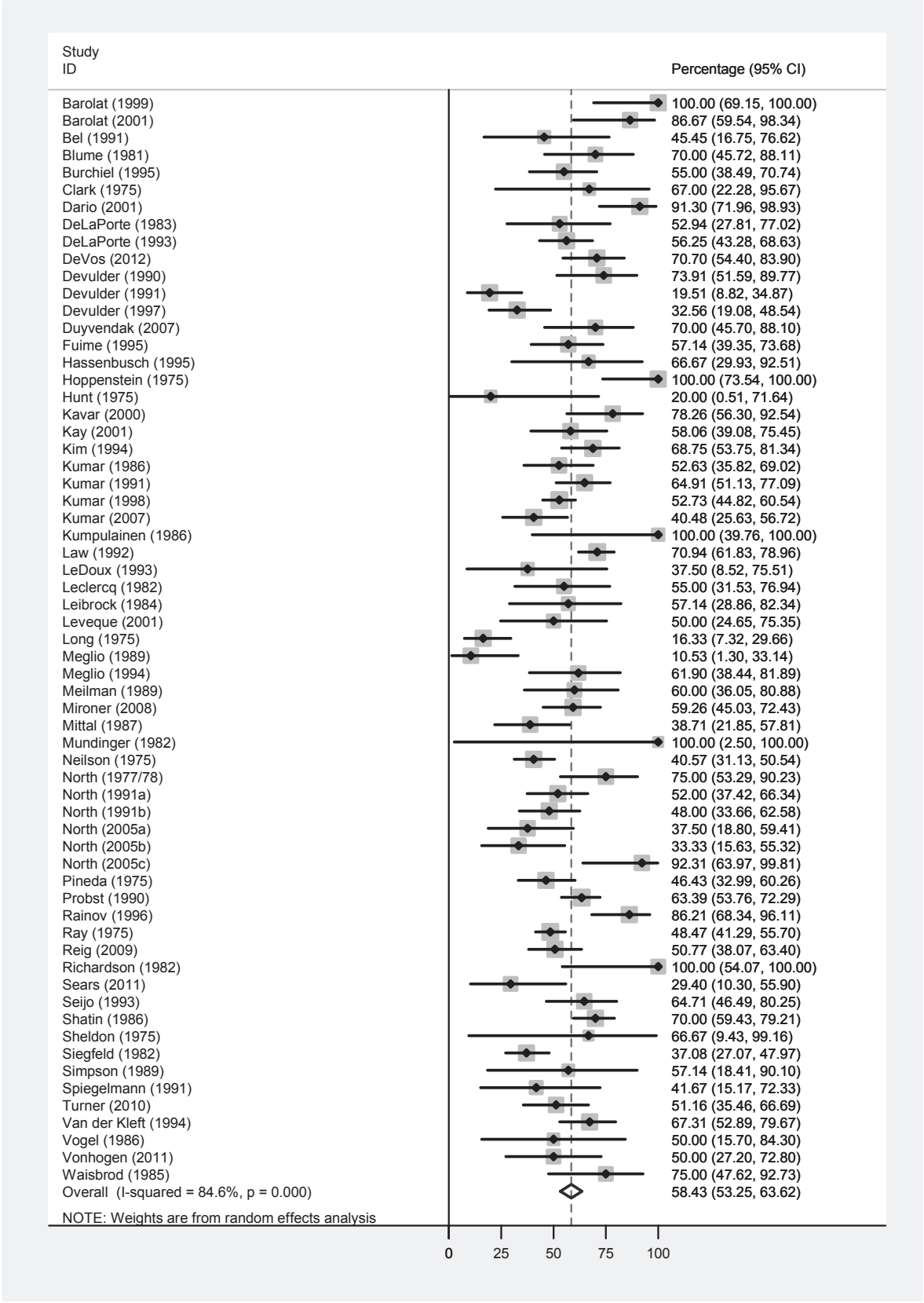
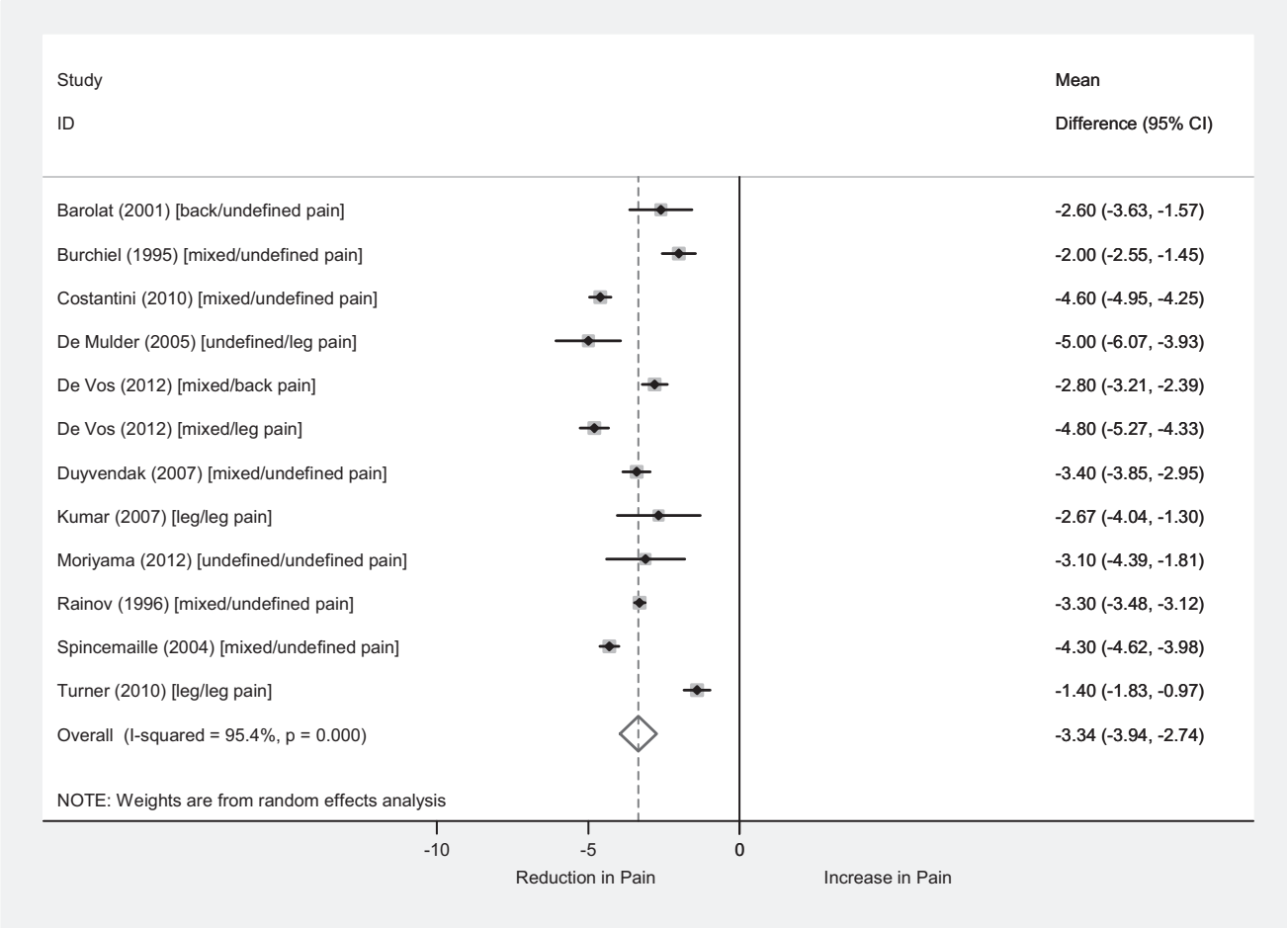



