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REVIEW

Comparative Effectiveness of Different Frequencies of Spinal Cord Stimulation for the Treatment of Patients with Failed Back Surgery Syndrome: Systematic Review and Network Meta-Analysis

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Purpose: Failed back surgery syndrome (FBSS) is a common and challenging complication after lumbar spine surgery, with around 30% of patients experiencing this condition post-surgery. Spinal cord stimulation (SCS) is a prevalent treatment for FBSS, yet there is a lack of systematic comparisons among different SCS frequencies. This first network meta-analysis (NMA) compared the effectiveness and superiority of different SCS frequencies for FBSS.

Material and Methods: Adhering to PRISMA guidelines, we searched PubMed, Web of Science, Embase, and CENTRAL for RCTs. Bayesian random-effects network meta-analysis assessed outcomes including pain reduction, functional capacity, and health-related quality of life.

Results: This NMA (11 RCTs; n=2275) revealed efficacy variations among SCS modalities. Based on surface under the cumulative ranking (SUCRA) rankings, subperception SCS (500–1200 Hz) had the highest probability for global pain relief (SUCRA=64.0%) and ≥50% pain reduction (SUCRA=75.3%; $P < 0.05$ vs low-frequency SCS). High-frequency SCS (10 kHz) was associated with higher SUCRA values for back pain (99.7%; $P < 0.05$ vs comparators; consistency $\chi^2=1.41$, $P = 0.703$) and leg pain (93.2%; $P < 0.05$ vs low-frequency SCS), suggesting a potential advantage. For functional outcomes, high-frequency SCS correlated with better ODI scores (SUCRA=85.0%), while subperception SCS showed higher probability for improved EQ-5D metrics (SUCRA=80.3%). All networks satisfied transitivity assumptions without significant inconsistency ($P > 0.05$).

Conclusion: This NMA suggests potential differential therapeutic profiles among SCS modalities for FBSS. HF-SCS (10 kHz) showed relatively higher SUCRA values for back pain (99.7%), leg pain (93.2%), and disability improvement (ODI 85.0%). Subperception SCS (500–1200 Hz) was associated with better probability for global pain relief (64.0%), ≥50% pain reduction (75.3%), and HRQoL outcomes (EQ-5D 80.3%). These findings warrant validation in head-to-head RCTs.

Keywords: failed back surgery syndrome (FBSS), spinal cord stimulation (SCS), frequency, back pain, leg pain

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Introduction

Failed Back Surgery Syndrome (FBSS) refers to intractable pain or discomfort in the lumbar spine, buttocks, or lower limbs that occurs after laminectomy or discectomy. FBSS is a common and challenging complication following lumbar spine surgery, with reports indicating that approximately 30% of patients experience FBSS after lumbar disc surgery.[1] As the number of lumbar spine surgeries has increased in recent years, the incidence of patients diagnosed with FBSS has also risen.[2]

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Spinal cord stimulation (SCS) is a widely accepted treatment for FBSS that has been used clinically for over 30 years. SCS employs electrical impulse signals to stimulate spinal cord nerves, effectively blocking the conduction of pain signals to provide relief. SCS can be classified into traditional/tonic low-frequency SCS, subperception SCS, high-frequency SCS, and burst SCS. Traditional low-frequency SCS operates at a frequency of about 40 to 60 Hz,[3] generating an anesthetic sensation that "covers" the painful area. High-frequency SCS utilizes electrical pulse frequencies ranging from 5 to 10 kHz, with 10 kHz being the most common, and does not produce abnormal sensations.[4] Subperception SCS functions at a frequency between low-frequency and high-frequency SCS, typically around 1000 Hz, and does not elicit abnormal sensations. Burst SCS mainly consists of 40 Hz stimulus clusters, each containing five 500 Hz spike pulses, and is less likely to cause abnormal sensations.[5]

The emergence of novel electrical stimulation modalities has introduced new ideas and options for SCS in the treatment of FBSS. As these innovative SCS techniques become more widely applied in clinical practice, the challenge of selecting the appropriate method arises, making a comparative evaluation of the effectiveness and advantages of different SCS modalities increasingly urgent.

Several reviews have evaluated the effectiveness of different SCS in patients with FBSS.[6] Studies have shown that SCS can significantly improve pain, daily functioning, and quality of life in these patients.[7,8] Previous studies have also demonstrated that novel electrical stimulation is superior to conventional low-frequency electrical stimulation for pain relief.[9–11] Some studies have grouped subperception SCS with traditional low-frequency SCS. North et al noted that traditional SCS (40–60 Hz) requires paresthesia coverage for therapeutic efficacy, whereas subperception SCS (1000–1200 Hz) functions without inducing sensory phenomena.[12] Regarding pain relief, subperception SCS is noninferior to conventional low-frequency SCS and may be an effective alternative for patients who do not respond to traditional therapy.[4] This mechanistic divergence is corroborated by two randomized, crossover, controlled trials by Sokal et al and Rigoard et al. These studies compared traditional low-frequency SCS (40–60 Hz) with subperception SCS (1000–1200 Hz) and found significant differences in pain relief between the two.[13,14] Consequently, our review classifies conventional low-frequency SCS and subperception SCS as separate therapeutic categories due to the pooling of these distinct modalities and divergent clinical efficacy profiles.

Additionally, there have been no network meta-analyses evaluating the effectiveness of different SCS modalities for FBSS, despite their advantages over traditional meta-analyses, such as improved statistical power through the use of direct and indirect estimations, the ability to compare treatments not originally assessed, and ranking capabilities.[15] The aim of our review was to conduct the first systematic network meta-analysis of RCT studies comparing different SCS frequencies for FBSS. We compared SCS with various frequencies directly and indirectly, and sequenced them to evaluate their effectiveness and superiority in terms of pain relief, daily functioning, and quality of life.

Materials and Methods

Data Sources and Search Strategies

The systematic review was meticulously conducted in full compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure methodological rigor and transparency.[16] This systematic review has been officially registered in PROSPERO (registration no. CRD42024496483). Bayesian random-effects models were employed for network meta-analysis to comprehensively evaluate treatment effects on pain relief, functional improvement, and quality of life enhancement. A thorough exploration of the database was conducted up to October 31, 2024, including PubMed, MEDLINE, Embase and Cochrane Central Register of Controlled Trials (CENTRAL), systematically searching for RCTs that described the use of SCS for FBSS. The retrieval strategy was meticulously developed and systematically executed by an experienced librarian in close collaboration with the study's principal investigator (X.F).

Inclusion and Exclusion Criteria

The analysis included only English-language prospective RCTs that compared two or more SCS frequency protocols in patients with failed FBSS. FBSS is defined as persistent back or leg pain following at least one lumbar surgery.[17] Inclusion criteria were: 1) randomized controlled trials, 2) comparisons of different frequencies of SCS, 3) study population with FBSS, and 4) reporting outcomes of back and/or leg pain and/or overall pain at baseline and follow-up. Exclusion criteria included: 1) fewer than 10 patients, 2) research subjects who have not been clearly diagnosed with FBSS or whose primary population is not FBSS, 3) review articles, case reports, case series, letters to the editor, commentaries, conference proceedings, laboratory science studies, and other non-relevant studies, and 4) studies that did not report outcomes of interest. If a trial reported multiple time points for the same outcome, we selected the three-month or closest follow-up outcome.

Screening Process

We imported the database-retrieved entries into EndNote 20.4.1 (Clarivate Analytics, Philadelphia, PA, USA) and removed duplicates, and evaluated them in relation to findings from other sources. The screening process comprised three distinct phases. Initially, two reviewers (QYY and ZCP) independently screened the articles by title, with any uncertain entries retained for further review. Next, all articles selected in the first stage underwent an abstract review, and any disagreements among the reviewers were resolved through discussion. Finally, full-text review was conducted for articles with eligible titles and abstracts, following predefined inclusion and exclusion criteria.

Data Collection

Two independent reviewers systematically extracted data using a standardized electronic form, with discrepancies resolved through consensus or third-party adjudication. From each included study, we collected study identifiers (first author, publication year, country), methodological characteristics (study design [RCT/RCD], follow-up duration, attrition rate), participant demographics (sample size, sex distribution, age [mean ± SD or median (IQR)], proportion of FBSS patients [range: 45–100%]), intervention specifications including spinal cord stimulation modality (conventional low-frequency [LF: 40–100 Hz], subperception stimulation [500–1200 Hz], high-frequency [HF: 10 kHz], or burst stimulation). The outcome measures included pain intensity assessed using the visual analog scale (VAS) and numeric pain rating scale (NPRS) at baseline and post-intervention with site-specific changes (back/leg/global), functional disability evaluated by the Oswestry Disability Index (ODI),[18] health-related quality of life measured with the EuroQol-5 Dimensions (EQ-5D),[19] and responder rate defined as either ≥50% pain reduction or ≥2-point improvement in pain related scores.

