Spinal Cord Stimulation – Rereview

Final Appendices

October 23, 2023

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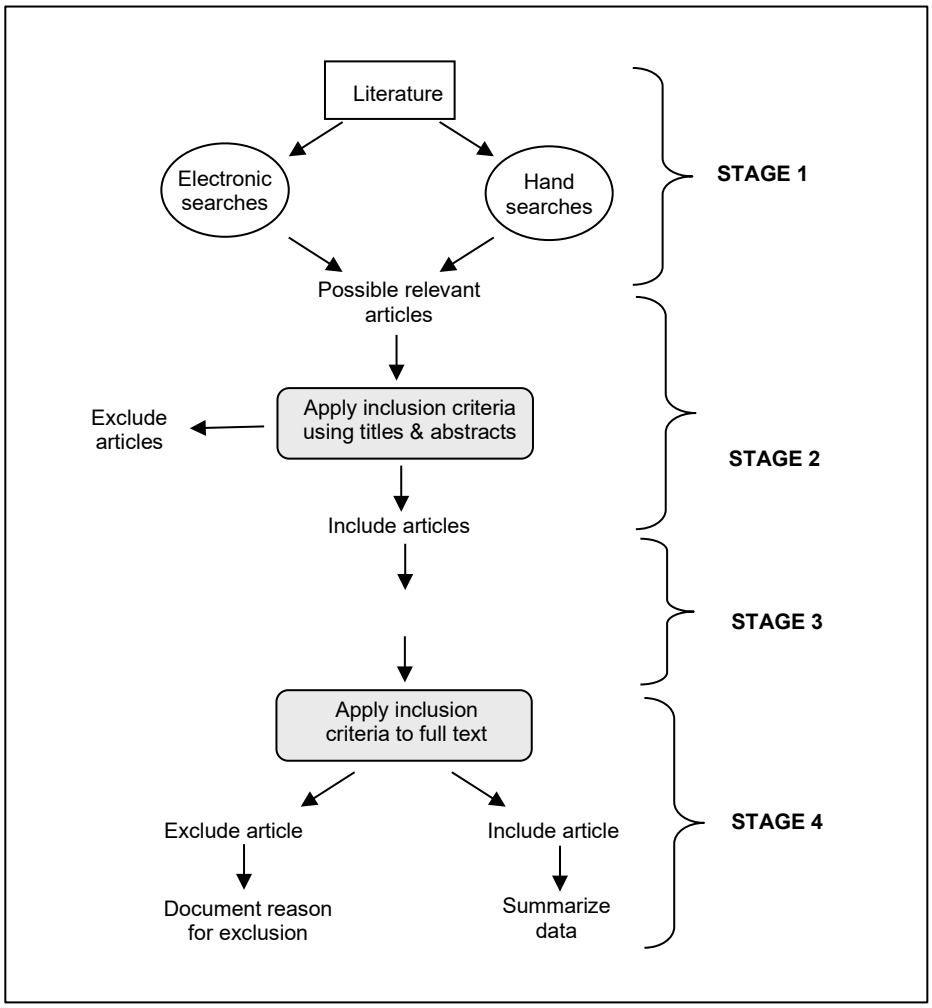
APPENDIX A. Algorithm for Article Selection



APPENDIX B. Search Strategies

Below is the search strategy for PubMed. Parallel strategies were used to search other electronic databases listed below. Keyword searches were conducted in the other listed resources. In addition, hand-searching of included studies was performed.

Appendix Table B1: PubMed Search Strategy; parallel searches in EMBASE, Cochrane
LIMITS: Humans, English
DATES: 2010 through June 6, 2023

1.	Spinal cord stimulation
2.	Chronic pain
3.	#1 AND #2
4.	Neuropathic pain
5.	Ischemic pain
6.	Ischaemic pain
7.	Failed back surgery syndrome
8.	Complex regional pain syndrome
9.	Dystrophy
10.	Causalgia
11.	Phantom limb pain
12.	Central pain
13.	Stroke pain
14.	Post-stroke pain
15.	Diabetic neuropathy
16.	Herpetic neuralgia
17.	Post-herpetic neuralgia
18.	Precision
19.	WaveWriter
20.	Vanta
21.	Intellis
22.	PrimeAdvanced
23.	SureScan
24.	Restore
25.	ReActiv8
26.	Evoke
27.	Senza
28.	Proclaim
29.	Prodigy
30.	Eterna
31.	#4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30
32.	#1 AND #31
33.	#3 OR #31 (FINAL SEARCH CODE)

Electronic Database Searches
The following databases have been searched for relevant information:

Cochrane Database of Systematic Reviews
Cochrane Registry of Clinical Trials (CENTRAL)
Database of Reviews of Effectiveness (Cochrane Library)
PubMed
ClinicalTrials.gov

Additional Economics, Clinical Guideline and Gray Literature Databases
Food and Drug Administration (FDA)
Google

APPENDIX C. Excluded Articles

Articles excluded as primary studies after full text review, with reason for exclusion.

Appendix Table C1. List of Excluded Articles

	Citation	Reason for exclusion after full-text review
1.	Schu S, Slotty PJ, Bara G, von Knop M, Edgar D, Vesper J. A prospective, randomised, double-blind, placebo-controlled study to examine the effectiveness of burst spinal cord stimulation patterns for the treatment of failed back surgery syndrome. Neuromodulation. 2014 Jul;17(5):443-50. doi: 10.1111/ner.12197. Epub 2014 Jun 19. PMID: 24945621.	Ineligible population (not SCS naïve)
2.	De Ridder D, Plazier M, Kamerling N, Menovsky T, Vanneste S. Burst spinal cord stimulation for limb and back pain. World Neurosurg. 2013 Nov;80(5):642-649.e1. doi: 10.1016/j.wneu.2013.01.040. Epub 2013 Jan 12. PMID: 23321375.	Ineligible intervention (not permanent implant, only trial SCS)
3.	Eldabe S, Duarte R, Gulve A, Williams H, Garner F, Brookes M, Madzinga G, Buchser E, Batterham AM. Analgesic Efficacy of "Burst" and Tonic (500 Hz) Spinal Cord Stimulation Patterns: A Randomized Placebo-Controlled Crossover Study. Neuromodulation. 2021 Apr;24(3):471-478. doi: 10.1111/ner.13321. Epub 2020 Nov 29. PMID: 33251662.	Ineligible population (not SCS naïve)
4.	Amirdelfan K, Yu C, Doust MW, Gliner BE, Morgan DM, Kapural L, Vallejo R, Sitzman BT, Yearwood TL, Bundschu R, Yang T, Benyamin R, Burgher AH, Brooks ES, Powell AA, Subbaroyan J. Long-term quality of life improvement for chronic intractable back and leg pain patients using spinal cord stimulation: 12-month results from the SENZA-RCT. Qual Life Res. 2018 Aug;27(8):2035-2044. doi: 10.1007/s11136-018-1890-8. Epub 2018 Jun 1. PMID: 29858746.	Ineligible comparator (two SCS types, no control group)
5.	Amirdelfan K, Webster L, Poree L, Sukul V, McRoberts P. Treatment Options for Failed Back Surgery Syndrome Patients With Refractory Chronic Pain: An Evidence Based Approach. Spine (Phila Pa 1976). 2017 Jul 15;42 Suppl 14:S41-S52. doi: 10.1097/BRS.0000000000002217. PMID: 28505029.	Ineligible comparator (two SCS types, no control group); ineligible outcome (proposes and analyzes remission cutoff)
6.	Eldabe S, Gilligan C, Taylor RS, Patel KV, Duarte RV. Issues in design, conduct, and conclusions of JAMA's Hara et al.'s randomized clinical trial of spinal cord burst stimulation versus placebo stimulation on disability in patients with chronic radicular pain after lumbar spine surgery. Pain Pract. 2023 Mar;23(3):232-233. doi: 10.1111/papr.13186. Epub 2022 Dec 11. PMID: 36504290.	Ineligible publication type (editorial)
7.	Feng X, Ye L. Comments on "Efficacy of Pulsed Radiofrequency or Short-Term Spinal Cord Stimulation for Acute/Subacute Zoster-Related Pain: A Randomized, Double-Blinded, Controlled Trial". Pain Physician. 2021 Sep;24(6):E893-E894. PMID: 34554710.	Ineligible publication type (letter to the editor)
8.	Kapural L, Patterson DG, Li S, et al. Multiphase Spinal Cord Stimulation in Participants With Chronic Back or Leg Pain: Results of the BENEFIT-02 Randomized Clinical Trial. Neuromodulation.	Ineligible intervention (trial phase only, not permanent implant); ineligible

	Citation	Reason for exclusion after full-text review
	2023 Aug 16;S1094-7159(23)00702-X. doi: 10.1016/j.neurom.2023.05.006.	comparator (two SCS types, no control group)
9.	Kapural L, Yu C, Doust MW, Gliner BE, Vallejo R, Sitzman BT, Amirdelfan K, Morgan DM, Brown LL, Yearwood TL, Bundschu R, Burton AW, Yang T, Benyamin R, Burgher AH. Novel 10-kHz High-frequency Therapy (HF10 Therapy) Is Superior to Traditional Low-frequency Spinal Cord Stimulation for the Treatment of Chronic Back and Leg Pain: The SENZA-RCT Randomized Controlled Trial. Anesthesiology. 2015 Oct;123(4):851-60. doi: 10.1097/ALN.0000000000000774. PMID: 26218762.	Ineligible comparator (two SCS types, no control group)
10.	Li X, Chen P, He J, Huang X, Tang D, Chen L, Wang X. Comparison of the Efficacy and Safety of Temporary Spinal Cord Stimulation versus Pulsed Radiofrequency for Postherpetic Neuralgia: A Prospective Randomized Controlled Trial. Pain Res Manag. 2022 Oct 11;2022:3880424. doi: 10.1155/2022/3880424. PMID: 36267666; PMCID: PMC9578922.	Ineligible intervention (temporary SCS); ineligible comparator (other neuromodulation [PRF])
11.	Liu B, Yang Y, Zhang Z, Wang H, Fan B, Sima L. Clinical Study of Spinal Cord Stimulation and Pulsed Radiofrequency for Management of Herpes Zoster-Related Pain Persisting Beyond Acute Phase in Elderly Patients. Pain Physician. 2020 Jun;23(3):263-270. PMID: 32517392.	Ineligible comparator (other neuromodulation [PRF])
12.	Mekhail N, Levy RM, Deer TR, Kapural L, Li S, Amirdelfan K, Hunter CW, Rosen SM, Costandi SJ, Falowski SM, Burgher AH, Pope JE, Gilmore CA, Qureshi FA, Staats PS, Scowcroft J, Carlson J, Kim CK, Yang MI, Stauss T, Poree L; Evoke Study Group. Long-term safety and efficacy of closed-loop spinal cord stimulation to treat chronic back and leg pain (Evoke): a double-blind, randomised, controlled trial. Lancet Neurol. 2020 Feb;19(2):123-134. doi: 10.1016/S1474-4422(19)30414-4. Epub 2019 Dec 20. PMID: 31870766.	Ineligible comparator (two SCS types, no control group)
13.	Perruchoud C, Eldabe S, Batterham AM, Madzinga G, Brookes M, Durrer A, Rosato M, Bovet N, West S, Bovy M, Rutschmann B, Gulve A, Garner F, Buchser E. Analgesic efficacy of high-frequency spinal cord stimulation: a randomized double-blind placebo-controlled study. Neuromodulation. 2013 Jul-Aug;16(4):363-9; discussion 369. doi: 10.1111/ner.12027. Epub 2013 Feb 20. PMID: 23425338.	Ineligible population (not SCS naïve)
14.	Vesper J, Gregor B, Slotty P. Burst or tonic stimulation? Results of a placebo controlled, double blinded, randomized study for the treatment of FBSS patients - 2 year follow-up. Pain Practice 2016;16(S1):74-75.	Ineligible population (not SCS naïve)
15.	Vesper J, Slotty PJ, Schu S. Burst or tonic stimulation? Results of a placebo controlled, double blinded, randomized study for the treatment of FBSS patients - 3 year follow-up. Neuromodulation 2017;20(7):e170.	Ineligible population (not SCS naïve)
16.	Sheng L, Liu Z, Zhou W, Li X, Wang X, Gong Q. Short-Term Spinal Cord Stimulation or Pulsed Radiofrequency for Elderly Patients with Postherpetic Neuralgia: A Prospective Randomized Controlled	Ineligible intervention (temporary SCS)

	Citation	Reason for exclusion after full-text review
	Trial. Neural Plast. 2022 Apr 27;2022:7055697. doi: 10.1155/2022/7055697. PMID: 35529453; PMCID: PMC9068337.	
17.	Schultz DM, Webster L, Kosek P, Dar U, Tan Y, Sun M. Sensor-driven position-adaptive spinal cord stimulation for chronic pain. Pain Physician. 2012 Jan-Feb;15(1):1-12. PMID: 22270733.	Ineligible comparator (two SCS types, no control group)
18.	van Eijs F, Smits H, Geurts JW, Kessels AG, Kemler MA, van Kleef M, Joosten EA, Faber CG. Brush-evoked allodynia predicts outcome of spinal cord stimulation in complex regional pain syndrome type 1. Eur J Pain. 2010 Feb;14(2):164-9. doi: 10.1016/j.ejpain.2009.10.009. Epub 2009 Nov 25. PMID: 19942463.	Ineligible outcome (predictors or treatment response)
19.	Wan CF, Song T. Efficacy of Pulsed Radiofrequency or Short-Term Spinal Cord Stimulation for Acute/Subacute Zoster-Related Pain: A Randomized, Double-Blinded, Controlled Trial. Pain Physician. 2021 May;24(3):215-222. PMID: 33988940.	Ineligible intervention (temporary SCS); ineligible comparator (other neuromodulation [PRF dorsal root ganglion])
20.	Wolter T, Kiemen A, Porzelius C, Kaube H. Effects of sub-perception threshold spinal cord stimulation in neuropathic pain: a randomized controlled double-blind crossover study. Eur J Pain. 2012 May;16(5):648-55. doi: 10.1002/j.1532-2149.2011.00060.x. Epub 2011 Dec 19. PMID: 22337509.	Ineligible population (not SCS naïve)
21.	Eisenberg E, Burstein Y, Suzan E, Treister R, Aviram J. Spinal cord stimulation attenuates temporal summation in patients with neuropathic pain. Pain. 2015 Mar;156(3):381-385. doi: 10.1097/01.j.pain.0000460342.69718.a2. PMID: 25599230.	Ineligible population (not SCS naïve)
22.	Eisenberg E, Burstein Y, Suzan E, Treister R, Aviram J. Spinal cord stimulation attenuates temporal summation in patients with neuropathic pain. Pain 2015;156(3):381-85	Ineligible population (not SCS naïve)
23.	North RB, Deruytter MM, Vangeneugden JJ, RaNopoulos C, Van Havenbergh T, Desai MJ, et al. Perioperative infections and prolonged SCS trial duration (PROMISE study). Neuromodulation 2018;21(3):e11.	Duplicate publication to North 2020
24.	Sweet J, Badjatiya A, Tan D, Miller J. Paresthesia-free highdensity spinal cord stimulation for postlaminectomy syndrome in a prescreened population: a prospective case series. Neuromodulation 2016;19(3):260-7. [DOI: 10.1111/ner.12357]; NCT05283863	Ineligible population (not SCS naïve); ineligible study design (n<10 total)
25.	Milbouw G, Leruth S. Spinal cord stimulation vs conventional medical management: a multicenter randomized controlled trial of patients with failed back surgery syndrome (PROCESS Study). Surgical Neurology 2007;68:192-204.	Ineligible study design - abstract only
26.	Mekhail N, Mehanny D, Armanyous S, Saweris Y, Costandi S. The impact of obesity on the effectiveness of spinal cord stimulation in chronic spine-related pain patients. Spine J. 2019 Mar;19(3):476-486. doi: 10.1016/j.spinee.2018.08.006. Epub 2018 Aug 22. PMID: 30142457.	Ineligible study design (no non-SCS control group)

	Citation	Reason for exclusion after full-text review
27.	Moriyama K, Murakawa K, Uno T, Oseto K, Kawanishi M, Saito Y, Taira T, Yamauchi M. A prospective, open-label, multicenter study to assess the efficacy of spinal cord stimulation and identify patients who would benefit. Neuromodulation. 2012 Jan-Feb;15(1):7-11; discussion 12. doi: 10.1111/j.1525-1403.2011.00411.x. Epub 2011 Dec 12. PMID: 22151729.	Ineligible study design (case series, not safety focused)
28.	Van Havenbergh T, Vancamp T, Van Looy P, Vanneste S, De Ridder D. Spinal cord stimulation for the treatment of chronic back pain patients: 500-Hz vs. 1000-Hz burst stimulation. Neuromodulation. 2015 Jan;18(1):9-12; discussion 12. doi: 10.1111/ner.12252. Epub 2014 Oct 22. PMID: 25339436.	Ineligible comparator (two SCS types, no control group)
29.	Avellanal M, Diaz-Reganon G, Orts A, Soto S. One-year results of an algorithmic approach to managing failed back surgery syndrome. Pain Res Manag. 2014 Nov-Dec;19(6):313-6. doi: 10.1155/2014/474510. Epub 2014 Sep 15. PMID: 25222573; PMCID: PMC4273710.	Ineligible study design (case series, not safety focused)
30.	Bondoc M, Hancu M, DiMarzio M, Sheldon BL, Shao MM, Khazen O, Pilitsis JG. Age as an Independent Predictor of Adult Spinal Cord Stimulation Pain Outcomes. Stereotact Funct Neurosurg. 2022;100(1):1-7. doi: 10.1159/000517426. Epub 2021 Jul 19. PMID: 34280929.	Ineligible study design (case series, not safety focused)
31.	Corallo F, De Salvo S, Floridia D, Bonanno L, Muscarà N, Cerra F, Cannistraci C, Di Cara M, Lo Buono V, Bramanti P, Marino S. Assessment of spinal cord stimulation and radiofrequency: Chronic pain and psychological impact. Medicine (Baltimore). 2020 Jan;99(3):e18633. doi: 10.1097/MD.0000000000018633. PMID: 32011443; PMCID: PMC7220179.	Ineligible comparator (other neuromodulation [pulsed SC RF])
32.	De Ridder D, Vanneste S, Plazier M, van der Loo E, Menovsky T. Burst spinal cord stimulation: toward paresthesia-free pain suppression. Neurosurgery. 2010 May;66(5):986-90. doi: 10.1227/01.NEU.0000368153.44883.B3. PMID: 20404705.	Ineligible comparator (two SCS types, no control group)
33.	Delmotte A, Jacques L, Kumar K, Poon K, Monlezun O, Roulaud M, Prevost A, Munson R, Guetarni F, Bataille B, Rigoard P. The Franco-Canadian multicolumn spinal cord stimulation prospective study: a subgroup analysis focusing on the decisive role of lead positioning. Neurochirurgie. 2015 Mar;61 Suppl 1:S83-9. doi: 10.1016/j.neuchi.2014.06.005. Epub 2014 Sep 22. PMID: 25245918.	Ineligible comparator (optimal vs. nonoptimal lead positioning for SCS, no control group)
34.	Dufka FL, Munch T, Dworkin RH, Rowbotham MC. Results availability for analgesic device, complex regional pain syndrome, and post-stroke pain trials: comparing the RReADS, RReACT, and RReMiT databases. Pain. 2015 Jan;156(1):72-80. doi: 10.1016/j.pain.0000000000000009. PMID: 25599303; PMCID: PMC4280280.	Ineligible outcome (non-clinical outcomes)
35.	El-Naggar AO, Reis CL, Hatheway JA, Schmidt TE, Pico TC, Sanapati MR, Abd-Elsayed A, Patel AS, Calodney A, Johanek L, Tan Y, McCammon S. Using Lower Amplitudes to Maintain Effective High Dose Spinal Cord Stimulation Therapy (SCS Dosing Pilot Study).	ineligible study design (case series, not safety focused)

	Citation	Reason for exclusion after full-text review
	Neuromodulation. 2021 Apr;24(3):532-539. doi: 10.1111/ner.13258. Epub 2020 Sep 18. PMID: 32946181.	
36.	Hagedorn JM, Falowski SM, Blomme B, Capobianco RA, Yue JJ. Burst spinal cord stimulation can attenuate pain and its affective components in chronic pain patients with high psychological distress: results from the prospective, international TRIUMPH study. Spine J. 2022 Mar;22(3):379-388. doi: 10.1016/j.spinee.2021.08.005. Epub 2021 Aug 20. PMID: 34419628.	Ineligible study design (case series, not safety focused)
37.	Huang M, Chen Q, Wu S, Huang J, Sun W, Yang S, Qian X, Xiao L. Treatment Efficacy and Technical Advantages of Temporary Spinal Nerve Root Stimulation Compared to Traditional Spinal Cord Stimulation for Postherpetic Neuralgia. Pain Physician. 2022 Sep;25(6):E863-E873. PMID: 36122270.	Ineligible comparator (other neuromodulation [spinal nerve root stimulation])
38.	Kim DD, Vakharyia R, Kroll HR, Shuster A. Rates of lead migration and stimulation loss in spinal cord stimulation: a retrospective comparison of laminotomy versus percutaneous implantation. Pain Physician. 2011 Nov-Dec;14(6):513-24. PMID: 22086092.	Ineligible comparator (SCS implant techniques [laminotomy vs. percutaneous], no control group)
39.	The impact of obesity on the effectiveness of spinal cord stimulation in chronic spine-related pain patients	Ineligible study design (case series, not safety focused)
40.	Moriyama K, Murakawa K, Uno T, Oseto K, Kawanishi M, Saito Y, Taira T, Yamauchi M. A prospective, open-label, multicenter study to assess the efficacy of spinal cord stimulation and identify patients who would benefit. Neuromodulation. 2012 Jan-Feb;15(1):7-11; discussion 12. doi: 10.1111/j.1525-1403.2011.00411.x. Epub 2011 Dec 12. PMID: 22151729.	Ineligible study design (case series, not safety focused)
41.	Abrecht CR, Greenberg P, Song E, Urman RD, Rathmell JP. A Contemporary Medicolegal Analysis of Implanted Devices for Chronic Pain Management. Anesth Analg. 2017 Apr;124(4):1304-1310. doi: 10.1213/ANE.0000000000001702. PMID: 28319551.	Ineligible intervention (not SCS, medication management)
42.	Ahmadi R, Hajiabadi MM, Unterberg A, Geist C, Campos B. Wireless Spinal Cord Stimulation Technology for the Treatment of Neuropathic Pain: A Single-Center Experience. Neuromodulation. 2021 Apr;24(3):591-595. doi: 10.1111/ner.13149. Epub 2020 Mar 31. PMID: 32232943.	Ineligible study design (case series, not safety focused)
43.	Tjepkema-Cloostermans MC, de Vos CC, Wolters R, Dijkstra-Scholten C, Lenders MW. Effect of Burst Stimulation Evaluated in Patients Familiar With Spinal Cord Stimulation. Neuromodulation. 2016 Jul;19(5):492-7. doi: 10.1111/ner.12429. Epub 2016 Apr 5. PMID: 27059278.	Ineligible population (not SCS naïve)
44.	van Eijs F, Geurts JW, Van Zundert J, Faber CG, Kessels AG, Joosten EA, van Kleef M. Spinal cord stimulation in complex regional pain syndrome type I of less than 12-month duration. Neuromodulation. 2012 Mar-Apr;15(2):144-50; discussion 150. doi: 10.1111/j.1525-1403.2011.00424.x. Epub 2012 Feb 13. PMID: 22329446.	Ineligible study design (case series, not safety focused)

	Citation	Reason for exclusion after full-text review
45.	Brill S, Defrin R, Aryeh IG, Zusman AM, Benyamini Y. Short- and long-term effects of conventional spinal cord stimulation on chronic pain and health perceptions: A longitudinal controlled trial. Eur J Pain. 2022 Oct;26(9):1849-1862. doi: 10.1002/ejp.2002. Epub 2022 Jul 7. PMID: 35761769; PMCID: PMC9543320.	Ineligible study design (not safety focused)
46.	Colombo EV, Mandelli C, Mortini P, Messina G, De Marco N, Donati R, Irace C, Landi A, Lavano A, Mearini M, Podetta S, Servello D, Zekaj E, Valtulina C, Dones I. Epidural spinal cord stimulation for neuropathic pain: a neurosurgical multicentric Italian data collection and analysis. Acta Neurochir (Wien). 2015 Apr;157(4):711-20. doi: 10.1007/s00701-015-2352-5. Epub 2015 Feb 3. PMID: 25646850.	Ineligible comparator (two SCS types, SCS trial vs. no trial)
47.	Garcia MA, Emami AS, Blau LE, Rutledge T. A pre- and post-implantable pain device procedure assessment model: psychiatric symptoms, functioning, and goals. Pain Manag. 2023 Mar;13(3):161-170. doi: 10.2217/pmt-2022-0087. Epub 2023 Apr 4. PMID: 37013940.	Ineligible study design (not safety focused)
48.	Abrecht CR, Gabriel RA, Dutton RP, Kaye AD, Michna E, Urman RD. National Perioperative Outcomes for Intrathecal Pump, Spinal Cord Stimulator, and Peripheral Nerve Stimulator Procedures. Pain Physician. 2015 Nov;18(6):547-54. PMID: 26606006.	Ineligible comparator (two SCS types, SCS vs. PNS)
49.	Al-Kaisy A, Van Buyten JP, Smet I, Palmisani S, Pang D, Smith T. Sustained effectiveness of 10 kHz high-frequency spinal cord stimulation for patients with chronic, low back pain: 24-month results of a prospective multicenter study. Pain Med. 2014 Mar;15(3):347-54. doi: 10.1111/pme.12294. Epub 2013 Dec 5. PMID: 24308759; PMCID: PMC4282782.	Ineligible study design (<5 years and/or n<500 for case series)
50.	Al-Mahfoudh R, Chan Y, Chong HP, Farah JO. Twiddler's syndrome in spinal cord stimulation. Acta Neurochir (Wien). 2016 Jan;158(1):147-54. doi: 10.1007/s00701-015-2627-x. Epub 2015 Nov 17. PMID: 26577635; PMCID: PMC4684581.	Ineligible outcome (twindler's syndrome)
51.	Amirdelfan K, Vallejo R, Benyamin R, Yu C, Yang T, Bundschu R, Yearwood TL, Sitzman BT, Gliner B, Subbaroyan J, Rotte A, Caraway D. High-Frequency Spinal Cord Stimulation at 10 kHz for the Treatment of Combined Neck and Arm Pain: Results From a Prospective Multicenter Study. Neurosurgery. 2020 Aug 1;87(2):176-185. doi: 10.1093/neuros/nyz495. PMID: 31792530; PMCID: PMC7360873.	Ineligible population (upper limb and/or neck)
52.	Bendersky D, Yampolsky C. Is spinal cord stimulation safe? A review of its complications. World Neurosurg. 2014; 82(6): 1359–1368, doi: 10.1016/j.wneu.2013.06.012, indexed in Pubmed: 23851231	Ineligible publication type (literature review)
53.	Benyamin R, Galan V, Hatheway J, Kim P, Choi D, Falowski S, Calodney A, Sweet J, Yu C, Kapural L, Provenzano D. Options: A Prospective, Open-Label Study of High-Dose Spinal Cord Stimulation in Patients with Chronic Back and Leg Pain. Pain Physician. 2020 Jan;23(1):87-98. PMID: 32013282.	Ineligible study design (<5 years and/or n<500 for case series)

	Citation	Reason for exclusion after full-text review
54.	Sharan AD, Riley J, Falowski S, et al. Association of Opioid Usage with Spinal Cord Stimulation Outcomes. Pain medicine (Malden, Mass) 2018;19:699-707. PMID: 29244102.	Duplicate study population
55.	Bir SC, Konar S, Maiti T, Nanda A, Guthikonda B. Neuromodulation in intractable pain management: outcomes and predictors of revisions of spinal cord stimulators. Neurosurg Focus. 2016 May;40(5):E4. doi: 10.3171/2016.3.FOCUS15634. PMID: 27132525.	Ineligible study design (<5 years and/or n<500 for case series)
56.	Bolash R, Creamer M, Rauck R, Vahedifar P, Calodney A, Fox I, Ozaktay C, Vanquathem N. Multi-waveform Spinal Cord Stimulation with High Frequency Electromagnetic Coupled (HF-EMC) Powered Implanted Electrode Array and Receiver for the Treatment of Chronic Back and Leg Pain (SURF Study). Pain Physician. 2022 Jan;25(1):67-76. PMID: 35051146.	Ineligible study design (<5 years and/or n<500 for case series)
57.	Chaudhry ZA, Najib U, Bajwa ZH, Jacobs WC, Sheikh J, Simopoulos TT. Detailed analysis of allergic reactions to spinal cord stimulator devices. J Pain Res 2013;6: 617–623.	Ineligible study design (case report)
58.	Daniels AH, McDonald CL, Basques BA, Hershman SH. Perioperative Management of Spinal Cord Stimulators and Intrathecal Pain Pumps. J Am Acad Orthop Surg. 2022 Sep 1;30(17):e1095-e1105. doi: 10.5435/JAAOS-D-22-00053. Epub 2022 Apr 18. PMID: 35439220.	Ineligible publication type (narrative review)
59.	Denisova NP, Rogov DY, Rzaev DA, Khabarova EA, Dmitriev AB. Spinal cord stimulation in the treatment of chronic pain syndromes. Zh Vopr Neirokhir Im N N Burdenko. 2016;80(2):47-52. English, Russian. doi: 10.17116/neiro201680247-52. PMID: 27070257.	Ineligible study design (case series, safety not stated a priori)
60.	Dombovy-Johnson ML, D'Souza RS, Ha CT, Hagedorn JM. Incidence and risk factors for spinal cord stimulator lead migration with or without loss of efficacy: a retrospective review of 91 consecutive thoracic lead implants. Neuromodulation 25(5), 731–737 (2022).	Ineligible study design (<5 years and/or n<500 for case series)
61.	Fitzgibbon DR, Stephens LS, Posner KL, Michna E, Rathmell JP, Pollak KA, Domino KB. Injury and Liability Associated with Implantable Devices for Chronic Pain. Anesthesiology. 2016 Jun;124(6):1384-93. doi: 10.1097/ALN.0000000000001122. PMID: 27054366.	Ineligible study design (<5 years and/or n<500 for case series)
62.	Galan V, Scowcroft J, Chang P, Li S, Staats P, Subbaroyan J, Caraway D. Ten kHz spinal cord stimulation for the treatment of chronic peripheral polyneuropathy: 12-Month results from prospective open-label pilot study. Pain Pract. 2021 Nov;21(8):898-906. doi: 10.1111/papr.13059. Epub 2021 Aug 25. PMID: 34251751.	Ineligible study design (<5 years and/or n<500 for case series)
63.	Goudman L, De Smedt A, Eldabe S, et al. High-dose spinal cord stimulation for patients with failed back surgery syndrome: a multicenter effectiveness and prediction study. Pain. 2021 Feb 1;162(2):582-590. doi: 10.1097/j.pain.0000000000002035.PMID: 32910099;	Ineligible study design (<5 years and/or n<500 for case series)

	Citation	Reason for exclusion after full-text review
64.	Hajiabadi MM, Vicheva P, Unterberg A, Ahmadi R, Jakobs M. A single-center, open-label trial on convenience and complications of rechargeable implantable pulse generators for spinal cord stimulation: The Recharge Pain Trial. Neurosurg Rev. 2023 Jan 14;46(1):36. doi: 10.1007/s10143-022-01940-y. PMID: 36640226; PMCID: PMC9840575.	Ineligible study design (<5 years and/or n<500 for case series)
65.	Higashiyama N, Tamura S, Sugawara T. Efficacy of Spinal Cord Stimulation for Failed Back Surgery Syndrome in Elderly Patients: A Retrospective Study. Pain Res Manag. 2023 May 9;2023:2136562. doi: 10.1155/2023/2136562. PMID: 37200968; PMCID: PMC10188261.	Ineligible study design (<5 years and/or n<500 for case series)
66.	Kaestner S, Claas A, Deinsberger W. A Retrospective Comparison of Long-Term Treatment Results of Subcutaneous Stimulation and Spinal Cord Stimulation for Chronic Neuralgia. Neuromodulation. 2023 Apr;26(3):676-680. doi: 10.1016/j.neurom.2022.02.226. Epub 2022 Apr 8. PMID: 35410768.	Ineligible study design (case series not focused on safety)
67.	Kunwald M, Gulisan HA, Bjarkam CR. Spinal cord stimulation in complex regional pain syndrome type 2. Dan Med J. 2022 Jun 15;69(7):A06210521. PMID: 35781126.	Ineligible study design (case series not focused on safety)
68.	La Grua M, Michelagnoli G. Rare adverse effect of spinal cord stimulation: micturition inhibition. Clin J Pain. 2010 Jun;26(5):433-4. doi: 10.1097/AJP.0b013e3181d2bdee. PMID: 20473052.	Ineligible study design (case report)
69.	Labaran L, Aryee JNA, Bell J, et al. Opioids and spinal cord stimulators: pre- and postoperative opioid use patterns and predictors of prolonged postoperative opioid use. Neurospine. 2020;17(1):246-253. doi:10.14245/ns. 1938308.154	Ineligible study design (retrospective database)
70.	Lee JJ, Sadrameli SS, Desai VR, Austerman RJ, Leonard DM, Dalm BD. Immediate Abdominal Pain after Placement of Thoracic Paddle Leads for Spinal Cord Stimulation: A Case Series. Stereotact Funct Neurosurg. 2018;96(6):400-405. doi: 10.1159/000495415. Epub 2019 Jan 3. PMID: 30605913.	Ineligible study design (<5 years and/or n<500 for case series)
71.	Levy R, Henderson J, Slavin K, et al. Incidence and avoidance of neurologic complications with paddle type spinal cord stimulation leads. Neuromodulation. 2011; 14(5): 412–422; discussion 422, doi: 10.1111/j.1525-1403.2011.00395.x, indexed in Pubmed: 21967534.	Ineligible study design (<5 years and/or n<500 for case series)
72.	Logé D, Vanneste S, Vancamp T, Rijckaert D: Long-term outcomes of spinal cord stimulation with percutaneously introduced paddle leads in the treatment of failed back surgery syndrome and lumboischialgia. Neuromodulation 16:537–545, 2013	Ineligible study design (case series not focused on safety)
73.	Maldonado-Naranjo AL, Golubovsky JL, Frizon LA, Hogue O, Lobel DA, Machado AG, Steinmetz MP, Nagel SJ. The Role of Additional Spine Surgery in the Management of Failed Back Surgery Syndrome, Complex Regional Pain Syndrome, and Intractable Pain in the Setting of Previous or Concurrent Spinal Cord Stimulation: Indications and Outcomes. World Neurosurg. 2019 May;125:e416-	Ineligible study design (case series not focused on safety)