**Figure 2.** Meta-analysis of pain relief following SCS.




Study (year) [location of CBLP pain/location of pain assessment]

Weighted pooled estimate shown as diamond as bottom of plot

**Figure 3.** Meta-analysis of change in pain score (0–10 scale) with SCS.

### Within-study Analysis

***Back vs. Leg Pain Outcome.*** Ten SCS studies reported both back and pain leg outcomes following SCS in the same individuals [ii, lix, lx, lxv, lxvii, lxx, xxxix, lxxiii, lxxvi, lxvii, lxx, xxxix, lxxiii, lxxvi, lii] (see Table 4). In the four studies in which pain was predominantly leg, three reported a higher level of pain relief for the leg than the back [lxv, xxxiv, lxx]. The fourth, a study in patients with FBSS on worker's compensation, found only a small reduction in leg pain relief up to 24-months, while the level of back pain got worse following SCS [lxxvi]. The one study undertaken in those with predominant back reported similar levels of pain relief at 6 and 24-months post-SCS in both leg and back [ii]. Consistent with this, the five studies with either mixed leg and back pain or a nondefined location of CBLP observed a similar magnitude of pain relief in the legs and back following SCS [lix, lxvii, lx, lxxiii, lii].

***Device-related Factors.*** Seven studies examined the association between device-related aspects of SCS and pain relief [xi, xxi, xxvii, lxvii, xxxvii, lxix, xli] (see Table 5). North et al. found that patients with FBSS with predominant leg pain randomized to lead placement by laminectomy experienced better pain relief than those allocated to percutaneous lead placement [lxix]. This observation was confirmed by a nonrandomized study [xxvii]. A single-center review of 182 individuals with FBSS over an average of 8.8 years follow-up