Quality Assessment of Evidence

Two independent reviewers (Q.Y.Y. and Z.C.P.) assessed the risk of bias using the revised Cochrane risk-of-bias tool for randomized trials (RoB 2.0).[20] The overall risk of bias was evaluated as low when all domains were assessed as low risk, high when at least one domain was high risk or multiple domains raised some concern, and some concern if the overall judgment was neither low nor high. To provide a comprehensive methodological evaluation, we employed the CINeMA (Confidence in Network Meta-Analysis) framework to assess the certainty of the evidence across six key domains (within-study bias, reporting bias, indirectness, imprecision, heterogeneity, and inconsistency).[21,22] This approach addresses issues specific to network meta-analysis that extend beyond the scope of RoB 2.0. Using the CINeMA framework, we examined intransitivity (violation of the transitivity assumption) by comparing key effect modifiers, including age, sex, and baseline pain scores, across studies that provided both direct and indirect evidence for each comparison.

Statistical Analysis

A frequency network meta-analysis (NMA) was performed using Stata 18.0 (command: mvmeta[23–25]). The analysis incorporated both direct and indirect evidence from a variety of SCS modalities. Prior to performing the NMA, the assumption of cross-sectionality was validated by assessing demographic comparability (age, sex, baseline pain score) and risk of bias distribution across studies. The presence of heterogeneity among the studies was addressed by implementing a random-effects model with restricted maximum likelihood estimation. This heterogeneity was then quantified using the τ^2 metric, which is commonly interpreted as follows: low < 0.04; low-moderate 0.04–0.16; moderate-high 0.16–0.36; high > 0.36.[8,26,27] It was hypothesized that a common τ^2 existed among the various contrasts, and that the correlation coefficient of the inter-study covariance matrix was equivalent to 0.5. The consistency between direct and indirect evidence was verified by means of a node-split analysis.[28]

Missing standard deviations of baseline changes were derived using correlation coefficients[25] or estimated from comparable studies. For data reported as median and range, means and standard deviations were calculated using the Hozo method.[29] Treatment effects were synthesized as pooled estimates with 95% confidence intervals.

The ensuing results are presented in the following ways: network plots were used to plot SCS pattern comparisons; forest plots were used to show pairwise treatment effects; and Surface Under Cumulative Ranking (SUCRA) values (range: 0–1) were used to objectively rank the interventions. This metric quantifies the relative superiority of each treatment option, where higher SUCRA scores indicate a greater likelihood of being among the most effective interventions.[26,30]

Results

Study Characteristics

A total of 1913 studies were identified after searching PubMed, MEDLINE, Embase, and Cochrane, and the search strategy is shown in Tables S1–S4. An additional 20 studies were identified after performing manual searches, such as reviewing references of included studies/reviews and additional searches for related/cited articles in PubMed. After eliminating duplicates, reviewing titles and abstracts, and reading the full text, our systematic review finalized 11 studies, as detailed in the flow chart (Figure 1). The list of data extracted from the included studies is in Table S5. Of the included articles, six studies were two-armed, three analyzed HF vs LF,[31–33] two analyzed subperception vs LF SCS,[4,12] one analyzed burst vs sham.[34] Four studies were three-armed, three of which analyzed burst vs subperception vs sham,[11,35] one study analyzed LF vs subperception vs burst,[13] and one study analyzed HF vs subperception vs sham.[36] There was also 1 study that was a four-arm study that analyzed burst vs subperception vs LF vs sham.[14] In the study by Kapural et al, 77% of patients were diagnosed with FBSS.[32] In two independent studies by North et al, one publication[4] reported 46% of patients with FBSS while the other[12] reported 45%. In Sokal et al's research, this proportion was 72%.[14] All other included studies enrolled only FBSS patients.

Table 1 provides a summary of the characteristics of the trials included in the systematic review and network meta-analysis.

Risk of Bias, Certainty of Evidence, and Consistency

Figure 2 presents the risk of bias for each trial, see Figure S1 and Table S6 for more details. One major limitation was the lack of sufficient details in some studies regarding the implementation of blinding for participants, investigators, and outcome assessors, with certain studies also failing to comprehensively report how the blinding process was conducted. For our consistency evaluation (ie, alignment of direct and indirect evidence), side-splitting results suggested there is no strong statistical evidence of global inconsistency was reported for most outcomes (Tables S7–S16). Consistency assessments also prompted vigilance over waist circumference data (P=0.08), which warrants more rigorous randomized controlled trials in the future. The τ2 result did not identify any high heterogeneity in the network, and most comparisons were low or low-moderate levels of heterogeneity (Tables S7–S16). After assessing the level of evidence using CINeMA, most of the results of the pairwise comparisons were of low or moderate confidence (Supplementary Material 1, Figures S2–S8 and Tables S17–S19). All networks met the principle of transitivity, endowing the validity of indirect comparisons (Supplementary Material 1, Figures S2–S8 and Tables S17–S19).

Synthesizing the Data

For each specific outcome, we generated network plots (Figures 3–8). Within these networks, edge thickness is proportional to the number of direct comparison trials (ranging from 3 to 12 studies), while edge length represents the inverse variance of the direct effect estimates. All metrics were standardized according to Cochrane network meta-analysis protocols to reflect evidence intensity and statistical precision.

We also created forest plots for pairwise comparisons (Figures 9–14). Orange dots denote the mean difference, with horizontal lines indicating 95% confidence intervals. Numerical results (mean difference [95% CI]) are listed adjacent to each comparison (eg, LF vs HF: 0.08 [−1.08, 1.24]).

Additionally, we present league tables (Tables S20–S25) and plots of average expected rankings alongside SUCRA cumulative probabilities for each treatment regimen (Figures 15–20). SUCRA values (range: 0–1) provide an objective

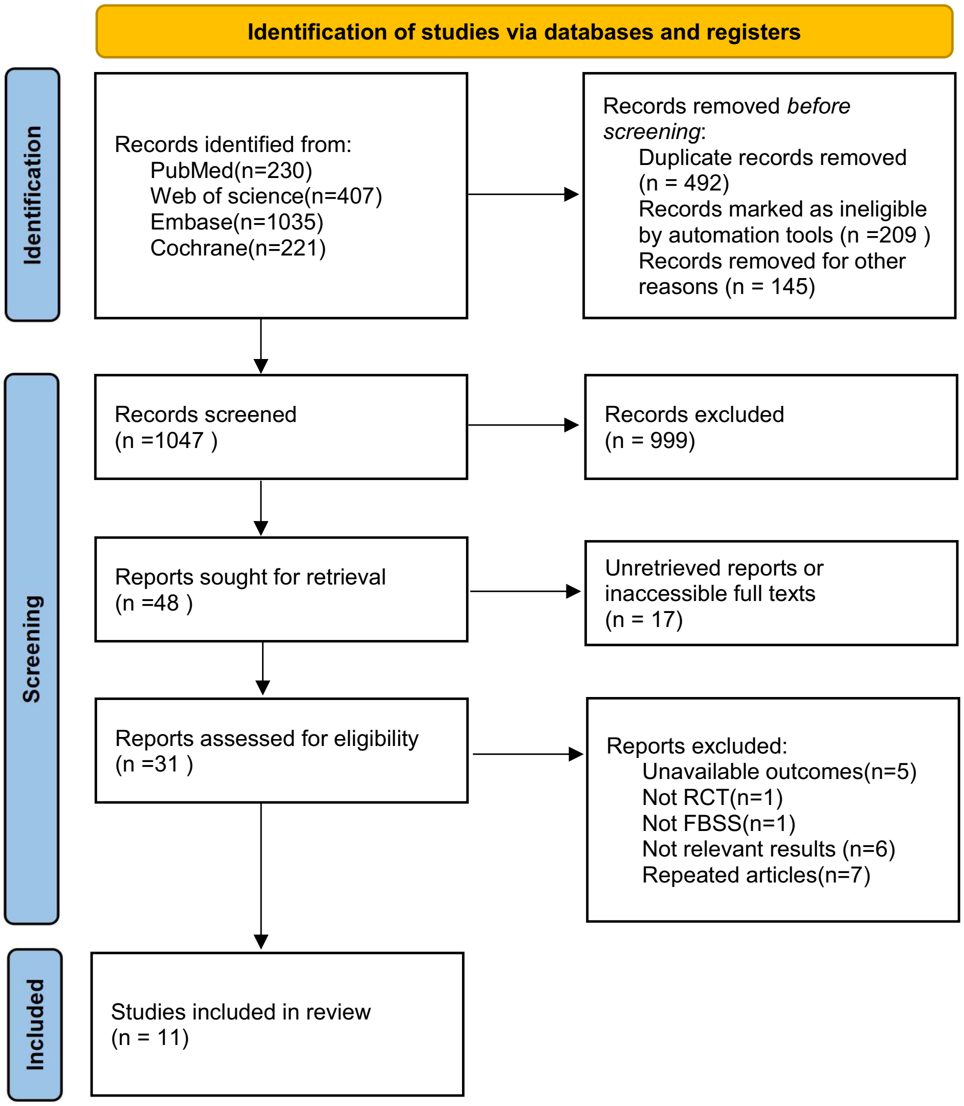

Figure 1 Flow diagram of preferred reporting items identified, included, and excluded for systematic reviews and meta-analyses (PRISMA).

intervention ranking by quantifying relative treatment superiority, with higher scores indicating greater likelihood of being among the most effective options. Specifically, SUCRA = 1.0 (100%) denotes the theoretically optimal treatment (consistent first rank), while 0 (0%) represents the least favorable option (consistent last rank); a value of 0.80 indicates an 80% probability of superiority over alternative regimens. Extended results are available in Figures S9–S14 and Tables S26–S31.