	Citation	Reason for exclusion after full-text review
	e423. doi: 10.1016/j.wneu.2019.01.091. Epub 2019 Jan 29. PMID: 30703586.	
74.	Mammis A, Bonsignore C, Mogilner AY. Thoracic radiculopathy following spinal cord stimulator placement: case series. Neuromodulation. 2013 Sep-Oct;16(5):443-7; discussion 447-8. doi: 10.1111/ner.12076. Epub 2013 May 17. PMID: 23682904.	Ineligible study design (<5 years and/or n<500 for case series)
75.	Motov S, Aftahy K, Jörger AK, Wagner A, Meyer B, Shiban E. High-frequency spinal cord stimulation in failed back surgery syndrome patients with predominant low back pain-single-center experience. Neurosurg Rev. 2021 Oct;44(5):2809-2818. doi: 10.1007/s10143-020-01462-5. Epub 2021 Jan 17. PMID: 33454835; PMCID: PMC8490248.	Ineligible study design (<5 years and/or n<500 for case series)
76.	Mutter UM, Bellut D, Porchet F, Schuknecht B. Spinal magnetic resonance imaging with reduced specific absorption rate in patients harbouring a spinal cord stimulation device - A single-centre prospective study analysing safety, tolerability and image quality. Acta Neurochir (Wien). 2013 Dec;155(12):2327-32. doi: 10.1007/s00701-013-1885-8. PMID: 24078115.	Ineligible publication type (evaluates specifically adapted MRI-protocal to SCS patients)
77.	Nissen M, Ikäheimo TM, Huttunen J, Leinonen V, Jyrkkänen HK, von Und Zu Fraunberg M. Gabapentinoids Associated With Lower Explantation Rate in 203 Patients With Spinal Cord Stimulation for Failed Back Surgery Syndrome. Neurosurgery. 2021 Sep 15;89(4):626-634. doi: 10.1093/neuros/nyab242. PMID: 34270731; PMCID: PMC8632751.	Ineligible study design (<5 years and/or n<500 for case series)
78.	Patel SK, Gozal YM, Saleh MS, Gibson JL, Karsy M, Mandybur GT. Spinal cord stimulation failure: evaluation of factors underlying hardware explantation. J Neurosurg Spine. 2019:1-6.	Ineligible study design (<5 years and/or n<500 for case series)
79.	Pope JE, Deer TR, Falowski S et al. Multicenter retrospective study of neurostimulation with exit of therapy by explant. Neuromodulation 2017;20:543–552	Ineligible study design (<5 years and/or n<500 for case series)
80.	Remacle TY, Bonhomme VL, Renwart HP, Remacle JM. Effect of Multicolumn Lead Spinal Cord Stimulation on Low Back Pain in Failed Back Surgery Patients: A Three-Year Follow-Up. Neuromodulation. 2017 Oct;20(7):668-674. doi: 10.1111/ner.12603. Epub 2017 May 2. PMID: 28464357.	Duplicate study population
81.	Russo M, Cousins MJ, Brooker C, Taylor N, Boesel T, Sullivan R, Poree L, Shariati NH, Hanson E, Parker J. Effective Relief of Pain and Associated Symptoms With Closed-Loop Spinal Cord Stimulation System: Preliminary Results of the Avalon Study. Neuromodulation. 2018 Jan;21(1):38-47. doi: 10.1111/ner.12684. Epub 2017 Sep 18. PMID: 28922517.	Duplicate study population
82.	ECRI. Senza Spinal Cord Stimulation System (Nevro Corp.) for Treating Chronic Pain. ECRI. 2022.	Ineligible study design (Not peer reviewed systematic review)
83.	Nevro Corp. Senza® Spinal Cord Stimulation (SCS) System SENZA Spinal Cord Stimulation Dossier. Nevro Corp. 2022.	Ineligible study design (Manufacturer dossier, not

	Citation	Reason for exclusion after full-text review
		peer reviewed systematic review)
84.	Russo M, Brooker C, Cousins MJ, Taylor N, Boesel T, Sullivan R, Holford L, Hanson E, Gmel GE, Shariati NH, Poree L, Parker J. Sustained Long-Term Outcomes With Closed-Loop Spinal Cord Stimulation: 12-Month Results of the Prospective, Multicenter, Open-Label Avalon Study. Neurosurgery. 2020 Sep 15;87(4):E485-E495. doi: 10.1093/neuros/nyaa003. Erratum in: Neurosurgery. 2020 Sep 1;87(3):611. PMID: 32023344; PMCID: PMC8184296.	Ineligible study design (<5 years and/or n<500 for case series)
85.	Sanchis-Lopez N, Romero-Garcia C, De Andres-Ibanez J, Martinez-Plumed R, Rodriguez-Gimillo P, Hernandez-Cadiz MJ, de Medrano VA. Medical Device Related Pressure Injury in the Treatment of Chronic Pain: An Early Sign of Explantation in Suspected Infection. Pain Physician. 2018 May;21(3):E235-E246. PMID: 29871379.	Ineligible study population (ITDD and SCS patients combined)
86.	Sears NC, Machado AG, Nagel SJ, et al. Long-term outcomes of spinal cord stimulation with paddle leads in the treatment of complex regional pain syndrome and failed back surgery syndrome. Neuromodulation. 2011; 14(4): 312–8; discussion 318, doi: 10.1111/j.1525- -1403.2011.00372.x, indexed in Pubmed: 21992424.	Ineligible study design (case series, safety not stated a priori)
87.	Simopoulos T, Yong RJ, Gill JS. Treatment of Chronic Refractory Neuropathic Pelvic Pain with High-Frequency 10-kilohertz Spinal Cord Stimulation. Pain Pract. 2018 Jul;18(6):805-809. doi: 10.1111/papr.12656. Epub 2018 Jan 11. PMID: 29106051.	Ineligible study design (<5 years and/or n<500 for case series)
88.	Stauss T, El Majdoub F, Sayed D et al. A multicenter real-world review of 10 kHz SCS outcomes for treatment of chronic trunk and/or limb pain. Ann Clin Transl Neurol 2019;6:496–507.	Ineligible study design (case series, safety not stated a priori)
89.	Spinal cord stimulation for failed back surgery syndrome: outcomes in a workers' compensation setting	Duplicate – already included in prior report, carried over to this re-review
90.	Van Buyten JP, Al-Kaisy A, Smet I, Palmisani S, Smith T. High-frequency spinal cord stimulation for the treatment of chronic back pain patients: results of a prospective multicenter European clinical study. Neuromodulation. 2013 Jan-Feb;16(1):59-65; discussion 65-6. doi: 10.1111/ner.12006. Epub 2012 Nov 30. PMID: 23199157.	Ineligible study design (<5 years and/or n<500 for case series)
91.	Verrills P, Salmon J, Russo M, Gliner B, Barnard A, Caraway D. 10 kHz spinal cord stimulation for chronic upper limb and neck pain: Australian experience. Eur Spine J. 2020 Nov;29(11):2786-2794. doi: 10.1007/s00586-020-06480-x. Epub 2020 Jun 30. PMID: 32607784.	Ineligible study design (<5 years and/or n<500 for case series)
92.	Viswanathan A, Phan PC, Burton AW. Use of spinal cord stimulation in the treatment of phantom limb pain: case series and review of the literature. Pain Pract. 2010 Sep-Oct;10(5):479-84. doi: 10.1111/j.1533-2500.2010.00374.x. PMID: 20412499.	Ineligible study design (<5 years and/or n<500 for case series)

	Citation	Reason for exclusion after full-text review
93.	Eldabe S, Buchser E, Duarte RV. Complications of spinal cord stimulation and peripheral nerve stimulation techniques: a review of the literature. Pain Med 2016;17:325–336.	Ineligible study design (older SR, checked bibliography for relevant studies.
94.	Shamji MF, Westwick HJ, Heary RF. Complications related to the use of spinal cord stimulation for managing persistent postoperative neuropathic pain after lumbar spinal surgery. Neurosurg Focus. 2015 Oct;39(4):E15. doi: 10.3171/2015.7.FOCUS15260. PMID: 26424339.	Ineligible study design (SR focused on non-RCTs)
95.	Pollard EM, Lamer TJ, Moeschler SM et al. The effect of spinal cord stimulation on pain medication reduction in intractable spine and limb pain: a systematic review of randomized controlled trials and meta-analysis. J Pain Res 2019;12: 1311–1324.	Ineligible study design (older SR, checked bibliography for relevant studies.
96.	Al-Kaisy A, Van Buyten JP, Carganillo R, et al. 10 kHz SCS therapy for chronic pain, efects on opioid usage: Post hoc analysis of data from two prospective studies. Sci Rep. 2019 Aug 7;9(1):11441. doi: 10.1038/s41598-019-47792-3	Ineligible study design (Case series not focused on safety)
97.	Al-Kaisy A, Van Buyten JP, Amirdelfan K, et al. Opioid-sparing effects of 10 kHz spinal cord stimulation: a review of clinical evidence. Ann N Y Acad Sci. 2020 Feb;1462(1):53-64. doi: 10.1111/nyas.14236. Epub 2019 Oct 2. PMID: 31578744	Ineligible publication type (narrative review)
98.	Asimakidou E, Matis GK. Spinal cord stimulation in the treatment of peripheral vascular disease: a systematic review - revival of a promising therapeutic option? Br J Neurosurg. 2022 Oct;36(5):555-563. doi: 10.1080/02688697.2021.1884189. Epub 2021 Mar 11. PMID: 33703962.	ineligible condition (peripheral vascular disease)
99.	Baranidharan G, Feltbower R, Bretherton B, Crowther T, Cooper L, Castino P, Radford H. One-Year Results of Prospective Research Study Using 10 kHz Spinal Cord Stimulation in Persistent Nonoperated Low Back Pain of Neuropathic Origin: Maiden Back Study. Neuromodulation. 2021 Apr;24(3):479-487. doi: 10.1111/ner.13345. Epub 2020 Dec 22. PMID: 33351230.	Ineligible study design (Case series not focused on safety)
100	Barpujari A, Erdek MA. Retrospective analysis on the effect of spinal cord stimulation on opioid consumption. Pain Manag. 2021 Mar;11(2):123-132. doi: 10.2217/pmt-2020-0016. Epub 2020 Dec 22. PMID: 33350351.	Ineligible study design (Case series not focused on safety)
101	Deer T, Slavin KV, Amirdelfan K, North RB, Burton AW, Yearwood TL, Tavel E, Staats P, Falowski S, Pope J, Justiz R, Fabi AY, Taghva A, Paicius R, Houden T, Wilson D. Success Using Neuromodulation With BURST (SUNBURST) Study: Results From a Prospective, Randomized Controlled Trial Using a Novel Burst Waveform. Neuromodulation. 2018 Jan;21(1):56-66. doi: 10.1111/ner.12698. Epub 2017 Sep 29. PMID: 28961366.	Ineligible comparator (burst vs. tonic stimulation)
102	Dougherty MC, Woodroffe RW, Wilson S, Gillies GT, Howard MA 3rd, Carnahan RM. Predictors of Reduced Opioid Use With Spinal Cord Stimulation in Patients With Chronic Opioid Use. Neuromodulation. 2020 Jan;23(1):126-132. doi: 10.1111/ner.13054. Epub 2019 Oct 10. PMID: 31602750.	Ineligible study design (case series not focused on safety)

	Citation	Reason for exclusion after full-text review
103	Falowski SM, Moore GA, Cornidez EG, Hutcheson JK, Candido K, Pena I, et al. Improved psychosocial and functional outcomes and reduced opioid usage following burst spinal cord stimulation. Neuromodulation. 2021 Apr;24(3):581-590. doi: 10.1111/ner.13226. Epub 2020 Jun 25. PMID: 32583937	Ineligible study design (case series not focused on safety)
104	Fraifeld EM, Hatheway JA, Ricker CN. Systemic Opioid Prescribing Patterns and Total Cost of Care in Patients Initiating Spinal Cord Stimulation Therapy: A Retrospective Analysis. Pain Med. 2021 Apr 20;22(4):784-799. doi: 10.1093/pm/pnab033. PMID: 33543759; PMCID: PMC8058769.	Ineligible study design (case series not focused on safety)
105	Gee L, Smith HC, Ghulam-Jelani Z, Khan H, Prusik J, Feustel PJ, McCallum SE, Pilitsis JG. Spinal Cord Stimulation for the Treatment of Chronic Pain Reduces Opioid Use and Results in Superior Clinical Outcomes When Used Without Opioids. Neurosurgery. 2019 Jan 1;84(1):217-226. doi: 10.1093/neuros/nyy065. PMID: 29538696.	Ineligible study design (<5 years and/or n<500 for case series)
106	Hartemann A, Attal N, Bouhassira D, Dumont I, Gin H, Jeanne S, Said G, Richard JL; Working Group on the Diabetic Foot from the French-speaking Society of Diabetology. Painful diabetic neuropathy: diagnosis and management. Diabetes Metab. 2011 Nov;37(5):377-88. doi: 10.1016/j.diabet.2011.06.003. Epub 2011 Aug 4. PMID: 21820345.	Ineligible publication type (narrative review)
107	Jensen TS, Karlsson P, Gylfadottir SS, Andersen ST, Bennett DL, Tankisi H, Finnerup NB, Terkelsen AJ, Khan K, Themistocleous AC, Kristensen AG, Itani M, Sindrup SH, Andersen H, Charles M, Feldman EL, Callaghan BC. Painful and non-painful diabetic neuropathy, diagnostic challenges and implications for future management. Brain. 2021 Jul 28;144(6):1632-1645. doi: 10.1093/brain/awab079. PMID: 33711103; PMCID: PMC8320269.	Ineligible study design (systematic review not focused on outcomes)
108	Jones MR, Orhurhu V, O'Gara B, Brovman EY, Rao N, Vanterpool SG, Poree L, Gulati A, Urman RD. Racial and Socioeconomic Disparities in Spinal Cord Stimulation Among the Medicare Population. Neuromodulation. 2021 Apr;24(3):434-440. doi: 10.1111/ner.13373. Epub 2021 Mar 15. PMID: 33723896.	Ineligible outcome (no outcome of interest)
109	Kaijankoski H, Nissen M, Ikäheimo TM, von Und Zu Fraunberg M, Airaksinen O, Huttunen J. Effect of Spinal Cord Stimulation on Early Disability Pension in 198 Failed Back Surgery Syndrome Patients: Case-Control Study. Neurosurgery. 2019 Jun 1;84(6):1225-1232. doi: 10.1093/neuros/nyy530. PMID: 30476235; PMCID: PMC6520102.	Ineligible outcome (no outcome of interest)
110	Kallewaard JW, Gültuna I, Hoffmann V, Elzinga L, Munnikes R, Verbrugge L, Minne V, Reiters P, Subbaroyan J, Santos A, Rotte A, Caraway D. 10 kHz Spinal Cord Stimulation for the Treatment of Failed Back Surgery Syndrome with Predominant Leg Pain: Results from a Prospective Study in Patients from the Dutch Healthcare System. Pain Pract. 2021 Jun;21(5):490-500. doi: 10.1111/papr.12973. Epub 2020 Dec 22. PMID: 33274545; PMCID: PMC8247309.	Ineligible study design (case series not focused on safety)

	Citation	Reason for exclusion after full-text review
111	Lamer TJ, Moeschler SM, Gazelka HM, Hooten WM, Bendel MA, Murad MH. Spinal Stimulation for the Treatment of Intractable Spine and Limb Pain: A Systematic Review of RCTs and Meta-Analysis. Mayo Clin Proc. 2019 Aug;94(8):1475-1487. doi: 10.1016/j.mayocp.2018.12.037. Epub 2019 Jul 3. PMID: 31279543.	Ineligible study design (older systematic review)
112	McClure JJ, Desai BD, Ampie L, You W, Smith JS, Buchholz AL. A Systematic Review of the Cost-Utility of Spinal Cord Stimulation for Persistent Low Back Pain in Patients With Failed Back Surgery Syndrome. Global Spine J. 2021 Apr;11(1_suppl):66S-72S. doi: 10.1177/2192568220970163. PMID: 33890806; PMCID: PMC8076810.	Ineligible study design (SR of cost-effectiveness studies; checked bibliography for relevant studies.
113	Niyomsri S, Duarte RV, Eldabe S, Fiore G, Kopell BH, McNicol E, Taylor RS. A Systematic Review of Economic Evaluations Reporting the Cost-Effectiveness of Spinal Cord Stimulation. Value Health. 2020 May;23(5):656-665. doi: 10.1016/j.jval.2020.02.005. Epub 2020 Apr 20. PMID: 32389232.	Ineligible study design (SR of cost-effectiveness studies; checked bibliography for relevant studies.
114	Schwarm FP, Stein M, Uhl E, Maxeiner H, Kolodziej MA. Spinal cord stimulation for the treatment of complex regional pain syndrome leads to improvement of quality of life, reduction of pain and psychological distress: a retrospective case series with 24 months follow up. Scand J Pain. 2020 Apr 28;20(2):253-259. doi: 10.1515/sjpain-2019-0081. PMID: 31743107.	Ineligible study design (<5 years and/or n<500 for case series)
115	Duarte RV, McNicol E, Colloca L, Taylor RS, North RB, Eldabe S. Randomized Placebo-/Sham-Controlled Trials of Spinal Cord Stimulation: A Systematic Review and Methodological Appraisal. Neuromodulation. 2020 Jan;23(1):10-18. doi: 10.1111/ner.13018. Epub 2019 Jul 15. PMID: 31305001; PMCID: PMC7004207.	Ineligible publication type (narrative review)
116	Akinlotan MA, Primm K, Bolin JN, Ferdinand Cheres AL, Lee J, Callaghan T, Ferdinand AO. Racial, Rural, and Regional Disparities in Diabetes-Related Lower-Extremity Amputation Rates, 2009-2017. Diabetes Care. 2021 Sep;44(9):2053-2060. doi: 10.2337/dc20-3135. Epub 2021 Jul 22. PMID: 34301733.	Ineligible outcome (not relevant to current report)
117	Al-Kaisy A, Van Buyten JP, Kapural, et al. 10 kHz spinal cord stimulation for the treatment of nonsurgical refractory back pain: subanalysis of pooled data from two prospective studies. Anaesthsia. 2020. 75;775-784. (SENZA-RCT the SENZA-EU)	Ineligible study design (sub-analysis of data from an already included RCT and a case series of the same device)
118	Chakravarthy K, Richter H, Christo PJ, Williams K, Guan Y. Spinal Cord Stimulation for Treating Chronic Pain: Reviewing Preclinical and Clinical Data on Paresthesia-Free High-Frequency Therapy. Neuromodulation. 2018 Jan;21(1):10-18. doi: 10.1111/ner.12721. Epub 2017 Nov 3. PMID: 29105244; PMCID: PMC5766402.	Ineligible publication type (narrative review)
119	Deer T, Abd-Elsayed A, Chakravarthy K, Rosenow JM, Falowski S, Petersen E, Pilitsis J, Hunter C, Sayed D, Schatman ME. Serious Issues in Authorship, Design, and Conclusions of JAMA Neurology Real-World Evidence Study on Spinal Cord Stimulation Outcomes and Costs as Compared to Conventional Medical Therapy. J Pain	Ineligible publication type (commentary)

	Citation	Reason for exclusion after full-text review
	Res. 2023 Jan 26;16:221-224. doi: 10.2147/JPR.S403031. PMID: 36726855; PMCID: PMC9885768.	
120	Eldabe S, Gilligan C, Taylor RS, Patel KV, Duarte RV. Issues in design, conduct, and conclusions of JAMA's Hara et al.'s randomized clinical trial of spinal cord burst stimulation versus placebo stimulation on disability in patients with chronic radicular pain after lumbar spine surgery. Pain Pract. 2023 Mar;23(3):232-233. doi: 10.1111/papr.13186. Epub 2022 Dec 11. PMID: 36504290.	Ineligible publication type (commentary)
121	Fantasia KL, Wirunsawanya K, Lee C, Rizo I. Racial Disparities in Diabetes Technology Use and Outcomes in Type 1 Diabetes in a Safety-Net Hospital. J Diabetes Sci Technol. 2021 Sep;15(5):1010-1017. doi: 10.1177/1932296821995810. Epub 2021 Mar 10. PMID: 33719610; PMCID: PMC8442173.	Ineligible outcome (not relevant to current report)
122	Feng H, Doherty P, Rotte A. Decreased Opioid Consumption and Durable Pain Relief in Patients Treated with 10 kHz SCS: A Retrospective Analysis of Outcomes from Single-Center. J Pain Res. 2021 Aug 24;14:2593-2600. doi: 10.2147/JPR.S312932. PMID: 34466027; PMCID: PMC8403026.	Ineligible study design (<5 years and/or n<500 for case series)
123	Galan V, Chang P, Scowcroft J, Li S, Staats P, Subbaroyan J. (Eds). A prospective clinical trial to assess high frequency spinal cord stimulation (HF-SCS) at 10 kHz in the treatment of chronic intractable pain from peripheral polyneuropathy. Presented at: The 22nd Annnual Meeting of the North American Neuromodulation Society; 2019. NV, USA (January 17–19, 2019)	Ineligible study design (<5 years and/or n<500 for case series)
124	Goudman L, De Smedt A, Eldabe S, et al. High-dose spinal cord stimulation for patients with failed back surgery syndrome: a multicenter effectiveness and prediction study. Pain. Published online September 1, 2020. doi: 10.1097/j.pain.0000000000002035]	Ineligible study design (<5 years and/or n<500 for case series)
125	Grider JS, Harned M. Cervical Spinal Cord Stimulation Using Monophasic Burst Waveform for Axial Neck and Upper Extremity Radicular Pain: A Preliminary Observational Study. Neuromodulation. 2020 Jul;23(5):680-686. doi: 10.1111/ner.13041. Epub 2019 Aug 29. PMID: 31468641.	Ineligible study design (case series, safety not stated a priori)
126	Gupta M, Ray M, Ladesich N, Gupta A. Health-Care Utilization and Outcomes with 10 kHz Spinal Cord Stimulation for Chronic Refractory Pain. J Pain Res. 2021 Dec 2;14:3675-3683. doi: 10.2147/JPR.S306126. PMID: 34880672; PMCID: PMC8648088.	Ineligible study design (<5 years and/or n<500 for case series)
127	Hagedorn JM, Falowski SM, Blomme B, Capobianco RA, Yue JJ. Burst spinal cord stimulation can attenuate pain and its affective components in chronic pain patients with high psychological distress: results from the prospective, international TRIUMPH study. Spine J. 2022 Mar;22(3):379-388. doi: 10.1016/j.spinee.2021.08.005. Epub 2021 Aug 20. PMID: 34419628.	Ineligible study design (<5 years and/or n<500 for case series)

	Citation	Reason for exclusion after full-text review
128	Harke H, Gretenkort P, Ladleif HU, Rahman S. Spinal cord stimulation in sympathetically maintained complex regional pain syndrome type I with severe disability. A prospective clinical study. Eur J Pain. 2005 Aug;9(4):363-73. doi: 10.1016/j.ejpain.2004.09.003. PMID: 15979016.	Ineligible study design (case series not focused on safety)
129	Isagulyan E, Slavin K, Konovalov N, Dorochov E, Tomsky A, Dekopov A, Makashova E, Isagulyan D, Genov P. Spinal cord stimulation in chronic pain: technical advances. Korean J Pain. 2020 Apr 1;33(2):99-107. doi: 10.3344/kjp.2020.33.2.99. PMID: 32235010; PMCID: PMC7136296.	Ineligible publication type (narrative review)
130	Khan H, Pilitsis JG, Prusik J, Smith H, McCallum SE. Pain Remission at One-Year Follow-Up With Spinal Cord Stimulation. Neuromodulation. 2018 Jan;21(1):101-105. doi: 10.1111/ner.12711. Epub 2017 Oct 23. PMID: 29058361.	Ineligible study design (<5 years and/or n<500 for case series)
131	Maatta J, Martikainen A, Pakarinen M, Ikaheimo TM, Nissen M, von Und Zu Fraunberg M, Viinamaki H, Huttunen J. High Level of Childhood Trauma Predicts a Poor Response to Spinal Cord Stimulation in Chronic Neuropathic Pain. Pain Physician. 2019 Jan;22(1):E37-E44. PMID: 30700077.	Ineligible outcome (childhood trauma)
132	Mekhail NA, Argoff CE, Taylor RS, Nasr C, Caraway DL, Gliner BE, Subbaroyan J, Brooks ES. High-frequency spinal cord stimulation at 10 kHz for the treatment of painful diabetic neuropathy: design of a multicenter, randomized controlled trial (SENZA-PDN). Trials. 2020 Jan 15;21(1):87. doi: 10.1186/s13063-019-4007-y. PMID: 31941531; PMCID: PMC6961392.	Ineligible publication type (protocol)
133	Mekhail N, Costandi S, Saweris Y, Armanyous S, Chauhan G. Impact of biological sex on the outcomes of spinal cord stimulation in patients with chronic pain. Pain Pract. 2022 Apr;22(4):432-439. doi: 10.1111/papr.13097. Epub 2021 Dec 9. PMID: 34845813.	Ineligible study design (secondary analysis of excluded study)
134	Moens M, Goudman L, Brouns R, Valenzuela Espinoza A, De Jaeger M, Huysmans E, Putman K, Verlooy J. Return to Work of Patients Treated With Spinal Cord Stimulation for Chronic Pain: A Systematic Review and Meta-Analysis. Neuromodulation. 2019 Apr;22(3):253-261. doi: 10.1111/ner.12797. Epub 2018 Aug 17. PMID: 30117650.	Ineligible outcome (return to work)
135	Odonkor CA, Orman S, Orhurhu V, Stone ME, Ahmed S. Spinal Cord Stimulation vs Conventional Therapies for the Treatment of Chronic Low Back and Leg Pain: A Systematic Review of Health Care Resource Utilization and Outcomes in the Last Decade. Pain Med. 2019 Dec 1;20(12):2479-2494. doi: 10.1093/pm/pnz185. PMID: 31498396.	Ineligible study design (older systematic review)
136	Rajkumar S, Yang LZ, Venkatraman V, Charalambous L, Parente B, Lee HJ, Lad SP. Health Care Resource Utilization of High-Frequency Spinal Cord Stimulation for Treatment of Chronic Refractory Low Back Pain. Neuromodulation. 2023 Jan;26(1):115-123. doi: 10.1016/j.neurom.2022.03.013. Epub 2022 Jul 21. PMID: 35871122.	Ineligible study design (<5 years and/or n<500 for case series)

	Citation	Reason for exclusion after full-text review
137	Simopoulos T, Sharma S, Wootton RJ, Orhurhu V, Aner M, Gill JS. Discontinuation of Chronic Opiate Therapy After Successful Spinal Cord Stimulation Is Highly Dependent Upon the Daily Opioid Dose. Pain Pract. 2019 Nov;19(8):794-799. doi: 10.1111/papr.12807. Epub 2019 Aug 13. PMID: 31199551.	Ineligible study design (case series not focused on safety)
138	Slavin KV. Commentary: High-Frequency Spinal Cord Stimulation at 10 kHz for the Treatment of Combined Neck and Arm Pain: Results From a Prospective Multicenter Study. Neurosurgery. 2020 Aug 1;87(2):E89-E90. doi: 10.1093/neuros/nyaa012. PMID: 31980832.	Ineligible publication type (commentary)
139	Taylor RS, Bentley A, Campbell B, Murphy K. High-frequency 10 kHz Spinal Cord Stimulation for Chronic Back and Leg Pain: Cost-consequence and Cost-effectiveness Analyses. Clin J Pain. 2020 Nov;36(11):852-861. doi: 10.1097/AJP.0000000000000866. PMID: 32769414; PMCID: PMC7671822.	Ineligible comparator (HF vs. LF SCS)
140	Thomson S, Huygen F, Prangnell S, De Andrés J, Baranidharan G, Belaïd H, Berry N, Billet B, Cooil J, De Carolis G, Demartini L, Eldabe S, Gatzinsky K, Kallewaard JW, Meier K, Paroli M, Stark A, Winkelmüller M, Stoevelaar H. Appropriate referral and selection of patients with chronic pain for spinal cord stimulation: European consensus recommendations and e-health tool. Eur J Pain. 2020 Jul;24(6):1169-1181. doi: 10.1002/ejp.1562. Epub 2020 Apr 4. PMID: 32187774; PMCID: PMC7318692.	Ineligible publication type (consensus and recommendations)
141	Ubbink DT, Vermeulen H. Spinal cord stimulation for non-reconstructable chronic critical leg ischaemia. Cochrane Database Syst Rev. 2013 Feb 28;2013(2):CD004001. doi: 10.1002/14651858.CD004001.pub3. PMID: 23450547; PMCID: PMC7163280.	Ineligible population (critical limb ischemia is excluded condition)
142	North, R. B., et al. (2011). "Spinal cord stimulation versus re-operation in patients with failed back surgery syndrome: an international multicenter randomized controlled trial (EVIDENCE study)." Neuromodulation 14(4): 330-335; discussion 335-336.	Ineligible publication type (protocol)
143	Farber SH, Han JL, Elsamadicy AA, Hussaini Q, Yang S, Pagadala P, Parente B, Xie J, Lad SP. Long-term Cost Utility of Spinal Cord Stimulation in Patients with Failed Back Surgery Syndrome. Pain Physician. 2017 Sep;20(6):E797-E805. PMID: 28934786; PMCID: PMC8358894.	ineligible publication type (not a full economic study)
144	Zinboonyahgoon, N., et al. (2023). "Cost-Utility and Cost-Effectiveness Analysis of Spinal Cord Stimulation for Chronic Refractory Pain in the Context of Developing Country." Pain Physician 26(1): 69-79.	ineligible publication type (not a full economic study)
145	Zucco, F., et al. (2015). "Cost-Effectiveness and Cost-Utility Analysis of Spinal Cord Stimulation in Patients With Failed Back Surgery Syndrome: Results From the PRECISE Study". Neuromodulation 18: 266–276	ineligible publication type (not a full economic study)
146	Scalone L, Zucco, Lavano, et al. Benefits in pain perception, ability function and health-related quality of life in patients with failed back surgery syndrome undergoing spinal cord stimulation in a	Ineligible study design (no comparator and not designed to evaluate safety)

	Citation	Reason for exclusion after full-text review
	clinical practice setting. Health Qual Life Outcomes. 2018 Apr 19;16(1):68. PMID: 29673357. DOI: 10.1186/s12955-018-0887-x	
147	Mekhail N, Deer TR, Poree L, Staats PS, Burton AW, Connolly AT, Karst E, Mehanny DS, Saweris Y, Levy RM. Cost-Effectiveness of Dorsal Root Ganglion Stimulation or Spinal Cord Stimulation for Complex Regional Pain Syndrome. Neuromodulation. 2021 Jun;24(4):708-718. doi: 10.1111/ner.13134. Epub 2020 Mar 9. PMID: 32153073.	Ineligible comparator (SCS vs. Dorsal root ganglion)
148	Hoelscher C, Riley J, Wu C, Sharan A. Cost-Effectiveness Data Regarding Spinal Cord Stimulation for Low Back Pain. Spine (Phila Pa 1976). 2017 Jul 15;42 Suppl 14:S72-S79. doi: 10.1097/BRS.0000000000002194. PMID: 28399549.	Ineligible study diesng (SR of cost-effectiveness studies, refererences checked for inclusion)
149	Rigoard P, Slavin K. Randomized Trial of Spinal Cord Stimulation in Chronic Pain: A Critical Review. Neuromodulation : journal of the International Neuromodulation Society 2023;26:476-7.	ineligible publication type (letter to the editor)
150	Prokopienko M, Sobstyl M. Spinal cord stimulation for treatment of complex regional pain syndrome: a single-centre retrospective case series study. Neurologia i neurochirurgia polska 2022;56:371-8.	Ineligible study design (case series not focused on safety)
151	Baird TA, Karas CS. The use of high-dose cervical spinal cord stimulation in the treatment of chronic upper extremity and neck pain. Surg Neurol Int 2019;10:109.	Ineligible study design (case report, not focused on safety)
152	Katz N, Dworkin RH, North R, et al. Research design considerations for randomized controlled trials of spinal cord stimulation for pain: Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials/Institute of Neuromodulation/International Neuromodulation Society recommendations. Pain 2021;162:1935-56.	Ineligible publication type (summary of meeting)
153	Lipman TH, Smith JA, Patil O, Willi SM, Hawkes CP. Racial disparities in treatment and outcomes of children with type 1 diabetes. Pediatr Diabetes 2021;22:241-8.	Ineligible study design (not SCS related/specific)
154	Mikhail N, Wali S, Brown AF. Ethnic Disparities in Diabetes. Endocrinol Metab Clin North Am 2021;50:475-90.	Ineligible outcome (ethnic disparities in diabetes)
155	Phonyiam R, Berry DC. Racial and Ethnic Disparities in Health Care and Health Outcomes for Pregnant Women With Diabetes. Nurs Womens Health 2021;25:437-49.	Ineligible outcome (racial and ethnic disparities in pregnant women with diabetes)
156	Prabhala T, Kumar V, Gruenthal E, et al. Use of a Psychological Evaluation Tool as a Predictor of Spinal Cord Stimulation Outcomes. Neuromodulation : journal of the International Neuromodulation Society 2019;22:194-9.	Ineligible outcome (Does not include any outcomes of interest)
157	Vowles KE, McEntee ML, Julnes PS, Frohe T, Ney JP, van der Goes DN. Rates of opioid misuse, abuse, and addiction in chronic pain: a systematic review and data synthesis. Pain 2015;156:569-76.	Ineligible study design (not SCS related/specific)
158	Brooker C, Russo M, Cousins MJ, Taylor N, Holford L, Martin R, Boesel T, Sullivan R, Hanson E, Gmel GE, Shariati NH, Poree L, Parker J. ECAP-Controlled Closed-Loop Spinal Cord Stimulation Efficacy and Opioid Reduction Over 24-Months: Final Results of	Ineligible study design (case series not focused on safety)*

	Citation	Reason for exclusion after full-text review
	the Prospective, Multicenter, Open-Label Avalon Study. Pain Pract. 2021 Jul;21(6):680-691. doi: 10.1111/papr.13008. Epub 2021 May 2. PMID: 33768664; PMCID: PMC8359972.	
159	Hagiwara,S.,Iwasaka,H.,Takeshima,N.,&Noguchi,T.(2019).Spinal cord stimulation reduces the risk of opioid use after lumbar spine surgery: a systematic review and meta-analysis of randomized controlled trials. Pain Physician, 22(4), 309-318.	Ineligible publication type (unable to locate in journal)*
160	Hamm-Faber TE, Gültuna I, van Gorp EJ, Aukes H. High-Dose Spinal Cord Stimulation for Treatment of Chronic Low Back Pain and Leg Pain in Patients With FBSS, 12-Month Results: A Prospective Pilot Study. Neuromodulation. 2020 Jan;23(1):118-125. doi: 10.1111/ner.12940. Epub 2019 Mar 12. PMID: 30860645.	Ineligible study design (case series not focused on safety)*
161	Ho E, Yazdanpanah N, Ho J, Drukman B, Chang A, Agarwal S. Parameters of Spinal Cord Stimulation in Complex Regional Pain Syndrome: Systematic Review and Meta-analysis of Randomized Controlled Trials. Pain Physician. 2022 Nov;25(8):521-530. PMID: 36375180.	Contains overlap with other larger systematic reviews included in the report*
162	Hussain N, Orhurhu V, D'Souza R. Spinal Cord Burst Stimulation vs Placebo Stimulation for Patients With Chronic Radicular Pain After Lumbar Spine Surgery. JAMA. 2023;329(10):845-6.	ineligible publication type (letter to the editor)*
163	Matis G, Chen L, Jain R, Doah Q. Clinical utilization of fast-acting sub-perception therapy (FAST) in SCS-implanted patients for treatment of mixed pain, Interventional Pain Medicine. 2022;1(4):100165.	Ineligible study design (case series not focused on safety)*
164	Metzger CS, Hammond MB, Paz-Solis JF, Newton WJ, Thomson SJ, Pei Y, Jain R, Moffitt M, Annecchino L, Doan Q. A novel fast-acting sub-perception spinal cord stimulation therapy enables rapid onset of analgesia in patients with chronic pain. Expert Rev Med Devices. 2021 Mar;18(3):299-306. doi: 10.1080/17434440.2021.1890580. Epub 2021 Mar 3. PMID: 33656411.	Ineligible study design (case series not focused on safety)*
165	Thomson S, Kallewaard JW, Gatzinsky K. Spinal Cord Burst Stimulation vs Placebo Stimulation for Patients With Chronic Radicular Pain After Lumbar Spine Surgery. JAMA. 2023;329(10):847.	ineligible publication type (letter to the editor)*
166	Jones et al, Spinal cord stimulators: An analysis of the adverse events reported to the Australian Therapeutic Goods Administration. J Patient Saf 2022; 18: 507-511.	Ineligible population (conditions and indications not included in the report)*
167	Duarte RV, Bentley A, Soliday N, Leitner A, Gulve A, Staats PS, Sayed D, Falowski SM, Hunter CW, Taylor RS. Cost-utility Analysis of Evoke Closed-loop Spinal Cord Stimulation for Chronic Back and Leg Pain. Clin J Pain. 2023 Oct 1;39(10):551-559. doi: 10.1097/AJP.0000000000001146. PMID: 37440335; PMCID: PMC10498882.	Ineligible comparator (Open vs. Closed loop SCS)*
168	North J, Loudermilk E, Lee A, Sachdeva H, Kaiafas D, Washabaugh E, et al. Outcomes of a Multicenter, Prospective, Crossover, Randomized Controlled Trial Evaluating Subperception Spinal Cord	Ineligible population (patients previously implanted with SCS)*

	Citation	Reason for exclusion after full-text review
	Stimulation at </=1.2 kHz in Previously Implanted Subjects. Neuromodulation. 2019	
169	Breel J, Wille F, Wensing AGCL, Kallewaard JW, Pelleboer H, Zuidema X, Bürger K, de Graaf S, Hollmann MW. A Comparison of 1000 Hz to 30 Hz Spinal Cord Stimulation Strategies in Patients with Unilateral Neuropathic Leg Pain Due to Failed Back Surgery Syndrome: A Multicenter, Randomized, Double-Blinded, Crossover Clinical Study (HALO). Pain Ther. 2021 Dec;10(2):1189-1202. doi: 10.1007/s40122-021-00268-7. Epub 2021 Jun 6. PMID: 34091818; PMCID: PMC8586063.	Ineligible comparator (HF vs. LF SCS)*
170	Fishman M, Cordner H, Justiz R, Provenzano D, Merrell C, Shah B, Naranjo J, Kim P, Calodney A, Carlson J, Bundschu R, Sanapati M, Mangal V, Vallejo R. Twelve-Month results from multicenter, open-label, randomized controlled clinical trial comparing differential target multiplexed spinal cord stimulation and traditional spinal cord stimulation in subjects with chronic intractable back pain and leg pain. Pain Pract. 2021	Ineligible comparator (compares different SCS modalities)*
171	Wallace MS, North JM, Phillips GM, Calodney AK, Scowcroft JA, Popat-Lewis BU, Lee JM, Washabaugh EP 3rd, Paez J, Bolash RB, Noles J, Atallah J, Shah B, Ahadian FM, Trainor DM, Chen L, Jain R. Combination therapy with simultaneous delivery of spinal cord stimulation modalities: COMBO randomized controlled trial. Pain Manag. 2023 Mar;13(3):171-184	Ineligible comparator (compares different SCS modalities)*

* Suggested in public comments and reviewed at full-text.