**Table 3. Meta-Regression Analysis of Included Studies Reporting SCS Pain Relief ($n$ = 59)**

| Predictors* | Univariable Coefficient (95% CI) *P* value | Multivariable† Coefficient (95% CI) *P* value |
|---|---|---|
| Study characteristics | | |
| Continent | −0.5 (−5.6 to 4.5) 0.83 | −11.1 (−26.4 to 4.2) 0.36 |
| Sample size | −0.1 (−0.2 to 0.1) 0.40 | −0.1 (−1.4 to 126) 1.00 |
| Publication year | 0.2 (−0.3 to 0.7) 0.46 | −2.4 (−4.6 to 43.1) 0.15 |
| Setting‡ | 0.1 (−13.1 to 13.4) 0.99 | 7.6 (−43.4 to 58.5) 0.99 |
| Comparative design§ | −0.2 (−17.4 to 17.0) 0.98 | −2.3 (39.9 to 35.4) 1.00 |
| Quality score¶ | 0.4 (−3.6 to 4.3) 0.86 | −1.1 (−2.6 to 0.4) 0.36 |
| Follow-up duration (56) | −0.3 (−0.7 to 0.06) 0.10 | 0.07 (−1.9 to 2.0) 0.93 |
| Baseline VAS pain (16) | 0.3 (−10.3 to 10.0) 0.95 | −4.9 (−26.1 to 16.2) 0.96 |
| Patient characteristics | | |
| Mean age (49) | −1.4 (−2.8 to 0.04) 0.06 | 1.8 (−2.4 to 6.1) 0.26 |
| Percent male (43) | 0.1 (−0.3 to 0.5) 0.56 | 1.0 (−0.3 to 2.3) 0.30 |
| Percent postop (53) | 0.1 (−0.5 to 0.8) 0.71 | ‖ |
| Duration of pain (33) | −0.2 (−0.3 to −0.05) 0.011 | 0.02 (−0.5 to 0.6) 0.92 |
| CBLP location** (29) | −4.0 (−15.8 to 7.7) 0.49 | ‖ |
| Worker's compensation (60) | 1.9 (−16.2 to 20.0) 0.84 | ‖ |
| SCS characteristics | | |
| Lead placement (47) | 3.2 (−4.8 to 11.4) 0.42 | ‖ |

*$N$ = 59 studies included unless otherwise stated.
†Based on $N$ = 12 studies and $P$ value adjusted for multiple testing.
‡Single centre vs. multicentre.
§Controlled vs. case series.
¶Number of quality criteria met (0–5).
‖Studies dropped due to colinearity.
**Predominantly leg vs. predominantly back vs. mixed.

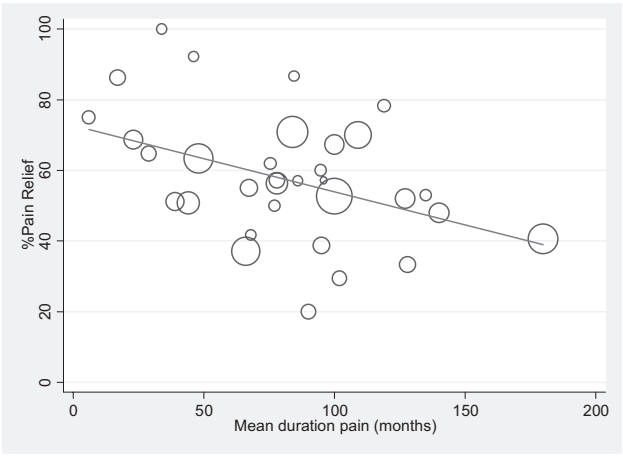



**Figure 4.** Plot of between study association of mean duration of pain vs. level of SCS pain relief.

reported differences between SCS devices in "time to failure"; a composite outcome taking into account trial stimulation failure, device complication, and loss of pain relief [xxi]. One study found multichannel stimulation parameters to be associated with a higher level of pain relief than a simple bipolar stimulation [xxxvii], while another found patients reported no difference between the two forms of stimulation [lxvii]. Pineda et al. found no difference in the proportions of patients reporting satisfactory or excellent pain relief between those who had received a unipolar electrode compared with those who got a bipolar electrode [xli].

***Patient-Related Factors.*** Eight studies reported the association between patient characteristics and pain relief following SCS [lvii, vi, lxiii, xxi, lxv, xxxvii, xxxvii, xli] (see Table 6). The study by Dario et al. reported higher levels pain relief with SCS in 10 individuals with predominant leg pain compared to 14 with leg only pain [vi]. Similarly, Pineda et al. found that of the individuals with back pain only, none achieved a satisfactory level of back pain relief following SCS [xli]. This compared with 40% of those with only leg and 49% of those with both leg and back. While, Kumar and colleagues [xxi] found a significant association between the time since back operation and pain relief with SCS (those with shortest time since operation having the greatest level of pain relief), three other studies reported no such association [lvii, lxiii, xxxvii]. No other patient-level characteristics were consistently found to be related to the level of pain relief following SCS.

## DISCUSSION

This systematic review of evidence base on pain relief following SCS quantifies the association between the level of pain relief and patient and technology-related factors.

