SUPPLEMENTARY MATERIAL

Table S1 PubMed search strategy

Search ID	Search term
#1	“spinal cord”[tiab] OR spine[tiab] OR spinal[tiab] OR epidural[tiab] OR “dorsal column*”[tiab] OR invasive[tiab] OR implant*[tiab] OR “spinal nerve*”[tiab] OR “spinal gangli*"[tiab] OR "spinal root*"[tiab] OR "nerve root*"[tiab] OR "dorsal gangli*"[tiab] OR "dorsal root*"[tiab]
#2	stimulation[tiab] OR stimulator[tiab] OR neuromodulation[tiab] OR neurostimulator[tiab]
#3	#1 AND #2
#4	"spinal cord stimulation"[mesh] OR "electric stimulation therapy"[mesh] OR scs[tiab] OR drg[tiab]
#5	#3 OR #4
#6	"Diabetic Neuropathies"[mesh]
#7	diabet*[tiab] AND (neuropath*[tiab] OR amyotroph*[tiab] OR polyneuropath*[tiab] OR mononeuropath*[tiab] OR neuralg*[tiab] OR pain*[tiab])
#8	#6 OR #7
#9	neuropathy[tiab] OR neuropathies[tiab] OR polyneuropath*[tiab] OR mononeuropath*[tiab]
#10	#8 OR #9
#11	#5 AND #10

Table S2 Cochrane Risk of Bias Assessment (performed using the RoB 2.0 tool) for randomized controlled trials

Unique ID	Petersen et al (2021)	**Study ID**	Petersen et al (2021)	**Assessor**	DE
Ref or Label	Petersen et al (2021)	**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	Conventional medical management (CMM) with adjunctive high-frequency 10 kHz SCS therapy	**Comparator**	Conventional medical management (CMM) alone	**Source**	Journal article(s)
Outcome	6 months: Pain intensity; Responder rate (at least 50% pain reduction)	**Results**		**Weight**	1

Domain	Signalling question	Response	Comments
Bias arising from the randomization process	1.1 Was the allocation sequence random?	Y	Computer generated randomization.
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	Y	Randomization was concealed.
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	N	Baseline characteristics appear to be well-balanced
	Risk of bias judgement	**Low**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	Y	Open-label study without blinding of participants or study personnel, or sham control
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	PN	No deviations were reported.
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	An ITT approach is reported, although there were 8 exclusions after exposure to the treatment during the screening trial.
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	N	Low level of missing data at 6 months: 10 kHz SCS plus CMM: 15%, 17 of 113; CMM: 9%, 9 of 103.
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	N	The level of missing data was not balanced between the arms. In addition, the missing participants were excluded from the 6-month analysis.
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	PN	Considering the 10 kHz SCS group, there were 8 exclusions after exposure to the treatment during the screening trial. The published article does not provide sufficient detail to confirm that the exclusions were not related to the pain outcome. However, individual patient data (IPD) confirmed that all 8 patients completed the trial, all were responders, and 6 had at least 75% pain relief; this suggests that the exclusions were probably not related to the pain outcome.
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	N	VAS is a validated pain intensity scale
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	N	
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	VAS score was patient-reported outcome (subjective scale). Since the trial was open-label in design, the assessor (ie, the patient) was aware of the treatment assignment.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	Y	Since the patient was aware of the intervention, they may have been influenced by expecting a benefit from 10 kHz SCS, or not perceiving CMM as a proper treatment. In addition, the patient was aware of being allowed to crossover at 6 months.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	PY	
	Risk of bias judgement	**High**	
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	PY	A summary of the trial protocol was published by Mekhail et al (2020). A statistical analysis plan (SAP) is also publicly available. However, it is not confirmed that the final SAP preceded the availability of unblinded outcome data to the trial investigators.
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	No apparent indications of reporting selectivity at 6 months from examination of the protocol and SAP.
	5.3 ... multiple eligible analyses of the data?	PN	
	Risk of bias judgement	**Low**	
Overall bias	**Risk of bias judgement**	**High**	

Unique ID	Slangen et al (2014)	**Study ID**	Slangen et al (2014)	**Assessor**	DE
Ref or Label	Slangen et al (2014)	**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	Best medical therapy with adjunctive LF-SCS therapy	**Comparator**	Best medical therapy (BMT) alone	**Source**	Journal article(s); Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
Outcome	6 months: Pain intensity; Responder rate (at least 50% pain reduction)	**Results**		**Weight**	1

Domain	Signalling question	Response	Comments
Bias arising from the randomization process	1.1 Was the allocation sequence random?	Y	Computer generated randomization.
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	NI	No information is provided regarding concealment; however, it is likely that the allocation was concealed since computer randomization was used.
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	N	Baseline characteristics appear to be well-balanced.
	Risk of bias judgement	**Low**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	Y	Open-label study without blinding of participants or study personnel.
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	PN	No deviations were reported.
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	ITT analysis was performed
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Y	Low level of missing data from each arm, but not balanced between the arms: LF-SCS 14% (3 of 22); CMM 7% (1 of 14). However, missing participants were treated as nonresponders.
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	N	NRS is a validated pain intensity scale
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	N	
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	NRS score was patient-reported outcome (subjective scale). Since the trial was open-label in design, the assessor (ie, the patient) was aware of the treatment assignment.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	Y	Since the patient was aware of the intervention, they may have been influenced by expecting a benefit from LF-SCS, or not perceiving BMT as a proper treatment.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	PY	
	Risk of bias judgement	**High**	
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	NI	Analysis intentions are not available, ie, no published protocol or statistical analysis plan
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	No apparent indications of reporting selectivity. The use of dichotomous responder status is standard in the SCS field (ie, not selective reporting). The analysis used the standard definition of treatment response (at least 50% pain reduction).
	5.3 ... multiple eligible analyses of the data?	PN	
	Risk of bias judgement	**Some concerns**	
Overall bias	**Risk of bias judgement**	**High**	