Global Pain Relief

Seven studies (583 patients) in total measured overall pain before and after different SCS treatments. All of which underwent NMA, and Figure 3 shows a network diagram of all eligible comparative endpoints. All 5 treatment frequencies(nodes) were connected to the network and no network inconsistencies were found [χ2 (3)=2.12, P=0.5469]. Figure 15 shows the expected mean rankings and SUCRA cumulative probability plots for each intervention. According to the SUCRA cumulative ranking plot, for global pain, the efficacy of SCS in patients with FBSS was ranked as follows: subperception SCS (64.0%), LF SCS (59.7%), burst SCS (59.6%), HF SCS (50.0%), and sham (16.7%). The reticular forest plot for two-by-two comparisons (Figure 9) showed no significant differences between the various SCSs.

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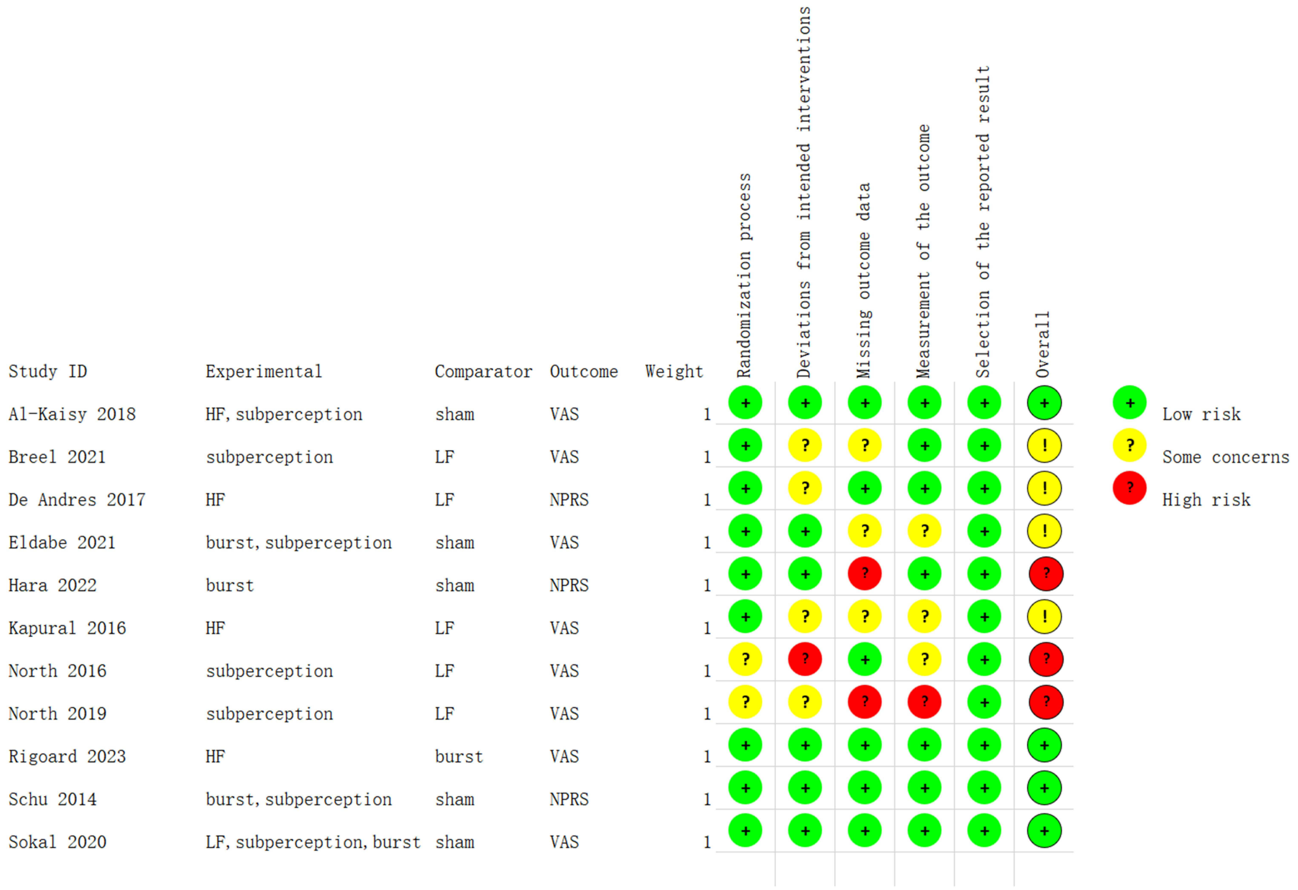
Table 1 Summarizes the Characteristics of the Trials Included in the Systematic Review and Network Meta-Analysis

Authors & Year	Type of Study	Country	Type of Spinal Cord Stimulation		No. of Patients	Follow-up	Sex, M/F	Mean age, y (SD)	Dropouts n (%)	Outcome measures	Pain	Population
Schu 2014[11]	RCD	Germany	Burst Subperception Sham	5 spikes at 500-Hz spike mode, 40-Hz burst mode, and 1-msec pulse width,3.4 ± 1.7 mA. 500-Hz, 370.8±135.4 µsec,5.5 ± 3.6 mA Off stimulation	20 20 29	1 week	7/13	58.6±10.2	0%	NRS ODI SF-MPQ	Global:8.3/4.7 Global:8.3/7.1 Global:8.3/8.3	FBSS
Kapural 2015[32]	RCT	America	HF LF	10K-Hz,30 msec,15mA 40~60Hz,300–600 msec,4~9mA	92 87	24 MO	108/71	54.6±12.4 55.2±13.4	13.6%	VAS CGIC PGIC ODI Patient satisfaction Responder rate	Back:7.4/2.4 Leg:7.1/2.4 Back: 7.8/4.5 Leg: 7.6/3.9	77% FBSS
De Andres 2017[31]	RCT	Spain	HF LF	10K-Hz,20 ls~1 ms,0 mA~15 mA 40Hz,300 ls~ 450 ms	26 29	3 MO	29/31	51.62±9.31 53.79±11.46	8%	NRPS ODI SF-12 PGIC	Global:7.6/6.0 Global:7.6/5.7	FBSS
Breel 2021[33]	RCD	Netherlands	LF LHF	30Hz,300 ls~450 ls 1000Hz,220 ls	26 26	1 MO	18/8	49±12 49±12	13.3%	VAS EQ-5D SF-36 Sleep Employment	Global:6.9/2.6 Global:6.9/2.7	FBSS
Hara 2022[34]	RCT	Norway	Burst Sham	5 spikes at 500-Hz spike mode, 40-Hz burst mode Off stimulation	91 89	3 MO	23/27	50 (45, 49)	16%	NPRS ODI EQ-5D	Back:6.8/5.7 Leg:7.3/5.9 Back: 6.8/6.1 Leg: 7.3/6.1	FBSS
Rigoard 2023[13]	RCD	France Belgium	LF Subperception Burst	10-100 Hz,10–500 µs,0.1–25 mA. 650–1200 Hz,10–500 µs 5 spikes at 500-Hz spike mode, 40-Hz burst mode,	20 20 20	3 MO	11/9	49.3±8.7	5%	VAS ODI EQ-5D PGIC Responder rate	Back:6.8/3.2 Leg:6.8/3.7 Back:6.8/3.3 Leg:6.8/3.02 Back: 6.8/3.8 Leg:6.8/5.9	FBSS
Eldabe 2021[35]	RCD	UK	Burst Subperception Sham	40 Hz, 250~500 µS 500Hz,480usec Off stimulation	18 17 18	9 Day	7/12	54±9	11.1%	VAS EQ-5D	Global: 7.6/5.8 Global: 7.6/4.25 Global: 7.6/5.25	FBSS
North 2020[12]	RCD	USA	Subperception LF	<1200Hz paresthesia-based SCS supraperception Based on abnormal sensation	123 124	3 MO	47/83	59.8±11.3	15%	VAS Responder rate	Global: 7.3/4.7 Back: 6.9/4.2 Leg: 6.1/3.9 Global: 7.3/5.1 Back: 6.9/4.8 Leg: 6.1/4.2	46% FBSS