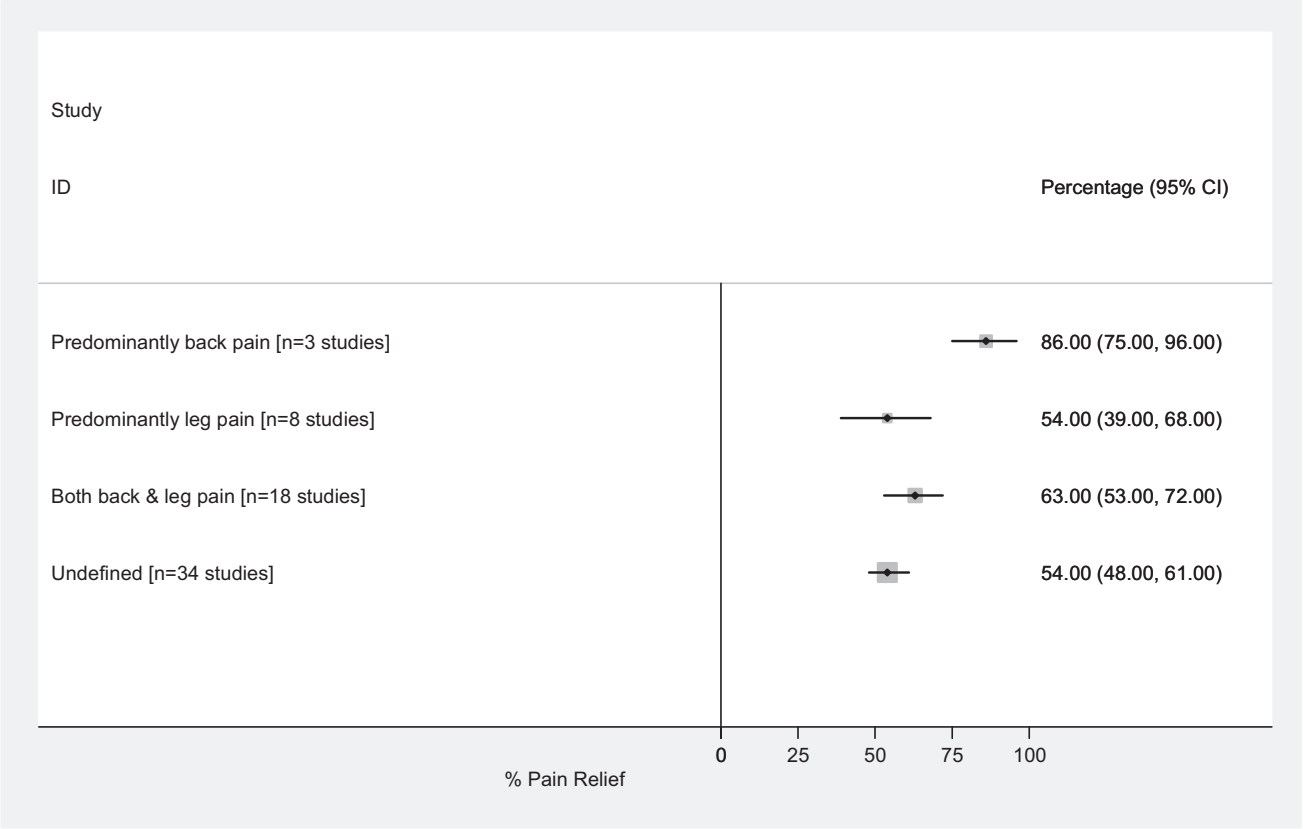



**Figure 5.** Stratified meta-analysis—pain relief following SCS by location of CBLP.

Our review included 74 studies in a total of 3,025 individuals with CBLP, the majority of which were post back surgery (ie, patients with FBSS). We found a substantial number of individuals experience important levels of pain reduction following SCS, that is, 53% (95% CI: 47% to 60%) achieving an equivalent of 50% more pain relief at a mean follow-up of 24 months. This is supported by a magnitude of reduction in pain score (on 0–10 scale) with SCS studies of −3.3 (95% CI: −3.9 to −2.7) that indicates a clinically important change (ie, a change of 2 or more units on 0–10 scale[27,28]). Although there was considerable heterogeneity across studies, we found no strong evidence that pain relief with SCS was limited to particular patients with CBLP subgroups. The one exception was the duration of pain, that is, those studies with the longest mean duration of pain reported a smaller magnitude of pain relief following SCS. However, we need to be cautious in this interpretation as this study level association was not seen in multivariable analysis, that is, adjusting for other study level characteristics. Two studies have shown that patients with FBSS receiving a surgical lead placement by laminectomy have superior analgesic outcomes compared with those who received a percutaneous lead placement.[13,29]

It is believed that SCS may be a more successful therapy for CBLP in those who present with pain predominantly in the legs than the low back.[12–14] While we sought to quantitatively explore the association between the level of SCS pain relief and the location of pain, because of the quality of reporting of the majority of included studies (few studies reported either the precise details of the location of pain pre-SCS, the pain outcome in both leg and back post-SCS), we were only able to partially do so. Although contemporary studies are better, only a minority of studies provide sufficient description of the entry criteria and assessment of participants to be able to reliably determine the location of their CBLP. Additionally, few studies have reported data on the level of pain relief in both the legs and the back. Accepting these limitations, SCS appears to be effective in reducing CBLP irrespective of back or leg pain location. Although increasing in the number, fewer SCS studies to date have reported outcomes of SCS in predominantly back pain populations. We identified no