APPENDIX D. Risk of Bias, Strength of Evidence, and QHES Determination

Each included comparative study is rated against pre-set criteria that resulted in a Risk of Bias (ROB) assessment and presented in a table. Assessment of RCTs followed appropriate criteria based on methods described in *the Cochrane Handbook for Systematic Reviews of Interventions*[1,2] and guidance from the Agency for Healthcare Research and Quality (AHRQ) *Methods Guide for Effectiveness and Comparative Effectiveness Reviews*[1]. In keeping with the AHRQ methods, each study was given a final rating of "good", "fair", or "poor" quality as described below in Table D1. Discrepancies in ratings between reviewers were resolved through discussion and consensus. The final quality assessments are provided in Appendix E.

Table D2 provides an example of the format used to assess ROB for comparative studies of testing/therapy. A "No" indicates that the criterion was not met; an "Unclear" indicates that the criterion could not be determined with the information provided or was not reported by the author. Risk of bias assessments were not conducted for case series; all were considered High risk of bias.

Appendix Table D1. Definition of the risk of bias categories

Rating	Description and Criteria
Good	• Least risk of bias; study results generally considered valid • Employ valid methods for selection, inclusion, and allocation of patients to testing; report similar baseline characteristics in different test groups; clearly describe attrition and have low attrition; use appropriate means for preventing bias (e.g., blinding of patients, care providers, and outcomes assessors); and use appropriate analytic methods (e.g., intention-to-treat analysis)
Fair	• Study is susceptible to some bias but not enough to necessarily invalidate results • May not meet all criteria for good quality, but no flaw is likely to cause major bias; the study may be missing information making it difficult to assess limitations and potential problems • This category is broad; studies with this rating will vary in strengths and weaknesses; some fair-quality studies are likely to be valid, while others may be only possibly valid
Poor	• Significant flaws that imply biases of various kinds that may invalidate results; the study contains "fatal flaws" in design, analysis, or reporting; large amounts of missing information; discrepancies in reporting or serious problems with intervention delivery • Study results are at least as likely to reflect flaws in the study design or execution as the true difference between the compared interventions • Considered to be less reliable than higher quality studies when synthesizing the evidence, particularly if discrepancies between studies are present

Appendix Table D2. Assessment of ROB for individual studies of therapy

Methodological Principle	Author 1, 2014	Author 2, 2012	Author 3, 2010
Study design			
Randomized controlled trial	■	■	■
Prospective cohort study			
Retrospective cohort study			
Case-control			
Case-series			
Random sequence generation*			
Statement of concealed allocation*			
Analysis according to random assignment (i.e., intention to treat)*			
Independent or blinded outcome assessment			
Outcome assessors independent or blinded			
Care providers blinded			
Patients blinded			
Complete follow-up of >80%			
<10% difference in follow-up between groups			
Patient characteristics comparable at baseline†			
Overall quality rating			

*Applies to randomized controlled trials only.
†Groups must be comparable on baseline characteristics or evidence of control for confounding presented (e.g., by restriction, matching, statistical methods)

Appendix Table D3. Rating overall Confidence in the Results of the Review (Dettori 2020).

High: No or 1 noncritical weakness	The systematic review provides an accurate and comprehensive summary of the results of the available studies that address the question of interest.
Moderate: More than 1 noncritical weakness*	The systematic review has more than 1 weakness but no critical flaws. It may provide an accurate summary of the results of the available studies that were included in the review.
Low: One critical flaw with or without noncritical weaknesses	The review has a critical flaw and may not provide an accurate and comprehensive summary of the available studies that address the question of interest.
Critically low: More than 1 critical flaw with or without noncritical weaknesses	The review has more than 1 critical flaw and should not be relied on to provide an accurate and comprehensive summary of the available studies.

* Multiple noncritical weaknesses may diminish confidence in the review, and it may be appropriate to move the overall appraisal down from moderate to low confidence.

Assessment of Economic Studies

Full formal economic analyses evaluate both costs and clinical outcomes of two or more alternative interventions. The four primary types are cost minimization analysis (CMA), cost-utility analysis (CUA), cost-effectiveness analysis (CEA), and cost-benefit analyses (CBA). Each employs different methodologies, potentially complicating critical appraisal, but some common criteria can be assessed across studies.

No standard, universally accepted method of critical appraisal of economic analyses is currently in use. A number of checklists [Canadian, BMJ, AMA] are available to facilitate critique of such studies. The Quality of Health Economic Studies (QHES) instrument developed by Ofman, et al. embodies the primary components relevant for critical appraisal of economic studies[3]. It also incorporates a weighted scoring process which was used as one factor to assess included economic studies. This tool has not yet undergone extensive evaluation for broader use but provides a valuable starting point for critique. Table D4 below provides a template of the instrument.

In addition to assessment of criteria in the QHES, other factors are important in critical appraisal of studies from an epidemiologic perspective to assist in evaluation of generalizability and potential sources of study bias.

Such factors include:

- Are the interventions applied to similar populations (e.g., with respect to age, gender, medical conditions, etc.)? To what extent are the populations for each intervention comparable and are differences considered or accounted for? To what extent are population characteristics consistent with "real world" applications of the comparators?
- Are the sample sizes adequate so as to provide a reasonable representation of individuals to whom the technology would be applied?
- What types of studies form the basis for the data used in the analyses? Data (e.g., complication rates) from randomized controlled trials or well-conducted, methodologically rigorous cohort studies for data collection are generally of highest quality compared with case series or studies with historical cohorts.
- Were the interventions applied in a comparable manner (e.g., similar protocols, follow-up procedures, evaluation of outcomes, etc.)?
- How were the data and/or patients selected or sampled (e.g., a random selection of claims for the intervention from a given year/source or all claims)? What specific inclusion/exclusion criteria or processes were used?

Were the outcomes and consequences of the interventions being compared comparable for each? (e.g., were all of the relevant consequences/complications for each intervention considered or do they primarily reflect those for one intervention?

Appendix Table D4. Assessment of Quality of Health Economic Studies Criteria

Question	Possible Points*	Criteria For Credit*
1. Was the study **objective** presented in a clear, specific, and measurable manner?	7	Authors must fully describe the objective; is it measurable?
2. Were the **perspective** of the analysis (societal, third-party payer, etc.) and reasons for its selection stated?	4	Authors must state perspective, provide rationale AND have done the correct analysis corresponding to the perspective
3. Were **variable estimates** used in the analysis from the best available source (ie, randomized controlled trial - best, expert opinion - worst)?	8	No credit if most of estimates are not from the best sources available
4. If estimates came from a **subgroup analysis**, were the groups prespecified at the beginning of the study?	1	
5. Was **uncertainty** handled by (1) statistical analysis to address random events, (2) sensitivity analysis to cover a range of assumptions?	9	NO credit if they do not give details regarding type of sensitivity analysis, methods (e.g. what assumptions or factors were varied/why), AND the results (what factors are influential, what is the range of ICERs, etc.)
6. Was **incremental analysis** performed between alternatives for resources and costs?	6	
7. Was the methodology for **data abstraction** (including the value of health states and other benefits) stated?	5	No credit if sources of model inputs and process of choosing model inputs not specified
8. Did the **analytic horizon allow time** for all relevant and important outcomes? Were benefits and costs that went beyond 1 year discounted (3% to 5%) and justification given for the discount rate?	7	No credit if time horizon is too short to allow for important outcomes
9. Was the **measurement of costs** appropriate and the methodology for the estimation of quantities and unit costs clearly described?	8	No credit if sources of cost data or methods of estimating costs not clearly described
10. Were the primary **outcome measure(s**) for the economic evaluation clearly stated and did they include the major short-term, long-term and negative outcomes included?	6	NO credit if major important outcomes are not included or if time horizon did not allow for important outcomes to be measured
11. Were the health outcomes **measures/scales valid** and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used?	7	No credit if sources of outcome data or not clearly described or if outcome data is not appropriate for the study population/outcome of interest (i.e. using utility weights from QOL measures that aren't validated or apply to a different population)
12. Were the **economic model** (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner?	8	Must provide explicit detail for methods and should be able to trace/identify specific components, how they were derived, etc.
13. Were the choice of economic model, main **assumptions, and limitations** of the study stated and justified?	7	NO credit if insufficient detail of model, assumptions AND limitations are provided (No credit if they do not provide justifications/rationale)
14. Did the author(s) explicitly discuss direction and magnitude of potential **biases?**	6	NO credit if no discussion of direction and magnitude of biases
15. Were the **conclusions/recommendations** of the study justified and based on the study results?	8	NO credit if conclusions/recommendations are stronger than warranted based on findings
16. Was there a statement disclosing the **source of funding** for the study?	3	
Total	100	

ICER = Incremental Cost-Effectiveness Ratio; QOL = quality of life.

* Study must fit criteria in order to receive full points. Partial credit is not given. If criteria is not met, then the question receives no points.

Determination of Overall Strength (Quality) of Evidence

The strength of evidence for the overall body of evidence for all *critical health outcomes* was assessed by one researcher following the principles for adapting GRADE (Grades of Recommendation Assessment, Development and Evaluation) as outlined by the Agency for Healthcare Research and Quality (AHRQ).[1] The strength of evidence was based on the highest quality evidence available for a given *primary* outcome. In determining the strength of body of evidence regarding a given *primary* outcome, the following domains were considered:

- **Risk of bias:** the extent to which the included studies have protection against bias.
- **Consistency:** the degree to which the included studies report results are similar in terms of range and variability.
- **Directness:** describes whether the evidence is directly related to patient health outcomes.
- **Precision:** describes the level of certainty surrounding the effect estimates.
- **Publication bias:** is considered when there is concern of selective publishing.

All AHRQ "required" and "additional" domains (risk of bias, consistency, directness, precision, and if possible, publication bias) were assessed. Bodies of evidence consisting of RCTs were initially considered as High strength of evidence (SoE), while those that comprised nonrandomized studies began as Low strength of evidence. The strength of evidence could be downgraded based on the limitations described above. There could also be situations where the *nonrandomized* studies could be upgraded, including the presence of plausible unmeasured confounding and bias that would decrease an observed effect or increase an effect if none was observed, presence of a dose-response relationship, and large magnitude of effect (strength of association) *if no downgrades for domains above*. Publication and reporting bias are difficult to assess. Publication bias is particularly difficult to assess with fewer than 10 RCTs (AHRQ methods guide). When publication bias was unknown in all studies and this domain is often eliminated from the strength of evidence tables for our reports. The final strength of evidence for each **primary** outcome was assigned an overall grade of high, moderate, low, or insufficient, which are defined as follows:

High— Very confident that effect size estimates lie close to the true effect for this outcome; there are few or no deficiencies in the body of evidence; we believe the findings are stable.

Moderate— Moderately confident that effect size estimates lie close to the true effect for this outcome; some deficiencies in the body of evidence; we believe the findings are probably stable but some doubt remains.

Low— Limited confidence that effect size estimates lie close to the true effect for this outcome; important or numerous deficiencies in the body of evidence; we believe that additional evidence is needed before concluding that findings are stable or that the estimate is close to the true effect.

Insufficient— We have no evidence, are unable to estimate an effect or have no confidence in the effect estimate for this outcome; OR no available evidence or the body of evidence has unacceptable deficiencies precluding judgment.

Similar methods for determining the overall quality (strength) of evidence related to economic studies have not been reported, thus the overall strength of evidence for outcomes reported in Key Question 4 was not assessed.

Appendix Table D5. Example methodology outline for determining overall strength of evidence (SoE):

All AHRQ "required" and "additional" domains* are assessed. Only those that influence the baseline grade are listed in table below.
Baseline strength: HIGH = RCTs. LOW = observational, cohort studies, administrative data studies.
DOWNGRADE: Risk of bias for the individual article evaluations (1 or 2); Inconsistency** of results (1 or 2); Indirectness of evidence (1 or 2); Imprecision of effect estimates (1 or 2); Sub-group analyses not stated *a priori* and no test for interaction (2)
UPGRADE (non-randomized studies): Large magnitude of effect (1 or 2); Dose response gradient (1) done for observational studies ***if no downgrade for domains above***

Outcome	Strength of Evidence	Conclusions & Comments	Baseline SOE	DOWNGRADE	UPGRADE
Outcome	**HIGH**	Summary of findings	**HIGH** RCTs	**NO** consistent, direct, and precise estimates	**NO**
Outcome	**MODERATE**	Summary of findings	**LOW** Cohort studies	**NO** consistent, direct, and precise estimates; high quality (moderately low ROB)	**YES** Large effect
Outcome	**LOW**	Summary of findings	**HIGH** RCTs	**YES (2)** Inconsistent Indirect	**NO**

*Required domains: risk of bias, consistency, directness, precision. Plausible confounding that would decrease observed effect is accounted for in our baseline risk of bias assessment through individual article evaluation. Additional domains: dose-response, strength of association, publication bias.
**Single study = "consistency unknown", may or may not be downgraded

Administrative Database Study evaluation

What constitutes a high quality administrative database study? What criteria?

Although the precise guidelines that should govern high quality administrative database studies are still under development a number of criteria that should be met in a high quality administrative database study have been suggested. The checklist below highlights many of these qualities as was used to provide an initial assessment of administrative data studies. Individual report topics may have unique aspects of coding, requirements for developing algorithms for subject identification and potential for misclassification that need to be considered as part of an assessment of bias risk and study limitations.

Appendix Table D6. Checklist for evaluating the quality of administrative database studies.

Methodological Principle	Author, year	Author, year	
Study design Administrative database comparative study Administrative database case-control study Administrative database case series	x	x	
Why database created clearly stated			
Description of database's inclusion/exclusion criteria			
Description of methods for reducing bias in database			
Codes and search algorithms reported			
Rationale for coding algorithm reported			
Code accuracy reported			
Code validity reported			
Clinical significance assessed			
Is the period of data consistent with the outcome data?			
Statement regarding whether data stems from single or multiple hospital admissions			
Statement regarding whether data stems from single or multiple procedures			
Accounting for clustering			
Number of criteria met (maximum: 12)			

APPENDIX E. Study Quality: Risk of Bias evaluation

Appendix Table E1. Quality (Risk of Bias) Assessment: Crossover RCTs

Methodological Principle	Al-Kaisy 2018 (FBSS)	Hara 2022 (Radiculopathy after back surgery)	Sokal 2020 (FBSS)	Kriek 2016 (CRPS)
Study design				
Randomized Cross-over trial	■	■	■	■
Random sequence generation	Yes	Yes	Unclear	Yes
Concealed allocation	Yes	Yes	Unclear	Yes
Outcome assessors independent or blinded	Yes	Yes	Unclear	Yes
Care providers blinded	Unclear	Yes	Yes	Unclear
Patients blinded	Yes	Yes	No**	Yes
Complete outcome data available	No	Yes	Yes	Yes
Groups comparable at baseline/first period*	Unclear	Unclear	Unclear	Unclear
Washout, mitigation, or test carryover effect†	Yes	Unclear††	No	Unclear‡‡
Analysis for correlated data‡	Yes (pair-wise)	Yes	Yes§§	Yes
Report protocol-specified outcomes§	Unclear	Yes	No***	Unclear
Study quality	**Fair**	**Good**	**Poor**	**Fair**

* based on differences at the start of the first period only

†Is there a sufficient washout period, sufficient mitigation strategies for carryover effect or evaluation (tests) for carry-over

‡ e.g., repeated measures analyses, paired analyses, appropriate modeling

§ Do outcomes reported follow what was specified in the trial protocol (e.g., primary outcomes reported, study doesn't add outcome not specified in registered protocol); credit not given if no registered protocol.

** Authors state: Patients only felt paraesthesia during the tonic LF stimulation condition. Therefore, the present trial can be considered to be semi-blinded. In tonic mode patients were always aware of active stimulation and knew when it was switched on.

†† Authors state that outcomes measures were obtained prior to the testing period and at the end of each allocation period, indicating that this ensured a sufficient washout period from the preceding treatment.

‡‡ 2 day washout, but testing for period effect reported but state that it unclear whether this was adequate to counteract possible carryover effects.

§§ Authors report Bayesian model.

*** no reporting of disability scores or EQ-5D as specified in protocol.

Appendix Table E2. Quality (Risk of Bias) Assessment: RCTs (FBSS and CLBP)

	FBSS			NSRBP
Methodological Principle	**Riogard 2019 PROMISE trial‡**	**Kumar 2007 (index); Kumar 2008 (f/u); Manca 2008 (f/u) PROCESS trial**	**North 2005**	**Kapural 2022**
Study design				
Randomized controlled trial	■	■	■	■
Random sequence generation	Yes	Yes	Yes	Yes
Concealed allocation	Yes	Yes	Yes	Yes
Intention to treat	Yes	Yes	Yes	Yes
Outcome assessors independent or blinded	No	No	No	No
Care providers blinded	No	No	No	No
Patients blinded	No	No	No	No
Complete follow-up of ≥80%	Yes	Yes	No	Yes
<10% difference in follow-up between groups	No	Yes	No	No
Groups comparable at baseline*	Yes	No	Unclear	Yes
Reported specified outcomes†	Yes	Yes	Yes	Yes
Quality (Risk of Bias)	Fair (Moderate)	Fair (Moderate)	Fair (Moderate)	Fair (Moderate)

Unclear indicates that the study had insufficient detail to determine whether criteria were met

*Groups must be comparable on a robust set of baseline characteristics or present evidence that controlling of confounding presented was performed.

† Do outcomes reported follow what was specified in the trial protocol (e.g., primary outcomes reported, study doesn't add outcome not specified in registered protocol); credit not given if no registered protocol.

‡ Medtronic funded the study and was involved in the study design, data collection, data analysis, data interpretation, and writing of the report. The corresponding author had access to all the data in the study and had final responsibility for the decision to submit for publication.

Appendix Table E3. Quality (Risk of Bias) Assessment: RCTs (Painful diabetic neuropathy)

Methodological Principle	De Vos 2014 (index); Duarte 2016 (f/u)	Slangen 2014 (index); Van Beek 2015 (f/u)	Petersen 2021 (index); Petersen 2022 (f/u) SENZA-PDN trial
Study design			
Randomized controlled trial	■	■	■
Random sequence generation	Yes	Yes	Yes
Concealed allocation	Unclear	Unclear	Unclear‡
Intention to treat	Yes	Yes	Yes
Outcome assessors independent or blinded	No	No	No
Care providers blinded	No	No	No
Patients blinded	No	No	No
Complete follow-up of ≥80%	Yes	Yes	Yes
<10% difference in follow-up between groups	Yes	Yes at 3 mos. (86% vs. 93%); No at 6 mos. (86% vs. 100%)	No at 3 mos. (78% vs. 93%) and 6 mos. (77% vs. 90%)
Groups comparable at baseline*	Yes	Yes	Yes
Reported specified outcomes†	Yes	Yes	Yes
Quality (Risk of Bias)	**Fair (Moderate)**	**Fair (Moderate)**	**Fair (Moderate)**

Unclear indicates that the study had insufficient detail to determine whether criteria were met

*Groups must be comparable on a robust set of baseline characteristics or present evidence that controlling of confounding presented was performed.

† Do outcomes reported follow what was specified in the trial protocol (e.g., primary outcomes reported, study doesn't add outcome not specified in registered protocol); credit not given if no registered protocol

‡ Authors state the following: "Steps were taken to mitigate bias, including random sequence generation and concealed treatment allocation." I do not see where concealment is described.

Appendix Table E4. Quality (Risk of Bias) Assessment: RCTs (CRPS)

Methodological Principle	Kemler 2000 (index); Kemler 2004 (f/u); Kemler 2008 (f/u)	Canos-Verdecho, 2021
Study design		
Randomized controlled trial	■	■
Random sequence generation	Yes	Unclear
Concealed allocation	Unclear	Unclear
Intention to treat	Yes	Yes
Outcome assessors independent or blinded	No	No
Care providers blinded	No	No
Patients blinded	No	No
Complete follow-up of ≥80%	Yes	Yes
<10% difference in follow-up between groups	Yes	No HF- and LF-SCS vs. CMM (91% vs. 86% vs. 76%)
Groups comparable at baseline*	No but controlled for in multivariate analysis	No
Reported specified outcomes†	Yes	Yes
Quality (Risk of Bias)	**Fair (Moderate)**	**Poor (High)**

CMM = Conventional medical management; HF = High-frequency; LF = Low frequency; SCS = Spinal cord stimulator.
Unclear indicates that the study had insufficient detail to determine whether criteria were met
*Groups must be comparable on a robust set of baseline characteristics or present evidence that controlling of confounding presented was performed.
† Do outcomes reported follow what was specified in the trial protocol (e.g., primary outcomes reported, study doesn't add outcome not specified in registered protocol); credit not given if no registered protocol.

Appendix Table E5. Quality (Risk of Bias) Assessment: NRSI (Comparative)

Methodological Principle	Perez, 2021	Turner, 2010
Did the study attempt to enroll a random sample or consecutive patients meeting inclusion criteria (inception cohort) from same underlying population?	Yes	Yes
Were the groups comparable at baseline on key prognostic factors?	No*	No*
Did the article report attrition?	Yes	Yes
Overall loss to followup acceptable? (≤20%) Differential loss to followup acceptable? (≤10%)	No	Yes
Were the outcomes investigated prespecified and defined?	Yes	Yes
Did the study clearly describe and use accurate methods for ascertaining outcomes, exposures, and potential confounders?	Yes	Yes
Were outcome assessors and/or data analysts blinded to treatment?	No	No
Did the study perform appropriate statistical analyses on potential confounders or otherwise control for confounding (e.g. restriction, stratification, matching)?	Yes	Yes
Was the duration of follow-up reasonable for investigated events?	Yes	Yes
Quality (Risk of Bias)	Fair (Moderate)	Fair (Moderate)

Unclear indicates that the study had insufficient detail to determine whether criteria were met

* Authors report that they adjusted for key factors.

Appendix Table E6. Checklist for Evaluating the Quality of Administrative Database Studies

Methodological Principle	Dhruva 2023	Vu 2022	Lad 2014
Study design Administrative database comparative study Administrative database case-control study Administrative database case series	x	x	
Why database created clearly stated	Y	Y	Y
Description of database's inclusion/exclusion criteria	Y	Y	Y
Description of methods for reducing bias in database	N	N	N
Codes and search algorithms reported	Y	Y	Y
Rationale for coding algorithm reported	Y	Y	Y
Code accuracy reported	Y	N	N
Code validity reported	N	N	N
Clinical significance assessed	Y	Y	Y
Is the period of data consistent with the outcome data?	Y*	Y	Y
Statement regarding whether data stems from single or multiple hospital admissions	N	N	N
Statement regarding whether data stems from single or multiple procedures	N	N	N
Accounting for clustering	Y†	N	N
Number of criteria met (maximum: 12)	8	6	6

* 24 months - but authors say the following: "Sixth, chronic pain is a diagnosis that often lasts longer than the 6-month clean period that we used and some patients were excluded because of insufficient longitudinal data, which may limit study generalizability; however, characteristics between included and excluded patients were not clinically different."
† A generalized estimating equation was used to account for correlation of outcomes within matched clusters during follow-up.

Appendix Table E7. QHES Assessment of U.S. Cost-effectiveness studies

Question	Possible Points*	Hollingworth 2011	Patel 2022
1. Was the study **objective** presented in a clear, specific, and measurable manner?	7	7	7
2. Were the **perspective** of the analysis (societal, third-party payer, etc.) and reasons for its selection stated?	4	4	0
3. Were **variable estimates** used in the analysis from the best available source (ie, randomized controlled trial - best, expert opinion - worst)?	8	8	8
4. If estimates came from a **subgroup analysis**, were the groups prespecified at the beginning of the study?	1	0	1
5. Was **uncertainty** handled by (1) statistical analysis to address random events, (2) sensitivity analysis to cover a range of assumptions?	9	0	0
6. Was **incremental analysis** performed between alternatives for resources and costs?	6	6	6
7. Was the methodology for **data abstraction** (including the value of health states and other benefits) stated?	5	5	0
8. Did the **analytic horizon allow time** for all relevant and important outcomes? Were benefits and costs that went beyond 1 year discounted (3% to 5%) and justification given for the discount rate?	7	7	0
9. Was the **measurement of costs** appropriate and the methodology for the estimation of quantities and unit costs clearly described?	8	8	8
10. Were the primary **outcome measure(s**) for the economic evaluation clearly stated and did they include the major short-term, long-term and negative outcomes included?	6	6	6
11. Were the health outcomes **measures/scales valid** and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used?	7	7	7
12. Were the **economic model** (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner?	8	8	0
13. Were the choice of economic model, main **assumptions, and limitations** of the study stated and justified?	7	7	0
14. Did the author(s) explicitly discuss direction and magnitude of potential **biases?**	6	6	6
15. Were the **conclusions/recommendations** of the study justified and based on the study results?	8	8	8
16. Was there a statement disclosing the **source of funding** for the study?	3	3	3

Question	Possible Points*	Hollingworth 2011	Patel 2022
Total	**100**	**90**	**60**

* Study must fit criteria in order to receive full points. Partial credit is not given. If criteria is not met, then the question receives no points.

Appendix Table E8. QHES Assessment of Non-U.S. Cost-effectiveness studies

Question	Possible Points*	Deloitte 2019	Kumar 2013	Rojo 2021	Slangen 2016	Annemans 2014	Kemler 2010
1. Was the study **objective** presented in a clear, specific, and measurable manner?	7	7	7	7	7	7	7
2. Were the **perspective** of the analysis (societal, third-party payer, etc.) and reasons for its selection stated?	4	4	4	4	4	4	4
3. Were **variable estimates** used in the analysis from the best available source (ie, randomized controlled trial - best, expert opinion - worst)?	8	8	0	0	8	0	8
4. If estimates came from a **subgroup analysis**, were the groups prespecified at the beginning of the study?	1	0	1	1	0	1	1
5. Was **uncertainty** handled by (1) statistical analysis to address random events, (2) sensitivity analysis to cover a range of assumptions?	9	9	9	9	9	9	9
6. Was **incremental analysis** performed between alternatives for resources and costs?	6	6	6	6	6	6	6
7. Was the methodology for **data abstraction** (including the value of health states and other benefits) stated?	5	5	5	5	0	5	5
8. Did the **analytic horizon allow time** for all relevant and important outcomes? Were benefits and costs that went beyond 1 year discounted (3% to 5%) and justification given for the discount rate?	7	7	7	7	7	7	7
9. Was the **measurement of costs** appropriate and the methodology for the estimation of quantities and unit costs clearly described?	8	8	8	8	8	0	8
10. Were the primary **outcome measure(s**) for the economic evaluation clearly stated and did they include the major short-term, long-term and negative outcomes included?	6	6	6	0	6	6	6
11. Were the health outcomes **measures/scales valid** and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used?	7	7	7	7	7	7	7
12. Were the **economic model** (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner?	8	8	8	8	8	8	8
13. Were the choice of economic model, main **assumptions, and limitations** of the study stated and justified?	7	7	7	0	7	7	7

Question	Possible Points*	Deloitte 2019	Kumar 2013	Rojo 2021	Slangen 2016	Annemans 2014	Kemler 2010
14. Did the author(s) explicitly discuss direction and magnitude of potential **biases?**	6	0	0	0	0	6	0
15. Were the **conclusions/recommendations** of the study justified and based on the study results?	8	8	8	8	8	8	8
16. Was there a statement disclosing the **source of funding** for the study?	3	0	3	3	3	0	3
Total	**100**	**90**	**86**	**73**	**88**	**81**	**94**

* Study must fit criteria in order to receive full points. Partial credit is not given. If criteria is not met, then the question receives no points.

Appendix Table E9. Trial Funding and Conflict of Interest Details

	Study, year	COI
Chronic Low Back Pain		
Parallel Trials	Rigoard 2019 (Promise Trial)	Medtronic funded the study and was involved in the study design, data collection, data analysis, data interpretation, and writing of the report. The corresponding author had access to all the data in the study and had final responsibility for the decision to submit for publication. Multiple authors had COI with industry.
	Kumar 2007 (PROCESS trial)	All logistical aspects of the study were managed and funded by Medtronic Inc. The trial was designed and supervised by a Trial Steering Committee that consisted of four external advisors and two representatives from Medtronic Inc. Data were collected and analysed by Med Inc. under the direction of the committee. The manuscript was written by the independent members who had full, non-restricted access to the data. E. Buchser, R.S. Tay and the Johns Hopkins University (R. North's employer) have received financial reimbursement as consultants for Medtronic.
	Kapural 2022	Funded by Nevro Corp. Dr. Kapural: scientific advisory board for Nalu, Biotronik, Medtronic, and Presidio; consultant for Saluda and Nevro; and research contracts with Nevro, Neuros, Avanos, Medtronic, NeuraLace, and Gimmer Medical. Dr. Jameson: consultant for Nevro, Abbott, Saluda, Boston Scientific, SI Bone, Vertos, and ControlRad; and research support from Saluda, Boston Scientific, Abbott, and Nevro. Dr. Calodney: consultant for Nevro Medtronic and Boston Scientific; research support from Medtronic, Nevro, Stryker, and PainTeq. Dr. Pillitsis: consultant for Boston Scientific, Nevro, Medtronic, Saluda, and Abbott; grant support from Medtronic, Boston Scientific, Abbott, Nevro, NIH 2R01CA166379-06, and NIH U44NS115111; medical advisor for Aim Medical Robotics and Karuna; and stock equity in Aim Medical Robotics. Dr. Petersen: research support from Medtronic, Neuros Medical, Nevro, ReNeuron, SPR, and Saluda; consultant for Abbott Neuromodulation, Medtronic Modulation, Neuros Medial, Nevro, Saluda, Biotronik, and Vertos; and stock options from SynerFuse and neuro42. Dr. Lad: consultant for Nevro. Dr. Yu: consultant for Nevro. Dr. Sayed consultant for and clinical or research support for the study described from Nevro. Dr. Goree: consultant for Abbott and Stratus Medical; and research support from Mainstay Medical and SPR. Dr. Rubenstein: employee of and stock ownership in Nevro. Ms. Azalde: employee of Nevro Corp. Dr. Caraway: employee of Nevro.
	North 2005	Medtronic, Inc., provided funding for this study. RBN (first author) recently sold the assets of Stimsoft, Inc., a company developing pain stimulator technology, to Medtronic; Johns Hopkins University received a share of the proceed.
Crossover Trials	Al-Kaisy 2018	This study was sponsored by Medtronic Inc (Minnesota, USA). Adnan Al-Kaisy received travel sponsorship and speaker fees from Medtronic and Nevro Corp, he is the principal investigator in separate studies sponsored by Medtronic, Nevro Corp and Abbot and he has financial interest in Micron Device LLC. Stefano Palmisani received speaker fees and sponsorships to attend professional meetings from Nevro Corp

	Study, year	COI
		and Medtronic; David Pang received sponsorship to attend professional meetings from Medtronic and Nevro Corp. Ye Tan and Sheryl McCammon are employees of Medtronic. The remaining authors have no conflicts of interest to disclose.
	Hara 2022	The trial was funded by the Liaison Committee for Education, Research, and Innovation in Central Norway. COI Disclosures: None reported.
	Sokal 2020	This research received no external funding. COI Disclosures: Paweł Sokal reports non-financial support from Medtronic and Boston Scientific. Agnieszka Malukiewicz and Marcin Rudaś report non-financial support from Boston Scientific. Sara Kierońska, Joanna Murawska, Cezary Guzowski, Marcin Rusinek, Dariusz Paczkowski, and Mateusz Krakowiak report no conflicts of interest.
Painful Diabetic Neuropathy		
Parallel Trials	De Vos 2014	This study was sponsored by St. Jude Medical, which was not involved in the interpretation and analysis of the data. The authors would thank Dr J.A.M. van der Palen (University of Twente) for his help with data analysis. Dr K. Meier received teaching fees from St Jude Medical and is a paid consultant for Biolab Technology. The other authors report no conflict of interest.
	Slangen 2014	This study was supported by Medtronic, which provided a grant for the employment of R.S. for 3 years. No other potential conflicts of interest relevant to this article were reported. Medtronic was not involved in the analysis and interpretation of the data or in writing the manuscript.
	Petersen 2021 (SENZA-PDN Trial)	This study was funded by Nevro Corp. Role of the Funder/Sponsor: The sponsor participated in the design of the study in collaboration with an outside expert advisory committee as well as the conduct of the study by supporting patient optimization in collaboration with the investigators and monitoring data at the sites. The research site investigators and staff were responsible for all data collection and management via entry into a secure database. The sponsor participated in the analysis and interpretation of the data along with the authors and an independent biostatistician. The sponsor also participated in the preparation, review, and approval of the manuscript and decision to submit the manuscript for publication in collaboration with the authors.
Complex Regional Pain Syndrome		
Crossover Trials	Kriek 2017	This investigator-initiated study was supported by a grant from St. Jude Medical (Plano, TX, USA). The design, performance, analysis and submission of this trial were independently performed by our research group. COI: FH is a paid consultant for Grünenthal GmbH; DdR has a patent on burst stimulation and is a paid consultant for St. Jude Medical. The remaining authors declare no conflict of interest.
	Kemler 2000	Supported by a grant (OG 96-006) from the Dutch Health Insurance Council.

	Study, year	COI
Parallel Trials	Canos-Verdecho 2021	This study was not sponsored by any device manufacturer. The investigators took care to minimize the role of manufacturers' representatives in device adjustment and patient management.

COI = Conflict of Interest; PDN = Painful diabetic neuropathy.