North 2016[4]	RCD	USA	Subperception LF	<1000Hz Paresthesia-based SCS supraperception Based on abnormal sensation	22 22	3week	14/4	57.3±10.3	0%	NPRS PGIC ODI Responder rate	Global:6.18/3.7 Global:6.18/6.1	45% FBSS
Sokal 2020[14]	RCD	Poland	LF Subperception Burst Sham	40-60 Hz, 250–500 μs 1KHz, 120 μs, 3 Amp 40 Hz, 250~500 μS 5 spikes at 500-Hz spike mode, 40-Hz burst mode, Off stimulation	18 18 18 18	2week	11/7	54.26	0%	VAS	Global:8.13/ 4.18 Global:8.13/ 5.17 Global:8.13/ 5.27 Global:8.13/ 5.42	72% FBSS
Al-Kaisy 2018[36]	RCD	UK	Sham Subperception HF	Off stimulation 1200Hz,80 Isec 5882Hz,30Isec	24 24 24	3week	16/8	47.9 (33, 60)	0%	VAS PGIC	Back:7.75/4.83 Back:7.75/4.51 Back:7.75/3.32	FBSS

Notes: Responder rate, defined as 50% pain improvement or 2-point decrease in pain score.

Abbreviations: HF, high frequency spinal cord stimulation; LF, low frequency spinal cord stimulation; Burst, burst spinal cord stimulation; Subperception, subperception spinal cord stimulation; sham, off the spinal cord stimulation; VAS, visual analog scale; NRS, numerical rating scale; NPRS, numerical pain rating scale; ODI, Oswestry Disability Index; EQ-5D, EuroQol Five Dimensions Questionnaire; CGIC, clinical global impression; PGIC, patients' global impression of change; SF-MPQ, McGill pain questionnaire short-form.



Study ID	Experimental	Comparator	Outcome	Weight	Randomization process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall
Al-Kaisy 2018	HF, subperception	sham	VAS	1	🟢 +	🟢 +	🟢 +	🟢 +	🟢 +	🟢 +
Breel 2021	subperception	LF	VAS	1	🟢 +	🟡 ?	🟡 ?	🟢 +	🟢 +	🟡 !
De Andres 2017	HF	LF	NPRS	1	🟢 +	🟡 ?	🟢 +	🟢 +	🟢 +	🟡 !
Eldabe 2021	burst, subperception	sham	VAS	1	🟢 +	🟢 +	🟡 ?	🟡 ?	🟢 +	🟡 !
Hara 2022	burst	sham	NPRS	1	🟢 +	🟢 +	🔴 ?	🟢 +	🟢 +	🔴 ?
Kapural 2016	HF	LF	VAS	1	🟢 +	🟡 ?	🟡 ?	🟡 ?	🟢 +	🟡 !
North 2016	subperception	LF	VAS	1	🟡 ?	🔴 ?	🟢 +	🟡 ?	🟢 +	🔴 ?
North 2019	subperception	LF	VAS	1	🟡 ?	🟡 ?	🔴 ?	🔴 ?	🟢 +	🔴 ?
Rigoard 2023	HF	burst	VAS	1	🟢 +	🟢 +	🟢 +	🟢 +	🟢 +	🟢 +
Schu 2014	burst, subperception	sham	NPRS	1	🟢 +	🟢 +	🟢 +	🟢 +	🟢 +	🟢 +
Sokal 2020	LF, subperception, burst	sham	VAS	1	🟢 +	🟢 +	🟢 +	🟢 +	🟢 +	🟢 +

🟢 + Low risk
🟡 ? Some concerns
🔴 ? High risk

Figure 2 Plot of the risk of bias for each trial.

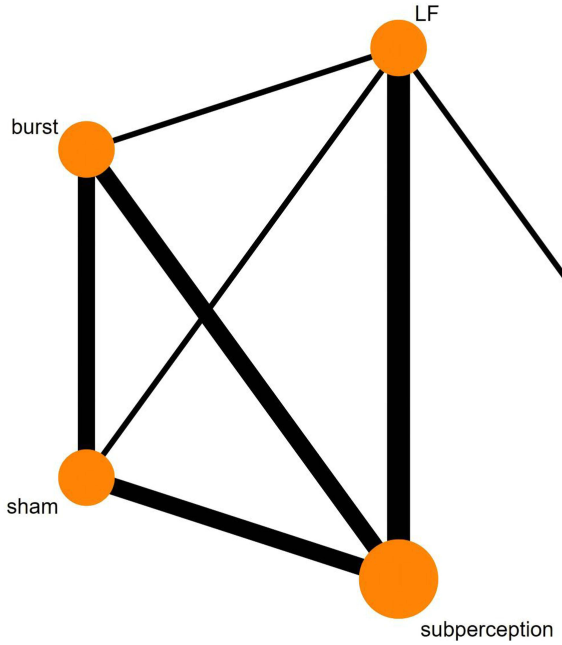


Figure 3 Network geometry of spinal cord stimulation (SCS) modalities for global pain.

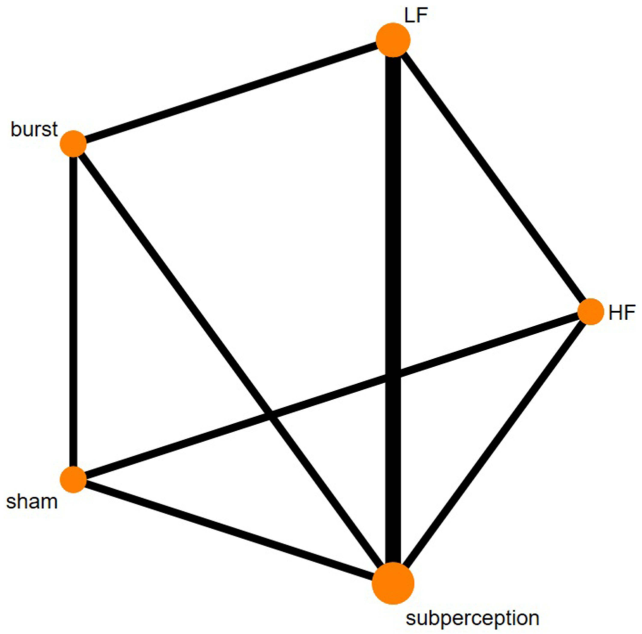


Figure 4 Network geometry of spinal cord stimulation (SCS) modalities for back pain.

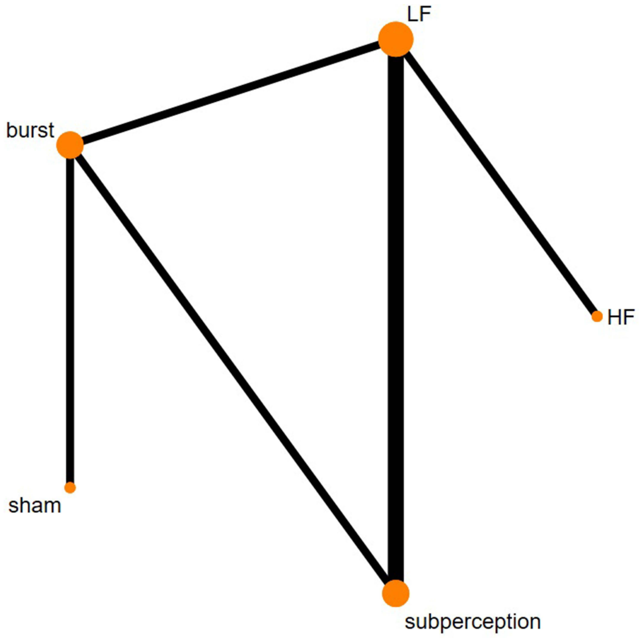


Figure 5 Network geometry of spinal cord stimulation (SCS) modalities for leg pain.