**Table 4. Within Study Assessment: Comparison of Back vs. Leg Pain Outcome**

| Study | Design | Population and Period of Follow-up | Findings | Comment |
|---|---|---|---|---|
| Barolat (2001)[ii] | Case series | 41 intractable low back pain.<br>Predominant back pain.<br>Follow-up to 24 mo | Pain relief*<br>6 months—Leg pain: 19/21 (92%), Back pain: 17/21 (83%) $P = 0.38^{\dagger}$<br>24 months—Leg pain: 13/15 (88%), Back pain: 10/15 (67%) $P = 0.20^{\dagger}$ | *Pain relief > 2 on 5-pt scale<br>$^{\dagger}P$ value calculated by authors of this report |
| De Mulder (2005)[lix] | Case series | 20 FBSS with chronic leg and back pain. Location of pain undefined<br>Follow-up 13 month | Pain score*<br>Leg pain pre-SCS: mean 7.4 (SD 2.8)<br>Leg pain post-SCS: mean 2.8 (SD 4.0), $P < 0.001$*<br>Back pain pre-SCS: mean 7.8 (SD 2.0)<br>Back pain post-SCS: mean 3.4 (SD 4.5), $P < 0.001$*, $P = 0.66^{\dagger}$^ | Pain VAS—read off graph<br>*compared with pre-SCS<br>^comparing post-SCS leg and back pain<br>$^{\dagger}P$ value calculated by authors of this report |
| de Vos (2012)[lx] | Case series | 41 FBSS with both leg and back pain<br>Follow-up 12 month | Pain score*<br>Leg pain pre-SCS: mean 8.0 (SD 0.8)<br>Leg pain post-SCS: mean 4.3 (SD 1.7)<br>Back pain pre-SCS: mean 7.0 (SD 1.2)<br>Back pain post-SCS: mean 4.2 (SD 2.1) $P = 1.00^{\dagger}$^<br>Pain relief<br>Leg pain: 29/41 (71%), Back pain: 21/41 (51%) $P = 0.07^{\dagger}$ | Pain VAS—read off graph<br>^comparing post-SCS leg and back pain<br>$^{\dagger}P$ value calculated by authors of this report |
| Kumar (2007)[lxv] | RCT | 52 FBSS. Predominant leg.<br>Follow-up 6 month | Pain relief*<br>6 months—leg pain: 23/42 (55%), back pain: 14/42 (33%), $P = 0.05^{\dagger}$<br>12 months—leg pain; 16/42 (38%), back pain: 13/42 (31%), $P = 0.49^{\dagger}$<br>24 months—leg pain: 17/42 (40%), back pain: 11/42 (26%), $P = 0.21^{\dagger}$<br>Pain score^<br>Baseline—leg pain: mean 76.0 (SD 13.0), back pain: 34.5 (24.3) $P < 0.0001^{\dagger}$<br>6-months change in score—leg pain: mean −26 (95% CI: −40.4 to −13.0, $P < 0.0001$), back pain: mean −11.0 (−25.0 to −3.0, $P = 0.008$) | *≥ 50% pain relief<br>$^{\dagger}P$ value calculated by authors of this report<br>^VAS pain |
| Mironer (2008)[lxvii] | Case series | 54 chronic low back and/or lower extremity pain. Location of pain undefined<br>Follow-up mean 9.3 month | Pain relief*<br>Leg pain: 34/54 (63%)<br>Back pain: 31/54 (58%) $P = 0.64^{\dagger}$ | *≥ 50% pain relief<br>$^{\dagger}P$ value calculated by authors of this report |
| North (2005c)[lxx] | RCT | 20 FBSS. Predominantly leg pain.<br>Up to 24 month follow-up | Pain relief<br>6 months follow-up<br>Back pain: 8/16 (50%)<br>Leg pain: 14/16 (88%) $P = 0.02^{\dagger}$ | *≥ 50% pain relief and patient satisfaction<br>$^{\dagger}P$ value calculated by authors of this report |

**Table 4. (Continued)**

| Study | Design | Population and Period of Follow-up | Findings | Comment |
|---|---|---|---|---|
| | | | 24 months follow-up<br>Back pain: 6/13 (46%)<br>Leg pain: 12/13 (88%) $P = 0.01^{\dagger}$ | |
| Ohnmeiss (1996)[xxxix] | Case series | 38 intractable leg pain.<br>Predominantly leg pain.<br>Up to 24 month follow-up | Pain score*<br>Mean leg pain<br>Preop: 7.38<br>6 week: 4.18, $P < 0.05$+<br>6 month: 5.55, $P < 0.05$+<br>12 month: 6.27, $P < 0.05$+<br>Mean back pain<br>Preop: 5.35<br>6 week: 4.71, $P < 0.05$ +<br>6 month: 5.35<br>12 month: 5.70 | *Pain VAS<br>+Compared with pre-op score |
| Rigoard (2012)[lxxiii] | Case series | 11 FBSS<br>Chronic back & leg pain<br>3 & 6 month follow-up | Pain score*<br>Mean leg pain<br>Preop: 7.6<br>3 month: 0.5<br>6 month: 0.5, $P < 0.05$ +<br>Mean back pain<br>Preop: 7.8<br>3 month: 1.5<br>6 month: 1.5, $P < 0.05$+ | *Pain VAS<br>+Compared with pre-op score |
| Turner (2010)[lxxvi] | Non RCT | 51 FBSS. Predominantly leg pain.<br>Up to 24 month | Pain score*<br>Leg pain<br>Pre-SCS: mean 7.7 (SD 1.0) $N = 51$<br>6 month post-SCS: mean 6.3 (SD 2.3) $N = 51$<br>12 month post-SCS: mean 6.8 (SD 1.9) $N = 47$<br>24 month post-SCS: mean 6.3 (SD 2.0) $N = 43$<br>Back pain<br>Pre-SCS: mean 6.0 (SD 1.9) $N = 51$<br>6 month post-SCS Not reported<br>12 month post-SCS: mean 6.8 (SD 2.1) $N = 47$, $P = 1.00^{\dagger}$^<br>24 month post-SCS: mean 6.6 (SD 1.8) $N = 43$, $P = 0.33^{\dagger}$^<br>Pain relief**<br>Leg pain<br>6 month 9/52 (18%) | *Pain rating on 0–10<br>\<br>^Comparison of leg vs. back<br>$^{\dagger}P$ value calculated by authors of this report<br>**≥ 50% pain relief |