APPENDIX F. Data Abstraction of Included Studies

Appendix Table F1. Efficacy and Safety Results: Crossover RCTs for FBSS and CRPS

	Function	Pain	Medication use	QOL/other	Adverse events
FBSS, Back pain					
Al-Kaisy 2018	N= 24 **ODI (mean, range)** Baseline: 53% (32% to 78%) Follow-up: NR	N= 24 **VAS pain** mean (SD) 0-10 scale Baseline: VAS back 7.75 (1.13) VAS leg 3.06 (2.25) **Results only reported across all sequences** **VAS back** mean (SD), range 1200 Hz 4.51 (1.87), 0.07 to 7.03. 3030 Hz 4.57 (2.09), 0.10 to 8.77. 5882 Hz 3.22 (1.98), 0 to 6.30. Sham 4.83 (2.45), 0 to 9.43 P-value (modeled across frequencies) p=0.002 **Mean percent reductions in low back pain scores** Sham 34.9%, 1200 Hz, 40.6%, 3030 Hz 39.8%, 5882 57.1%, **VAS Leg** mean (SD) Baseline: 3.06 (2.55) Follow-up 1200 Hz: 2.37 (NR)	NR	Patients Global Impression of Change (PGIC) **No change** 1200 Hz: 25% (6/24) 3030 Hz: 16.7% (4/24) 5882 Hz: 8.3% (2/24) Sham: 37.5% (9/24) **Somewhat Better** 1200 Hz: 58.3% (14/24) 3030 Hz: 70.8% (17/24) 5882 Hz: 50% (12/24) Sham: 41.7% (10/24) **Better** 1200 Hz: 16.7% (4/24) 3030 Hz: 12.5% (3/24) 5882 Hz: 41.7% (10/24) Sham: 20.8% (5/24)	**Withdrawal due to AE (NOS)** Screening: 1.9% (1/23) Trial: 2.6% (1/39)

	Function	Pain	Medication use	QOL/other	Adverse events
		3030 Hz: 2.20 (NR) 5882 Hz: 1.81 (NR) Sham: 2.51 (NR) No statistical difference between mean leg pain scores during crossover phase among frequency groups, 0.367			
Hara 2022	N= 50 **ODI Points** (mean, 95% CI) Baseline: 44.7 (41.4 to 47.9) Burst Stimulation 34.0 (30.0 to 38.1) Δ from baseline -10 (-14 to 7.2) Placebo Stimulation 35.4 (31.3 to 39.4) Δ from baseline -9.3(-12.7 to -5.9) Between group change (change scores) -1.3 (-3.9 to 1.3), p=0.32	N= 50 **NRS (0-10 score)** (mean, 95% CI) **Leg pain** Baseline 7.3 (6.8 to 7.7) Burst 5.9 (5.3 to 6.4) Placebo 6.1 (5.6 to 6.6) Between group change MD, −0.2 (95% CI −0.7 to 0.2), p=0.32 **Back pain** Baseline: 6.8 (6.4 to 7.3) Burst 5.7 (5.2 to 6.2) Placebo: 6.1 (5.6 to 6.6) Between group change MD, −0.4 (95% CI −0.8 to 0.04), p= 0.07	N= 50 **Baseline pain medications:** Opioid: 36% (18/50) Gabapentinoids: 34% (17/50) Acetaminophen: 34% (17/50) NSAIDs: 10% (5/50) Antidepressants: 6% (3/50) Follow-up: NR	N= 50 **5-Dimension EuroQol index (0 to 1 scale)** (mean, 95% CI) Baseline 0.21 (0.13 to 0.28) Burst 0.48 (0.39 to 0.56) Placebo 0.44 (0.35 to 0.53) Between group change MD 0.04 (−0.03 to 0.11), p=0.32 **Physical activity level** (mean, 95% CI) **Steps/day** Baseline 6775 (5651 to 7899) Burst 7561 (6411 to 8710)	**Any AE** Within 12 weeks: 18% (9/50) **Pulse generator replacement** Within 12 weeks: 2% (1/50) **Lead revision** Within 12 weeks: 4% (2/50) **Deep infection requiring removal** Within 12 weeks: 2% (1/50) **Unintentional durotomy** Within 12 weeks: 6% (3/50)

	Function	Pain	Medication use	QOL/other	Adverse events
				Placebo 7155 (6006 to 8305) Between group change (change scores 405 (−422 to 1233), p = 0.34 **Hours/day walking or standing** Baseline: 3.8 (3.3 to 4.3) Burst 4.0 (3.5 to 4.4) Placebo 4.0 (3.6 to 4.4) Between group change MD −0.02 (−0.4 to 0.3), p = 0.89	**Anaphylactic reaction** Within 2 weeks: 0% (0/50) **Superficial infection (antibiotics)** Within 12 weeks: 2% (1/50) **Micturition problems** Within 12 weeks: 2% (1/50) **Post-op hematoma, pneumonia, thromboembolism, cardiovascular complication, urinary tract infection** Within 12 weeks: 0% (0/50)
Sokal 2020	**ODI:** Based on Bayesian modeling, authors state that ODI score was noticeably higher after the trial vs. before but did not reach significance. Data only available for 8 participants; SCS mode(s) NR. Median (IQR) Before: 19 (15) After: 30.5 (10)	**VAS (0-10 scale)** **Mean, SD** Δ from baseline Modeled VAS (predicted marginal means of mean VAS) **Observed effects*** Mean, (SD) 1 KHz: Baseline: 5.17 (1.40) Follow-up (change from baseline): 3.04 (1.47) % pain reduction	Changes in medications taken by treatments are not reported; based on modeling, authors report that total number of medications did not differ by treatment; opioid taken in approximately half of patients (z = 49%, (21%, 79%); NSAIDs by approximately two	NR	**Unavoidable IPG removal (NOS)** Timing NR: 16.7% (3/18) **IPG, electrode removal, unsatisfactory pain relief** Timing NR: 13% (n=NR) **IPG replacement; depleted battery** 43 weeks: 5.6% (1/18) **Electrode replacement (dysfunction)**

	Function	Pain	Medication use	QOL/other	Adverse events
		LF tonic: Baseline: 4.18 (1.76) Follow-up (change from baseline): 4.07 (2.11) Cluster tonic: Baseline: 5.27 (1.33) Follow-up (change from baseline): 2.80 (1.63) Sham: Baseline: 5.42 (1.22) Follow-up (change from baseline): 2.73 (1.70) **Bayesian Model: predicted marginal means of mean VAS scores** 1 KHz: 5.21 (SE 0.22) LF tonic: 4.39 (SE 0.56) Cluster tonic: 5.35 (SE 0.37) Sham: 5.38 (SE 0.42)	thirds of patients (z = 72%, (39%, 91%); Anticonvulsants were *not* taken in 81% (71%, 88%) of patients		Timing NR: 5.6% (1/18) **Delayed allergic reaction** 56 weeks: 5.6% (1/18)

	Function	Pain	Medication use	QOL/other	Adverse events
CRPS					
Kriek 2016	NR	**VAS (0-100 scale)** Mean, SE, (95% CI) Baseline: 72.74 (2.56) Across crossover period: Placebo: 63.74 (3.51) (95% CI 56.56 to 70.91) Standard: 39.83 (4.7) (95% CI 30.19 to 49.47) 500 Hz: 40.13 (4.94) (95% CI 30.02 to 50.24) 1200 Hz: 42.89 (4.79) (95% CI 33.09 to 52.70) Burst: 47.98 (5.26) (95% CI 37.22 to 58.75) **McGill NRS (0-10 scale)** Mean, SE, (95% CI) Baseline Average pain: 7.14 (0.25) (95% CI NR) Minimal pain: 5.36 (0.38) (95% CI NR) Maximum pain: 8.82 (0.17) (95% CI NR) Pain during exertion: 8.93 (0.21) (95% CI NR) Across crossover period: Placebo Average pain: 7.07 (0.28) (95% CI 6.50 to 7.63) Minimal pain: 5.59 (0.42) (95% CI 4.73 to 6.45) Maximum pain: 8.35 (0.27) (95% CI 7.80 to 8.90)	NR	**Global perceived effect (1-7 scale)** Mean, SE (95% CI) Satisfaction Sham: 3.52 (0.35) (95% CI 2.79 to 4.24) Standard: 5.28 (0.29) (95% CI 4.69 to 5.86) 500 Hz: 5.31 (0.27) (95% CI 4.76 to 5.86) 1200 Hz: 4.97 (0.26) (95% CI 4.43 to 5.50) Burst: 4.72 (0.34) (95% CI 4.02 to 5.43) Improvement Sham: 3.79 (0.27) (95% CI 3.24 to 4.34) Standard: 4.93 (0.20) (95% CI 4.53 to 5.34) 500 Hz: 5.00 (0.23) (95% CI 4.53 to 5.47) 1200 Hz: 4.72 (0.21) (95% CI 4.29 to 5.15) Burst: 4.55 (0.24) (95% CI 4.06 to 5.05)	**Serious AEs** Across crossover period: 0% (0/29) **Electrode dislocation** Across crossover period: 10.3% ((3/29) **Stimulation stopped involuntarily** Across crossover period: 3.4% (1/29) **Stimulation switches off** Across crossover period: 3.4% (1/29) **Electrode reconfiguration required** Across crossover period: 8 events (n=NR) **Pulse width adjusted** Across crossover period: 27 events (n=NR) **Comfortable paresthesia not reached** Across crossover period: 8 events (n=NR) **Itching and/or rash** Across crossover period: 6.9% (2/29)

	Function	Pain	Medication use	QOL/other	Adverse events
		Pain during exertion: 8.41 (0.27) (95% CI 7.86 to 8.97) Standard Average pain: 4.70 (0.40) (95% CI 3.89 to 5.50) Minimal pain: 3.17 (0.40) (95% CI 2.35 to 4.00) Maximum pain: 6.31 (0.45) (95% CI 5.39 to 7.23) Pain during exertion: 6.35 (0.45) (95% CI 5.42 to 7.27) 500 Hz Average pain: 5.10 (0.45) (95% CI 4.18 to 6.03) Minimal pain: 3.57 (0.47) (95% CI 2.63 to 4.54) Maximum pain: 6.86 (0.44) (95% CI 5.96 to 7.76) Pain during exertion: 6.66 (0.46) (95% CI 5.71 to 7.61) 1200 Hz Average pain: 5.31 (0.46) (95% CI 4.36 to 6.26) Minimal pain: 3.69 (0.49) (95% CI 2.68 to 4.70) Maximum pain: 6.52 (0.53) (95% CI 5.43 to 7.61) Pain during exertion: 6.86 (0.49) (95% CI 5.86 to 7.87) Burst Average pain: 5.66 (0.49) (95% CI 4.65 to 6.66)			**Stimulation could not be set high enough** Across crossover period: 3 events (n=NR) **Standard stimulation with 60 Hz** Across crossover period: 3.4% (1/29) **Axial paresthesia** Across crossover period: 3.4% (1/29) **Headache** Across crossover period: 4 events (n=NR) **Converted to standard stimulation** Across crossover period: 3 events (n=NR) **Stimulation discontinued** Across crossover period: 1 event (n=NR)

	Function	Pain	Medication use	QOL/other	Adverse events
		Minimal pain: 4.31 (0.49) (95% CI 3.31 to 5.31) Maximum pain: 7.28 (0.46) (95% CI 6.33 to 8.22) Pain during exertion: 7.35 (0.48) (95% CI 6.35 to 8.34)			

AE = adverse events; CI = confidence interval; CRPS = complex regional pain syndrome; FBSS = failed back surgery syndrome; HF = high frequency; Hz = Hertz; IPG = implanted pulse generator; KHz= kilohertz; LF = low frequency; MD= mean difference; NOS = not otherwise specified; NR = not reported; NRS = numerical rating scale; NSAID = non-steroid anti-inflammatory drugs; ODI = Oswestry Disability Index; PGIC = Patients Global Impression of Change; QoL = quality of life; SD = standard deviation; SE = standard error; VAS = visual analogue scale.

* These effects do not account for correlated data. Results are from one sample t-tests for VAS change scores.

Appendix Table F2. Efficacy Results Table: Parallel RCTs for CLBP (No Surgery) and FBSS

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
Kapural, 2022	3 months, 6 months (prior to crossover [allowed after 6 months])	NR	*PP analysis*: 10KHz HF-SCS + CMM (n=65) vs. CMM (n=75) **Mean VAS back % change in score (SD)** 3 months: -74.1% (25.9%) vs. 0.41% (20.8%) 6 months: -72.0% (32.0%) vs. 6.2% (21.7%)	*ITT analysis*: 10KHz HF-SCS + CMM (n=83) vs. CMM (n=76) **Pain responder (>=50% pain relief), 3 months:** 74.3% (62/83) vs. 1.3% (1/76) *PP analysis*:	*PP analysis*: 10KHz HF-SCS + CMM (n=65) vs. CMM (n=75) **Mean change in opioid use (mg morphine equivalent dose, % change), 6 months**: -17.7 (-45.8%) vs. 1.1 (12.1%)	*PP analysis*: 10KHz HF-SCS + CMM (n=65) vs. CMM (n=75) **Patient's Global Impression of Change, 6 months** "Better" or "A great deal better": 70.8% (46/65) vs. 1.3% (1/75) Little, somewhat, or moderately better: 24.7% (16/65) vs. 5.4% (4/75) No change or almost the same: 4.6% (3/65) vs. 93.3% (70/75)

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
				10KHz HF-SCS + CMM (n=65) vs. CMM (n=75) **Pain responder (>=50% pain relief)** 3 months: 80.9% (55/68) vs. 1.3% (1/75) 6 months: 80.0% (52/65) vs. 2.7% (2/75) **ODI responder (>=10pt reduction)** 1 month: 67.7% (46/68) vs. 8.1% (6/75) 3 months: 80.9% (55/68) vs. 12.0% (9/75) 6 months: 78.5% (51/65) vs. 4.0% (3/75)	**Proportion of patients modifying daily opioid dose (n/Ns back calculated based on PP analysis)** Increased: 6% (4/65) vs. 49% (37/75) Stable: 28% (18/65) vs. 34% (26/75) Decreased: 44% (27/65) vs. 17% (13/75) Stopped: 22% (16/65) vs. 0%	**EQ-5D-5L (mean (SD, estimated from graph))** Baseline: 0.58 (0.12) vs. 0.56 (0.13) 3 months: 0.79 (0.14) vs. 0.56 (0.12) 6 months: 0.78 (0.11) vs. 0.52 (0.16)
Kapural, 2022, continued *Considered as case series*	12 months (after cross-over)	n=64 SCS patients followed Mean ODI total score remained at a 22.5 (SD 16.4) point reduction from baseline to 12 months	n=64 SCS patients followed Mean back and leg pain scores both sustained a mean VAS score < 2.5 cm (2.1 and 1.8, respectively).	NR	n=64 SCS patients followed The average percent change in opioid daily dose from baseline was a statistically significant reduction at all time points, with the reduction remaining at	n=64 SCS patients followed Mean EQ5D-5L index score remained 0.20 (SD 0.15) points above baseline.

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
					an average 49.6% at 12 months.	
Rigoard, 2019	6 months	*ITT analysis*: SCS + OMM (n=110) vs. OMM (n=108) **ODI mean (SD)** Baseline: 55.0 (14.6) vs. 54.8 (14.4) 6 months: 46.9 (17.9) vs. 53.1 (17.1) *As treated analysis*: SCS + OMM (n=79) vs. OMM (n=117) **ODI mean (SD)** Baseline: 55.9 (14.6) vs. 54.4 (14.0) 6 months: 46.9 (17.9) vs. 53.2 (16.4) *Completers analysis*: SCS+OMM (n=92) vs. OMM (n=104) **ODI mean (SD)** Baseline: 55.0 (14.2) vs. 55.0 (14.3) 6 months: 45.3 (17.7) vs. 53.2 (17.1)	*ITT analysis*: SCS + OMM (n=110) vs. OMM (n=108) **NPRS low back pain mean (SD)** Baseline: 7.5 (1.2) vs. 7.6 (1.2) 6 months: 6.0 (2.1) vs. 7.2 (1.9) **NPRS leg pain mean (SD)** Baseline: 5.4 (1.9) vs. 5.3 (2.1) 6 months: 4.2 (2.4) vs. 5.4 (2.4) *As treated analysis*: SCS + OMM (n=79) vs. OMM (n=117) **NPRS low back pain mean (SD)** Baseline: 7.5 (1.2) vs. 7.5 (1.2) 6 months: 5.4 (2.1) vs. 7.3 (1.8) **NPRS leg pain mean (SD)**	*ITT analysis*: SCS + OMM (n=110) vs. OMM (n=108) **Low back pain responder (>=50% reduction in lower back pain)**: 13.6% (15/110) vs. 4.6% (5/108) **Low back pain responder (>=30% reduction in lower back pain)**: 28.2% (31/110) vs. 13.0% (14/108) **Low back pain responder (>=2-point reduction in lower back pain)**: 30.9% (34/110) vs. 12.0% (13/108) **Leg pain responder (>=50% reduction in lower back pain)**: 30.0% (33/110) vs. 8.3% (9/108)	*As treated analysis*: SCS + OMM (n=79) vs. OMM (n=117) **Opioid use (mg morphine equivalent) mean (SD)**: Baseline: 59.5 (114.5) vs. 57.5 (69.1) 6 months: 58.5 (121.1) vs. 64.8 (83.1) **Opioid use** Baseline: 74.7% (59/79) vs. 78.6% (92/117) 6 months: 67.1% (53/79) vs. 78.6% (92/117) Other medications also reported Non-drug procedures also reported	*ITT analysis*: SCS + OMM (n=110) vs. OMM (n=108) **SF-36 PCS HRQoL mean (SD)** Baseline: 24.55 (7.13) vs. 24.72 (6.70) 6 months: 29.82 (9.78) vs. 26.06 (6.59) *As treated analysis*: SCS + OMM (n=79) vs. OMM (n=117) **SF-36 PCS HRQoL mean (SD)** Baseline: 24.08 (6.73) vs. 24.53 (6.83) 6 months: 31.58 (10.04) vs. 25.66 (6.60) **SF-36 MCS HRQoL mean (SD)** Baseline: 41.15 (14.55) vs. 40.71 (14.24) 6 months: 42.53 (14.26) vs. 41.38 (14.64) **EQ-5D-5L mean (SD)** Baseline: 0.31 (0.27) vs. 0.36 (0.23) 6 months: 0.49 (0.27) vs. 0.38 (0.27) **PSQI mean (SD)**

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
			Baseline: 5.2 (1.9) vs. 5.3 (2.0) 6 months: 3.7 (2.4) vs. 5.4 (2.4) **EQ-VAS mean (SD)** Baseline: 42.9 (22.1) vs. 49.4 (23.2) 6 months: 54.1 (23.1) vs. 50.1 (23.8) *Completers analysis*: SCS+OMM (n=92) vs. OMM (n=104) **NPRS low back pain mean (SD)** Baseline: 7.5 (1.2) vs. 7.6 (1.2) 6 months: 5.8 (2.1) vs. 7.2 (1.9) **NPRS leg pain mean (SD)** Baseline: 5.3 (1.8) vs. 5.2 (2.1) 6 months: 3.9 (2.4) vs. 5.3 (2.5)	*As treated analysis*: SCS + OMM (n=79) vs. OMM (n=117) **Low back pain responder (>=50% reduction in lower back pain)**: 20.3% (16/79) vs. 3.4% (4/117) **Low back pain responder (>=30% reduction in lower back pain)**: 39.2% (31/79) vs. 12.0% (14/117) **Low back pain responder (>=2-point reduction in lower back pain)**: 43.0% (34/79) vs. 11.1% (13/117) **Leg pain responder (>=50% reduction in lower back pain)**: 40.5% (32/79) vs. 8.5% (10/117)		Baseline: 13.1 (4.1) vs. 12.3 (4.2) 6 months: 10.8 (5.0) vs. 11.6 (4.7) *Completers analysis*: SCS+OMM (n=92) vs. OMM (n=104) **SF-36 PCS HRQoL mean (SD)** Baseline: 24.06 (6.80) vs. 24.61 (6.78) 6 months: 30.35 (9.98) vs. 26.00 (6.67)

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
				Completers analysis: SCS+OMM (n=92) vs. OMM (n=104) **Low back pain responder (>=50% reduction in lower back pain)**: 16.3% (15/92) vs. 4.8% (4/117) **Low back pain responder (>=30% reduction in lower back pain)**: 33.7% (31/92) vs. 13.5% (14/104) **Low back pain responder (>=2-point reduction in lower back pain)**: 37.0% (34/92) vs. 12.5% (13/104) **Leg pain responder (>=50% reduction in lower back pain)**: 35.9% (33/92) vs. 8.7% (9/104)		

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
Riogard, 2019, continued *Considered as case series*	12 and 24 months *(after cross-over at 6 months)* "The primary and secondary reported outcomes all showed durability to the **12- and 24-month follow-ups** in the 10- kHz SCS group with significant improvement seen at these timepoints in the patients that started SCS after crossing over from CMM."	**12 months** *SCS as randomized (68/110 continued)* • Mean (SD) improvement in ODI: 10.7 (18.6) (n=66), p < 0.001 *SCS after CMM (54/108 patients crossed over)* • NR **24 months** *SCS as randomized (63/110 continued)* • Mean (SD) improvement in ODI: 9.4 (15.2) (n=63), p < 0.001 *SCS after CMM (53/108 patients crossed over)* • NR	**12 months** *SCS as randomized (68/110 continued)* • Mean (SD) LBP improvement (change from baseline): 2.3 (2.2) (n=68), p < 0.001 *SCS after CMM (54/108 patients crossed over)* • Mean (SD) LBP improvement (change from baseline): 3.0 (2.0), p < 0.001 **24 months** *SCS as randomized (63/110 continued)* • Mean (SD) LBP improvement (change from baseline): 2.2 (2.0) (n=63), p < 0.001 *SCS after CMM (53/108 patients crossed over)* • Mean (SD) LBP improvement (change from	**12 months** *SCS as randomized (68/110 continued)* • ≥50% reduction in LBP: 26.5% (18/68), p < 0.001 *SCS after CMM (54/108 patients crossed over)* • ≥50% reduction in LBP: 38.9% (21/54), p < 0.001 **24 months** *SCS as randomized (63/110 continued)* • ≥50% reduction in LBP: 20.6% (13/63), p < 0.001 *SCS after CMM (53/108 patients crossed over)* • ≥50% reduction in LBP: 37.7% (20/53), p < 0.001	NR	**12 months** *SCS as randomized (68/110 continued)* • Mean (SD) improvement in EQ-5D-5L: 0.17 (0.30) (n=66), p < 0.001 • Mean (SD) improvement in SF-36 PCS: 6.92 (8.30), p < 0.001 *SCS after CMM (54/108 patients crossed over)* • NR **24 months** *SCS as randomized (63/110 continued)* • Mean (SD) improvement in EQ-5D-5L: 0.18 (0.29), (n=63) • Mean (SD) improvement in SF-36 PCS: 6.45 (8.71), p < 0.001 *SCS after CMM (53/108 patients crossed over)* • NR

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
			baseline): 2.7 (2.2), p < 0.001			
Kumar, 2007	6 months	*Primary data analysis*: SCS + CMM (n=50) vs. CMM (n=44) **ODI mean (SD)** Baseline: 57.4 (12.5) vs. 55.2 (15.4) 6 months: 44.9 (18.8) vs. 56.1 (17.9)	*Primary data analysis*: SCS + CMM (n=50) vs. CMM (n=44) **VAS back pain mean (SD)** Baseline: 54.5 (24.3) vs. 44.8 (23.2) 1 month: 38 (NR) vs. 47 (NR) 3 months: 41 (NR) vs. 51 (NR) 6 months: 40.6 (24.9) vs. 51.6 (26.7) **VAS leg pain mean (SD)** Baseline: 76.0 (13.0) vs. 73.4 (14.0) 1 month*: 38 (NR) vs. 69 (NR) 3 months*: 35 (NR) vs. 68 (NR) 6 months: 39.9 (26.3) vs. 66.6 (24.0)	*Primary data analysis*: SCS + CMM (n=50) vs. CMM (n=44) **Leg pain >=50% relief** 1 month: 47% (24/50) vs. 2% (1/44) 3 months: 56% (23/50) vs. 9% (4/44) 6 months: 48% (24/50) vs. 9% (4/44) **Leg pain >=30% relief**: 64% (32/50) vs. 18% (8/44) **Leg pain >=80% relief**: 22% (11/50) vs. 7% (3/44)	*Primary data analysis*: SCS + CMM (n=50) vs. CMM (n=44) **Opioid use (mg morphine daily equivalent) mean (SD)** Baseline Low: 63.9 (131) vs. 57.2 (129) High: 72.3 (148) vs. 71.8 (170) 6 months Low: 68.3 (139) vs. 96.9 (214) High: 76.8 (146) vs. 125 (281) **Opioid use** Baseline: 65% (34/52) vs. 58% (28/48) 6 months: 56% (28/50) vs. 70% (31/44) Other medications also reported Non-drug therapy also reported	*Primary data analysis*: SCS + CMM (n=50) vs. CMM (n=44) **SF-36 Physical functioning** Baseline: 24.5 (NR) vs. 21.6 (NR)* 6 months: 38.1 (23.0) vs. 21.8 (16.2) **SF-36 Mental health** Baseline: 51 (NR) vs. 55 (NR)* 6 months: 62.6 (22.2) vs. 50.1 (23.3) **Patient satisfaction**: 66% (33/50) vs. 18% (8/44)

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
Kumar, 2008 [f/u to Kumar, 2007] *Considered as case series*	12 and 24 months *(after crossover at 6 months)*	*SCS as randomized (42/52 continued SCS)* **Mean ODI (SE)[*]** • 12 months: 48 (4) • 24 months: 45 (4) • p=0.0002 vs. baseline for both	*SCS as randomized (42/52 continued SCS)* **Mean VAS leg pain (SE)[*]** • 12 and 24 months: 4.5 (0.5), p<0.0001 vs. baseline **Mean back pain (SE), VAS:** • 12 months: 4.5 (0.5) • 24 months: 4.8 (0.5) • p=0.21 vs. baseline for both	Authors presented an "illustrative analysis" (since the number of patients randomized to and remaining in the CMM group was deemed too small [n = 11] to undertake a companion analysis): • At 24 months, 46 of the 52 patients randomized to SCS and 41 of the 48 patients randomized to CMM were available for follow-up. • In the "modified ITT" or "treated-as-intended" analysis (outcomes assigned to randomized group with crossover considered a failure), 17 SCS patients (37%) vs. 1 CMM patient (2%) achieved the primary outcome	*SCS as randomized (42/52 continued SCS)* Neither analgesic drug intake nor nondrug therapy showed a clear pattern of change (no data provided).	*SCS as randomized (42/52 continued SCS)* **Mean EQ-5D (SE)[*]** • 12 months: 0.38 (0.13) • 24 months: 0.42 (0.10) • p<0.0001 vs. baseline for both

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
				of ≥50% leg pain relief (P < 0.003). • In the most conservative scenario (i.e., assuming patients who withdrew or were lost to follow-up in the SCS group were failures and their counterparts in the CMM group were successes), 17 (33%) of 52 patients randomized to SCS and 8 (17%) of 48 patients randomized to CMM achieved the primary outcome of ≥50% leg pain relief (P = 0.07).		
Manca, 2008 [f/u to Kumar, 2007]	6 months	NR	NR	NR	*ITT analysis*: SCS + CMM (n=52) vs. CMM (n=48) **Oral/transdermal opioids**: 75% (39/52) vs. 77% (37/48)	*ITT analysis*: SCS + CMM (n=52) vs. CMM (n=48) **EQ-5D weighted index score** Baseline: 0.13 (0.30) vs. 0.18 (0.31) 3 months: 0.49 (0.31) vs. 0.22 (0.31) 6 months: 0.47 (0.32) vs. 0.25 (0.30)

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
					Other medications also reported Non-drug therapy also reported	
North, 2005	Mean 2.9 (1.1) years	NR	NR	*"Long term" follow-up as randomized no crossover*: SCS (n=15) vs. Reoperation (n=12) **Success (>=50% pain relief and patient satisfaction with treatment)**: 60% (9/15) vs. 25% (3/12)	*"Long term" follow-up as randomized*: SCS (n=23) vs. Reoperation (n=26) Opioid use Stable or decreased: 87% (20/23) vs. 58% (15/26) Increased: 13% (3/23) vs/ 42% (11/26)	NR

CLBP = Chronic lower back pain; CMM = Conventional medical management; EQ-5D = EuroQol 5D; FBSS = Failed back surgery syndrome; f/u = follow-up; GPE = Global Perceived Effect; HF = High frequency; HRQoL = Health related quality of life; ITT = Intention-to-treat; kHz = Kilohertz; LF = Low frequency; MCS = Mental component summary; NR = Not reported; NRPS = Numerical Pain Rating Scale; ODI = Oswestry Disability Index; PCS = Physical component summary; PP = Per protocol; PSQI = Pittsburgh Sleep Quality Index; QoL = Quality of life; SCS = Spinal cord stimulator; SD = Standard deviation; SF-36 = 36-item Short Form; VAS = Visual analogue scale.

* Estimated from graph.

Appendix Table F3. Efficacy Results: Parallel RCTs for PDN

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
De Vos 2014	26 weeks	NR	*ITT analysis* SCS + CMM (n=40) vs. CMM (n=20) **VAS Pain** Baseline: 73 (16) vs. 67 (1.8) 26 weeks: 31 (28) vs. 67 (21), p<0.001 **MPQ** Baseline: 13 (5) vs. 13 (3) 26 weeks: 8 (7) vs. 13 (4), p<0.01 **MPQ Pain Rating Index:** Baseline: 27 (13) vs. 24 (9) 26 weeks: 15 (14) vs. 26 (10), p<0.01	*ITT analysis* SCS + CMM (n=40) vs. CMM (n=20) **>50% VAS Pain reduction** 26 weeks: 63% (25/40) vs. 5% (1/20)	*ITT analysis* SCS + CMM (n=40) vs. CMM (n=20) **Opioid Use** Baseline: 45% (18/40) vs. 55% (11/20) 26 weeks: 38% (15/40) vs. 55% (11/20) **No analgesics**[*] Baseline: 15% (6/40) vs. 15% (3/20) 26 weeks: 23% (9/40) vs. 5% (1/20) **MQS III** Baseline: 10.6 (9.7) vs. 9.2 (7.8) 26 weeks: 7.7 (8.7) vs. 10.1 (8.2)	*ITT analysis* SCS + CMM (n=40) vs. CMM (n=20) **Global Impression of Change pain reduction** 26 weeks: 73% (29/40) vs. 17% (3/20), p<0.001 **MPQ QoL** Baseline: 16 (5) vs. 15 (6) 26 weeks: 8 (7) vs. 14 (6), p<0.001 **EQ5D** Baseline: 50 (19) vs. 46 (17) 26 weeks: 61 (22) vs. 41 (20), p<0.01 **Patient Satisfaction** 26 weeks: 80% (8/10) vs. 40% (4/10), p<0.001
Duarte 2016[†]	26 weeks	NR	*As randomized* SCS + CMM vs. CMM **VASPI** Baseline: 73 (16) (n=40) vs. 67 (18) (n=20), MD -6 (95% CI -15 to 3) p>0.05	*As randomized* SCS + CMM vs. CMM **Minimal clinically important reduction in pain intensity (10% to 30%)** 26 weeks: 11% (4/36) vs. 33% (6/18)	NR	*As randomized* SCS + CMM vs. CMM **EQ VAS** Baseline: 50 (19) (n=40) vs. 48 (16) (n=20), MD -1 (95% CI -11 to 8) p>0.05

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
			26 weeks: 29 (27) (n=36) vs. 66 (22) (n=18), MD 37 (95% CI 22 to 52) p<0.001	**Moderate important reduction in pain intensity (30% to 50%)** 26 weeks: 8% (3/36) vs. NR **Substantial clinical reduction in pain intensity (>50%)** 26 weeks: 67% (24/36) vs. 6% (1/18)		26 weeks: 61 (23) (n=36) vs. 41 (20) (n=18), MD -20 (95% CI -34 to -7), p<0.01 **EQ-5D index** Baseline: 0.27 (0.26) (n=40) vs. 0.47 (0.31) (n=20), MD 0.2 (95% CI 0.05 to 0.36), p<0.05 26 weeks: 0.65 (0.28) (n=36) vs. 0.44 (0.33) (n=18), MD -0.21 (95% CI -0.39 to -0.04) p<0.05
Slangen 2014	26 weeks	*ITT analysis* SCS + CMM (n=22) vs. CMM (n=14) **MOS SF-36 – PCS[‡]** Baseline: 27.9 (7.5) vs. 31.7 (7.9) 13 weeks: 33.2 (9.6) vs. 32.9 (6.6), p>0.05 26 weeks: 32.3 (10.5) vs. 30.5 (7.4) **MOS SF-36 – MCS[‡]** Baseline: 44.7 (13.5) vs. 45.3 (11.8) 13 weeks: 51.4 (10.5) vs. 44.9 (12.4), p>0.05 26 weeks: 49.3 (11.5) vs. 46.7 (12.0), p>0.05	*ITT analysis* SCS + CMM (n=22) vs. CMM (n=14) **NRS – day** Baseline: 7.1 (1.7) vs. 6.5 (1.7) 13 weeks: 3.5 (2.4) vs. 6.7 (1.8), p<0.001 26 weeks: 4.0 (2.9) vs. 6.5 (1.9), p<0.001 **NRS – night** Baseline: 6.3 (2.5) vs. 7.3 (1.8) 13 weeks: 3.3 (2.7) vs. 6.9 (2.0), p<0.001 26 weeks: 3.9 (3.1) vs. 6.4 (2.1), p<0.001	*ITT analysis* SCS + CMM (n=22) vs. CMM (n=14) **Treatment success[§]** 13 weeks: 73% (16/22) vs. 0% (0/14), p<0.001 26 weeks: 59% (13/22) vs. 7% (1/14), p<0.009 OR = 18.8 (95% CI 2.1 to 170.2) **Treatment success during daytime** 26 weeks: 41% (9/22) vs. 0% (0/14), p<0.001 **Treatment success during nighttime**	*ITT analysis* SCS + CMM (n=22) vs. CMM (n=14) **Opioid use**: NR **Reduction in pain medication** 26 weeks: 32% (7/22) vs. 0% (0/14) **No medication change** 26 weeks: 55% (12/22) vs. 64% (9/14) **Stopped medication usage** 26 weeks: 9% (2/22) vs. 0% (0/14)	*ITT analysis* SCS + CMM (n=22) vs. CMM (n=14) **EQ-5D – utility score** Baseline: 0.25 (0.31) vs. 0.33 (0.32) 13 weeks: 0.54 (0.32) vs. 0.41 (0.3), p>0.05 26 weeks: 0.50 (0.33) vs. 0.33 (0.29), p>0.05 **EQ-5D – current health** Baseline: 53.9 (18.5) vs. 54.6 (16.7) 13 weeks: 63.2 (17.4) vs. 58.8 (13.0), p>0.05 26 weeks: 57.6 (24.3) vs. 56.5 (14.2), p>0.05 **BDI** Baseline: 13.2 (7.3) vs. 13.7 (6.4)

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
			mBPI-DPN - PSI Baseline: 7.1 (1.5) vs. 6.3 (1.8) 13 weeks: 4.0 (2.5) vs. 6.1 (1.8), p<0.01 26 weeks: 4.0 (2.8) vs. 6.5 (2.1), p<0.001 **mBPI-DPN - PII** Baseline: 6.0 (1.9) vs. 5.3 (2.0) 13 weeks: 3.0 (2.1) vs. 5.6 (1.8), p<0.001 26 weeks: 3.5 (2.6) vs. 5.5 (1.5), p<0.01 **NPS – Deep pain** Baseline: 8.2 (1.5) vs. 7.6 (1.5) 13 weeks: 4.9 (3.1) vs. 7.3 (1.6), p<0.01 26 weeks: 6.3 (2.9) vs. 7.4 (1.8) p>0.05 **NPS – Surface pain** Baseline: 6.0 (3.3) vs. 6.5 (2.4) 13 weeks: 4.1 (3.2) vs. 7.2 (2.1), p<0.01 26 weeks: 3.6 (3.4) vs. 6.4 (2.1), p<0.01	26 weeks: 36% (8/22) vs. 7% (1/14), p<0.01 **Treatment success (≥6 on PGIC for pain)** 13 weeks: 68% (15/22) vs. 0% (0/14), p<0.001 26 weeks: 55% (12/22) vs. 0% (0/14), p<0.001 **Treatment success adjusted for sex** 26 weeks: OR = 24.7 (95% CI 2.4 to 250.2)	**Increased medication usage** 26 weeks: 0% (0/22) vs. 29% (4/14) **Medication changed to another category of neuropathic pain medication** 26 weeks: 0% (0/22) vs. 7% (1/14)	13 weeks: 12.1 (9.0) vs. 12.7 (5.2), p>0.05 26 weeks: 13.0 (9.8) vs. 14.4 (6.3), p>0.05