Unique ID	de Vos et al (2014)	**Study ID**	de Vos et al (2014)	**Assessor**	DE
Ref or Label	de Vos et al (2014)	**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	Best medical therapy with adjunctive LF-SCS therapy	**Comparator**	Best medical therapy (BMT) alone	**Source**	Journal article(s); Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
Outcome	6 months: Pain intensity; Responder rate (at least 50% pain reduction)	**Results**		**Weight**	1

Domain	Signalling question	Response	Comments
Bias arising from the randomization process	1.1 Was the allocation sequence random?	Y	Block stratified randomization is likely to be computer based.
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	NI	No information is provided regarding concealment; however, it is likely that the allocation was concealed if computer randomization was used.
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	N	Baseline characteristics appear to be well-balanced (no statistically significant differences between the groups).
	Risk of bias judgement	**Low**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	Y	Open-label study without blinding of participants or study personnel.
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	PN	No deviations were reported.
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	ITT analysis was performed
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Y	Low and balanced level of missing data in each arm: LF-SCS 10%, 4 of 40; BMT 10%, 2 of 20. The authors presented an ITT analysis.
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	N	VAS is a validated pain intensity scale
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	N	
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	VAS score was patient-reported outcome (subjective scale). Since the trial was open-label in design, the assessor (ie, the patient) was aware of the treatment assignment.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	Y	Since the patient was aware of the intervention, they may have been influenced by expecting a benefit from LF-SCS, or not perceiving BMT as a proper treatment. In addition, the patient was aware of being allowed to crossover at 6 months.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	PY	
	Risk of bias judgement	**High**	
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	NI	Analysis intentions are not available, ie, no published protocol or statistical analysis plan
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	No apparent indications of reporting selectivity. The use of dichotomous responder status is standard in the SCS field (ie, not selective reporting). The analysis used the standard definition of treatment response (at least 50% pain reduction).
	5.3 ... multiple eligible analyses of the data?	PN	
	Risk of bias judgement	**Some concerns**	
Overall bias	**Risk of bias judgement**	**High**	

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Title
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Section 1 Introduction, final paragraph
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Section 1 Introduction, final paragraph
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Section 2.1 Eligibility
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Section 2.2 Search Strategy
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Supplementary Material Table S1
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Section 2.3 Selection Process
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Section 2.4 Data Extraction and Outcomes
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Section 2.4 Data Extraction and Outcomes
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	N/A
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Section 2.5. Study Risk of Bias Assessment
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Section 2.6. Summary Measures
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	N/A (no meta-analysis performed)
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Section 2.7. Data synthesis
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Section 2.7. Data synthesis
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	N/A (no meta-analysis performed)
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	N/A (no meta-analysis performed)

Section and Topic	Item #	Checklist item	Location where item is reported
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	N/A (no meta-analysis performed)
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	N/A (no meta-analysis performed)
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	N/A (no meta-analysis performed)
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Section 3.1. Study Selection, Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	N/A
Study characteristics	17	Cite each included study and present its characteristics.	Section 3.2. Characteristics of Included Studies, Table 1
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Section 3.3. Risk of Bias in Studies (Performed for RCTs)
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Section 3.4. Outcomes in Painful Diabetic Neuropathy; Section 3.5. Outcomes in Other Painful Peripheral Neuropathies and Mixed Etiology Populations; Table 2; Table 3.
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	N/A (no meta-analysis performed)
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	N/A (no meta-analysis performed)
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	N/A (no meta-analysis performed)
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N/A (no meta-analysis performed)
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	N/A (no meta-analysis performed)
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	N/A (no meta-analysis performed)
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Section 4.1. Interpretation of Results
	23b	Discuss any limitations of the evidence included in the review.	Section 4.2. Strengths and Limitations of the Review
	23c	Discuss any limitations of the review processes used.	Section 4.2. Strengths and Limitations of the Review

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
	23d	Discuss implications of the results for practice, policy, and future research.	Section 4.3. Implications for Practice, Policy, and Future Research
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Figure 1
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Figure 1, DOI
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	See Funding and Author Contributions
Competing interests	26	Declare any competing interests of review authors.	See Conflicts of Interest
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	N/A

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit: http://www.prisma-statement.org/

PRISMA 2020 for Abstracts Checklist

Section and Topic	Item #	Checklist item	Reported (Yes/No)
TITLE			
Title	1	Identify the report as a systematic review.	Yes
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	Yes
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	Yes
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	Yes
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	Yes
Synthesis of results	6	Specify the methods used to present and synthesise results.	Yes
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.	Yes
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured).	Yes
DISCUSSION			
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).	No (see manuscript)
Interpretation	10	Provide a general interpretation of the results and important implications.	Yes
OTHER			
Funding	11	Specify the primary source of funding for the review.	No (see manuscript)
Registration	12	Provide the register name and registration number.	No (see manuscript)

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71