**Table 4. (Continued)**

| Study | Design | Population and Period of Follow-up | Findings | Comment |
|---|---|---|---|---|
| | | | 12 month 7/47 (15%)<br>24 month 9/43 (21%)<br>Back pain<br>Not reported | |
| Van Buyten (1999)[iii] | Case series | 17 FBSS. Both leg and back pain<br>24 month | Generic pain*<br>Pre-SCS: mean 9.4<br>Post-SCS: mean 4.7, $P < 0.0001$<br>Back pain*<br>Pre-SCS: mean 9.7<br>Post-SCS: mean 4.6, $P < 0.0001$<br>Leg pain*<br>Pre-SCS: mean 9.5<br>Post-SCS: mean 3.6, $P < 0.0001$<br>"Comparable VAS changes were reported at the interim follow-up for global, back and leg pain" | *VAS (0–10) pain score |

randomized controlled evidence of SCS in this subpopulation.

### Comparison with Previous Reviews

The level of pain relief seen in this update review is consistent (ie, the 95% CIs overlap) with the findings of our 2005 meta-analysis—62% (95% CI: 56% to 69%) achieving an equivalent of 50% or more pain relief following SCS at a mean follow-up of 26 months.[11] In this present study, we only found the duration of pain to be predictive of the level of pain relief following SCS, while the previous meta-analysis identified a number of predictors (ie, duration of study follow-up, type of pain [CBLP vs. FBSS] and study setting [single vs. multicenter]). This difference probably reflects the somewhat different evidence base between the two analyses—we excluded some studies from the previous review (eg, abstracts only, mixed case series that did not specifically report outcomes in those with CBLP) and a number of studies, published since, have been included in this review.

Previous systematic reviews of SCS for CBLP have not formally quantified the difference in level of pain relief with SCS according to the location of CBLP or whether pain assessment was specific to either the legs or back or aspects of SCS technological innovation.[5,11,17,18,30] However, a number of these issues have been qualitatively reviewed in the "Pain Practice Parameters for the Use of Spinal Cord Stimulation in the Treatment of Chronic Neuropathic Pain" report.[9] This report gave a "level B" recommendation (ie, uncertain validity) that pain is most likely to be treated successfully by SCS if: "*The pain location is radicular or radiating than axial in distribution (predominant low back pain is more difficult to treat)….*".

### Strengths and Limitations

We made every effort to reduce potential bias in this review. We used comprehensive electronic searches, including the searching of reference lists of included studies and previous reviews. However, we did find evidence of small-study bias that may reflect some level of publication bias. By including only studies that reported pain outcomes in CBLP individuals, we sought to minimize confounding due to the effects of SCS on other indications. We found several potential biases in the included studies: methodological details were often poorly reported with respect to the use of prospective