Back Pain Relief

Five studies (730 patients) measured back pain before and after treatment with different SCSs. Figure 4 shows the network plot of all eligible comparisons for this endpoint. All 5 administrative modalities (nodes) were connected to the network, and no network inconsistencies were observed [$\chi 2$ (3)=1.41, P=0.7032]. Figure 16 shows the anticipated average rankings and SUCRA cumulative probability plots for each intervention, according to which, for back pain, the efficacy rankings were in descending order, HF SCS (99.7%), subperception SCS (64.6%), burst SCS (47.2%), LF SCS

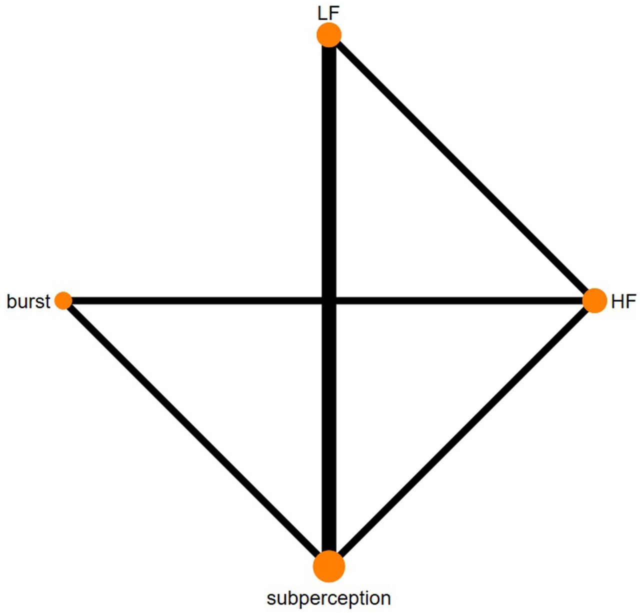


Figure 6 Network geometry of spinal cord stimulation (SCS) modalities for responder rate (50% of pain im-provement or 2-point decrease).

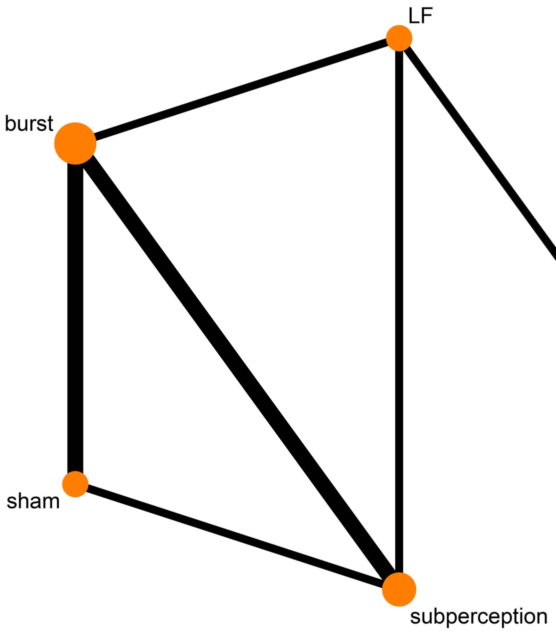


Figure 7 Network geometry of spinal cord stimulation (SCS) modalities for ODI (Oswestry Disability Index).

(26.3%), and sham (12.2%). In accordance with the reticulated forest plot, HF SCS was superior to other SCSs in relieving back pain, and the difference was statistically significant (Figure 10).

Leg Pain Relief

A total of 4 studies (658 patients) measured leg pain scores before and after different SCS treatments. The network plot of all eligible comparisons for this endpoint is shown in Figure 5. All 5 administrative modalities (nodes) were connected to the network, and no network inconsistency was observed [χ2 (1)=0.03, P=0.8633]. The expected mean rankings and SUCRA cumulative probability plots for each intervention are shown in Figure 17. According to the probability ranking graph SUCRA

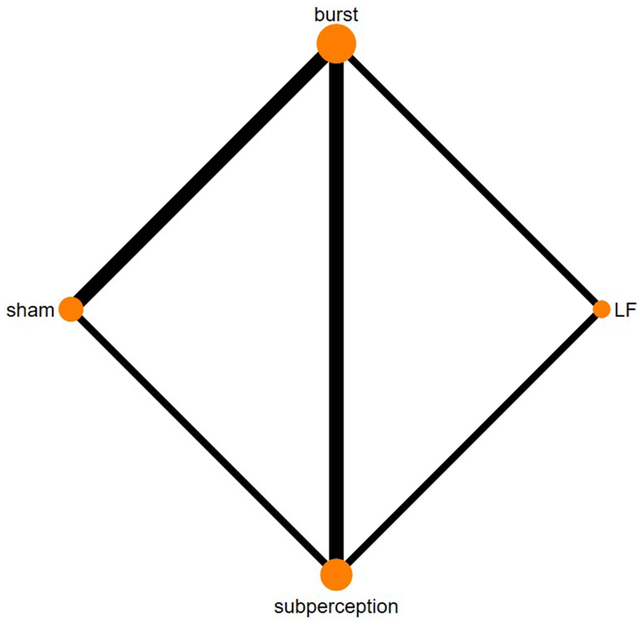


Figure 8 Network geometry of spinal cord stimulation (SCS) modalities for EQ-5D (used to describe health-related quality of life).

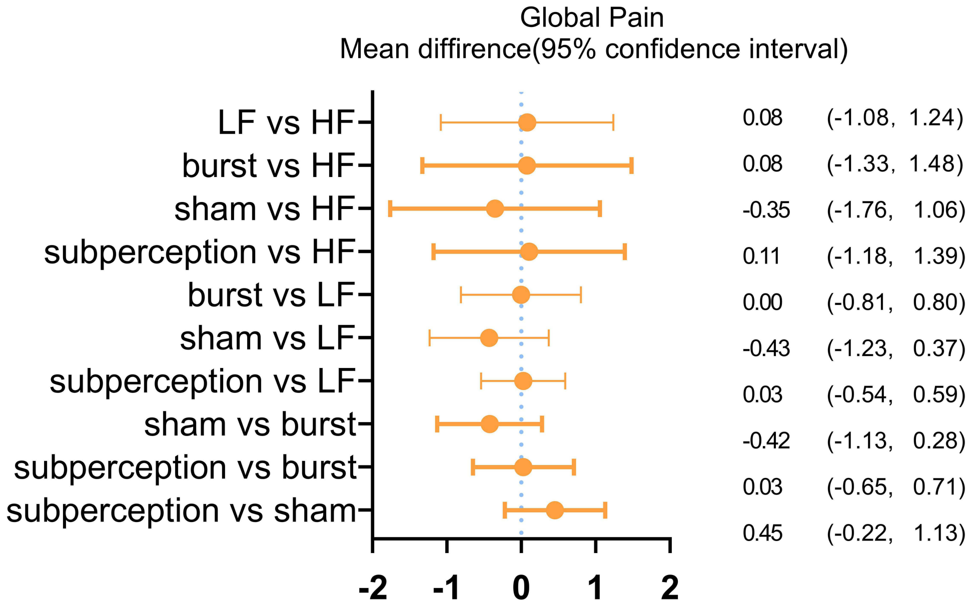


Figure 9 Forest plot of network effect sizes between different frequencies of SCS for global pain.

cumulative probability plot, it is known that for leg pain, the efficacy rankings were HF SCS (93.2%), subperception SCS (68.4%), LF SCS (40.6%), burst SCS (33.3%), and sham (14.6%) in that order. According to the reticulated forest plot, HF relieved leg pain better than traditional LF SCS, and the difference was statistically significant (Figure 11).

Responder Rate

A total of 4 studies (400 patients) measured responder rates before and after treatment with different SCSs. Figure 6 displays a network plot that covers all eligible comparisons made for this endpoint. All 4 administrative modalities (nodes) were connected to the network, and no network inconsistency was observed [χ2 (1)=0.00, P=0.9648]. The expected mean rankings and SUCRA cumulative probability plots for each intervention are shown in Figure 18.

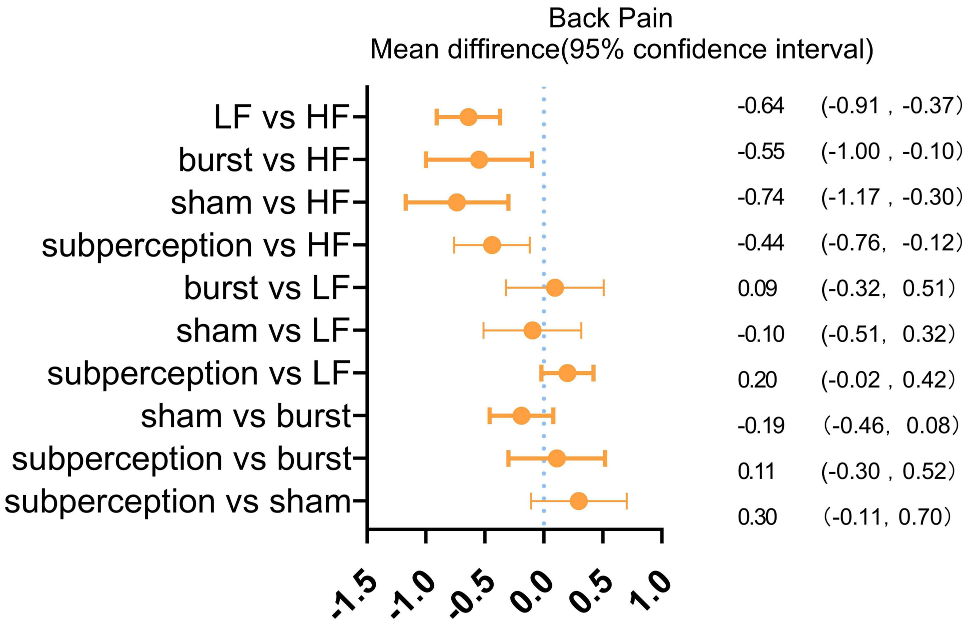


Figure 10 Forest plot of network effect sizes between different frequencies of SCS for back pain.