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
			NPS – Intensity Baseline: 8.0 (1.5) vs. 7.6 (1.5) 13 weeks: 4.5 (2.8) vs. 7.3 (1.6), p<0.001 26 weeks: 4.3 (3.0) vs. 7.3 (2.0), p<0.001 **NPS – Unpleasantness** Baseline: 7.9 (1.8) vs. 7.6 (1.7) 13 weeks: 5.1 (2.9) vs. 7.2 (1.7), p<0.01 26 weeks: 5.4 (2.8) vs. 7.5 (1.6), p<0.01 **NPS – Coldness** Baseline: 4.2 (3.6) vs. 4.9 (4.0) 13 weeks: 2.6 (2.9) vs. 5.0 (3.3), p>0.05 26 weeks: 2.2 (2.7) vs. 5.6 (3.1) p<0.05 **NPS – Hotness** Baseline: 6.9 (2.7) vs. 6.7 (3.5) 13 weeks: 2.7 (2.9) vs. 6.5 (2.4), p<0.001 26 weeks: 2.9 (3.3) vs. 6.3 (2.5), p<0.01			

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
			NPS – Dullness Baseline: 7.6 (2.1) vs. 7.7 (2.4) 13 weeks: 4.5 (2.8) vs. 7.6 (1.9), p<0.001 26 weeks: 4.6 (3.5) vs. 7.6 (1.7), p<0.001 **NPS – Sharpness** Baseline: 7.9 (1.9) vs. 7.3 (2.4) 13 weeks: 4.0 (3.1) vs. 7.5 (1.6), p<0.001 26 weeks: 5.0 (3.3) vs. 7.7 (1.7), p<0.01 **NPS – Sensitivity** Baseline: 7.6 (2.5) vs. 6.5 (2.4) 13 weeks: 4.1 (2.8) vs. 7.4 (2.1), p<0.001 26 weeks: 5.0 (3.4) vs. 7.1 (2.2), p<0.05 **NPS – Itching** Baseline: 3.9 (3.1) vs. 3.6 (3.3) 13 weeks: 1.9 (2.6) vs. 2.8 (2.5), p>0.05 26 weeks: 1.6 (2.6) vs. 4.2 (3.2), p<0.05			

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
Van Beek 2015 [f/u to Slangen 2014] *Considered as case series*	104 weeks (after crossover at 6 months) "The data demonstrate a sustained effect of SCS on pain relief in PDPN after 24 months"	NR	*SCS group as randomized, patients who continued treatment through 12 months (n=16) and 24 months (n=15)* **NRS pain score, mean (SD) – Day** • 12 months: 4.1 (2.7) • 24 months: 4.0 (3.0) • p<0.001 vs. baseline for both timepoints **NRS pain score, mean (SD) – Night** • 12 months: 3.6 (2.7) • 24 months: 3.5 (3.0) • p<0.001 vs. baseline for both timepoints	*SCS group as randomized, patients who continued treatment through 12 months (n=16) and 24 months (n=15)* **≥50% relief of pain intensity on NRS - Day** • 12 months: 35% (6/17) • 24 months: 47% (8/17) **≥50% relief of pain intensity on NRS - Night** • 12 months: 53% (9/17) • 24 months 35% (6/17) **Treatment success** (≥50% relief of pain intensity on a NRS for 4 days during the daytime or nighttime or "(very) much improved" for pain and sleep on the PGIC scale)	NR	*SCS group as randomized, patients who continued treatment through 12 months (n=16) and 24 months (n=15)* **SF-36 MCS, mean (SD)** • 12 months: 49.1 (12.3), p <0.05 vs. baseline • 24 months: 50.4 (14.7), p=NS vs. baseline **SF-36 PCS, mean (SD)** • 12 months: 32.8 (8.7) • 24 months: 31.9 (7.6) • p <0.05 vs. baseline at both timepoints **BDI, mean (SD)** • 12 months: 12.5 (8.4) • 24 months: 12.8 (10.4) • p=NS at both timepoints

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
				• 52 weeks: 71% (12/17) • 104 weeks: 65% (11/17)		
Peterson 2021	26 weeks	*Per protocol* SCS + CMM (n=88) vs. CMM (n=96) **Improvement in motor, sensory, or reflex testing** 13 weeks: 72.4% (63/87) vs. 6.4% (6/94), MD 66% (95% CI 55.4% to 76.6%), p<0.001 26 weeks: 61.9% (52/84) vs. 3.3% (3/92), MD 58.6% (47.6% to 69.6%), p<0.001	*Per protocol* SCS + CMM (n=88) vs. CMM (n=96) **VAS pain** Baseline: 7.6 (95% CI 7.3 to 7.9) vs. 7 (95% CI 6.7 to 7.3) 26 weeks: 1.7 (95% CI 1.3 to 2.1) vs. 6.9 (95% CI 6.5 to 7.3) **VAS pain ≤ 3** 13 weeks: 78.4% (69/88) vs. 5.2% (5/96), MD 73.2% (95% CI 63.5% to 82.9%) p<0.001 **Worsening pain** 26 weeks: 2% (2/87) vs. 52% (48/93) **DN4 Score** Baseline: 6.5 (95% CI 6.3 to 6.7) (n=113) vs. 6.4 (95% CI 6.2 to 7.6) n=103)	*ITT* SCS + CMM vs. CMM **50% or more pain relief on VAS without observed deterioration on neurological examination, *known responder status***** 26 weeks: 79% (75/95) vs. 5% (5/94), MD 73.6% (95% CI 64.2% to 83%) p<0.001 **50% or more pain relief on VAS without observed deterioration on neurological examination, *True ITT*** 26 weeks: 66.4% (75/113) vs. 11.7% (12/103), p<0.001 *Per protocol* SCS + CMM vs. CMM	NR	Per protocol SCS + CMM vs. CMM **Mean change in EQ-5D-5L index** 26 weeks: 0.13 (0.16) vs. -0.03 (0.13), p<0.001 **Mean change in EQ-5D-5L VAS** 26 weeks: 15.9 (21.6) vs. -1.7 (23), p<0.001

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
			26 weeks: 3.5 (95% CI 3.2 to 3.8) (n=87) vs. 6.5 (95% CI 6.3 to 6.7) (n=93)	**Responders (≥50% pain relief from baseline VAS)** 26 weeks: 85.1% (74/87) vs. 5.4% (5/93), p<0.001 **Remission of pain (VAS ≤3 sustained for 26 weeks)** 26 weeks: 60.2% (53/88) vs. 1.1% (1/95), p<0.001 **Clinical PDN (DN4 score ≥3)** Baseline: 98.9% (83/83) vs. 96.7% ((88/91) 26 weeks: 64.3% (54/84) vs. 95.6% (87/91)		
Petersen 2022 [f/u to Petersen 2021] *Considered as a case series*	52 weeks	*HF SCS as randomized (continued SCS)* **Neurological improvements, particularly improved sensory function**: 68% (52/76)	*HF SCS as randomized (continued SCS)* **Mean lower limb pain VAS:** 1.7 (95% CI 1.3–2.1), representing 77.1% mean pain relief. *Crossover group (from CMM to SCS)*	*HF SCS as randomized (continued SCS)* **Treatment responder, (≥50% pain relief from baseline)**: 86% (72/84) *Crossover group (from CMM to SCS)*	NR	NR

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
		Crossover group (from CMM to SCS) **Neurological improvements, particularly improved sensory function:** 62% (32/52); similar to the originally assigned 10-kHz SCS group	**Mean lower limb pain VAS:** • Baseline: 7.2 cm (95% CI 6.8–7.6) • 6 months (prior to crossover): no change • 52 weeks (after crossover): 2.0 cm (95% CI 1.6–2.4), mean 70.3% pain relief (95% CI 63.4–77.1, P < 0.001); similar to the originally assigned 10-kHz SCS group	**Treatment responder, (≥50% pain relief from baseline)**: 84% (49/58); similar to the originally assigned 10-kHz SCS group		
Petersen 2023 [f/u to Petersen 2021] *Considered as a case series*	104 weeks	Investigators assessed neurological function versus study baseline in all implanted patients. **clinically meaningful improvement over study baseline in sensory, motor, or reflex function, without worsening in any category.** • 65.7% (95% CI, 57.5%–73.1%) (92/140) of all 10	**Mean lower limb pain on VAS** • After 24 months of 10 kHz SCS, the score in the group of all implanted patients decreased from a preimplantation mean of 7.6 cm (95% CI, 7.3–7.8) to 1.5 cm (95% CI, 1.2–1.8; p<0.001), a **mean reduction** of 79.9% (95% CI, 76.3%–83.6%; p<0.001).	**Responders (≥50% pain relief from baseline or preimplantation)** • 90.1% (95% CI, 84.1%–94.0%) (128/142) of the implanted patients at 24 months **Profound responders (≥80% pain relief from baseline or preimplantation)** • 65.5% (95% CI, 57.4%–72.8%	NR	**EQ-5D-5L index** • Among all implanted patients, the mean EQ-5D-5L index value increased by 0.146 (95% CI, 0.117–0.175; P<0.001) from preimplantation to 24 months, with the improvement in HRQoL consistent between the original 10 kHz SCS+CMM group and the CMM-to-10 kHz SCS+CMM crossover cohort (p=0.37)

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
		kHz SCS implanted individuals • Most of the neurological gains were observed in sensory function: 65.0% (95% CI, 56.8%–72.4%) (91/140) of participants assessed showed improvement • Neurological and sensory improvement outcomes were similar between the original 10 kHz SCS+CMM group and the CMM-to-10 kHz SCS+CMM crossover cohort, with the initial 10 kHz SCS recipients showing higher improvement rates that reached statistical significance for neurological function at 24	• Pain relief and percentage pain relief at 24 months were consistent between the original 10 kHz SCS+CMM group and the CMM-to-10 kHz SCS+CMM crossover cohort (p=0.22 for pain relief and p=0.12 for percentage pain relief) **Mean DN4 scores** • Among all implanted patients, scores decreased from a preimplantation mean of 6.6 (95% CI, 6.3–6.9) to 3.5 (95% CI, 3.1-3.9; p<0.001) after 24 months of 10 kHz SCS. • At 24 months, DN4 results were comparable between the original 10 kHz SCS+CMM group and the CMM-to-10 kHz SCS+CMM crossover cohort (p=0.14).	(93/142) of the implanted patients at 24 months **No patients had increased pain relative to baseline**. **DN4 score <4** • The proportion with a DN4 score < 4 increased from 3.9% (95% CI, 1.8%-8.2%) (5/154) to 48.9% (95% CI, 40.8-57.1) (69/141); p<0.001 • At 24 months, DN4 results were comparable between the original 10 kHz SCS+CMM group and the CMM-to-10 kHz SCS+CMM crossover cohort (p=0.14).		

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
		months post-implantation (P =.048 for neurological improvement and P =.076 for sensory improvement).				

BDI = Beck's Depression Inventory; CI = confidence interval; CMM = conventional medical management; DN4 = Douleur Neuropathique en 4 Questions; EQ = EuroQol; EQ5D = EuroQoL 5D Form; F/U = follow-up; GPE = global perceived effect; ITT = intention-to-treat; mBPI-DPN = Brief Pain Inventory- Diabetic Peripheral Neuropathy; MCS = mental component summary; MD = mean difference; MOS = medical outcomes study; MPQ = McGill Pain Questionnaire; MPQ III = Medication Quantification Scale III; NPS = Neuropathic Pain Scale; NR = not reported; NRS = numerical rating scale; OR = odds ratio; PCS = physical component summary; PDN = painful diabetic neuropathy; PII = pain interference index; PSI = pain severity index; QoL = quality of life; SCS = spinal cord stimulator; SF-36 = 36-Item Short Form Survey; VAS = visual analogue scale; VASPI = visual analogue scale for pain intensity.
*Authors also report use of NSAIDs (baseline: 15% vs. 10%, 6 months: 8% vs. 10%), antidepressants (baseline: 35% vs. 45%, 6 months: 33% vs. 40%), anticonvulsants (baseline: 58% vs. 35%, 6 months: 45% vs. 35%), acetaminophen (baseline: 30% vs. 30%, 6 months: 18% vs. 30%).
† Does not use ITT analyses for main outcomes.
‡ MOS SF-36 measures PCS and MCS and is converted to a 0–100 scale, with higher scores indicating higher levels of functioning or well-being.
§ ≥50% relief of pain intensity on an NRS for 3 days during daytime or nighttime or a score of ≥6 on a 7-point Likert scale.
** Only those patients with known status.

Appendix Table F4. Efficacy Results Table: Parallel RCTs for CRPS

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
Kemler 2000	6 months	NR	*ITT analysis:* SCS + PT (n=36) vs. PT (n=18)	*ITT analysis:* SCS + PT (n=36) vs. PT (n=18)	NR	*ITT analysis:* SCS + PT (n=36) vs. PT (n=18) **GPE**

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
			• **VAS score**, change from baseline (mean ± SD): -2.4 ± 2.5 vs. 0.2 ± 1.6, p<0.001 [pain relief similar for pts with affected hand and those with affected foot (data NR)] • **MPQ** pain-rating index: NR *Randomized treatment received analysis:* SCS + PT, implant received (n=24) vs. PT (n=18) • **VAS score**, change from baseline (mean ± SD): -3.6 ± 2.0 vs. 0.2 ± 1.6, p<0.001 • **MPQ** pain-rating index: p=0.02 in favor of SCS (data NR)	• "**Success":** ≤ 50% pain relief on VAS *OR* GPE ≥ 6: 56% (20/36) vs. NR		• Percent of patients with GPE score* ≥ 6: 39% (14/36) vs. 6% (1/18), p=0.01 **HR-QoL** (VAS; 0=death, 100=perfect health) • Percent change from baseline (mean ± SD): 6% ± 22% vs. 3% ± 18%, p=0.58 **Nottingham Health Profile pain component**: NR **EQ-5D**: NR **Self-Rating Depression Scale**: NR **Patient Satisfaction:** NR *Randomized treatment received analysis:* SCS + PT, implant received (n=24) vs. PT (n=18) **GPE** • Percent of patients with GPE score* ≥ 6: 58% (14/24) vs. 6% (1/18), p< 0.001

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
						HR-QoL (VAS; 0=death, 100=perfect health) • Percent change from baseline (mean ± SD): 11 ± 23% vs. 3 ± 18%, p=NR **Nottingham Health Profile pain component**: • Patients with affected hand: p= 0.02 in favor of SCS (data NR) • Patients with affected foot: p=0.008 in favor of SCS (data NR) **EQ-5D**: NR **Self-Rating Depression Scale**: NR **Patient Satisfaction:** NR
Kemler 2004 [f/u of Kemler 2000 RCT]	24 months	NR	*ITT analysis:* SCS + PT (n=36) vs. PT (n=18) • **VAS score**, change from baseline (mean ± SD): -2.1 ± 2.8 vs. 0.0 ± 1.5, p=0.001 [pain relief similar for pts with affected hand and those with affected foot (data NR)]	*ITT analysis:* SCS + PT (n=36) vs. PT (n=18) • "**Success":** ≤ 50% pain relief on VAS *OR* GPE ≥ 6: 57% (20/35) vs. NR	**NR**	*ITT analysis:* SCS + PT (n=36) vs. PT (n=18) **GPE** • Percent of patients with GPE score* ≥ 6: 42.9% (15/36) vs. 6% (1/18), p=0.01 Score • 1: 2.6% (1/35) vs. 12.5% (2/16) • 2: 5.7% (2/35) vs. 12.5% (2/16) • 3: 11.4% (4/35) vs. 43.8% (7/16) • 4: 25.7% (9/35) vs. 18.8% (3/16) • 5: 11.4% (4/35) vs. 6.3% (1/16)

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
			• **VAS** pain, from graph 3 months: 4.6 (1.9) vs. 7.2 (1.9) 6 months: 4.3 (2.2) vs. 7.4 (2.2) 12 months: 4.4 (2.2) vs. 7.0 (2.3) 24 months: 4.5 (2.2) vs. 7.0 (2.4) • **MPQ** pain-rating index: NR *Randomized treatment received analysis:* SCS + PT, implant received (n=24) vs. PT (n=16) • **VAS score**, change from baseline (mean ± SD): -3.0 ± 2.7 vs. 0.0 ± 1.9, p NR • **MPQ** pain-rating index: p=0.02 in favor of SCS (data NR)			• 6: 42.9% (15/35) vs. 6.3% (1/16) • 7: 0% vs. 0% **HR-QoL** (VAS; 0=death, 100=perfect health) • Percent change from baseline (mean ± SD): 7% ± 20% vs. 12% ± 18%, p=0.41 **Nottingham Health Profile pain component**: NR **EQ-5D**: NR **Self-Rating Depression Scale**: NR **Patient Satisfaction:** NR *Randomized treatment received analysis:* SCS + PT, implant received (n=24) vs. PT (n=16) **GPE** • Percent of patients with GPE score* ≥ 6: 63% (15/24) vs. 6.3% (1/16), p< 0.001 **HR-QoL** (VAS; 0=death, 100=perfect health)

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
						• Percent change from baseline (mean ± SD): 12 ± 21% vs. -1 ± 12%, p=NR **Nottingham Health Profile pain component**: • Patients with affected hand: p= 0.02 in favor of SCS (data NR) • Patients with affected foot: p=0.008 in favor of SCS (data NR) **EQ-5D**: NR **Self-Rating Depression Scale**: NR **Patient Satisfaction:** NR
Kemler 2008 [f/u of Kemler 2000 RCT]	60 months	NR	*ITT analysis:* SCS + PT (n=31) vs. PT (n=13) • **VAS score**, change from baseline (mean ± SD): -1.7 ± 2.3 vs. -1.0 ± 2.9, p=0.25 [pain relief similar for pts with affected hand and those with affected foot (data NR)]	*ITT analysis:* SCS + PT (n=31) vs. PT (n=13) • "**Success":** ≤ 50% pain relief on VAS *OR* GPE ≥ 6: 35% (11/31) vs. NR	**NR**	*ITT analysis:* SCS + PT (n=31) vs. PT (n=13) **GPE** • Percent of patients with GPE score* ≥ 6: 23% (7/31) vs. 15% (2/13), p=0.24 **HR-QoL** (VAS; 0=death, 100=perfect health) • Percent change from baseline (mean ± SD): 6% ± 22% vs. 3% ± 18%, p=0.58

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
			• **VAS** pain, from graph (SD NR for all) 36 months: 5.2 vs. 6.3 48 months: 5.1 vs. 5.9 60 months: 5.0 vs. 5.9 • **MPQ** pain-rating index: NR			**Nottingham Health Profile pain component**: • Mobility change from baseline: 7 (15) vs. 5 (28), p=0.81 • Pain change from baseline: -7 (27) vs. -5 (27), p=0.82 • Sleep change from baseline: -15 (30) vs. -12 (34), p=0.74 • Energy change from baseline: 5 (43) vs. 2 (55), p=0.88 • Social isolation change from baseline: 4 (18) vs. 1 (20), p=0.66 • Emotional reaction change from baseline: -2 (27) vs. -5 (26), p=0.74 **EQ-5D** • Change from baseline: 16 (25) vs. 19 (46), p=0.80 **Self-Rating Depression Scale** • Change from baseline: 0 (9) vs. -3 (11), p=0.47 **Patient Satisfaction:** NR
Canos-Verdecho, 2021†	12 months	LF-SCS (n=12) vs. 10-kHz (n=10) vs. Conventional (n=19) **ODI**	LF-SCS (n=12) vs. 10-kHz (n=10) vs. Conventional (n=19) NRS Pain Baseline: 9.2(0.2) vs. 9.3 (0.3) vs. 8.3 (0.5), p=0.203	NR	NR	LF-SCS (n=12) vs. 10-kHz (n=10) vs. Conventional (n=19) SF-12 Total Baseline: 344.2 (43.7) vs. 193.5 (34.8) vs. 393.1 (50.4), p=0.304

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
		Baseline: 58.5 (4.3) vs. 65.0 (6.6) vs. 32.4 (4.4), p=0.001 1 month: 18.5 (3.4) vs. 26.0 (3.3) vs. 32.4 (4.4), p=0.069 3 months: 17.3 (3.0) vs. 29.4 (3.4) vs. 31.5 (4.4), p=0.045 6 months: 16.8 (3.0) vs. 31.2 (3.6) vs. 22.9 (4.5), p=0.113 12 months: 17.0 (3.0) vs. 33.2 (4.8) vs. 22.0 (4.7), p=0.089	1 month: 3.9 (0.4) vs. 2.8 (0.5) vs. 8.0 (0.5), p=0.001 3 months: 3.5 (0.2) vs. 3.4 (0.5) vs. 6.9 (0.5), p=0.005 6 months: 3.6 (0.3) vs. 3.9 (0.4) vs. 5.7 (0.6), p=0.024 12 months: 3.6 (0.3) vs. 4.5 (0.7) vs. 5.3 (0.8), p=0.257 DN-4 Neuropathic pain Baseline: 6.7 (0.3) vs. 6.9 (0.4) vs. 6.5 (0.3), p=0.187 1 month: 3.9 (0.7) vs. 3.5 (0.5) vs. 6.0 (0.3), p=0.001 3 months: 3.8 (0.6) vs. 3.9 (0.3) vs. 5.7 (0.4), p=0.005 6 months: 3.9 (0.6) vs. 3.8 (0.3) vs. 4.9 (0.5), p=0.290 12 months: 3.8 (0.6) vs. 4.1 (0.4) vs. 44 (0.7), p=0.834			1 month: 648.7 (74.5) vs. 579.5 (54.2) vs. 392.0 (50.4), p=0.040 3 months: 717.9 (59.97) vs. 558.0 (58.0) vs. 433.1 (52.0), p=0.039 6 months: 709.2 (56.9) vs. 538.5 (59.5) vs. 494.5 (54.5), p=0.008 12 months: 729.6 (58.3) vs. 517.5 (70.7) vs. 505.0 (54.6), p=0.229 SF-12 Physical Baseline: 133.3 (16.0) vs. 87.5 (11.3) vs. 146.0 (30.0), p=0.304 1 month: 264.6 (42.5) vs. 212.5 (21.1) vs. 146.0 (30.0), p=0.039 3 months: 279.2 (41.6) vs. 190.0 (18.7) vs. 148.7 (32.3), p=0.029 6 months: 268.7 (36.4) vs. 180.0 (20.6) vs. 193.4 (37.5), p=0.233 12 months: 283.3 (38.7) vs. 170.0 (24.4) vs. 201.3 (38.4), p=0.150 SF-12 Emotional Baseline: 210.8 (34.8) vs. 106.0 (26.6) vs. 252.6 (32.0), p=0.304 1 month: 384.2 (46.6) vs. 367.0 (46.6) vs. 252.6 (32.0), p=0.015 3 months: 438.7 (35.2) vs. 368.0 (49.1) vs. 290.2 (33.5), p=0.024 6 months: 440.4 (35.2) vs. 358.5 (51.0) vs. 306.6 (32.8), p=0.042 12 months: 446.2 (35.1) vs. 347.5 (56.5) vs. 309.2 (32.5), p=0.38

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
						Sleep (MOS-SS) Baseline: 2.7 (0.2) vs. 3.0(0.1) vs. 2.0 (0.2), p=0.001 1 month: 1.4 (0.2) vs. 1.6 (0.3) vs. 2.0 (0.2), 0.122 3 months: 1.2 (0.2) vs. 1.7 (0.3) vs. 2.0 (0.2), p=0.030 6 months: 1.2 (0.2) vs. 1.8 (0.3) vs. 1.9 (0.2), p=0.087 12 months: 1.2 (0.2) vs. 1.9 (0.3) vs. 1.8 (0.2), p=0.107 PGI-I Baseline: 4.0 (0.1) vs. 4.0 (0.1) vs. 3.68 (0.1), p=0.010 1 month: 1.9 (0.1) vs. 1.8 (0.2) vs. 3.63 (0.1), p=0.001 3 months: 1.7 (0.1) vs. 1.9 (0.2) vs. 3.2 (0.2), p=0.001 6 months: 1.7 (0.1) vs. 2.2 (0.2) vs. 2.7 (0.2), p=0.006 12 months: 1.8 (0.2) vs. 2.3 (0.3) vs. 2.5 (0.3), p=0.172 CGI-I Baseline: 3.2 (0.2) vs. 3.1 (0.1) vs.2.9 (0.1), p=0.171 1 month: 1.3 (0.1) vs. 1.2 (0.1) vs. 2.8 (0.2), p=0.001 3 months: 1.2 (0.1) vs. 1.2 (0.1) vs. 2.3 (0.1), p=0.001

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
						6 months: 1.2 (0.1) vs. 1.3 (0.1) vs. 2.1 (0.2), p=0.001 12 months: 1.3 (0.1) vs. 1.5 (0.2) vs. 1.9 (0.2), p=0.082

CRPS = complex regional pain syndrome; F/U = Follow-up; GPE = Global perceived effect; ITT = intention to treat; MPQ = McGill Pain Questionnaire; NR = not reported; PT = physical therapy; QoL = Quality of life; RCT = randomized controlled trial; SCS = spinal cord stimulation; SD = standard deviation; VAS = visual analog scale.
*GPE scores range from 1 to 7 and are defined as follows: 1 = worst ever, 2 = much worse, 3 = worse, 4 = not improved and not worse, 5 = improved, 6 = much improved, 7 = best ever
†Canos-Verdecho, 2021: P-values provided derived from ANOVA or chi-squared test with Yates connection

Appendix Table F5. Efficacy Results: Non-randomized Studies of Interventions

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
Turner 2010	104 weeks	SCS vs. pain clinic vs. usual care *Modified per-protocol analysis** **≥2-point improvement in RDQ score, % (n/N):** 104 weeks: 51% (22/43) vs. 41% (14/34) vs. 44% (27/61) **RDQ score, mean (SD)** Baseline: 21.1 (2.1) vs. 20.1 (2.5) vs. 20.0 (2.4) 104 weeks: 18.1 (4.8) vs. 17.9 (4.7) vs. 17.5 (5.1)	SCS vs. pain clinic vs. usual care *Modified per-protocol analysis** **≥50% VAS leg pain relief, % (n/N)** 104 weeks: 16% (7/43) vs. 15% (5/34) vs. 21% (13/61) **VAS leg pain score, mean (SD):** Baseline: 7.7 (10.0) vs. 7.3 (1.1) vs. 7.2 (1.1) 104 weeks: 6.3 (2.0) vs. 6.2 (2.1) vs. 5.7 (2.1)	SCS vs. pain clinic vs. usual care *Modified per-protocol analysis** **≤50% reduction in VAS leg pain; RDQ improvement of ≥2 points; and less than daily opioid usage** 104 weeks: 5% (2/43) vs. 3% (1/34) vs. 10% (6/61) *Per-protocol analysis** **≤50% reduction in VAS leg pain; RDQ**	SCS vs. pain clinic vs. usual care *Modified per-protocol analysis** **Less than daily opioid usage, % (n/N):** 104 weeks: 21% (9/43) vs. 32% (11/34) vs. 34% (21/61) **Medications taken in past month for leg/back pain‡, % (n/N)** Opioid: 84% (36/47) vs. 74% (25/34) vs. 71% (43/61) Benzodiazepine/sedative-hypnotic/anti-anxiety: 19%	SCS vs. pain clinic vs. usual care *Modified per-protocol analysis** **SF-36 Mental Health, mean (SD)** Baseline: 33.6 (12.4) vs. 32 (13.1) vs. 35.6 (10.4) 104 weeks: 38.7 (13.7) vs. 36.8 (11.9) vs. 36.3 (12.9)

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
		Adjusted† mean difference (SCS vs. pain clinic): 0.5 (95% CI -1.4 to 2.4) Adjusted mean difference SCS vs. usual care): 0.1 (95% CI -1.6 to 1.7) **Ability to perform daily tasks, % (n/N)** 104 weeks: Much/somewhat better: 33% (14/43) vs. 21% (7/34) vs. 26% (16/61) About the same: 34% (15/43) vs. 32% (11/34) vs. 41% (25/61) Much/somewhat worse: 33% (14/43) vs. 47% (16/34) vs. 33% (20/61) **≥2-point improvement in RDQ score, % (n/N):** 104 weeks (SCS vs. pain clinic only) 61% (16/27) vs. 47% (10/22 **Working, % (n/N)** 104 weeks (SCS vs. pain clinic only) : 30% (8/27) vs. 26% (6/22) **Claim closed, % (n/N)**	Adjusted† MD (SCS vs. pain clinic): 0.4 (95% CI -0.6 to 1.3) Adjusted MD (SCS vs. usual care): -0.2 (95% CI -1.0 to 0.6) **VAS back pain score, mean (SD)** 104 weeks: 6.6 (1.8) vs. 6.6 (1.8) vs. 6.3 (2.3) *Per-protocol analysis** **≥50% VAS leg pain relief, % (n/N):** 104 weeks (SCS vs. pain clinic only): 30% (8/27) vs. 26% (6/22)	**improvement of ≥2 points; and less than daily opioid usage** 104 weeks (SCS vs. pain clinic): 9% (2/27) vs. 5% (1/22)	(8/47) vs. 15% (5/34) vs. 20% (12/61) Muscle relaxant: 37% (16/47) vs. 27% (9/34) vs. 25% (15/61) Antidepressant: 16% (7/47) vs. 12% (4/34) vs. 15% (9/61) Anticonvulsant: 33% (14/47) vs. 6% (2/34) vs. 16% (10/61) Non-opioid analgesic: 23 % (10/47) vs. 21% (7/34) vs. 18% (11/61) *Per-protocol analysis** **Less than daily opioid usage, % (n/N)** 104 weeks (SCS vs. pain clinic only): 17% (5/27) vs. 42% (9/22)	

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
		104 weeks (SCS vs. pain clinic only): SCS: 30% (8/27) vs. 45% (10/22)				
Perez 2021	104 weeks	SCS vs. CMM **ODI, % (95% CI)[§]** Baseline: 59.37% (95% CI 55% to 65%) (n=39) vs. 50.87% (95% CI 47% to 55%) (n=45), MD 8.5, p=0.63 12 weeks: 39.64% (95% CI 33% to 43%) (n=38) vs. 43.82% (95% CI 38% to 50%) (n=39), p=0.36 26 weeks: 36.4% (95% CI 29.8% to 34%) (n=36) vs. 46.71% (95% CI 40% to 54%) (n=34), p=0.04 52 weeks: 38.48% (95% CI 33% to 45%) (n=34) vs. 44.94% (95% CI 38% to 53%) (n=30), p=0.21 78 weeks: 37.07% (95% CI 29.8% to 44%) (n=34) vs. 34.57% (95% CI 25% to 37%) (n=28), p=0.51 104 weeks: 35.4% (95% CI 37.5% to 43%) (Δ score from baseline -	SCS vs. CMM **PD-Q, mean (95% CI)[§]** Baseline: 19.49 (95% CI 17.5 to 22) (n=39) vs. 14.56 (95% CI 13 to 16.5) (n=45), MD 4.93, p=0.0008 12 weeks: 12.42 (95% CI 9.5 to 15.2) (n=38) vs. 12.87 (95% CI 10 to 16) (n=39), p=0.74 26 weeks: 11.3 (95% CI 8.7 to 14) (n=36) vs. 14.65 (95% CI 11.4 to 17.5) (n=34), p=0.08 52 weeks: 11.53 (95% CI 9 to 14) (n=34) vs. 12.13 (95% CI 9 to 15.1) (n=30), p=0.87 78 weeks: 10.15 (95% CI 7.5 to 13) (n=34) vs. 10.64 (95% CI 7.6 to 14.2) (n=28), p=0.75 104 weeks: 9.3 (95% CI 7 to 12) (n=33) (Δ score from baseline -9.79, p<0.001) vs. 14.08 (95% CI 10.2 to 18) (Δ score from baseline -0.64,	SCS vs. CMM **Significantly different reduction of 30% in pain at present moment, % (n/N)[**]** 104 weeks: 51% (15/29) vs. 11% (3/23), p<0.001 **Significantly different reduction of 30% in strongest pain in the past month, % (n/N)[**]** 104 weeks: 41% (12/29) vs. 2% (<1/23), p<0.001 **Significantly different reduction of 30% in average intensity of pain in the past month, % (n/N)[**]** 104 weeks: 51% (15/29) vs. 9% (2/23), p<0.001 **Significant reduction of 50% in pain at the**	SCS vs. CMM **Opioid use, % (n/N)[††]** Baseline: 79.49% (31/39) vs. 39.58% (19/46), p=0.0004 104 weeks: 31% (n=NR) vs. 25% (n=NR), p=0.72 No other differences were significant between baseline and 104 weeks for all other pharmacological treatment.	SCS vs. CMM **EQ-5D-3L, mean (95% CI)[§]** Baseline: 0.22 (95% CI 0.13 to 0.33) (n=39) vs. 0.32 (95% CI 0.23 to 0.42) (n=45), MD -0.1, p=0.15 12 weeks: 0.41 (95% CI 0.3 to 0.42) (n=36) vs. 0.43 (95% CI 0.43 to 0.45) (n=37), p=0.83 26 weeks: 0.5 (95% CI 0.48 to 0.63) (n=34) vs. 0.35 (95% CI 0.24 to 0.48) (n=33), p=0.07 52 weeks: 0.52 (95% CI 0.39 to 0.65) (n=33) vs. 0.46 (95% CI 0.34 to 0.58) (n=28), p=0.50 78 weeks: 0.51 (95% CI 0.39 to 0.63) (n=31) vs. 0.41 (95% CI 0.25 to 0.55) (n=21), p=0.30 104 weeks: 0.63 (95% CI 0.52 to 0.74) (n=30) (Δ score from baseline 0.39, p<0.001) vs. 0.34 (95% CI 0.2 to 0.48) (n=23) (Δ score from baseline -0.01, p>0.05), MD -8.52 p=0.0029 **EQ-VAS, mean (95% CI)[§]**

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
		23.25, p<0.001) (n=33) vs. 43.92% (95% CI 35% to 52.5%) (Δ score from baseline -6.47, p>0.05) (n=25), MD -8.52, p=0.21 **Ability to endure without painkillers, % (n=NR)** Baseline: 0% (n=NR) vs. 17.8% (n=NR) 104 weeks: 21.4% (n=NR) vs. 13% (n=NR)	p>0.05) (n=25), MD -4.78, p=0.051 **Pain at present moment**[**] 104 weeks: Δ score from baseline -3.31 (p<0.001) vs. -0.52 (p>0.05) **Strongest pain during the past week**[**] 104 weeks: Δ score from baseline -3.34 (p<0.001) vs. -0.7 (p<0.05) **Average pain intensity during the past 4 weeks**[**] Δ score from baseline: -2.76 (p<0.001) vs. -0.48 (p>0.05)	**present moment, % (n/N)**[**] 104 weeks: 36% (10/29) vs. 4% (1/23), p<0.001 **Significant reduction of 50% in strongest pain in the past month, % (n/N)**[**] 104 weeks: 23% (7/29) vs. 0% (0/23), p<0.001 **Significant reduction of 50% in average intensity of pain the past month, % (n/N)**[**] 104 weeks: 18% (5/29) vs. 0% (0/23), p<0.01 **Reduction of ≥50% pain, % (n=NR)** 104 weeks: 48.72% (n=NR) vs. 8.7% (n=NR), p<0.001 **Pain relief greater than 50%, % (n/N)**[‡‡] 104 weeks: 13% (n=NR) vs. NR **Pain relief greater than 60%, % (n/N)**[‡‡]		Baseline: 21.36 (95% CI 13 to 29) (n=39) vs. 17.62 (95% CI 10 to 26) (n=45), MD 3.74 p=0.51 12 weeks: 38.58 (95% CI 28 to 49.5) (n=36) vs. 22.62 (95% CI 13 to 32), p=0.02 26 weeks: 45.56 (95% CI 35 to 57) (n=34) vs. 20.42 (95% CI 13 to 29) (n=33), p=0.0063 52 weeks: 36.15 (95% CI 26 to 47) (n=33) vs. 29.21 (95% CI 18 to 40) (n=28), p=0.35 78 weeks: 42.48 (95% CI 30.5 to 55) (n=31) vs. 40.52 (95% CI 28 to 54) (n=21), p=0.76 104 weeks: 46.3 (95% CI 36 to 57) (n=30) (Δ score from baseline 24.97, p<0.001) vs. 27.13 (95% CI 17 to 37) (n=23) (Δ score from baseline 12.39, p<0.05), MD 19.17 p=0.0081 **HADS, mean (SD NR)** Baseline: 21.33 (NR) vs. 19.39 (NR) 104 weeks: 9.72 (NR) (n=26) (Δ score from baseline -11.62, p<0.001) vs. 8.61 (NR) (n=23) (Δ score from baseline -10.78, p<0.001), MD 1.11 p>0.05 **HADS Anxiety** 12 weeks: No difference between SCS vs. CMM.