**Table 5. Within Study Assessment: SCS Procedure-Related Predictors**

| Study | Design | Comparison | Population and period of follow-up | Findings | Comment |
|---|---|---|---|---|---|
| Devulder (1997)[xi] | Case series | Battery type | 69 FBSS<br>Location of pain undefined<br>Mean follow-up 30 month | Complications*<br>Radiofrequency: 23/27 (85%)<br>Internalized battery: 25/42 (53%) $P = 0.02^{\dagger}$ | *Electrode reinterventions<br>†*P* value calculated by authors of this report |
| Kumar (1998)[xxi] | Case series | Type of electrode | 182 chronic postlaminectomy pain<br>Location of pain undefined<br>Mean follow-up 8.8 year | Time to failure*<br>Resume & Pisces-Quadripolar electrodes significantly more reliable than Pisces-Sigma electrodes (hazard ratio = 0.49, $P < 0.001$; hazard ratio = 0.45, $P < 0.01$, respectively). No significant difference in reliability Resume vs. Pisces-Quadripolar systems. | *Failure of trial stimulation, device complication, loss of pain relief |
| Leveque (2001)[xxvii] | Case series | Implant technique | 23 FBSS<br>Location of pain undefined<br>Mean 34 month follow-up | Pain relief*<br>Laminectomy 12/14 (86%)<br>Pecutaneous 6/9 (67%), $P = 0.28$<br>Postop pain score<br>Laminectomy mean 4.6 (range 0–9)<br>Pecutaneous mean 6.1 (range 0–10) | *Excellent or good pain relief |
| Mironer (2008)[lxvii] | Case series | Stimulation parameters | 54 chronic low back and/or lower extremity pain<br>Location of pain undefined<br>Mean 9.3 month | Pain relief*<br>Single stimulation: 6/9 (65%)<br>Multi stimulation: 25/44 (56%) $P = 0.58^{\dagger}$ | *50% pain relief<br>†*P* value calculated by authors of this report |
| North (1991b)[xxxvii] | Case series | Type of electrode | 50 FBSS<br>Location of pain undefined<br>Mean follow-up 5.0 years | Success*<br>Programmable multichannel implants significantly better than simple bipolar electrodes (coefficient+; 1.231, $P = 0.047$) | *≥ 50% pain relief and patient satisfaction<br>+logistic regression |
| North (2005b)[lxix] | RCT | Implant technique | 24 FBSS<br>Leg pain ≥ back pain<br>Up to 2.9 years follow-up | Success*<br>Mean 1.9 years follow-up<br>Laminectomy 10/12 (83%)<br>Pecutaneous 5/12 (42%), $P = 0.04$<br>Mean 2.9 years follow-up<br>Laminectomy 5/12 (42%)<br>Pecutaneous 3/12, (25%) $P = 0.91$<br>Activities of daily living<br>"Improvement greater with laminectomy. Not statistically significant"+<br>Complications<br>Percutaneous 5/12 (42%)<br>Laminectomy 1/12 (8%) | *≥ 50% pain relief and patient satisfaction<br>+ no inferential statistics reported |
| Pineda (1975)[xli] | Case series | Type of electrode | 56 unsuccessful lumbar disc surgery<br>Back, leg, and mix of back and leg pain<br>Follow-up duration not reported | Pain relief*<br>Unipolar: 14/28 (50%)<br>Biopolar: 12/28 (43%), $P = 0.59^{\dagger}$ | * "satisfactory" or "excellent" pain relied (no definition)<br>†*P* value calculated by authors of this report |

**Table 6. Within Study Assessment—Patient Characteristics**

| Study | Design | Comparison | Population & Period of Follow-up | Findings | Comment |
|---|---|---|---|---|---|
| Burchiel (1995)[lviii] | Case series | Age, gender, education, pain, compensation for injury, prior back operations, duration of pain | 40 chronic leg & back pain<br>Mix of leg and back pain<br>Mean follow-up 5.6 year | Pain relief*<br>age $r^2 = 0.53$, $P = 0.004$ +<br>gender $r^2 = 0.17$, $P = 0.17$ +<br>pain location $r^2 = 0.23$, $P = 0.3$ +<br>compensation $r^2 = 0.11$, $P = 0.5$ +<br>pain operations $r^2 = 0.29$, $P = 0.1$ +<br>pain duration $r^2 = 0.09$, $P = 0.6$+ | *≥ 50% pain relief and patient satisfaction<br>+multivariate regression-based analysis |
| Dario (2001)[vi] | Non RCT | Location of CBLP | 24 FBSS<br>Mix of leg and back pain<br>Follow-up to 84 month | Pain score*<br>Leg only pain ($n = 14$)<br>Pre-SCS pain: mean 85 (range 77–92)<br>Post-SCS pain: mean 22 (range 17–24)<br>Predominant leg pain ($n = 10$)<br>Pre-SCS pain: mean 45 (range 39–50)<br>Post-SCS pain: mean 40 (range 36–45)<br>"$P < 0.01$ between groups" | |
| Fiume (1995)[lxiii] | Case series | Number of surgical operations, duration and severity of symptoms, time since first operation, gender, pain location | 55 FBSS with radicular pain<br>Location of pain not reported<br>Mean follow-up 55 month | Pain relief*<br>"There was no relationship between the success rate and number of surgical operations, duration and severity of symptoms, time since first operation."<br>Female: 15/22 (69%)<br>Male: 13/31 (43%) $P = 0.06$†<br>"patients with predominant pain did better" | *≥ 50% pain relief<br>†$P$ value calculated by authors of this report |
| Kumar (1998)xxi | Case series | Age<br>Gender<br>Number of previous back operations<br>Time since last back operation<br>Worker's compensation | 182 chronic postlaminectomy pain<br>Location of pain not reported<br>Mean follow-up 8.8 year | Successful pain relief*<br>< 51 years: 48/91 (53%)<br>> 51 years: 39/74 (53%)<br>$P = 0.99$†<br>Male: 74/140 (53%)<br>Female: 13/25 (52%)<br>$P = 0.94$†<br>1: 9/29 (47%)<br>2: 23/40 (58%)<br>3: 26/56 (46%)<br>4: 14/24 (48%)<br>> 4: 15/26 (58%) "no correlation"+<br>0–3 month: 17/18 (94%)<br>3–6 month: 31/39 (79%)<br>6–9 month: 22/40 (55%)<br>9–12 month: 14/36 (40%)<br>> 12 month: 3/39 (9%),<br>regression coeff. −0.86, $P < 0.05$<br>Workers comp claim: 30/56 (54%)<br>No workers comp: 57/109 (52%) $P = 0.88$† | *50% pain relief<br>†$P$ value calculated by authors of this report<br>+no inferential statistics reported |
| Kumar (2007)[lxv] | RCT | Number of previous back surgeries | 94 FBSS<br>Leg > back pain<br>Follow-up 6 mo | Pain relief*<br>< 3 vs. ≥ 3: $P = 0.95$ +<br>trend favoring < 3 | *≥ 50% pain relief<br>+Subgroup analysis (interaction test |