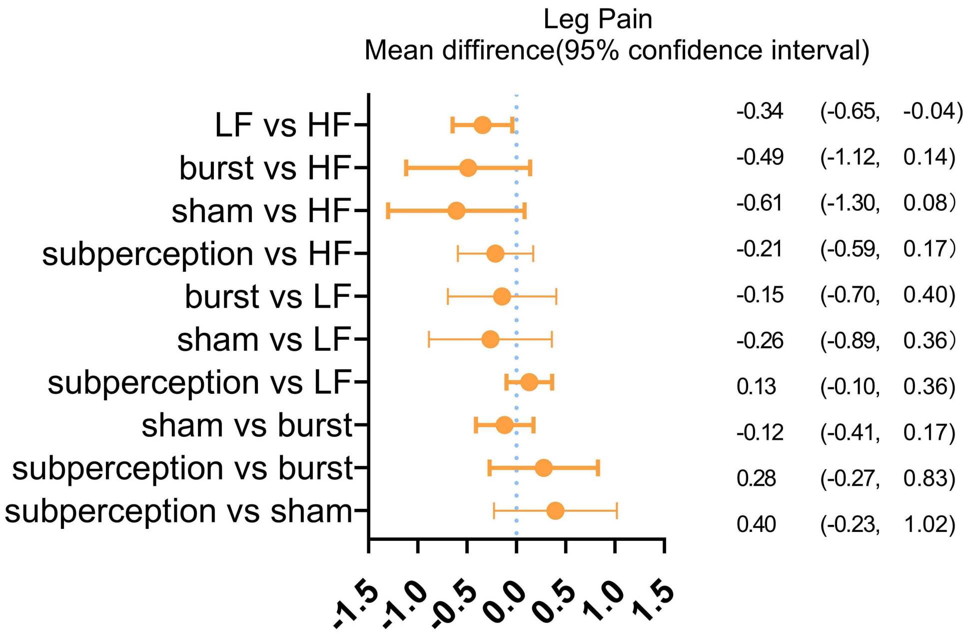


Figure 11 Forest plot of network effect sizes between different frequencies of SCS for leg pain.

According to the probability ranking plot SUCRA cumulative probability plot, the qualitative analysis of SCS for pain relief in FBSS patients in terms of response rate showed that the efficacy rankings were subperception SCS (75.3%), HF SCS (69.6%), burst SCS (44.2%), and LF SCS (10.8%) in that order. According to the reticulated forest plot (Figure 12), Patients with subperception SCS had a higher level of pain relief response than those with LF SCS.

ODI Improvement

A total of 4 studies (360 patients) measured ODI scores before and after treatment with different SCSs. The network plot of all eligible comparisons for this endpoint is shown in Figure 7. All 5 management modalities (nodes) were connected

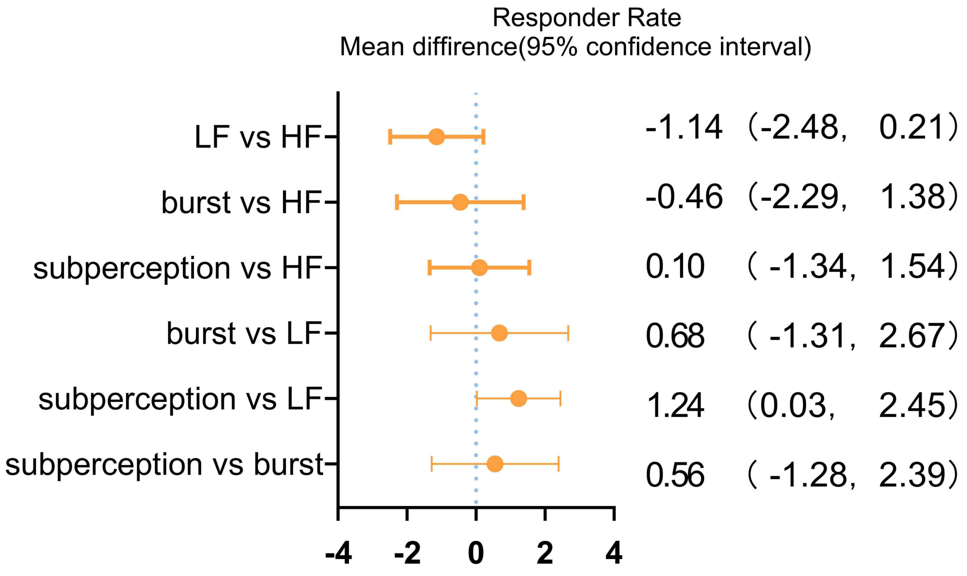


Figure 12 Forest plot of network effect sizes between different frequencies of SCS for responder rate.

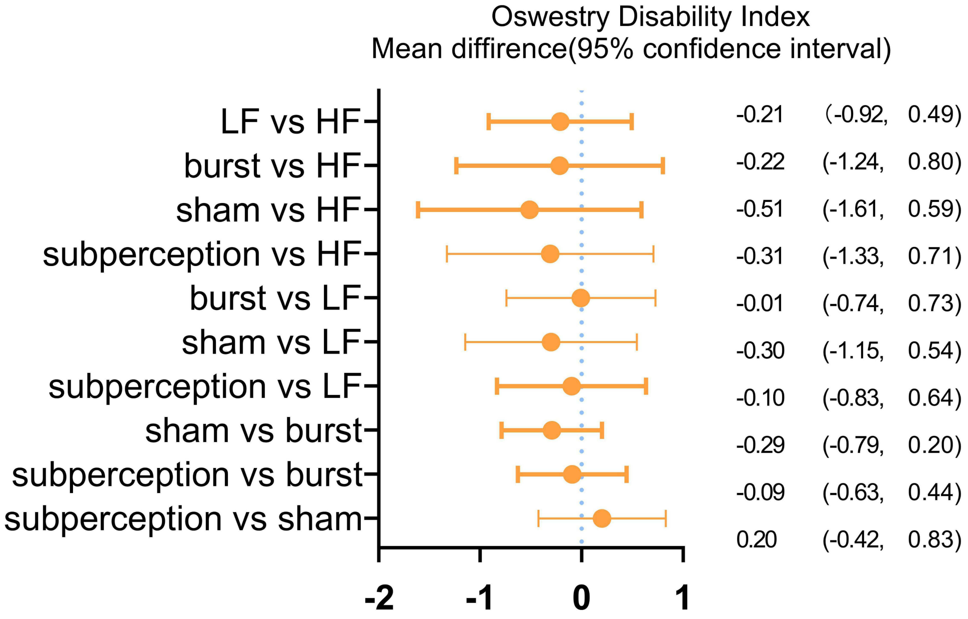


Figure 13 Forest plot of network effect sizes between different frequencies of SCS for ODI.

to the network, and no network inconsistency was observed [$\chi2(2)=3.16$, P=0.1646]. The expected mean rankings and SUCRA cumulative probability plots for each intervention are shown in Figure 19. According to the probability ranking plot SUCRA cumulative probability plot shows that the order ranking of SCSs for improvement of lumbar function in FBSS patients was HF SCS (85.0%), burst SCS (64.4%), LF SCS (64.4%), subperception SCS (30.8%), and sham (5.1%) in that order. None of the differences were statistically different according to the reticular forest plot (Figure 13).

EQ-5D Improvement

A total of 4 studies measured A total of 4 studies (618 patients) measured EQ-5D scores before and after different SCS treatments. The network plot of all eligible comparisons for this endpoint is shown in Figure 8. All 5 administrative modalities (nodes) were connected to the network, and no network inconsistency was observed [$\chi2$ (1)=1.90, P=0.1681].