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
				104 weeks: 71% (n=NR) vs. NR **Pain relief greater than 70%, % (n/N)‡‡** 104 weeks: 16% (n=NR) vs. NR		26 weeks: No difference between SCS vs. CMM. 52 weeks: No difference between SCS vs. CMM. 78 weeks: No difference between SCS vs. CMM. 104 weeks: Δ score from baseline -5.77 (p<0.001) vs. -5.61 (p<0.001), No difference between SCS vs. CMM from baseline to 104 weeks. MD 0.6, p>0.05 **HADS Depression** 12 weeks: No difference between SCS vs. CMM. 26 weeks: No difference between SCS vs. CMM. 52 weeks: No difference between SCS vs. CMM. 78 weeks: 78 weeks: Difference between SCS vs CMM, p=0.0249. 104 weeks: Δ score from baseline -5.85 (p<0.001) vs. -5.17 (p<0.001), No difference between SCS vs. CMM from baseline to 104 weeks. MD 0.51, p>0.05
Dhruva 2023	104 weeks	NR	NR	NR	SCS vs. CMM, *propensity matched analyses* **Number of opioid scripts, mean (SD)** 52 weeks: 8.9 (7.8) (n=1,260) vs. 8.2 (8.2) (n=6,300)	NR

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
					13 to 104 weeks: 7.4 (7.6) (n=1,260) vs. 7.4 (8.0) (n=6,300) **Chronic opioid use** 52 weeks: 54.9% (692/1260) vs. 51.8% (3260/6300)), adjusted[§§] OR 1.14 (95% CI 1.01 to 1.29) 13 to 104 weeks: 49% (617/1260)vs. 47.6% (2998/6300), adjusted[§§] OR 1.06 (95% CI 0.94 to 1.20) **Long-acting opioid use** 52 weeks: 22.5% (282/1260) vs. 18.5% (1165/6300), adjusted[§§] OR 1.28 (95% CI 1.11 to 1.49) 13 to 104 weeks: 18.3% (231/1260)) vs. 16.3% (1028/6300), adjusted[§§] OR 1.16 (95% CI 0.99 to 1.36) **High MME** 52 weeks: 64.7% (815/1260) vs. 50.3% (3169/6300), adjusted[§§] OR 1.81 (95% CI 1.60 to 2.04) 13 to 104 weeks: 44.7% (563/1260) vs. 43.7% (2755/6300), adjusted[§§] OR 1.04 (95% CI 0.92 to 1.18) **Opioid discontinuation (among patients taking**	

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
					opioids during 6-month baseline period) 52 weeks: 3.1% (31/996) vs. 10% (385/4858), p<0.001 13 to 104 weeks: 17.1% (170/996) vs. 18% (876/4858), p=0.47 1-104 weeks: 2.1% (21/966) vs. 5.9% (285/4858), p<0.001 **Average MME, (mean SD)** 52 weeks: 33.0 (60.7) (n=1260) vs. 33.6 (66.4) (n=6300) 104 weeks: 27.1 (49.2) (n=1260) vs. 28.5 (56.8) (n=6300)	
Vu 2022	12 to 65 weeks	NR	NR	NR	SCS vs. no SCS[***] **Odds of being opioid-naïve at follow-up** 65 weeks: adjusted[†††] OR 0.90 (95% CI 0.85 to 0.96) **Odds of being on long-term opioids (LOT)[‡‡‡] at follow-up (12-65 weeks),*propensity score adjusted analyses:*** Primary analysis (≥6 prescriptions/year) *Patients on opioids* (n=5,607 vs. 56,034): adjusted[†††] OR 0.93 (95% CI 0.87 to 0.98)	NR

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
					Opioid naïve patients (n=16,766 vs. 167,636): adjusted[†††] OR 0.92 (95% CI 0.87 to 0.98) <u>Most stringent analysis (≥10 prescriptions/year)</u> *Patients on opioids* (n=4,783vs. 47,780): adjusted[†††] OR 0.93 (95% CI 0.87 to 0.98) *Opioid naïve patients*[§§§] (n=16,255 vs. 162,539): adjusted[†††] OR 0.87 (95% CI 0.81 to 0.95) <u>Most liberal definition (≥4 prescriptions/year) of LOT analysis</u> *Patients on opioids* (n=6,013 vs. 60,094): adjusted[†††] OR 0.94 (95% CI 0.89 to 1.00) *Opioid naïve patients* (n=17,334 vs. 173,328): adjusted[†††] OR 0.98 (95% CI 0.93 to 1.03) **Reduction in long-term opioid use** 65 weeks: unadjusted OR 0.93 (95% CI 0.87 to 0.98)	

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
					Patients that were opioid-naïve at baseline[****] **Patients requiring long-term opioid treatment** 65 weeks: 7.6% (n=NR) vs. 7.0% (n=NR), mean difference -0.6% (95% CI -1.0% to -0.2%) **Patient odds of starting long-term opioid use** 65 weeks: unadjusted OR 0.92 (95% CI 0.87 to 0.98) Patients on long-term opioid treatment at baseline **Patients requiring long-term opioid treatment** 65 weeks: 69.2% (n=6225) vs. 70.3% (n=74,585), mean difference -1.1% (95% CI -2.3% vs. 0.2%)	
Lad 2014	104 weeks	NR	NR	NR	SCS vs. reoperation Unmatched cohort (n=111 vs. n=6386) **Number of prescription medications filled, mean (SD)** 52 weeks: 45 (42) vs. 43 (40) 104 weeks: 92 (86) vs. 84 (78) **Post-op opioid use**	NR

Author (year)	F/U	Function	Pain	Success	Opioid Use	Secondary Outcomes In this order: • GPE/global impression of change • QoL • Anxiety and Depression • Patient Satisfaction
					52 weeks: 66.7% (74/111) vs. 67.9% (4334/6386) 104 weeks: 71.2% (79/111) vs. 71.2% (4544/6386) <u>Matched cohort (n=111 vs. n=111)</u>†††† **Number of prescription medications filled, mean (SD)** 52 weeks: 45 (42) vs. 38 (34), p=0.42 104 weeks: 92 (86) vs. 75 (71), p=0.28 **Post-op opioid use** 52 weeks: 66.7% (74/111) vs. 65.8% (73/111), p=0.89 104 weeks: 71.2% (79/111) vs. 66.7% (74/111), p=0.47	

CI = confidence interval; CMM = conventional medical management; F/U = follow-up; HADS = Hospital Anxiety and Depression Scale; MD = mean difference; NR = not reported; NRSI = non-randomized studies of intervention; NSAIDs = Non-steroid anti-inflammatory drugs; OR = odds ratio; PC = pain clinic; PD-Q = PainDETECT Questionnaire; RDQ = Roland-Morris Disability Questionnaire; SCS = spinal cord stimulator; SD = standard deviation; SF-36 = 36-item Short Form Survey; SNRI = Serotonin and norepinephrine re-uptake inhibitors; TCA = Tricyclic antidepressant; UC = usual care; VAS = visual analogue scale.

* Modified per-protocol analysis was defined by the treatment received during the first year of the study: SCS (only trial stimulation was required); PC (pain clinic evaluation performed), and UC (patients did not undergo SCS trial or PC evaluation). Per-protocol analysis was used to compare SCS (patients underwent permanent implantation of SCS device) vs PC (some pain clinic treatment was received).

† Adjusted for baseline differences between groups in the following characteristics: age, gender, RDQ score, leg pain intensity, duration of work time loss compensation, disability benefit other than workers' compensation, unilateral vs bilateral leg pain, legal representation, and SF-36 mental health scores.

‡ Adjusted for baseline value of the outcome measure being assessed.

§ 95% confidence intervals very crudely estimated from figures. Difficult to be precise to due the quality of images.

** Authors report figures for pain at present moment, strongest pain during the past month, and average pain during the past month for each follow-up, but figures are too distorted to estimate from.

†† Authors report that SCS patients were offered pharmacological treatment throughout the trial, but n's are only reported at baseline.

‡‡. Presented as is reported by authors in text. Unclear if these are not cumulative rates.
§§ Propensity score matching balanced baseline characteristics by modeling the probability of receiving permanent SCS vs. CMM as a function of 65 baseline predictors among patients with 52 weeks or longer follow-up. Variables assessed for associated with SCS included: CMM, index calendar year, and demographic characteristics, clinician specialty for cohort entry, 31 medical and mental health comorbidities using the Elixhauser index, and additional pain-related musculoskeletal conditions using the Chronic Conditions Data Warehouse algorithm. A greedy matching algorithm with a caliper width of 20% of the SD of the logit of the propensity score was used. To balance cohort entry diagnosis, matching was performed separately within patients with or without FBSS.
*** At baseline defined opioid-naive patients as those who received at most 2 opioid prescriptions in the year prior to PLS index date or an SCS implant to account for prescriptions written for nonspinal indications (eg, procedures, injuries), whereas LOT was defined as receiving at least 6 opioid prescriptions in this time frame
At the primary end point, we defined patients on LOT as those who received at least 6 opioid prescriptions within the 12-month period of 3 to 15 months after their PLS index date and/or SCS implant to control for opioid prescriptions provided in the 3-month postsurgical period and because many patients receive more than a 1-month supply of opioid medications in a single prescription (particularly with out-of-state telehealth) or receive prescriptions from out-of-network clinicians during vacations or stays at secondary residences.
††† Propensity score matching included similar covariates asin multivariable logistic regression and defined the distance with logistic regression using the nearest neighbor method and selected matches within caliper distance of 0.2 SD of the logit propensity score, with a matching ratio of 1:10 without replacement. Covariates included age, Charlson Score, Sex, race, smoking status, alcohol abuse, depression disorder, anxiety diagnosis, psychosis diagnosis, antidepressant use, benzodiazepine use, and antipsychotics use.
‡‡‡ Clinically questionable according to authors.
§§§ Defined as receiving at most 2 opioid prescriptions per year.
**** Defined as receiving at least 6 opioid prescription per year.
†††† Propensity score calculated using a multivariate logistic regression with surgery type as the outcome and age, year of surgery, Charlson index, postoperative follow-up time, and insurance as predictors and using the SAS macro with greedy algorithm.

Appendix Table F6. Safety Results: Parallel RCTs for CLBP (No Surgery) and FBSS

Author (year)	F/U	Revisions and Removals	Other SCS device related complications or side effects	Complications unrelated to SCS	Mortality
Kapural, 2022	6 months	*As treated analysis*: SCS + CMM (n=145) vs. NR **Explantation due to SAE**: 2.07% (3/145) vs. NR **Explantation due to loss of efficacy**: 0% (0/145) **Lead Revision (3 due to dislodgement, 2 due to lack of therapeutic effect)**: 3.45% (5/145) vs. NR	*As treated analysis*: SCS + CMM (n=145) vs. NR **Any serious SCS related AE**: 3.45% (5/145) vs. NR **Any SCS/study related AE**: 24.14% (35/145) vs. NR **Serious AE**	*ITT analysis*: SCS + CMM (n=83) vs. CMM (n=76) **Withdrawal due to AE**: 3.61% (3/83) vs. 0% *As treated analysis*: SCS + CMM (n=145) vs. NR	NR

Author (year)	F/U	Revisions and Removals	Other SCS device related complications or side effects	Complications unrelated to SCS	Mortality
		Serious AE Implant site infection (leading to explantation and reimplantation): 1.38% (2/145) vs. NR Poor wound healing (lead to explant): 0.69% (1/145) vs. NR	Osteomyelitis (did not receive permanent implant): 0.69% (1/145) vs. NR	**Withdrawal due to AE**: 2.76% (4/145) vs. 0% **Serious AE** Lethargy (narcotics related): 0.69% (1/145) vs. NR	
Rigoard, 2019	6 months	**Surgical intervention to address AE**: 11.8% (12/102) vs. NR Implant site infection requiring surgery: 4.9% (5/102) vs. NR Implant site pain requiring surgery: 1.0% (1/102) vs. NR Device deployment issue requiring surgery: 2.0% (2/102) vs. NR Device battery issue requiring surgery: 1.0% (1/102) vs. NR Device stimulation issue requiring surgery: 2.0% (2/102) vs. NR Paresthesia requiring surgery: 2.0% (2/102) vs. NR	**Any serious SCS related AE**: 12.7% (13/102) vs. NR* **Any SCS/study related AE**: 17.6% (18/102) vs. NR	**Withdrawal due to AE**: 1.0% (1/102) vs. 0.9% (1/107) *ITT analysis* **Any AE - non-SCS related**: 36.4% (40/110) vs. 40.7% (44/108) *PP analysis* **Any AE - non-SCS related**: 43.5% (40/92) vs. 42.3% (44/104)	None
North, 2020	6 months	NR	Surgical site infection (seven overt implant site infections with wound breakdown, one implant site cellulitis, and one extradural abscess. In four patients, the infection was identified after implantation of the complete SCS system): 5.2% (9/174) vs. NR *>10 day implant trial vs. <=10 day implant trial* **Surgical site infection 90 days**: 24.1% (7/29) vs. 1.4% (2/145)	NR	NR

Author (year)	F/U	Revisions and Removals	Other SCS device related complications or side effects	Complications unrelated to SCS	Mortality
Kumar, 2007	12 months	*Any patient receiving electrode/permanent implant (n=84)* **Total device-related surgery**: 24% (20/84) • Lead migration: 10% (8/84) • Lead/extension fracture/torqued contacts: 1% (1/84) • IPG migration: 1% (1/84) • Loss of therapeutic effect/loss of paresthesia/unpleasant paresthesia: 1% (1/84) • Issue with surgical technique: 5% (4/84) • Infection/wound breakdown: 6% (5/84) • Pain at IPG/incision site: 1% (1/84)	*Any patient receiving electrode/permanent implant (n=84)* **Total device-related complications**: 32% (27/84) **Lead/extension fracture/torqued contacts**: 1% (1/84) **Loss of therapeutic effect/loss of paresthesia/unpleasant paresthesia**: 6% (5/84) **Infection/wound breakdown**: 2% (2/84) **Pain at IPG/incision site**: 5% (4/84) **IPG pocket fluid collection**: 5% (4/84)	*Adverse event group*: SCS (n=52) vs. CMM (n=48) **Withdrawal due to AE**: NR **At least 1 non-SCS related AE**: 35% (18/52) vs. 52% (25/48) • At least 1 drug AE: 4% (2/52) vs. 21% (10/48) • At least 1 extra pain event: 0% vs. 4% (2/48) • At least 1 new illness/injury/condition: 25% (13/52) vs. 23% (11/48) • At least 1 worsening of pre-existing condition: 13% (7/52) vs. 15% (7/48)	
Manca, 2008	6 months	*As randomized*: SCS (n=52) vs. CMM (n=48) **Device-related surgery**: 25% (13/52) vs. N/A **Lead replacement**: 4% (2/52) vs. N/A **IPG reprogramming**: 73% (36/52) vs. N/A	*As randomized*: SCS (n=52) vs. CMM (n=48) **Hospitalization**: 23% (12/52) vs. N/A	*As randomized*: SCS (n=52) vs. CMM (n=48) **Withdrawal due to AE**: NR	NR
Kumar, 2008	24 months	*Received SCS (n=42)* **Total requiring surgical revision**: 31% (13/42) • Electrode migration: 14% (6/42) • Lead/extension fracture/torqued contacts: 2% (1/42) • IPG migration: 2% (1/42)	*Received SCS (n=42)* **Lead/extension fracture/torqued contacts**: 5% (2/42)	*Received SCS (n=42)* **Withdrawal due to AE**: NR **New injury/illness/condition related to FBSS pain**: 17% (7/42)	NR

Author (year)	F/U	Revisions and Removals	Other SCS device related complications or side effects	Complications unrelated to SCS	Mortality
		• Loss of therapeutic effect/loss of paresthesia/unpleasant paresthesia: 5% (2/42) • Issue with surgical technique: 5% (2/42) • Infection/wound breakdown: 5% (2/42) • Pain at IPG/incision site: 2% (1/42)	**Loss of therapeutic effect/loss of paresthesia/unpleasant paresthesia**: 7% (3/42) **Infection/wound breakdown**: 5% (2/42) **Pain at IPG/incision site**: 10% (4/42) **IPG pocket fluid collection**: 5% (2/42)	**Worsening of pre-existing condition related to FBSS pain**: 17% (7/42)	

AE = Adverse event; CLBP = Chronic low back pain; CMM = Conventional medical management; FBSS = Failed back surgery syndrome; f/u = follow-up; IPG = Implantable pulse generator; ITT = Intention-to-treat; NR = Not reported; PP = Per protocol; SCS = Spinal cord stimulator.
* Additional supp table (S10) with different data.

Appendix Table F7. Safety Results: Parallel RCTs for PDN

Author (year)	F/U	Revisions and Removals	Other SCS device related complications or side effects	Complications unrelated to SCS	Mortality
De Vos 2014	26 weeks	*ITT analysis* SCS + CMM (n=40) vs. CMM (n=20) **Revision** 26 weeks: 5% (2/40)* vs. 0% (0/20)	*ITT analysis* SCS + CMM (n=40) vs. CMM (n=20) **Any AE** 26 weeks: 7 events vs. 0 events **Pain due to implanted pulse generator** 26 weeks: 5% (2/40) vs. 0% (0/20) **Electrode lead migration** 26 weeks: 3% (1/40) vs. 0% (0/20) **Coagulopathy** 26 weeks: 3% (1/40)† vs. 0% (0/20)	*ITT analysis* SCS + CMM (n=40) vs. CMM (n=20) **Any AE** 26 weeks: 4 events vs. 6 events **Infection during trial stimulation** 26 weeks: 5% (2/40) vs. 10% (2/20) **Femur fracture** 26 weeks	NR

Author (year)	F/U	Revisions and Removals	Other SCS device related complications or side effects	Complications unrelated to SCS	Mortality
			Incomplete overlap of paresthesia with painful area during trial stimulation 26 weeks: 5% (2/40) vs. 0% (0/20)	26 weeks: 3% (1/40) vs. 0% (0/20) **Cardiac arrest** 26 weeks: 3% (1/40) vs. 0% (0/20) **MI** 26 weeks: 0% (0/40) vs. 5% (1/20) **Atrial fibrillation** 26 weeks: 0% (0/40) vs. 5% (1/20) **Coronary bypass surgery** 26 weeks: 0% (0/40) vs. 5% (1/20) **Carotid artery stenosis** 26 weeks: 0% (0/40) vs. 5% (1/20)	
Duarte 2016	26 weeks	NR	NR	NR	NR
Slangen 2014	26 weeks	NR	*ITT analysis* SCS + CMM (n=22) vs. CMM (n=14) **Serious AEs** 26 weeks: 9.1% (2/22)‡ vs. 0% (0/14) **Withdrawel due to AE**	NR	*ITT analysis* SCS + CMM (n=22) vs. CMM (n=14) **Mortality**

Author (year)	F/U	Revisions and Removals	Other SCS device related complications or side effects	Complications unrelated to SCS	Mortality
			26 weeks: 9.1% (2/22) vs. 0% (0/14) **Dural puncture leading to postdural puncture headache** Baseline: 5% (1/22)[§] vs. 0% (0/14) **Infection** 6 weeks: 5% (1/22)[**] vs. 0% (0/14)		5% (1/22)[††] vs. 0% (0/14)
Van Beek 2015 [24-month f/u of Slangen 2014 RCT]	103 weeks	SCS + CMM (n=17) **New pulse generator implanted** 103 weeks 11.8% (2/17) **Stimulation lead revision** 103 weeks 23.5% (4/17) **SCS explant** 6 weeks: 5.8% (1/17)[‡‡]	SCS + CMM (n=17) **Infection** 6 weeks: 5.8% (1/17)[§§]		NR
Peterson 2021	26 weeks	*ITT analysis* SCS + CMM (n=113) vs. CMM (n=103) **Device explant due to infection** 26 weeks: 2% (2/90) vs. 0% (0/103)	*ITT analysis* SCS + CMM (n=113) vs. CMM (n=103) **Any AE** 26 weeks: 12.4% (14/113) vs. 0% (0/103) **Serious AEs (not defined)** 26 weeks: 1.8% (2/113) vs. 0% (0/103) **Withdrawal due to AE**	NR	NR

Author (year)	F/U	Revisions and Removals	Other SCS device related complications or side effects	Complications unrelated to SCS	Mortality
			26 weeks: 5.3% (6/113) vs. 1.9% (2/103) **Stimulation related neurological deficits** 26 weeks: 0% (0/90) vs. 0% (0/103) **Infection** 26 weeks: 2.7% (3/113) vs. 0% (0/103) **Wound dehiscence** 26 weeks: 1.8% (2/113) vs. 0% (0/103) **Impaired healing** 26 weeks: 0.9% (1/113) vs. 0% (0/103) **Device extrusion** 26 weeks: 0.9% (1/113) vs. 0% (0/103) **Incision site pain** 26 weeks: 0.9% (1/113) vs. 0% (0/103) **Implantable pulse generator site discomfort** 26 weeks: 0.9% (1/113) vs. 0% (0/103) **Lead migration** 26 weeks: 0.9% (1/113) vs. 0% (0/103)		

Author (year)	F/U	Revisions and Removals	Other SCS device related complications or side effects	Complications unrelated to SCS	Mortality
			Contact dermatitis 26 weeks: 0.9% (1/113) vs. 0% (0/103) **Urticaria** 26 weeks: 0.9% (1/113) vs. 0% (0/103) **Radiculopathy** 26 weeks: 0.9% (1/113) vs. 0% (0/103) **Uncomfortable stimulation** 26 weeks: 0.9% (1/113) vs. 0% (0/103) **Gastroesophageal reflux** 26 weeks: 0.9% (1/113) vs. 0% (0/103) **Myalgia** 26 weeks: 0.9% (1/113) vs. 0% (0/103) **Arthralgia** 26 weeks: 0.9% (1/113) vs. 0% (0/103) **Hyporeflexia** 26 weeks: 0.9% (1/113) vs. 0% (0/103)		
Petersen 2022	52 weeks	SCS + CMM (n=90) + SCS crossover (n=64) group (N=154)***	SCS + CMM (n=90) + SCS crossover (n=64) group (N=154)***	NR	NR

Author (year)	F/U	Revisions and Removals	Other SCS device related complications or side effects	Complications unrelated to SCS	Mortality
[12-month f/u of Petersen 2021 RCT]		**Surgical explant due to infection** 52 weeks: 3.2% (5/154) **Surgical explant due to loss of efficacy** 52 weeks: 0% (0/154) **SCS location revision** 52 weeks: 1.3% (2/154)††† **Lead migration requiring further revision** 52 weeks: 0.6% (1/154)†††	**Infections** 52 weeks: 5.2% (8/154)		
Petersen 2023	104 weeks	SCS + CMM (n=84) + SCS crossover (n=58) (N=134) **Device explants due to lack of efficacy**: 0% (0/134) Cumulative (N=154) **Device explants due infection**: 3.2% (5/154), 4 patients exited the study while 1 continued after reimplantation. **Revision surgery to:** **reposition or replace IPG**: 3.2% (5/154); **reposition or replace lead due to migration**: 1.9% (3/154)	SCS + CMM (n=84) + SCS crossover (n=58) (N=134) **Stimulation-related neurological deficits**: 0% (0/134) Cumulative (N=154) **Study related serious AE (not defined)**: 4.5% (7/154) **Procedure related infection**: 5.2% (8/154)	NR	Cumulative (N=154) **Mortality unrelated to device**: 1.9% (3/154)

AE = Adverse event; CMM = conventional medical management; F/U = follow-up; ITT = intention-to-treat; MI = myocardial infarction; NR = not reported; PDN = painful diabetic neuropathy; SCS = spinal cord stimulator.
* 1 Due to the electrode lead migration, 1 due to incomplete overlap of parasthesia during trial stimulation.
† Coagulopathy complicated the implantation and resulted in prolonged hospitalization.
‡ 1 death, 1 infection during explant.
§ This occurred during the trial stimulation. This same patient eventually died.
** This patient recovered, but not fully, and developed an autonomic neuropathy.
†† This is the same patient as the dural puncture. The dural puncture lead to a large subdural hematoma; the patient fell into a coma and never woke up.
‡‡ This is the same patient that had an infection at 6 weeks; and is also reported in Slangen 2014.
§§ This is the same patient as reported in Slangen 2014.
*** Does not differentiate between patients before and after crossover.

††† 3 patients in total had revision surgery.

Appendix Table F8. Safety Results: Parallel RCTs for CRPS

Author (year)	F/U	Revisions and Removals	Other SCS device related complications or side effects	Complications unrelated to SCS	Mortality
Kemler 2000	6 months	*SCS group, permanent implant received* (24/24 available):* **Summary:** 11 total complications requiring revision occurred in 25% of patients (6/24) **Revision of electrode:** • Repositioning of electrode: 21% (5/24) ○ successful in 4/5 in 1 procedure ○ 1/5 required 3 procedures • Replacement of electrode: 4% (1/24) ○ due to defective electrode **Revision of pulse generator**: 8% (2/24) • due to painful pulse generator pocket **Total removal and reimplantation of system**: 4% (1/24) • due to clinical signs of infection (implant removed, antibiotics given, reimplantation performed when patient recovered)	*SCS group, implant received* (24/24 available):* **Complications (not leading to revision) include:** • Dural puncture: 8% (2/24) ○ associated headache: 1/2	NR	**Mortality:** 0% (0/36) vs. 0% (0/18)
Kemler 2004 [f/u of Kemler 2000 RCT]	24 months	*SCS group, permanent implant received* (24/24 available):* **Cumulative** **Summary:** 22 total complications requiring revision occurred in 37.5% of patients (9/24) **Revision of electrode:**	*SCS group, implant received* (24/24 available):* **Side effects** • Change of amplitude by bodily movements: 79.2% (19/24) • Paresthesiae in other body parts: 54.2% (13/24)	NR	**Mortality** 0% (0/36) **vs.** 0% (0/18)

Author (year)	F/U	Revisions and Removals	Other SCS device related complications or side effects	Complications unrelated to SCS	Mortality
		• Repositioning of electrode: 33.3% (8/24) • Replacement of electrode: 8.3% (2/24) **Revision of pulse generator**: 29.2% (7/24) **Total removal and reimplantation of system**: 4% (1/24) **Explantation of system**: 12.5% (3/24)	• Pain/irritation from extension lead/plug: 45.8% (11/24) • Pain/irritation from pulse generator: 41.7% (10/24) • More pain in other body parts: 29.2% (7/24) • Disturbed urination: 16.7% (4/24) • Movements or cramps due to elevated amplitude: 12.5% (3/24)		
Kemler 2008 [f/u of Kemler 2000 RCT]	60 months	**Cumulative** **Summary:** 29 total complications requiring revision occurred in 42% of patients (10/24) **Revision of electrode:** • Repositioning of lead: 11 instances (n=NR) • Replacement of lead: 6 instances (n=NR) **Revision/replacement of pulse generator**: 54.1% (13/24) **Total removal and reimplantation of system (infection)**: 4.2% (1/24) **Explantation of system**: 8.3% (2/24)	NR	NR	NR
Canos-Verdecho, 2021	12 months	None reported	LF-SCS (n=12) vs. 10-kHz (n=10) vs. Conventional (n=19)	None reported	None reported

Author (year)	F/U	Revisions and Removals	Other SCS device related complications or side effects	Complications unrelated to SCS	Mortality
			Parasthesias in annoying way with postural changes: 41.7% (5/12) vs. 0% vs. 0% Occipital headache: 0% vs. 10% (1/10) vs. 0% Generator discomfort: 8.3% (1/12) vs. 0% vs. 0%		

HF = High frequency; kHz = kilohertz; LF = Low frequency; NR = Not reported; RCT = Randomized control trial; SCS = Spinal cord stimulator.

* Kemler (2000, 2004, 2008): Reported complications only for patients randomized to receive SCS. Thus, the final follow-up (60 months) excluded the 4 patients randomized to CMM alone who crossed over and received permanent implants; similarly, 2 CMM patients who had crossed over by 24 months were excluded.

Appendix Table F9. Safety Results: Non-randomized Studies of Interventions

Author (year)	F/U	Revisions and Removals	Other SCS device related complications or side effects	Complications unrelated to SCS	Mortality
Turner 2010	104 weeks	N = 27 patients underwent permanent device implantation **Revision of electrode/lead:** 15% (4/27) **Revision of generator:** 11% (3/27) **Total removal and replacement of system:** 4% (1/27) **Total removal of system: 22% (6/27)***	N = 28 patients underwent attempted implantation of a permanent device **Implantation terminated due to dural puncture and CSF leak:** 4% (1/28) **Superficial skin/wound infection:** 11% (3/28) **Persistent pain over SCS components†:** 18% (5/28) N = 51 patients underwent at least trial stimulation **AE associated with trial stimulation:** 16% (8/51)	NR	SCS (n=51) vs. pain clinic (n=68) vs. usual care (39) **Mortality:** 2% (1/51) vs. 0% (0/68) vs. 0% 0/39)

Author (year)	F/U	Revisions and Removals	Other SCS device related complications or side effects	Complications unrelated to SCS	Mortality
			Symptoms of unknown etiology (ie., dizziness, increased back or leg pain): 9.8% (5/51) **Fluid leaking at electrode entry site:** 2% (1/51) **Severe post-spinal headache:** 2% (1/51) **Extensive epidural abscess that necessitated irrigation, debridement, and a T2-L3 hemilaminotomy; one day following surgery, the patient had respiratory arrest and was placed on mechanical ventilation:** 2% (1/51)		
Perez 2021		SCS vs. CMM **Underwent further neurostimulator implant** 104 weeks: 0% (0/39) vs. 4.3% (2/46) **Minor reoperations** 104 weeks: 7.7% (3/39) vs. 0% (0/46)	NR	NR	NR
Dhruva 2023	104 weeks	SCS (n=1260) **Removal and/or revision** *Any* 52 weeks: 17.2% (217/1260) 104 weeks: 22.1% (279/1260)[‡] *Revision of lead/generator* 52 weeks: 14.6% (184/1260) 104 weeks: 6.0% (75/1260) *Lead removal* 52 weeks: 7.5% (95/1260) 104 weeks: 4.0% (50/1260) *Generator removal*	SCS (n=1260) **Any SCS-related complication[§]** (other than removal or revision) 52 weeks: 14.0% (176/1260) 104 weeks: 17.9% (226/1260) *Breakdown of lead/generator* 52 weeks: 4.4.% (56/1260) 104 weeks: 1.3% (16/1260) *Displacement of lead/generator* 52 weeks: 1.8% (22/1260) 104 weeks: NA	NR	NR

Author (year)	F/U	Revisions and Removals	Other SCS device related complications or side effects	Complications unrelated to SCS	Mortality
		52 weeks: 1.8% (23/1260) 104 weeks: NA	*Infection/inflammation of lead/generator* 52 weeks: 2.1% (26/1260) 104 weeks: NA *Other mechanical complications of lead/generator* 52 weeks: 9.3% (117/1260) 104 weeks: 4.1% (51/1260)		
Vu 2022	12 to 65 weeks	NR	NR	NR	NR
Lad 2014	12 weeks	NR	NR	SCS vs. reoperation Unmatched cohort **Any complications** Index: 5.1% (20/395) vs 11.7% (18/16060) 4 weeks: 6.65% (25/376) vs. 14.35% (2225/15504) 12 weeks: 6.51% (22/338) vs. 14.42% (2074/14386) **Renal complications** Index: 1.3% (5/395) vs. 0.95% (152/16060) 4 weeks: 1.52% (6/376) vs. 1.39% (224/15504) 12 weeks: 1.52% (6/338) vs. 1.5% (241/14386) **Cardiac complications** Index: 0.76% (3/395) vs. 0.55% (89/16060)	SCS vs. reoperation Unmatched cohort **Mortality** Index: 0% (0/395) vs. 0.12% (20/16060)

Author (year)	F/U	Revisions and Removals	Other SCS device related complications or side effects	Complications unrelated to SCS	Mortality
				4 weeks: 0.76% (3/376) vs. 0.81% (130/15504) 12 weeks: 1.01% (4/338) vs. 0.87% (139/14386) **Neurological complications** Index: 0.51% (2/395) vs. 1.13% (181/16060) 4 weeks: 0.76% (3/376) vs. 1.31% (210/15504) 12 weeks: 1.01% (4/338) vs. 1.37% (220/14386) **DVT/PE** Index: 0.25% (1/395) vs. 0.76% (122/16060) 4 weeks: 0.51% (2/376) vs. 1.32% (212/15504) 12 weeks: 1.01% (4/338) vs. 1.51% (243/14386) **Pulmonary complications** Index: 0.76% (3/395) vs. 2.07% (332/16060) 4 weeks: 1.01% (4/376) vs. 2.71% (435/15504) 12 weeks: 1.27% (5/338) vs. 2.86% (460/14386) **Infection** Index: 0% (0/395) vs. 0.27% (43/16060)	

Author (year)	F/U	Revisions and Removals	Other SCS device related complications or side effects	Complications unrelated to SCS	Mortality
				4 weeks: 0% (0/376) vs. 0.66% (106/15504) 12 weeks: 0% (0/338) vs. 0.81% (130/14386) **Wound** Index: 1.27% (5/395) vs. 5.75% (923/16060) 4 weeks: 2.03% (8/376) vs. 7.29% (1170/15504) 12 weeks: 2.78% (11/338) vs. 7.60% (1221/14386)	

AE = adverse event; DVT = deep vein thrombosis; F/U = follow-up; NR = not reported; NRSI = non-randomized studies of intervention; PC = pain clinic; PE = pulmonary embolism; SCS = spinal cord stimulation; UC = usual care.
*study reported that 19% (5/27) of patients underwent total explantation of system, but another patient was apparently not included in this total and had explantation 20 months after the original implantation; this rate includes this additional patient.
† Not clear whether this lead to revision in any patients.
‡ 10% of these were without complication. Authors indicated this may have suggested lack of effectiveness.
§ Included breakdown, displacement, other complications, and infection of the lead and/or generator. Details NR.

Appendix Table F10. Summary of other pain outcomes reported by FBSS trials

Author, year	Outcome	Definition	Timing	Conv. SCS % (n/N)	CMM % (n/N)	RR (95% CI)
Rigoard, 2019 **PROMISE Study**	**LBP responder**	≥30% reduction in LBP on NPRS (0-10)	6 mos.	28.2% (31/110)	13.0% (14/108)	2.17 (1.23, 3.85)
ITT analyses		2-point improvement in LBP pain on NPRS (0-10)	6 mos.	30.9% (34/110)	12.0% (13/108)	2.57 (1.44, 4.59)

Kumar, 2007 **PROCESS Study** **ITT analysis**	**Leg pain responder**	≥30% reduction in leg pain on VAS (0-10)	6 mos.	64% (32/50)	18% (8/44)	3.52 (1.82, 6.81)
		≥80% reduction in leg pain on VAS (0-10)	6 mos.	22% (11/50)	7% (3/44)	3.23 (0.96, 10.83)

CI = Confidence interval; CMM = Conventional medical management; FBSS = Failed Back Surgery Syndrome; ITT = Intention-to-treat; LBP = Low back pain; NPRS = Numerical Pain Rating Scale; RR = Risk ratio; SCS = Spinal cord stimulator; VAS = Visual analogue scale.