**Table 6. (Continued)**

| Study | Design | Comparison | Population & Period of Follow-up | Findings | Comment |
|---|---|---|---|---|---|
| | | Duration of diagnosis of FBSS | | < 12 vs. ≥ 12 months: $P = 0.20$ + | ^includes both SCS and usual medical care intervention received |
| North (1991b)[xxxvii] | Case series | Gender, duration of follow-up, time since 1st operation, number of previous operations, pain location | 50 FBSS<br>Location of pain not reported<br>Mean follow-up 5.0 year | Success*<br>Males significantly poorer than simple bipolar electrodes (coefficient+; 1.231, $P = 0.047$)<br>"No significant association for duration of follow-up, time since 1st operation, number of previous operations, pain location (axial vs. radicular)" | *≥ 50% pain relief and patient satisfaction<br>+logistic regression |
| North (2005a)[xxxviii] | RCT | Age, gender, number of previous operations, workers compensation | 50 FBSS<br>Back > leg pain<br>Mean follow-up 2.9 year | Success*<br>"No association of age, gender, number of previous operations, workers compensation with outcome" | *≥ 50% pain relief and patient satisfaction |
| Pineda (1975)[xli] | Case series | Location of pain | 56 unsuccessful lumbar disc surgery<br>Duration of follow-up not reported | Pain relief*<br>Back pain: 0/6 (0%)<br>Leg pain: 2/5 (40%)<br>Leg & back pain: 22/45 (49%) | *Excellent or satisfactory pain relief |

design, population selection, and independent outcome blinding. Therefore, there was potential for selection and assessment bias.

As outlined above, the principle limitation of this study was the failure by more than half of the included studies to report sufficient details to enable us to assess the factors that may be predictive of pain relief, including the precise location of pain. CBLP and FBSS are heterogeneous descriptors; identification of specific pain predictors can allow stratification of this broad group of patients and, thereby, the optimization of therapy. Another limitation is the risk of ecological fallacy with meta-regression. An association between pain relief and patient and technology factors at a study level may not reflect such an association within a study and, therefore, at the level of individual with CBLP. To overcome such criticism, we used multivariable analysis; therefore, adjusting for what might be potential confounders. Additionally, we have reported within-study analyses to check whether they were consistent with our meta-regression analysis.

## Implications

A number of international clinical guidelines currently recommend SCS as evidence-based treatment for the management of CBLP following back surgery (ie, FBSS).[7,9,30] The PROCESS trial reported that 24% ($n = 51$) of 214 preselected individuals with FBSS did not enter the trial specifically because of their predominant lower back pain component.[1] Targeting and the effective management of axial back pain has become a focus for recent technological innovation in neuromodulation. This has seen the development and use of multipolar SCS electrodes, hybrid peripheral nerve stimulation systems, and alternative stimulation techniques.[12] Well-conducted trials, using contemporary technological advances in neurostimulation, in individuals with predominant back pain, are needed. Future publications need to better report inclusion and screening processes in sufficient detail to allow a better understanding of factors that may predict the success of SCS, including details on the technology used, the precise location of pain location, pain duration, and level of opioid prior to therapy. In addition to the assessment of patient-related outcomes, such as health-related quality of life and functional capacity, studies should collect pain outcomes in both the leg and back, to enable better understanding of the target of neurostimulation.

We are aware of two randomized trials of SCS currently being undertaken in back pain. The first is a

multicenter French study that aims to compare the analgesic efficacy of mono-column SCS (using longitudinal and transverse electric stimulation) versus mono-column SCS (using axial stimulation, represented by quadripolar or octopolar lead; ESTIMET, NCT01628237). A total of 115 patients with lumbar pain will be randomly allocated to each of the SCS approaches and their leg and back pain, function, level of depression, health-related quality, and costs at 6- and 12-month postrandomization. Second, a multi-country randomized trial (PROMISE, NCT01697358) is ongoing. Two hundred and twelve patients with FBSS presenting with predominant back pain will be randomized to SCS using a tripolar 16-contact lead plus optimal medical management as compared to optimal medical management alone in a postoperative CBLP population with predominant back pain. This parallel designed trial aims to assess outcomes at 6 to 24-months including leg and back pain relief, health-related quality of life, functional capacity, and costs.

## CONCLUSIONS

This systematic review and meta-analysis supports SCS as an effective pain relieving treatment for CBLP in patients with or without a prior history of back surgery and presenting as predominantly leg pain. Randomized controlled trials are needed to confirm the effectiveness and cost-effectiveness of SCS in the CBLP population with predominant low back pain and examine patient and technology-related factors that may be predictive of SCS success.

## ACKNOWLEDGEMENTS

This study was sponsored by Medtronic, Inc. The planning, conduct, and conclusions of this report are those of the authors and not the company. All the authors have received consultancy fees past and present from Medtronic.

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## SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

**Appendix S1**. Search strategy.

**Appendix S2**. Citation of included studies.

**Appendix S3.** Citation of study excluded on full paper review.

**Figure S1**. Funnel plot for small study bias—pain relief following SCS.