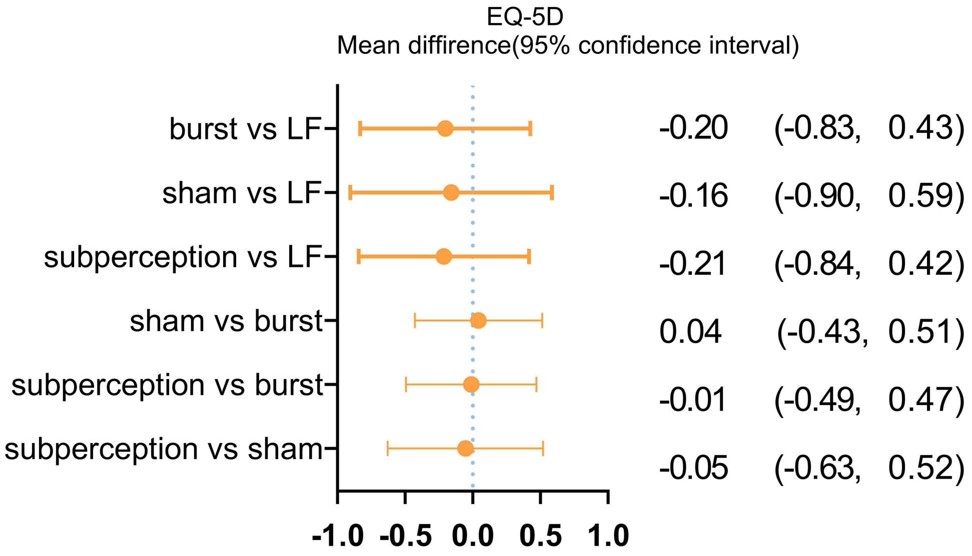


Figure 14 Forest plot of network effect sizes between different frequencies of SCS for EQ-5D.

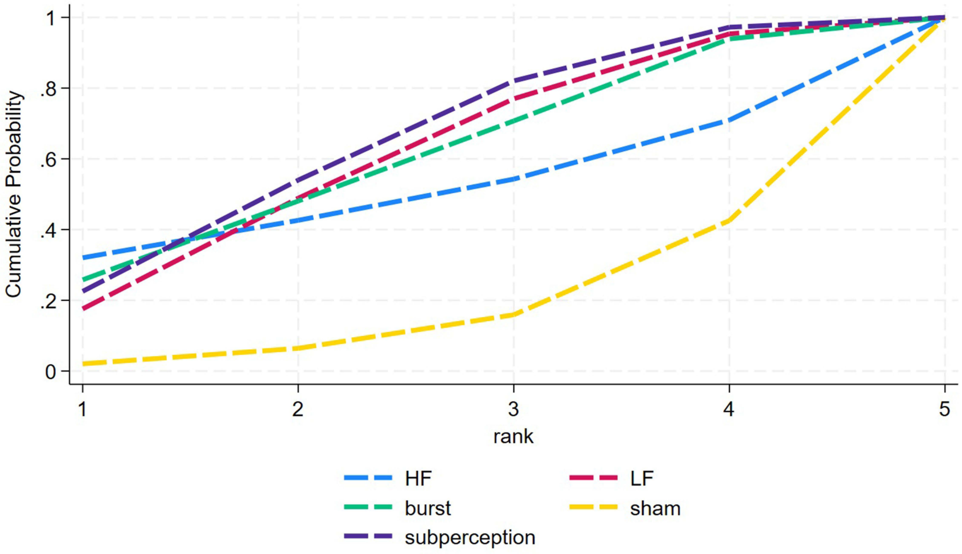


Figure 15 Plots of SUCRA values for each SCS to global pain.

The expected mean rankings and SUCRA cumulative probability plots for each intervention are shown in Figure 20. According to the probability ranking plot SUCRA cumulative probability plot shows that the effect of SCS on the improvement of healthy quality of life of FBSS patients in the order of subperception SCS (80.3%), LF SCS (64%), burst SCS (48.7%), sham (29%), and HF SCS (28%) in descending order. None of the differences were statistically different according to the forest plot of the two-by-two comparison (Figure 14).

Discussion

Our network meta-analysis comprehensively evaluated the efficacy of different SCS frequencies in FBSS. This study addresses a notable literature gap by distinctly comparing traditional low-frequency SCS with subperception SCS—modalities frequently conflated in prior analyses despite evidence suggesting divergent mechanisms of action and clinical outcomes. Results suggest subperception SCS may be associated with superior global pain improvement, with higher rates of ≥50% pain responders versus traditional low-frequency SCS ($P < 0.05$).

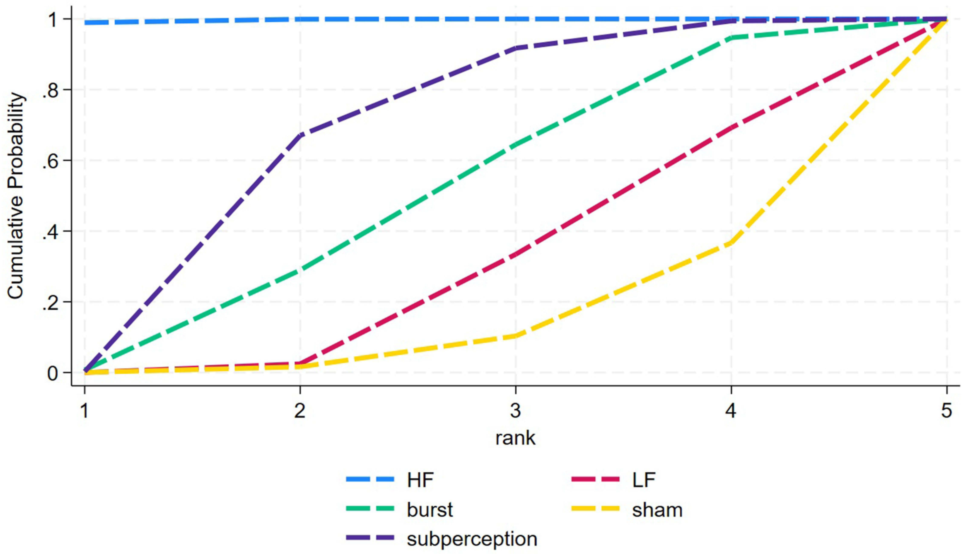


Figure 16 Plots of SUCRA values for each SCS to back pain.

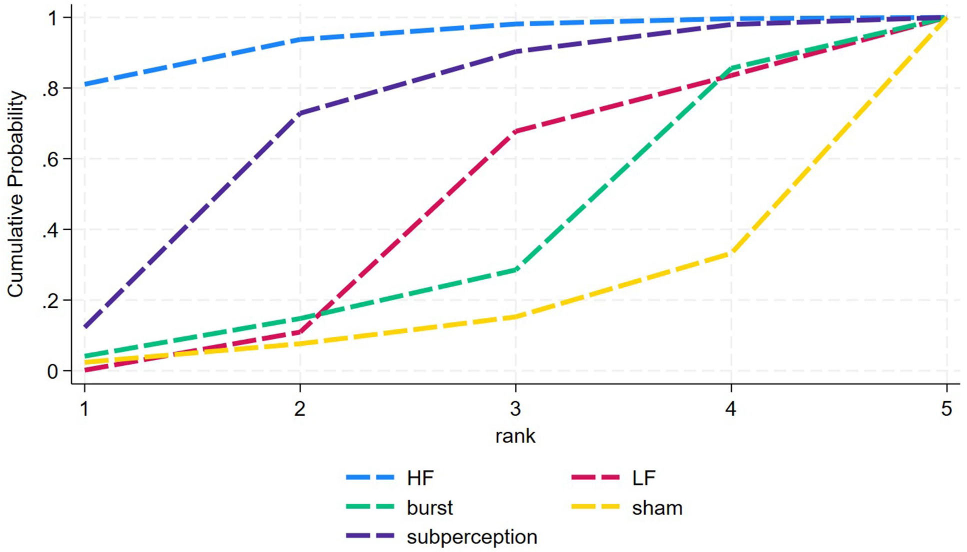


Figure 17 Plots of SUCRA values for each SCS to leg pain.

Current research indicates that SCS can significantly alleviate pain in patients with FBSS and improve their quality of life. Kurt et al confirmed the benefits of SCS from multiple perspectives,[7] while Nissen et al conducted a 20-year follow-up study of 224 patients, demonstrating the sustained therapeutic effects of SCS.[37] However, with the increasing variety of SCS methods available, selecting the appropriate option has become a challenge. This study compared the efficacy of different frequencies of SCS commonly used in patients with FBSS to provide evidence for clinical selection.