Appendix Table F11. Summary of other opioid use outcomes reported by FBSS trials:

Author, year	Outcome	Timing	Response	HF (10 kHz) SCS % (n/N)	CMM % (n/N)	RR (95% CI)
Kapural, 2022 **PP analyses**	Proportion of patients modifying daily opioid dose	6 mos.	Increased	6% (4/65)	49% (37/75)	0.12 (0.05, 0.33)
			Stable	28% (18/65)	34% (26/75)	0.80 (0.48, 1.32)
			Decreased	44% (27/65)	17% (13/75)	2.40 (1.35, 4.25)
			Stopped	22% (16/65)	0% (0/75)	-

CI = Confidence interval; CMM = Conventional medical management; FBSS = Failed back surgery syndrome; HF = High-frequency; kHz = Kilohertz; PP = Per protocal; RR = Risk ratio; SCS = Spinal cord stimulator.

Appendix Table F12. Summary of other secondary outcomes reported by FBSS trials: Quality of Life

Author, year	Outcome	Timing	SCS Mean (SD)	CMM Mean (SD)	MD (95% CI)
Kapural, 2022 **HF (10 kHz) SCS** **PP analyses**	EQ-5D-5L (-0.224 to 1, best)	3 mos.	0.79 (0.14) (n=68)	0.56 (0.12) (n=75)	0.23 (0.19, 0.27)
		6 mos.	0.78 (0.11) (n=65)	0.52 (0.16) (n=75)	0.26 (0.23, 0.29)
Rigoard, 2019 **PROMISE Study**	EQ-5D-5L (-0.224 to 1, best)	6 mos.	0.49 (0.27) (n=78)	0.38 (0.27) (n=117)	0.11 (0.03, 0.19)
	EQ-VAS	6 mos.	54.1 (23.1)	50.1 (23.8)	4.00 (-2.76, 10.76)

Conventional SCS **As-treated analyses (unless otherwise indicated)**	(0-100, best)		(n=78)	(n=117)	
	SF-36 PCS (0-100, best) – *ITT analysis*	6 mos.	29.82 (9.78) (n=110)	26.06 (6.59) (n=108)	3.76 (1.53, 5.99)
	SF-36 PCS (0-100, best) – *PP analysis*	6 mos.	30.35 (9.98) (n=92)	26.00 (6.67) (n=104)	4.35 (1.98, 6.72)
	SF-36 PCS (0-100, best)	6 mos.	31.58 (10.04) (n=78)	25.66 (6.60) (n=117)	5.92 (3.58, 8.26)
	SF-36 MCS (0-100, best)	6 mos.	42.53 (14.26) (n=78)	41.38 (14.64) (n=117)	1.15 (-3.01, 5.31)
Manca, 2008 (f/u to Kumar, 2007) **ITT analyses**	EQ-5D weighted index (-0.224 to 1, best)	3 mos.	0.49 (0.31) (n=52)	0.22 (0.31) (n=48)	Adj. 0.27 (0.15, 0.39)
		6 mos.	0.47 (0.32) (n=52)	0.25 (0.30) (n=48)	Adj. 0.23 (0.12, 0.35)

CI = Confidence interval; CMM = Conventional medical management; EQ-5D = EuroQol 5D; EQ-VAS = EuroQol Visual analogue scale; f/u = follow-up; HF = High frequency; ITT = Intention-to-treat; kHz = Kilohertz; MCS = Mental component summary; MD = Mean difference; PCS = Physical component summary; PP = Per protocal; SCS = Spinal cord stimulator; SD = Standard deviation; SF-36 = 36-Item Short form.

* The utility scores were weighted against a large sample of the UK population.

† adjusted for baseline imblanace on EQ-5D weighted index score.

Appendix Table F13. Summary of other secondary outcomes reported by FBSS trials: Patients Satisfaction and Global Impression of Change.

Author, year	Outcome	Timing	Response	SCS % (n/N)	CMM % (n/N)	RR (95% CI)
Rigoard, 2019 PROMISE Study **Conventional SCS** **As treated analyses**	Patient Satisfaction	6 mos.	Somewhat or very satisfied	82.1% (65/79)	53.9% (63/117)	1.53 (1.26, 1.86)
Kumar, 2007 PROCESS Study **Conventional SCS** **ITT analysis**	Patient Satisfaction	6 mos.	Satisfied with pain relief	66% (33/50)	18% (8/44)	3.63 (1.88, 7.01)
			Would choose treatment again	86% (43/50)	50% (22/44)	1.72 (1.25, 2.36)

Kapural, 2022 **HF (10 kHz) SCS** **PP analyses**	Patient's Global Impression of Change	6 mos.	Better or a great deal better	70.8% (46/65)	1.3% (1/75)	53.08 (7.53, 374.24)
			Little, somewhat, or moderately better	24.7% (16/65)	5.4% (4/75)	4.62 (1.62, 13.11)
			No change or almost the same	4.6% (3/65)	93.3% (70/75)	0.05 (0.02, 0.15)

CI = Confidence interval; CMM = Conventional medical management; FBSS = Failed Back Surgery Syndrome; HF = High frequency; ITT = Intention-to-treat; kHz = Kilohertz; PP = Per protocol; RR = Risk ratio; SCS = Spinal cord stimulator.
* Numerators back-calculated using % given in text and numbers for as treated analysis.

Appendix Table F14. Summary of secondary outcomes reported by Kemler trial: Quality of Life and Depression Scales.

Author, year	Outcome	Timing	Conv. SCS Mean (SD)	PT Mean (SD)	MD (95% CI) in change scores, or p-value
Kemler 2000, 2004, 2008 **ITT analyses**	EQ-5D overall health VAS (0-100, best)	Baseline	47 (19) (n=36)	42 (19) (n=18)	**5 (-0.48, 10.48)** (vs control)
		6 mos.	Change score: 6 (22) (n=36)	Change score: 3 (18) (n=18)	**3 (-2.61, 8.61)** (vs control)
		24 mos.	Change score: 7 (20) (n=35)	Change score: 12 (18) (n=16)	**-5 (-10.63, 0.63)** (vs control)
		60 mos.	Change score: 16 (25) (n=31)	Change score: 19 (46) (n=13)	**-3 (-16.53, 10.53)** (vs control)
	NHP – pain component (scale NR)	Baseline	NR	NR	
		6 mos.	Data NR; improvement with SCS		hand (p=0.02) foot (p=0.008)
		24 mos.	Data NR; p=NS for between-group difference		p=NS
		60 mos.	Change score: -7 (27) (n=31)	Change score: -5 (27) (n=13)	**-2 (-10.92, 6.92)** p=0.82
	Self-Rating Depression Scale	Baseline	NR	NR	
		60 mos.	Change score: 0 (9) (n=31)	Change score: -3 (11) (n=13)	**3 (-0.45, 6.45)** p=0.47

CI = Confidence interval; EQ-5D = EuroQol 5D; ITT = Intention-to-treat; MD = Mean difference; NHP = Nottingham Health Profile; NR = Not reported; NS = Not significant; PT = Physical therapy; SCS = Spinal cord stimulator; SD = Standard deviation; VAS = Visual analogue scale.

Appendix Table F15. Summary of secondary outcomes reported by Canos-Verdecho trial: Quality of Life and Global Impression of Change Scales.

Author, year	Outcome	Timing	10 kHz SCS (n=10) Mean (SE)	Conv. SCS (n=12) Mean (SE)	CMM (n=19) Mean (SE)	10 kHz SCS vs. CMM MD (95% CI)	Conv. SCS vs. CMM MD (95% CI)
Canos-Verdecho, 2021 **ITT analyses**	SF-12 Physical	Baseline	87.5 (11.3)	133.3 (16.0)	146.0 (30.0)	**-58.5 (-84.91, -32.09)**	**-12.7 (-41.44, 16.04)**
		3 mos.	190.0 (18.7)	279.2 (41.6)	148.7 (32.3)	**41.3 (10.24, 72.36)**	**130.5 (82.08, 178.92)**
		6 mos.	180.0 (20.6)	268.7 (36.4)	193.4 (37.5)	**-13.4 (-47.12, 20.32)**	**75.3 (30.16, 120.44)**
		12 mos.	170.0 (24.4)	283.3 (38.7)	201.3 (38.4)	**-31.3 (-67.7, 5.10)**	**82 (34.81, 129.19)**
	SF-12 Emotional	Baseline	106.0 (26.6)	210.8 (34.8)	252.6 (32.0)	**-146.6 (-182.87, -110.33)**	**-41.8 (-84.45, 0.85)**
		3 mos.	368.0 (49.1)	438.7 (35.2)	290.2 (33.5)	**77.8 (22.33, 133.27)**	**148.5 (105.19, 191.81)**
		6 mos.	358.5 (51.0)	440.4 (35.2)	306.6 (32.8)	**51.9 (-4.88), 108.68)**	**133.8 (90.64), 176.95)**
		12 mos.	347.5 (56.5)	446.2 (35.1)	309.2 (32.5)	**38.3 (-23.42, 100.02)**	**137.0 (93.99, 180.01)**
	Total SF-12	Baseline	193.5 (34.8)	344.2 (43.7)	393.1 (50.4)	**-199.6 (-246.17, -153.03)**	**-48.9 (-102.45, 4.64)**
		3 mos.	558.0 (58.0)	717.9 (59.97)	433.1 (52.0)	**124.9 (58.93, 190.87)**	**284.8 (217.15, 352.45)**
		6 mos.	538.5 (59.5)	709.2 (56.9)	494.5 (54.5)	**44.0 (-23.64, 111.64)**	**214.7 (149.33, 280.07)**
		12 mos.	517.5 (70.7)	729.6 (58.3)	505.0 (54.6)	**12.5 (-65.19, 90.19)**	**224.6 (157.99, 291.21)**
	Global impression of change – Patient	Baseline	4.0 (0.1)	4.0 (0.1)	3.7 (0.1)	**0.3 (-1.08, 1.68)**	**0.3 (-1.08, 1.68)**
		3 mos.	1.9 (0.2)	1.7 (0.1)	3.2 (0.2)	**-1.3 (-3.26, 0.66)**	**-1.5 (-3.45, 0.45)**
		6 mos.	2.2 (0.2)	1.7 (0.1)	2.7 (0.2)	**-0.5 (-2.46, 1.46)**	**-1.0 (-2.95, 0.95)**
		12 mos.	2.3 (0.3)	1.8 (0.2)	2.5 (0.3)	**-0.2 (-2.61, 2.21)**	**-0.7 (-3.1, 1.7)**
	Global impression of change – Clinician	Baseline	3.1 (0.1)	3.2 (0.2)	2.9 (0.1)	**-0.2 (-1.18, 1.58)**	**0.3 (-1.09, 1.69)**
		3 mos.	1.2 (0.1)	1.2 (0.1)	2.3 (0.1)	**-1.1 (-2.48), 0.28)**	**-1.1 (-2.48, 0.38)**
		6 mos.	1.3 (0.1)	1.2 (0.1)	2.1 (0.2)	**-0.8 (-2.75, 1.15)**	**-0.9 (-2.85, 1.05)**
		12 mos.	1.5 (0.2)	1.3 (0.1)	1.9 (0.2)	**-0.4 (-2.36, 1.56)**	**-0.6 (-2.55, 1.35)**

CI = confidence interval; CMM = Conventional medical management; kHz = Kilohertz; MD = Mean difference; SF-12 = 12 item Short Form; SCS = Spinal cord stimulator; SE = Standard error.

Appendix Table F16. Device/Hardware Related Adverse Events Reported by Parallel RCTs Across all Diagnoses and SCS types.

Device/Hardware AAI Subcategory	Outcome (author reported)	Author, year	Dx	SCS	F/U	Any AE, % (n/N)	No. events (any)	Serious AE, % (n/N)	No. events (serious)
Total hardware related AEs	Total hardware related AE	Kumar, 2007	FBSS	Conv.	12 mos.	13.1% (11/84)	13	NR	NR
	Total hardware related AE requiring revision					11.9% (10/84)	NR	n/a	n/a
IPG explant (with or without replacement)	Explantation (due to implant site infection)*	Kapural, 2022	NSRBP	10 kHz	12 mos.	1.4% (2/145)	2	n/a	n/a
	Explantation (due to loss of therapeutic effect)	Kapural, 2022	NSRBP	10 kHz	12 mos.	0% (0/145)	n/a	n/a	n/a
	Total removal and replacement of system due to infection at receiver site	North, 2005	FBSS	Conv.	mean 2.9 years	3% (1/31)	NR	n/a	n/a
	Explant, due to infection	Petersen, 2021	PDN	10 kHz	6 mos.	2.2% (2/90)	2	n/a	n/a
		Petersen, 2022	PDN	10 kHz	12 mos.	3.2% (5/154)	NR	n/a	n/a
		Petersen, 2023	PDN	10 kHz	24 mos.	3.2% (5/154)†	NR	n/a	n/a
		Slangen, 2014	PDN	Conv.	6 mos.	5.3% (1/19)	NR	n/a	n/a
	Explant due to loss of efficacy	Petersen, 2022	PDN	10 kHz	12 mos.	0% (0/154)	n/a	n/a	n/a
		Petersen, 2023	PDN	10 kHz	24 mos.	0% (0/134)	n/a	n/a	n/a
	Implant removal (and reimplantation), due to infection‡	Kemler, 2000	CRPS	Conv.	6 mos.	4.2% (1/24)	NR	n/a	n/a
	Explantation of system	Kemler, 2004	CRPS	Conv.	24 mos.§	NR	3	n/a	n/a
	Explantation of system	Kemler, 2008	CRPS	Conv.	60 mos.	NR	3	n/a	n/a
Device failure/ malfunction	Device deployment issue	Rigoard, 2019	FBSS	Conv.	6 mos.	2.0% (2/102)	2	0% (0/102)	0
					24 mos.	1.1% (2/174)	2	0% (0/174)	0
					6 mos.	2.0% (2/102)	2	0% (0/102)	0

Device/Hardware AAI Subcategory	Outcome (author reported)	Author, year	Dx	SCS	F/U	Any AE, % (n/N)	No. events (any)	Serious AE, % (n/N)	No. events (serious)
	Device deployment issue - **requiring surgery**				24 mos.	1.1% (2/174)	2	0% (0/174)	0
	Device stimulation issue	Rigoard, 2019	FBSS	Conv.	6 mos.	NR	NR	2.0% (2/102)	2
	Device stimulation issue - **requiring surgery**				6 mos.	NR	NR	2.0% (2/102)	2
	Device stimulation issue				24 mos.	5.2% (9/174)	12	NR	3
	Paresthesia	Rigoard, 2019	FBSS	Conv.	6 mos.	2.0% (2/102)	2	0% (0/102)	0
	Paresthesia - **requiring surgery**				6 mos.	2.0% (2/102)	2	0% (0/102)	0
	Paresthesia				24 mos.	2.3% (4/174)	4	NR	1
	Burning sensation				24 mos.	0.6% (1/174)	1	0% (0/174)	0
	Hypoesthesia				24 mos.	0.6% (1/174)	1	0% (0/174)	0
	Uncomfortable stimulation	Petersen, 2021	PDN	Conv.	6 mos.	0.9% (1/113)	1	NR	NR
	Incomplete overlap of paresthesia with painful area **requiring a second electrode lead**	De Vos, 2014	PDN	Conv.	6 mos.	5.6% (2/36)	NR	NR	NR
	Perceiving paresthesia in an annoying way/with discomfort with postural changes	Canos-Verdecho, 2021	CRPS	Conv.	12 mos.	41.7% (5/12)	NR	NR	NR
	Change of amplitude by bodily movements	Kemler, 2004	CRPS	Conv.	24 mos.	NR	19	NR	NR
	Paresthesia in other body parts					NR	13	NR	NR
	Movements or cramps resulting from elevated amplitude					NR	3	NR	NR
	Loss of therapeutic effect, loss of paresthesia, or unpleasant paresthesia	Kumar, 2007	FBSS	Conv.	12 mos.	7.1% (6/84)	6	NR	NR
	Loss of therapeutic effect, loss of paresthesia, or unpleasant paresthesia - **requiring surgery**					1.2% (1/84)	NR	NR	NR
	Therapeutic product ineffective	Rigoard, 2019	FBSS	Conv.	24 mos.	1.1% (2/174)	2	0% (0/174)	0

Device/Hardware AAI Subcategory	Outcome (author reported)	Author, year	Dx	SCS	F/U	Any AE, % (n/N)	No. events (any)	Serious AE, % (n/N)	No. events (serious)
	Therapeutic response decrease					1.1% (2/174)	2	0% (0/174)	0
IPG revision or replacement	Device dislocation	Rigoard, 2019	FBSS	Conv.	24 mos.	1.7% (3/174)	3	0% (0/174)	0
	IPG migration requiring surgery	Kumar, 2007	FBSS	Conv.	12 mos.	1.2% (1/84)	1	NR	NR
	IPG repositioning (due to implant site pain)	Kapural, 2022	NSRBP	10 kHz	12 mos.	2.0% (3/145)	NR	NR	NR
	Device extrusion	Petersen, 2021	PDN	10 kHz	6 mos.	0.9% (1/113)	1	NR	NR
	IPG revision (NOS)	Petersen, 2022	PDN	10 kHz	12 mos.	1.3% (2/154)	2	NR	NR
	IPG reposition or replacement	Petersen, 2023	PDN	10 kHz	24 mos.	3.2% (5/154)	NR	NR	NR
	Pain pulse generator pocket (requiring revision)	Kemler, 2000	CRPS	Conv.	6 mos.	8.3% (2/24)	NR	8.3% (2/24)	NR
	Pulse generator pocket revision	Kemler, 2004	CRPS	Conv.	24 mos.[§]	NR	7	NR	NR
		Kemler, 2008	CRPS	Conv.	60 mos.	NR	8	NR	NR
	IPG replacement	Kemler, 2004	CRPS	Conv.	24 mos.	NR	1	NR	NR
		Kemler, 2008	CRPS	Conv.	60 mos.	54.2% (13/24)	17	NR	NR
Lead/electrode failure/migration	Lead/extension fracture/torqued contacts	Kumar, 2007	FBSS	Conv.	12 mos.	2.4% (2/84)	2	NR	NR
	Lead migration				12 mos.	9.5% (8/84)	10	NR	NR
	Lead migration	Petersen, 2021	PDN	10 kHz	6 mos.	0.9% (1/113)	1	NR	NR
	Lead revision due to lead migration	Petersen, 2022	PDN	10 kHz	12 mos.	0.6% (1/154)	1	NR	NR
		Petersen, 2023	PDN	10 kHz	24 mos.	1.9% (3/154)	NR	NR	NR
	Electrode lead migration	De Vos, 2014	PDN	Conv.	6 mos.	2.8% (1/36)	NR	NR	NR
	Lead revision (dislodgement or lack of therapeutic effect)	Kapural, 2022	NSRBP	10 kHz	12 mos.	3.4% (5/145)	NR	NR	NR
	Lead revision (lead dislodgement)				12 mos.	2.1% (3/145)	NR	NR	NR
	Lead revision (lack of therapeutic effect)				12 mos.	1.4% (2/145)	NR	NR	NR
	Lead revision due to electrode migration or malposition	North, 2005	FBSS	Conv.	mean 2.9 years	10% (3/31)	NR	NR	NR
	Lead migration **requiring surgery**	Kumar, 2007	FBSS	Conv.	12 mos.	9.5% (8/84)	10	NR	NR

Device/Hardware AAI Subcategory	Outcome (author reported)	Author, year	Dx	SCS	F/U	Any AE, % (n/N)	No. events (any)	Serious AE, % (n/N)	No. events (serious)
	Lead/extension fracture/torqued contacts **requiring surgery**	Kumar, 2007	FBSS	Conv.	12 mos.	1.2% (1/84)	1	NR	NR
	Defective lead **requiring replacement**	Kemler, 2000	CRPS	Conv.	6 mos.	4.2% (1/24)	NR	NR	NR
	Unsatisfactory positioning of the electrode **requiring revision**	Kemler, 2000	CRPS	Conv.	6 mos.	20.8% (5/24)	7††	NR	NR
	Repositioning of lead	Kemler, 2004	CRPS	Conv.	24 mos.**	NR	8	NR	NR
		Kemler, 2008	CRPS	Conv.	60 mos.	NR	11	NR	NR
	Replacement lead	Kemler, 2004	CRPS	Conv.	24 mos.	NR	2	NR	NR
		Kemler, 2008	CRPS	Conv.	60 mos.	NR	6	NR	NR
Device battery issue	Device battery issue	Rigoard, 2019	FBSS	Conv.	6 mos.	1.0% (1/102)	1	0% (0/102)	0
	Device battery issue - **requiring surgery**				6 mos.	1.0% (1/102)	1	0% (0/102)	0
	Device battery issue				24 mos.	0.6% (1/174)	1	0% (0/174)	0

AE = Adverse event; CRPS = Complex Regional Pain Syndrome; Dx = Diagnosis; FBSS = Failed Back Surgery Syndrome; F/U = Follow-up; IPG = Implantable pulse generator; KhZ = Kilohertz; NOS = not otherwise specified; NR = Not reported; NSRBP = Non-surgery related back pain; PDN = Painful diabetic neuropathy; SCS = Spinal cord stimulator.
*Same 2 people who had severe infection requiring device removal listed under Biological events, infections.
† Four patients exited the study while 1 patient continued the study after reimplantation.
‡ This is same person who had severe infection requiring device removal listed under Biological events, infections.
§ 1 occurred at 12 months and 2 occurred at 24 months.
** All occurred by 12 months.
†† 1 patients needed 3 procedures.

Appendix Table F17. Biological Adverse Events Reported by Parallel RCTs Across all Diagnoses and SCS Types.

Biological AAI Subcategory	Outcome	Author, year	Dx	SCS	F/U	Any AE, % (n/N)	No. events (any)	Serious AE, % (n/N)	No. events (serious)
Any Event	SCS-related: Total biological events	Kumar, 2007	FBSS	Conv.	12 mos.	19.0% (16/84)	16	7.1% (6/84)*	NR
	Study-related AE – serious (NOS)	Petersen, 2023	PDN	10 kHz	24 mos.	NR	NR	4.5% (7/154)	NR
	Any event (excluding dural puncture)	Kemler, 2000	CRPS	Conv.	6 mos.	25.0% (6/24)	11	NR	NR

Biological AAI Subcategory	Outcome	Author, year	Dx	SCS	F/U	Any AE, % (n/N)	No. events (any)	Serious AE, % (n/N)	No. events (serious)
Infection, cellulitis	Implant site infection	Rigoard, 2019	FBSS	Conv.	6 mos.	6.9% (7/102)	8	4.9% (5/102)[*]	7
					24 mos.	4.0% (7/174)	8	NR	7
	Implant site cellulitis				6 mos.	1.0% (1/102)	1	0% (0/102)	---
					24 mos.	0.6% (1/174)	1	0% (0/174)	---
	Extradural abscess				24 mos.	NR	NR	0.6% (1/174)	1
	Infection/wound breakdown	Kumar, 2007	FBSS	Conv.	12 mos.	8.3% (7/84)	7	6.0% (5/84)[*]	NR
	Implant site infection (required implant removal)[†]	Kapural, 2022	NSRBP	10 kHz	12 mos.	3.4% (5/145)	NR	1.4% (2/145)	2
	Infection (requiring abx and implant removal)[‡]	Kemler, 2000	CRPS	Conv.	6 mos.	4.2% (1/24)	NR	4.2% (1/24)[*]	NR
	Infection	Slangen, 2014	PDN	Conv.	6 mos.	NR	NR	5.3% (1/19)	NR
		Petersen, 2021	PDN	10 kHz	6 mos.	2.7% (3/113)[§]	3	NR	NR
		Petersen, 2022	PDN	10 kHz	12 mos.	5.2% (8/154)[**]	NR	NR	NR
		Petersen, 2023	PDN	10 kHz	24 mos.	5.2% (8/154)[**]	NR	NR	NR
		De Vos, 2014	PDN	Conv.	6 mos.	2.8% (1/36)[††]	NR	NR	NR
Possible surgical/technical complications	SCS-related: Technique	Kumar, 2007	FBSS	Conv.	12 mos.	4.8% (4/84)	5	4.8% (4/84)	NR
	Extradural hematoma	Rigoard, 2019	FBSS	Conv.	24 mos.	NR	NR	0.6% (1/174)	1
	Post procedural complication (NOS)				24 mos.	NR	NR	0.6% (1/174)	1
	Transient CSF leakage	Kapural, 2022	NSRBP	10 kHz	12 mos.	2.0% (3/145)	NR	NR	NR
	Dural puncture	Kemler, 2000	CRPS	Conv.	6 mos.	8.3% (2/24)[‡‡]	NR	NR	NR
	Occipital headache	Canos-Verdecho, 2021	CRPS	10 kHz	12 mos.	10% (1/10)	NR	NR	NR
	Neurostimulator pocket, fluid collection	Kumar, 2007	FBSS	Conv.	12 mos.	4.8% (4/84)	4	0% (0/84)[§§]	---
Implant or incision site pain, swelling, dehiscence	Implant site pain	Rigoard, 2019	FBSS	Conv.	6 mos.	NR	NR	1.0% (1/102)[*]	1
					24 mos.	3.4% (6/174)	6	NR	2
	Implant site swelling				24 mos.	0.6% (1/174)	1	0% (0/174)	---

Biological AAI Subcategory	Outcome	Author, year	Dx	SCS	F/U	Any AE, % (n/N)	No. events (any)	Serious AE, % (n/N)	No. events (serious)
	Procedural pain				24 mos.	1.1% (2/174)	2	NR	0
	Implant/incision site pain/discomfort	Kumar, 2007	FBSS	Conv.	12 mos.	6.0% (5/84)	5	1.2% (1/84)*	
	Implant/incision site pain/discomfort	Kapural, 2022	NSRBP	10 kHz	12 mos.	4.8% (7/145)	NR	NR	NR
	IPG site pain/discomfort	Petersen, 2021	PDN	10 kHz	6 mos.	0.9% (1/113)	1	NR	NR
	Incision site pain				6 mos.	0.9% (1/113)	1	NR	NR
	Wound dehiscence				6 mos.	1.8% (2/113)	2	NR	NR
	IPG site pain/discomfort	De Vos, 2014	PDN	Conv.	6 mos.	5.6% (2/36)	NR	NR	NR
	IPG site pain/discomfort	Canos-Verdecho, 2021	CRPS	Conv.	12 mos.	10% (1/10)	NR	0% (0/10)	---
	IPG site pain/irritation	Kemler, 2004	CRPS	Conv.	24 mos.	NR	10	NR	NR
	Pain/irritation from extension lead or plug				24 mos.	NR	11	NR	NR
Skin-related complications	Contact dermatitis	Rigoard, 2019	FBSS	Conv.	24 mos.	0.6% (1/174)	1	0% (0/174)	NR
	Contact dermatitis	Petersen, 2021	PDN	10 kHz	6 mos.	0.9% (1/113)	1	NR	NR
	Urticaria				6 mos.	0.9% (1/113)	1	NR	NR
Neurological injury	Neuro/sensory deficit	Kapural, 2022	NSRBP	HF SCS	12 mos.	NR	NR	0.7% (1/145)	0.7% (1/145)
	Autonomic neuropathy	Slangen, 2014	PDN	Conv.	6 mos.	NR	NR	5.3% (1/19)	NR
	Monoparesis	Rigoard, 2019	FBSS	Conv.	24 mos.	0.6% (1/174)	NR	NR	NR
	Simulation related neurological deficits	Petersen, 2021	PDN	10 kHz	6 mos.	0% (0/113)	0	0% (0/113)	---
		Petersen, 2023	PDN	10 kHz	24 mos.	0% (0/134)	0	0 (0/134)	---
Other - serious	Back pain	Rigoard, 2019	FBSS	Conv.	6 mos.	NR	NR	1.0% (1/102)	1
					24 mos.	2.3% (4/174)	5	NR	3
	Abdominal pain lower				24 mos.	NR	NR	0.6% (1/174)	1
	Musculoskeletal pain				24 mos.	NR	NR	0.6% (1/174)	1
	Pulmonary edema				6 mos.	NR	NR	1.0% (1/102)	1
					24 mos.	NR	NR	0.6% (1/174)	1
	UTI				6 mos.	NR	NR	1.0% (1/102)	1

Biological AAI Subcategory	Outcome	Author, year	Dx	SCS	F/U	Any AE, % (n/N)	No. events (any)	Serious AE, % (n/N)	No. events (serious)
					24 mos.	NR	NR	0.6% (1/174)	1
	Lethargy	Kapural, 2022	NSRBP	10 kHz	12 mos.	NR	NR	0.7% (1/145)	1
	Osteomyelitis				12 mos.	NR	NR	0.7% (1/145)	1
	Poor wound healing				12 mos.	NR	NR	0.7% (1/145)	1
Other – non serious or seriousness NR	Abdominal pain	Rigoard, 2019	FBSS	Conv.	24 mos.	0.6% (1/174)	1	0% (0/174)	NR
	Pelvic pain				6 mos.	1.0% (1/102)	1	0% (0/102)	NR
					24 mos.	0.6% (1/174)	1	0% (0/174)	NR
	Arthralgia	Petersen, 2021	PDN	10 kHz	6 mos.	0.9% (1/113)	1	NR	NR
	GI reflux				6 mos.	0.9% (1/113)	1	NR	NR
	Hyporeflexia				6 mos.	0.9% (1/113)	1	NR	NR
	Impaired healing				6 mos.	0.9% (1/113)	1	NR	NR
	Myalgia				6 mos.	0.9% (1/113)	1	NR	NR
	Radiculopathy				6 mos.	0.9% (1/113)	1	NR	NR
	Coagulopathy prolonging hospitalization	De Vos, 2014	PDN	Conv.	6 mos.	2.8% (1/36)	NR	NR	NR
	Disturbed urination	Kemler, 2004	CRPS	Conv.	24 mos.	NR	4	NR	NR
	More pain in other body parts				24 mos.	NR	7	NR	NR

Abx = antibiotics; AE = Adverse event; CRPS = Complex Regional Pain Syndrome; Dx = Diagnosis; FBSS = Failed Back Surgery Syndrome; F/U = Follow-up; GI = Gastrointestinal; IPG = Implantable pulse generator; KhZ = Kilohertz; NOS = Not otherwise specified; NR = Not reported; NSRBP = Non-surgery related back pain; PDN = Painful diabetic neuropathy; SCS = Spinal cord stimulator; UTI = Urinary tract infection.

* These events required surgical intervention to resolve.

† Same two people who had severe device removal for serious infection listed under Device/Hardware related AE table.

‡ This is same person who had device removal due to infection listed under IPG explant in Device/Hardware related AEs table.

§ Two required explant and are included under explant also.

** 5 required explant and are included under explant in Table F16.

†† Resolved, patient had permanent implant.

‡‡ With headache in one patient.

§§ No surgery required for any case.

Appendix Table F18. Explant Rates from Case Series, Database Studies, and Registries

Author, year	N	Study type	Follow-up	% (n/N)
Any, total, explant (Author reported sum)				
Rosenberg, 2016	620	Case series	1 year	4.0% (25/620)
Van Buyten, 2017	955	Case series	2 years	18.8% (180/955)
Dupre, 2018	595	Case series	2 years	27.7% (165/595)
Hagedorn, 2021	744	Case series	2 years	10.2% (76/744)
Remacle 2020	54	Case series	6 years	57.4% (31/54)
Al-Kaisy, 2020	718	Registry	5 years	17.8% (NR) (IPG)
Al-Kaisy, 2020	718	Registry	10 years	25.2% (181/718) (overall)
Rauck, 2023	1289	Registry	3 years	7.6% (98/1289)
Han 2017	8727	Admin	3 years	9.2% (805/8727)
Hussain 2022	52,070	Admin	2 years	6.0% (3104/52070)
Due to infection				
Bendel, 2017	2737	Case series	NR	1.9% (52/2737)
Van Buyten, 2017	955	Case series	2 years	4.8% (46/955)
Hagedorn, 2021	744	Case series	2 years	2.2% (16/744)
Kumar & Wilson, 2007	336	Case series	8.1 years	3.0% (10/336)
North, 1993	249	Case series	7.1 (1.5-20.4) years	5% (12/249)
Thomson, 2017	298	Case series	7.5 years	2.3% (7/298) (fatal) 0.3% (1/298) (nonfatal)
Kumar & Toth, 1998	164	Case series	8.8 (0.67-17) years	4.9% (8/164)
Nissen, 2018	175	Case series	6 years	0.6% (1/175)
Kay 2001	72	Case series	5.2 (1-13) years	4% (3/72)
Remacle 2020	54	Case series	6 years	3.7% (2/54)
Remacle 2020 (late electrode)	54	Case series	6 years	5.6% (3/54)
van Beek, 2017	40	Case series	Median 5yrs	5% (2/40)
Sanchez-Ledesma, 1989	36	Case series	5.5 years	3% (1/36)
Brinzeu, 2018	402	Registry	2 years	1.0% (4/402)
Due to Infection/wound dehiscence				
Dupre, 2018	595	Case series	2 years	2.5% (15/595)
Van Buyten, 2017	955	Case series	2 years	4.8% (46/955)
Due to inadequate pain relief, loss of efficacy, lack of efficacy, inadequate benefit				
Van Buyten, 2017	955	Case series	2 years	9.8% (94/955)
Hagedorn, 2021	744	Case series	2 years	5.2% (39/744)
Dupre, 2018	595	Case series	2 years	20.3% (121/595)
Thomson, 2017	298	Case series	7.5 years	3.02% (9/298)
Nissen, 2018	175	Case series	6 years	19.4% (34/175)
Kay 2001	72	Case series	5.2 (1-13) years	1% (1/72)
van Beek, 2017	40	Case series	Median 5yrs	15% (6/40)
Hoikkanen, 2021	27	Case series	6 years	25.9% (7/27)
Rauck, 2023	1289	Registry	3 years	2.5% (32/1289)
Al-Kaisy, 2020	718	Registry	10 years	16.6% (119/718)
Brinzeu, 2018	402	Registry	2 years	2.0% (8/402)
Due to pain, discomfort at IPG, electrode, intolerable pain				
Van Buyten, 2017	955	Case Series	2 years	0.4% (4/955)
Hagedorn, 2021	744	Case Series	2 years	1.1% (8/744)
Dupre, 2018	595	Case Series	2 years	6.1% (31/595)
Nissen, 2018	175	Case Series	6 years	0.6% (1/175)
Kay, 2021	72	Case Series	5.2 years	8.3% (6/72)

Remacle, 2020	54	Case Series	6 years	9.3% (5/54)
Due to device malfunction (IPG or electrode), electrode migration, electrode dysfunction, no longer joinable				
Thoson, 2017	298	Case Series	7.5 years	0.3% (1/298)
Nissen, 2018	175	Case Series	6 years	0.6% (1/175)
Remacle, 2020	54	Case Series	6 years	1.9% (1/54)
Remacle, 2020	54	Case Series	6 years	3.7% (2/54)
Remacle, 2020	54	Case Series	6 years	13.0% (7/54)

IPG = Implantable pulse generator.