In Morales and Karri's systematic reviews, it was shown that HF SCS provided better pain relief compared to low-frequency SCS.[10,38] Our analysis reveals that HF SCS is potentially the most effective option for relieving back and leg pain. SUCRA values and statistical significance indicate its superiority in these areas: 99.7% for back pain ($P < 0.05$ vs comparators; consistency $\chi^2 = 1.41$, $P = 0.703$) and 93.2% for leg pain ($P < 0.05$ vs low-frequency SCS). Conversely, subperception SCS exhibits potential in overall pain management and quality of life enhancement. SUCRA analysis showed that subperception SCS (500–1200 Hz) had the highest probability of providing global pain relief (64.0%),

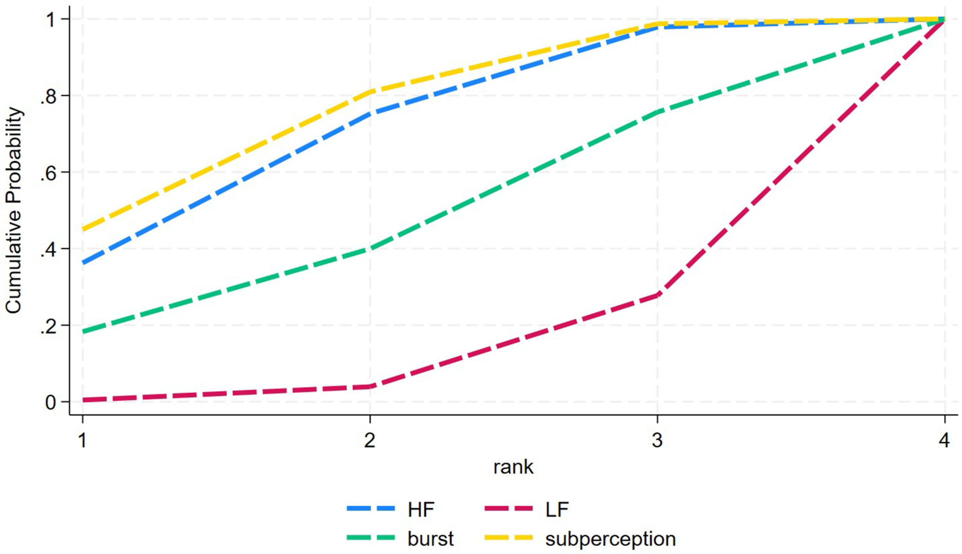


Figure 18 Plots of SUCRA values for each SCS to responder rate.

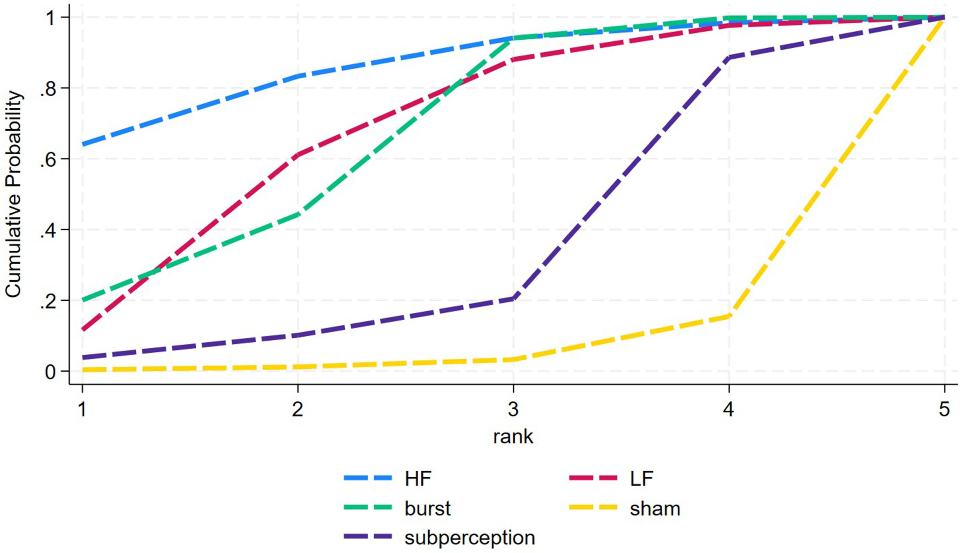


Figure 19 Plots of SUCRA values for each SCS to ODI.

a responder rate of ≥50% (75.3%), and an improvement in health-related quality of life (EQ-5D, 80.3%). Therefore, subperception SCS may be clinically applicable in managing overall pain and improving quality of life.

As SCS technology evolves, the emergence of novel modalities provides a broader spectrum of options for clinicians and patients alike. To our knowledge, this study is the most comprehensive and up-to-date systematic review and network meta-analysis, covering almost the entire range of available data on the frequency of SCS usage for patients with failed back surgery syndrome. By rigorously applying the CINeMA quality assessment approach, we enhanced the credibility of the findings. This network meta-analysis lays the groundwork for such inquiries and emphasizes the need for further exploration into the optimal use of SCS in FBSS management.

However, our study has some limitations. First, the included trials had different follow-up periods. We conducted a subgroup analysis and a sensitivity analysis. For the former, we divided the stimulation follow-up into long-term (one month) and short-term (less than one month) subgroups (see Table S32 for details). For the latter, we compared all

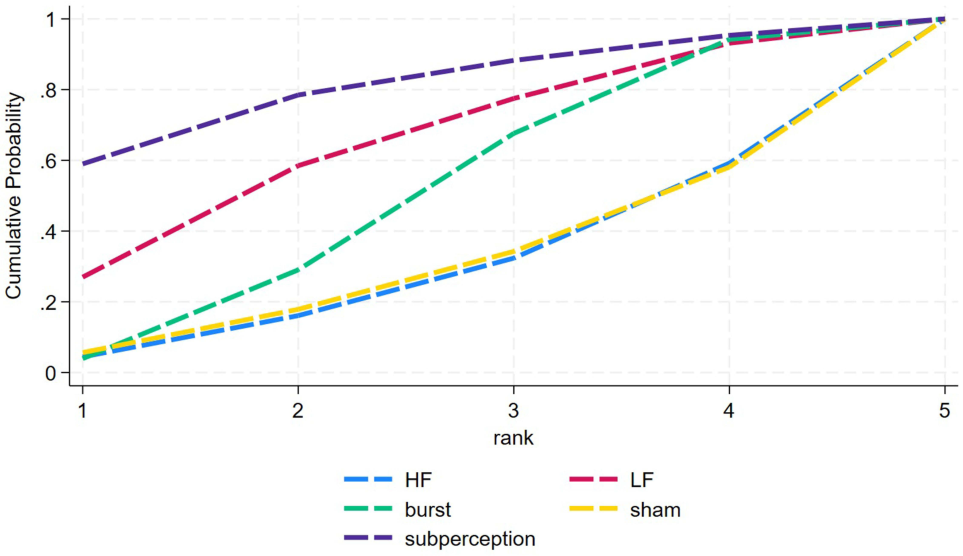


Figure 20 Plots of SUCRA values for each SCS to EQ-5D.

included studies with those that had a follow-up period of up to three months (see Figure S15 for details). Although these variations in follow-up duration did not alter the overall conclusions, they may have introduced heterogeneity and influenced the interpretation of the results. Second, some of the included studies did not exclusively involve FBSS patients. These studies were included for the following reasons: First, due to limitations in sample size, studies that included only FBSS patients lacked key data, such as VAS/ODI scores. Second, in studies that did not include only FBSS patients, the primary study population was still FBSS patients, accounting for 45–77% of the total. The remainder were patients with CRPS and other SCS indications. Since the mechanisms and SCS response profiles were consistent with FBSS, we included these studies to enhance statistical power. However, the effect estimates may be imprecise, which limits the overall accuracy and generalizability. Additionally, despite our efforts to contact the authors, some trials lacked sufficient information to accurately assess randomization, task concealment, and investigator blinding. Additionally, SCS trials may be biased due to non-standardized blinding, open-label designs, and manufacturer funding. Results from different studies may also be inconsistent.[39,40] In some cases, this results in a lower level of evidence. Additionally, limited literature exists on certain SCS frequencies, resulting in less precise effect estimates compared to other frequencies. Therefore, these relative efficacy estimates must be confirmed by directly comparing SCS modes in randomized controlled trials with adequate sample sizes.

Conclusion

This NMA suggests potential differences in therapeutic profiles among SCS modalities for FBSS. HF-SCS (10 kHz) showed relatively higher SUCRA values for back pain (99.7%), leg pain (93.2%), and disability improvement (ODI 85.0%). Subperception SCS (500–1200 Hz) was associated with better probability for global pain relief (64.0%), ≥50% pain reduction (75.3%), and HRQoL outcomes (EQ-5D 80.3%). These relative efficacy estimates require confirmation in adequately powered RCTs directly comparing SCS modalities.

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Disclosure

All authors report no conflicts of interest in this work; no financial relationships with any organizations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

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