Appendix Table F19. IPG revision or replacement from Case Series, Database Studies, and Registries

Author, year	N	Study type	Follow-up	% (n/N)
Any, total, IPG Revision or Replacement (Author reported sum)				
Rosenberg, 2016	620	Case Series	1 year	3.1% (19/620)
Geurts, 2013	84	Case Series	5.2 years (Median)	60.7% (51/84)
Hoikkanen, 2021	27	Case Series	6 years	63.0% (17/27)
Brinzeu, 2018	402	Registry	2 years	15.9% (64/402)
Due to infection				
Sanchez-Ledesma, 1989	36	Case Series	5.5 years	2.7% (1/36)
Due to pain/discomfort at IPG site/pocket				
Kumar & Wilson, 2007	336	Case Series	8.2 years	1.5% (5/336)
Thomson, 2017	298	Case Series	7.5 years	2.0% (6/298)
Nissen, 2018	175	Case Series	6 years	1.7% (3/175)
Geurts, 2013	84	Case Series	5.2 years (Median)	8.3% (7/84)
Kay, 2021	72	Case Series	5.2 years	5.6% (4/72)
van Beek, 2017	40	Case Series	5 years (Median)	2.5% (1/40)
Hoikkanen, 2021	27	Case Series	6 years	11.1% (3/27)
Zuidema, 2023	19	Case Series	8-10 years	31.6% (6/19)
Rauck, 2023	1289	Registry	3 years	0.9% (12/1289)
Due to malfunction of IPG/electrode, intolerable pain				
Nissen, 2018	175	Case Series	6 years	6.3% (11/175)
Kay, 2021	72	Case Series	5.2 years	1.4% (1/72)
Hoikkanen, 2021	27	Case Series	6 years	7.4% (2/27)
Due to IPG displacement/migration				
Kumar & Wilson, 2007	336	Case Series	8.2 years	1.2% (4/336)
Kay. 2021	72	Case Series	5.2 years	1.4% (1/72)*
Rauck, 2023	1289	Registry	3 years	1.2% (16/1289)
Brinzeu, 2018	402	Registry	2 years	0.5% (2/402)
Due to battery failure, electrical leak, charging problems				
Kumar & Wilson, 2007	336	Case Series	8.2 years	1.2% (4/336)
Nissen, 2018	175	Case Series	6 years	11.4% (20/175)
Kumar & Toth, 1998	164	Case Series	8.8 years	1.2% (2/164)
Geurts, 2013	84	Case Series	5.2 years	26.2% (22/84)
Kay, 2021	72	Case Series	5.2 years	22.2% (16/72)
van Beek, 2017	40	Case Series	5 years	32.5% (13/40)
Hoikkanen, 2021	27	Case Series	6 years	29.6% (8/27)
Zuidema, 2023	19	Case Series	8-10 years	78.9% (15/19)
Rauck, 2023	1289	Registry	3 years	1.1% (14/1289)
Deer, 2016	614	Registry	2 years	0.5% (3/614)
Brinzeu, 2018	402	Registry	2 years	1.5% (6/402)

IPG: Implantable Pulse Generator.
*Due to pregnancy.

Appendix Table F20. Lead or electrode events from Case Series, Database Studies, and Registries

Author, year	N	Study type	Follow-up	% (n/N)
Any, total, Lead/electrode Revision or Replacement (Author reported sum)				
Thomson, 2017	298	Case Series	7.5 years	4.0% (12/298)
van Beek, 2017	40	Case Series	5 years (Median)	22.5% (9/40)
Labaran, Jaine, 2020	12297	Database	1 year	3.4% (413/12297)
Lead fracture/failure				
Mekhail, 2011	527	Case Series	3.4 years	15.8% (83/527)
Kumar & Wilson, 2007	336	Case Series	8.1 years	6.4% (27/336)
North, 1993	298	Case Series	7.1 years	7.4% (22/298)*
Kleiber, 2016	212	Case Series	13 years	3.8% (8/212)
Kumar & Toth, 1998	164	Case Series	8.8 years	3.6% (6/164)
Geurts, 2013	84	Case Series	5.2 years	8.3% (7/84)
Kay, 2001	72	Case Series	5.2 years	6.9% (5/72)
Zuidema, 2023	19	Case Series	8-10 years	42.1% (8/19)
Deer, 2016	614	Registry	2 years	1.1% (7/614)
Brinzeu, 2018	402	Registry	2 years	6.2% (25/402)
Lead migration/mispositioning				
Rosenberg, 2016	620	Case Series	1 year	3.2% (20/620)
Mekhail, 2011	527	Case Series	3.4 years	22.6% (119/527)
Kumar & Wilson, 2007	336	Case Series	8.1 years	26.7% (90/336)
Kleiber, 2016	212	Case Series	13 years	1.4% (3/212)
Nissen, 2018	175	Case Series	6 years	1.1% (2/175)
Kumar & Toth, 1998	164	Case Series	8.8 years	33.5% (55/164)
Geurts, 2013	84	Case Series	5.2 years	27.4% (23/84)
Kay, 2001	72	Case Series	5.2 years	11.1% (8/72)
Sanchez-Ledesma, 1989	36	Case Series	5.5 years	2.8% (1/36)
Hoikkanen, 2021	27	Case Series	6 years	22.2% (6/27)
Rauck, 2023	1289	Registry	3 years	5.0% (65/1289)
Deer, 2016	614	Registry	2 years	6.5% (40/614)
Brinzeu, 2018	402	Registry	2 years	6.0% (24/402)
Inadequate/inappropriate parasthesia/pain, high impedance				
Kumar & Wilson, 2007	336	Case Series	8.1 years	6.0% (20/336)
Kay, 2001	72	Case Series	5.2 years	26.4% (19/72)
Rauck, 2023	1289	Registry	3 years	5.4% (69/1289)

* Out of total systems implanted

Appendix Table F21. Infection rates from Case Series, Database Studies, and Registries

Author, year	N	Study type	Follow-up	% (n/N)
Deep/serious/fatal infection or infection leading to hospital readmission or revision/removal of device				
Mekhail, 2011	527	Case Series	3.4 years	3.2% (22/527)
Thomson, 2017	321	Case Series	7.5 years	0.4% (1/321)*
Kleiber, 2016	212	Case Series	13 years	3.8% (8/212)
Nissen, 2018	175	Case Series	6 years	3.4% (6/175)
Lanner, 2007	88	Case Series	5 years	8.0% (7/88)
Geurts, 2013	84	Case Series	5.2 years	1.2% (1/84)
Kay, 2001	72	Case Series	5.2 years	1.4% (1/72)
Hoikkanen, 2021	27	Case Series	6 years	3.7% (1/27)
Elsamadicy, 2018	1521	Database	30 days	0.9% (14/1521)
Rauck, 2023	1289	Registry	3 years	3.9% (50/1289)

Superficial/not fatal/not serious infection not leading to revision/removal of device				
Mekhail, 2011	527	Case Series	3.4 years	1.9% (10/527)
Thomson, 2017	321	Case Series	7.5 years	0.9% (3/321)
Kleiber, 2016	212	Case Series	13 years	0.5% (1/212)
Geurts, 2013	84	Case Series	5.2 years	6.0% (5/84)
Kay, 2001	70	Case Series	5.2 years	5.7% (4/70)
Remacle, 2020	54	Case Series	6 years	9.3% (5/54)
Infection, unspecified				
Bendel, 2017	2737	Case Series	NR	2.5% (67/2737)
Kumar & Wilson, 2007	336	Case Series	8.1 years	1.5% (5/336)
Kumar & Toth, 1998	164	Case Series	8.8 years	0.6% (1/164)
Chivukula, 2014	28	Case Series	5+ years	3.6% (1/28)
Labaran, Jaine, 2020	12297	Database	1 year	4.3% (523/12297)
Falowski, 2019	6615	Database	1 year	3.1% (206/6615)
Deer, 2016	614	Registry	2 years	1.9% (18/614)
Brinzeu, 2018	402	Registry	2 years	4.2% (17/402)

*Infection was fatal, occurred during the trial stimulation period.

Appendix Table F22. Miscellaneous Events from Case Series, Database Studies, and Registries

Author, year	N	Study type	Follow-up	% (n/N)
CSF leak/dural tear				
Kumar & Wilson, 2007	336	Case Series	8.1 years	0.6% (2/336)
Kumar & Toth, 1998	164	Case Series	8.8 years	0.6% (1/164)
Chivukula, 2014	28	Case Series	5+ years	7.1% (2/28)
Brinzeu, 2018	402	Registry	2 years	0.7% (3/402)
Neurological deficit/paralysis/intraspinal abcess				
Rosenberg, 2016	620	Case Series	1 year	0.2% (1/620)
Kleiber, 2016	212	Case Series	13 years	0.9% (2/212)
Labaran, Jaine, 2020	12297	Database	1 year	0.2% (19/12297)
Cardiac complication/pulmonary embolism				
Kleiber, 2016	212	Case Series	13 years	0.5% (1/212)
Elsamadicy, 2018	1521	Database	30 days	0.3% (5/1521)*
Allergic reaction				
Deer, 2016	614	Registry	2 years	0.2% (1/614)
Brinzeu, 2018	402	Registry	2 years	0.7% (3/402)
Hematoma/seroma/hemorrhage				
Mekhail, 2011	707	Case Series	3.4 years	0.1% (1/707)†
Rosenberg, 2016	620	Case Series	1 year	0.3% (2/620)
Kumar & Wilson, 2007	336	Case Series	8.1 years	5.7% (19/336)
Kleiber, 2016	212	Case Series	13 years	1.9% (4/212)
Nissen, 2018	175	Case Series	6 years	0.6% (1/175)
Labaran, Jaine, 2020	12297	Database	1 year	0.5% (58/12297)‡
Labaran, Jaine, 2020	12297	Database	1 year	0.4% (52/12297)§
Deer, 2016	614	Registry	2 years	0.2% (1/614)
Brinzeu, 2018	402	Registry	2 years	1.2% (5/402)

CSF = Cerebrospinal fuid leak.
* Required hospital readmission
† Trial period included in reporting
‡ Hematoma
§ Seroma.

Appendix Table F23. Other Events Requiring Hospitalization/Emergency Department Visit from Case Series, Database Studies, and Registries

Author, year	N	Study type	Follow-up	% (n/N)
Kleiber, 2016	212	Case Series	13 years	0.9% (2/212)
Labaran, Jaine, 2020	12297	Database	1 year	17.2% (2116/12297)
Elsamadicy, 2018	1521	Database	30 days	0.7% (10/1521)
Brinzeu, 2018	402	Registry	2 years	20.9% (84/402)

APPENDIX G. Detailed Characteristics and Demographic Tables

Appendix Table G1. Demographics, Crossover RCTs

Author (year), Study Period, Country	Condition and pain duration	Population	SCS Intervention	Placebo	Follow-up (% followed)	Crossover	Funding/COI
Al-Kaisy 2018 Study period NR UK	FBSS. Diagnosis not described in detail. Inclusion criteria required patients to have undergone previous spinal surgery, to not be indicated for additional surgical treatment, and to have VAS back pain ≥6 cm. Duration: VAS ≥6 cm for at least 6 months Screening was not described. Exclusion criteria excluded patients with major psychiatric comorbidities, drug-related behavioral issues, or neurological abnormalities unrelated to FBSS.	N=53 Mean age: 48 years Female: 33% White: NR Black: NR Hispanic/ Latino: NR Asian: NR Other: NR	SCS Trial stimulation for up to 17 days: • Completed: 36/53 patients (68%). • Successful: 33/53 patients (62%) implanted with permanent device. • Randomized: 30/53 patients (57%) randomized to scheme. Threshold: ≥50% reduction in pain Permanent SCS specifications: • RestoreSensor • Rate: HF 1200, 3030, or 5882 Hz • Pulse width: 30, 60 or 180 µsec • Amplitude: NR	Placebo During "sham mode" the devise depleted batter without delivering any electrical charge to the leads or causing any noticeable heating of the IPG.	12 months 24/53 (45%)	Patients were randomized to one of the four settings (sham, 1200 Hz @ 180 µsec, 3030 Hz @ 60 µsec or 5882 Hz @ 30 µsec) for three weeks and then reprogrammed. This occurred for 4 phases (over 12 weeks), and then patients chose their preference to apply for 12-month follow-up.	Sponsored by Medtronic Three authors received fees from Medtronic and Nevro, and has financial interest in Micron Device LLC, one is a PI for a separate study sponsored by Medtronic, two authors are employees of Medtronic, and the other authors have no COIs.
Hara 2022	Prior lumbar surgery, chronic radicular pain. Defined as pain arising from 1 or more spinal	N=65 Mean age: 50 years	SCS Period 1: n=24 Period 2: n=25 Period 3: n=22	Placebo Period 1: n=26 Period 2: n=22 Period 3: n=22	12 months: 42/50 (84%)	Patients were randomized to either active stimulation or	Funded by the Liaison Committee for Education,

Author (year), Study Period, Country	Condition and pain duration	Population	SCS Intervention	Placebo	Follow-up (% followed)	Crossover	Funding/COI
Study period NR Norway	nerve roots, diagnosis based on pain characteristics, clinical examination, sensorimotor testing, and review of diagnostic imaging. Duration: ≥6 months Screening was not described. Patients were ineligible if they had unresolved psychiatric illness.	Female: 54% White: 100% Black: 0% Hispanic/ Latino: 0% Asian: 0% Other: 0%	Period 4: n=21 Trial stimulation for up to 14 days: • Completed: 50/65 patients (77%). • Randomized: 50/50 patients (100%) randomized to first 3 months, 47/50 (94%) to second 3 months, 44/50 (88%) to third 3 months, and 42/50 (84%) to fourth 3 months. Threshold: Reduction of ≥2 points on NRS for leg pain. Permanent SCS specifications: • Precision Novi • Rate: 40 Hz • 4 spikes per burst • Pulse width: NR • Amplitude: NR	Period 4: n=21 No stimulation. Further details NR.		placebo stimulation for 4 three month periods	Research, and Innovation in Central Norway No COIs reported.
Sokal 2020 Study period NR	FBSS (78% 18/23), CRPS (22%, 5/23). Diagnostic details NR. Symptom duration: ≥6 months	N=23 Mean age: 57 years Female: 48%	SCS Trial stimulation for up to 14 days:	Placebo IPG deactivated. Further details NR	8 weeks 18/23 (78%)	Patients were randomized to one of four treatments for 2 weeks at a time over 4	No funding One author reports non-financial support from Medtronic,

Author (year), Study Period, Country	Condition and pain duration	Population	SCS Intervention	Placebo	Follow-up (% followed)	Crossover	Funding/COI
Poland	Screening was not described. Patients were ineligible if they had evidence of an active disruptive psychiatric disorder.	White: NR Black: NR Hispanic/ Latino: NR Asian: NR Other: NR	• Completed: 16/17[*] patients (94%). • Successful: 13/17 patients (76%) implanted with permanent device. • Randomized: 18/23 patients (78%) randomized to scheme. (includes 5 patients who did not undergo trial stimulation) Threshold: ≥50% reduction in pain Permanent SCS specifications: • Precision Novi or Montage[†] • Rate: 1. LF tonic stimulation (40 to 60 Hz), 2. HF (1000 Hz), or 3. Clustered tonic (burst, 450 to 550 Hz in a cluster activated with 40 to 60 Hz) • Pulse width: 120 (HF), 250 to 500 (LF, burst) µsec • Amplitude: NR			follow-up periods.	three authors report non-financial support from Boston Scientific. All others report no COI.

Author (year), Study Period, Country	Condition and pain duration	Population	SCS Intervention	Placebo	Follow-up (% followed)	Crossover	Funding/COI
Kriek 2016 Study period NR Netherlands	CRPS. Patients were eligible if they had a confirmed diagnosis of CRPS in one single extremity that was therapy resistant and a VAS pain score ≥5, and an indication for SCS in accordance with Dutch national guidelines. Symptom duration ≥12 months Screening by a psychologist to rule out any psychological contraindication that might influence the outcome of the SCS trial.	N=43 Mean age: 42 years Female: 14% White: 97% Black: 0% Hispanic/ Latino: 0% Asian: 3% Other: 0%	SCS Trial stimulation for up to 14 days: • Completed: 35/40‡ patients (88%). • Successful: 35/40 patients (88%) implanted with permanent device. • Randomized: 33/40 patients (83%) randomized to scheme. Threshold: NR Permanent SCS specifications: • Eon • Rate: LF (40, 500 Hz), HF (1200 Hz), burst • Pulse width: NR • Amplitude: NR	Placebo Programming was performed with a 100 Hz stimulus to maintain an equal programming paradigm and sensation for the patient, but the IPG was switched off immediately after programming, and remained switched off during the 2 week test period.	3 month trial stimulation: 35/43 (81%) Crossover trial period: 33/43 (77%) Final follow-up completion: 28/43 (65%)	Following a 3 month trial stimulation for eligibility, patients were randomized one of five treatments for 2 weeks at a time for 5 phases with a 2 day washout. Upon completion, patients chose the setting they preferred and continued for 3 months follow-up.	Supported by a grant from St. Jude Medical. One author is a paid consultant of Gru€nenthal GmbH, one author owns a patent on burst stimulation and is a paid consultant for St. Jude Medical, all others report no COI.

COI = conflict of interest; CRPS = complex regional pain syndrome; FBSS = failed back surgery syndrome; HF = high=frequency; Hz = hertz IPG = implantable pulse generator; LF = low-frequency; NR = not reported; NRS = Numerical Rating Scale; PI = principle investigator; SCS = spinal cord stimulator; VAS = visual analogue scale; µsec = microsecond.

* Only 17 patients underwent trial stimulation. 6 other patients were unable to undergo percutaneous implantation, and underwent a one-stage surgery that included the implant of a surgical paddle electrode and a permanent IPG in the subcutaneous pocket. 1 of these patients was excluded from the final analysis due to disagreeing to further evaluation.

† Only one patient received the Montage IPG. All others were implanted with the Precision Novi.

‡ 3 patients had dropped out by the time trail stimulation occurred. 1 had reconsidered SCS therapy, 1 had discovered a malignancy, and 1 was wrongfully included.

Appendix Table G2. Demographics, Parallel RCTs for CLBP (No Surgery) and FBSS

Author (year), Study Period, Country	Condition and pain duration	Population	SCS Intervention	Comparator Intervention	Follow-up (% followed)	Crossover	Funding/COI
Kapural, 2022 Study period NR; recruitment period: NR United States	10-kHz SCS + CMM vs. CMM Chronic refractory lower back pain (100%) – "Nonsurgical refractory back pain (NSRBP)" • Degenerative disc disease: 72.3% vs. 68.4% • Spondylosis: 66.3% vs. 64.5% • Radiculopathy: 41.0% vs. 46.1% • Mild/moderate stenosis: 27.7% vs. 31.6% • Spondylolisthesis: 8.4% vs. 11.8% • Sacroiliac dysfunction: 3.6% vs. 6.6% Concurrent leg pain (total): 61% Duration of pain (Noted as median time since diagnosis): 8.50 yrs vs. 8.00 yrs	N=159 Mean age (range): 38 years (NR) Female: 60.2% vs. 52.6% White: 90.4% (75/83) vs. 96.1% (73/76) Black: 4.8% (4/83) vs. 2.6% (2/76) Hispanic/ Latino: NR Asian: 2.4% (2/83) vs. 0% American Indian or Alaska Native: 2.4%% (2/83) vs. 1.3% (1/76) Native Hawaiian/Other Pacific Islander: 1.2% (1/83) vs. 0% Other: 1.2% (1/83) vs. 0%	10-kHz SCS + CMM (n=83) [see comparator column for CMM description] Trial stimulation* for up to 14 days: • Successful†: 74/80 patients (92.5%), 69/80 (86.3%) went on to receive permanent SCS implant • Unsuccessful†: 7.5% (6/80) patients, excluded Permanent SCS specifications: • Senza, Nevro Corp. • HF • Rate: 10 kHz • Pulse width: 30 µsec • Amplitude adjusted to attain pain relief, otherwise NR	CMM alone (n=76) • best standard of care as determined for each individual patient by the study investigator • Timing NR	3 months (89.9%) Intention-to-treat analysis: • SCS + CMM: 83/83 • CMM alone: 76/76 Randomized treatment received analysis: • SCS implant: 68/83 CMM alone: 75/76 6 months (88.1%) Intention-to-treat analysis: • SCS + CMM: 83/83 • CMM alone: 76/76 Randomized treatment	Not permitted until 6 months follow-up	Nevro Corp./Several authors have significant industry-based COI

Author (year), Study Period, Country	Condition and pain duration	Population	SCS Intervention	Comparator Intervention	Follow-up (% followed)	Crossover	Funding/COI
					received analysis: • SCS implant: 65/83 • CMM alone: 75/76		
Rigoard, 2019 Study period NR; recruitment period: NR Europe/United States	Failed Back Surgery Syndrome: 100% Concurrent leg pain: 100% Duration of pain, years (SD): 6.7 (7.2)	N=218 Mean age (SD): 53.9 (11.5) Female: 60.6% White: NR Black: NR Hispanic/ Latino: NR Asian: NR Other: NR	Conventional SCS + OMM (n=110) [see comparator column for OMM description] Trial stimulation* (duration NR): • Successful†: 90/110 patients (81.8%), 82/110 (74.5%) went on to receive permanent SCS implant • Unsuccessful†: 18.2% (20/110) patients, 14 patients failed or declined and switched to OMM Permanent SCS specifications (6 months): • Pulse Generator + Specify 5-6-5 lead, Medtronic, Inc. • Pulse	OMM alone (n=108) Acupuncture, psychological/behavioural therapy, physiotherapy, spinal injections/blocks, epidural adhesiolysis, neurotomies. Timing NR	6 months Intention-to-treat analysis: • SCS + OMM: 110/110 • OMM alone: 108/108 As treated analysis: • SCS implant: 79/83 OMM alone: 117/121	Not permitted until 6 months follow-up (except for SCS patients that failed trial stimulation (n=14))	Medtronic, Inc./ Several authors have significant industry-based COI

Author (year), Study Period, Country	Condition and pain duration	Population	SCS Intervention	Comparator Intervention	Follow-up (% followed)	Crossover	Funding/COI
			• Rate: 90.6 Hz • Pulse width: 388.0 µsec • Amplitude: 3.07V				
North, 2020 See Rigoard, 2019	See Rigoard, 2019	See Rigoard, 2019	See Rigoard, 2019	See Rigoard, 2019	See Rigoard, 2019	See Rigoard, 2019	See Rigoard, 2019
Kumar, 2007 Study period NR; recruitment period: NR Europe/United States	Failed Back Surgery Syndrome: 100% Unilateral leg pain: 65% (65/100) Bilateral leg pain: 35% (35/100) Duration of pain, years (SD): NR	N=100 A vs. B Mean age (SD): 48.9 (10.0) vs. 52.0 (10.7) Female: 42% vs. 56% White: NR Black: NR Hispanic/ Latino: NR Asian: NR Other: NR	SCS + CMM (n=52) [see comparator column for OMM description] Trial stimulation* (duration NR): • Successful†: 43/52 patients (82.7%), 48/52 (92.3%) went on to receive permanent SCS implant • Unsuccessful†: 17.3% (9/52) patients Permanent SCS specifications (6 months) mean (SD): • Synergy System, Medtronic, Inc. • Pulse • Rate: 49 Hz (16.4) • Pulse width: 350 µsec (95.5)	CMM alone (n=48) Included oral medications (i.e. opioid, non-steroidal anti-inflammatory drug, antidepressant, anticonvulsant/antiepileptic and other analgesic therapies), nerve blocks, epidural corticosteroids, physical and psychological rehabilitative therapy, and/or chiropractic care Timing NR	6 months Primary analysis (not explained very well): • SCS + OMM: 50/52 • OMM alone: 43/48	Not permitted until 6 months	Medtronic, Inc./ Several authors have significant industry-based COI

Author (year), Study Period, Country	Condition and pain duration	Population	SCS Intervention	Comparator Intervention	Follow-up (% followed)	Crossover	Funding/COI
			• Amplitude: 3.7V (2.0)				
Manca, 2008 See Kumar, 2007	See Kumar, 2007	See Kumar, 2007	See Kumar, 2007	See Kumar, 2007	See Kumar, 2007	See Kumar, 2007	See Kumar, 2007
North, 2005 Study period NR; recruitment period: NR United States	FBSS: nerve root compression and radicular pain not resolved by initial back surgery: 100% Duration of pain, years (SD): NR	N=100 A vs. B Mean age: Range 26yrs to 76yrs Female: NR White: NR Black: NR Hispanic/ Latino: NR Asian: NR Other: NR	SCS (n=30) Trial stimulation* for ≥3 days: • Successful†: 17/24 patients (70.8%) and went on to receive permanent SCS implant • Unsuccessful†: 29.2% (7/24) patients Permanent SCS specifications (6 months) mean (SD): • Xtrel or Itrel generator + Resume electrode, Medtronic, Inc. • Pulse • Rate: NR • Pulse width: NR • Amplitude: NR	Reoperation (n=30) Laminectomy and/or foraminotomy and/or discectomy in all patients with or without fusion, with or without instrumentation Timing NR	"Long term" follow-up as randomized no crossover, 2.9 (1.1) years SCS: 15/30 Reoperation: 12/30	Not permitted until 6 months (except for SCS patients that failed trial stimulation (n=5))	Medtronic, Inc.

COI = Conflict of interest; CMM = Conventional medical management; HF = High frequency; kHz = Kilohertz; NR = Not reported; OMM = Optimal medical management; SCS = Spinal cord stimulator; SD = Standard deviation.

Appendix Table G3. Demographics, Parallel RCTs for PDN

Author (year), Study Period, Country	Condition and pain duration	Population	SCS Intervention	Comparator Intervention	Follow-up (% followed)	Crossover	Funding/COI
De Vos 2014 Study period NR; recruitment period: November 2008 to October 2012 Netherlands, Denmark, Belgium, Germany	PDN (100%) Mean pain duration: 7 years	N=60 Mean age (range): 59 years (NR) Female: 37% White: NR Black: NR Hispanic/ Latino: NR Asian: NR Other: NR	SCS + CMM[*] (n=40) [see comparator column for CMM description] Trial stimulation for 7 days maximum: • Successful: 37/40[†] patients (93%), went on to receive permanent SCS implant. • Unsuccessful: 3/40 patients, all dropped out of study. Permanent SCS specifications: • EonC, Eon, or Eon Mini • Constant current • Rate: 2 to 1200 Hz • Pulse width: 50 to 500 µsec • Amplitude 0 to 25.5 mA.	CMM[*‡] (n=20) Medication adjustments and other conventional pain treatments, such as physical therapy, were allowed at any time during the study, if needed	6 months 54/60 (90%) Intention-to-treat analysis: • SCS + CMM: 36/40 • CMM: 18/20 Randomized treatment received analysis: • SCS + CMM: 40/40 • CMM alone: 20/20	Not permitted until end 6 month follow-up	Sponsored by St. Jude Medical One author received teaching fees from St. Jude Medical and is a paid consultant for Biolab Technology.
Duarte 2016 See above	See above	See above	See above	See above[‡]	6 months: 54/60 (90%) Randomized treatment received analysis: • SCS + CMM: 36/40 • CMM alone: 18/20	See above	No funding No COI
Slangen 2014 Study period NR; recruitment period:	PDN (100%) Mean pain duration: 5.5 years	N=36 Mean age (range):	SCS + CMM (n=22) [see comparator column for CMM description]	CMM (n=14) CMM according to the international guidelines (5,7,15) and the	6 months: 30/36 (83%) Intention-to-treat analysis:	Details NR. Unsuccessful patients were followed at all time points,	Sponsored by Medtronic One author received a 3

Author (year), Study Period, Country	Condition and pain duration	Population	SCS Intervention	Comparator Intervention	Follow-up (% followed)	Crossover	Funding/COI
February 2010 to February 2013 Netherlands		57 years (18 to 80) Female: 33% White: NR Black: NR Hispanic/ Latino: NR Asian: NR Other: NR	Trial stimulation for 14 days: • Successful: 17/22 patients (77%), went on to receive permanent SCS implant. • Unsuccessful: 4/22 (18%) patients, • 1 patient died after attempted trial stimulation Permanent SCS specifications: • Synergy Versitrel or PrimeAdvanced • LF • Rate: 3 to 130 Hz • Pulse width: 60 to 450 µsec • Amplitude 0 to 10.5 mA.	treatment algorithm of Jensen et al. (6); Invasive therapy, such as intrathecal drug delivery, was not allowed	• SCS + CMM: 17/22 • CMM: 13/14 Randomized treatment received analysis: • SCS + CMM: 22/22 • CMM: 14/14	and considered as in the SCS group.	year grant from Medtronic
Van Beek 2015	See above	See above	See above	See above	24 months SCS + CMM 77.3% (17/22)	Patients were allowed to crossover at 6 months	Sponsored by Medtronic One author received a 3 year grant from Medtronic
Petersen 2021 Study period NR; Recruitment period: August 2017 to August 2019	PDN (100%) Median pain duration: 5.6 years	N=216 Mean age (range): 61 years (NR) Female: 63% White: NR Black: NR Hispanic/	SCS + CMM (n=113) [see comparator column for CMM description] Trial stimulation for 5 to 7 days: • Successful: 90/113 patients (80%), went on to receive permanent SCS implant.	CMM (n=103) May include a variety of non-invasive or minimally invasive treatments that comprise the standard of care for neuropathic limb pain. Investigators will follow their standard of care and/or	6 months: 184/216 (85%) Intention-to-treat analysis: • SCS + CMM: 91/113 • CMM: 93/103 Randomized treatment received analysis:	Patients in either treatment arm allowed to crossover to the alternative arm Crossovers at 6 months: 0% (0/87) vs.	Sponsored by Nevro Corp Authors have received fees from various private corporations

Author (year), Study Period, Country	Condition and pain duration	Population	SCS Intervention	Comparator Intervention	Follow-up (% followed)	Crossover	Funding/COI
		Latino: NR Asian: NR Other: NR	• Unsuccessful: 6/113 (5%) patients, included in 6 month analyses • 8/113 (8%) were excluded before trial SCS due to withdrawn consent, AEs, or loss to follow-up, and a further 8/113 (7%) were excluded following successful trial SCS due to declining permanent SCS, AE, or loss to follow-up Permanent SCS specifications: • Senza • HF • Rate: 10k Hz • Pulse width: 30-µsec • Amplitude: 0.5 to 3.5 mA	published clinical guidelines (Dworkin, 2010) to administer CMM to both treatment groups. Treatments include, but are not limited to, pharmacological agents, physical therapy, cognitive therapy, chiropractic care, nerve blocks, and other non-invasive or minimally invasive therapies.	• SCS + CMM: 113/113 • CMM: 103/103	81.7% (76/93), p<0.001 69% (64/93) received permanent device implants after crossover.	
Petersen 2022 See above [12-month f/u of Petersen 2021 RCT]	See above	See above	See above	See above	12 months: 71.3% (154/216) 79.6% (90/113) SCS + CMM group were combined with the 68.8% (64/93) crossover patients to make a new sample of n=154	See above 68.8% (64/93) received permanent device implants after crossover.	Sponsored by Nevro Corp Authors have received fees from various private corporations

CMM = conventional medical management; COI = conflict of interest; HF = high=frequency; LF = low-frequency; NR = not reported; PDN = painful diabetic neuropathy; SCS = spinal cord stimulator.

*For all patient's in SCS or conventional treatment groups, medication adjustments and other conventional pain treatments, such has physical therapy, were allowed at any time during the study, at the discretion of the treating physician and the patient.

† One further patient dropped out at 3 months due to joining a pharmacological gastroenterology study.

‡ Duarte 2016 refers to the control group as conventional medical practice, while De Vos 2014 refers to it as best medical therapy. Assumed to be the same treatment.

Appendix Table G4. Demographics, Parallel RCTs for CRPS

Author (year), Study Period, Country	Condition and pain duration	Population	SCS Intervention	Comparator Intervention	Follow-up (% followed)	Crossover	Funding/COI
Kemler 2000 Study period NR; recruitment period: March 1997 to July 1998 Netherlands	Chronic CRPS I (100%) • affecting the: hand (61%), foot (39%) • caused by: trauma (48%), surgery (44%), or developed spontaneously (7%) Duration of pain: 38 months	N=54 Mean age (range): 38 years (NR) Female: 69% White: Black: Hispanic/ Latino: Asian: Other:	SCS + PT (n=36) [see comparator column for PT description] Trial stimulation* for ≥7 days: • Successful†: 24/36 patients (67%), went on to receive permanent SCS implant • Unsuccessful†: 12/36 patients, went on to receive PT alone (crossed over) Permanent SCS specifications: • Rate: 85 Hz • Pulse width: 210 µsec • Amplitude (adjusted by patient): 0–10 V.	PT alone (n=18) • standardized program of graded exercises to improve strength, mobility, and function • 30 minutes twice/week for 6 months	6 months (100%) Intention-to-treat analysis: • SCS + PT: 36/36 • PT alone: 18/18 Randomized treatment received analysis: • SCS implant: 24/24 • PT alone: 18/18	12 to PT at trial failure, then no additional crossover	Grant from the Dutch Health Insurance Council; No COIs
Kemler 2004 See above [24-month f/u of Kemler 2000 RCT]	See above	See above	See above SCS + PT group (n=36): • implant: 24/24 • no implant: 11/12 • 1/12 patient excluded (received special implant) • 9/24 patients still undergoing PT**	See above PT group (n=18): • 16/18 • 2/18 patients excluded (crossed over) • 12/18 patients still undergoing PT**	24 months (94%; 51/54) Intention-to-treat analysis: • SCS + PT: 35/36 • PT alone: 16/18 Randomized treatment received analysis: • SCS implant: 24/24 • PT alone: 16/18	See above	See above
Kemler 2008 See above	See above	See above	See above SCS + PT group (n=36):	See above PT group (n=18):	60 months (81%; 44/54)	See above	See above

Author (year), Study Period, Country	Condition and pain duration	Population	SCS Intervention	Comparator Intervention	Follow-up (% followed)	Crossover	Funding/COI

[60-month f/u of Kemler 2000 RCT]			• implant: 22/24
			  • 2/24 lost to f/u
			• no implant: 9/12
			  • 1/12 excluded (received special implant)
			  • 2/12 lost to f/u
			• number of patients still undergoing PT** NR
				• 13/18
				• 4 excluded (crossed over)
				• 1 lost to f/u
				number of patients still undergoing PT** NR
					Intention-to-treat:
					• SCS + PT: 31/36
					• PT alone: 13/18
					
					Randomized treatment received analysis:
					• SCS implant: 20/24
					• PT alone: 13/18		

Canos-Verdecho, 2021	CRPS with upper limb involvement (100%)	N=41 Mean age (range): 49 years (NR) Female: 78.0% (32/41) White: 97.6% (40/41) Black: NR Hispanic/ Latino: NR Asian: NR Other: 2.4% (1/41)	Low frequency SCS (LF-SCS) (n=14) 10-kHz SCS (n=11) Trial stimulation* for 14 days: • Successful†: 12/14 patients (85.7%) in LF-SCS and 10/11 (90.9%) in 10-kHz SCS went on to receive permanent SCS implant • Unsuccessful†: 2/14 patients (14.3%) in Low frequency SCS (LF-SCS) and 1/11 (9.1%) in 10-kHz SCS were dropped from study pop Permanent LF-SCS specifications: • RestoreSensor, Intellis MEDTRONIC • Tonic, LF • Rate: 40-60 Hz • Pulse width: 250-400 MCS	Conventional Treatment (n=25) Included pharmacological, physical, and blockages	12 months: 41/50 Does not appear to use any ITT analysis	N/A	"Not sponsored by any device manufacturer" Author COI NR

Author (year), Study Period, Country	Condition and pain duration	Population	SCS Intervention	Comparator Intervention	Follow-up (% followed)	Crossover	Funding/COI
			Permanent LF-SCS specifications: • Senza system; Nevro Corp. • Type NR • Rate: 10 kHz • Pulse width: NR				

COI = Conflict of interest; CRPS = Complex regional pain syndrome; f/u = follow-up; HF = High frequency; Hz = Hertz; ITT = Intention-to-treat; LF= Low frequency; NR = Not reported; PT = Physical therapy; SCS = Spinal cord stimulator.

* Trial stimulation of SCS - devices used:

Kemler 2001, 2004, 2008: temporary electrode (model 3861, Medtronic, Minneapolis, MN): positioned in the in epidural space so the patient experienced paresthesia over the entire region of pain upon stimulation; external stimulator (model 3625, Medtronic).

Kumar 2007: device and length of trial stimulation NR.

North 2005: temporary electrode (3487A Pisces-Quad, Medtronic): placed in the percutaneous space, no other details given.

Turner 2010: device details NR, devices used determined by the treating physician.

† Trial stimulation of SCS – definition of success:

Kemler 2001: trial stimulation was considered successful if patients met either of the following criteria: (1) VAS score for the last four days of test stimulation was ≥ 50% lower than the score prior to randomization, and/or (2) the GPE score was ≥ 6 ("much improved").

Kumar 2007: trial stimulation was considered successful if patients met both of the following criteria: (1) ≥ 50% reduction in leg pain, and (2) ≥ 80% overlap of their pain with stimulation-induced paresthesia.

North 2005: trial stimulation was considered successful if patients met all of the following criteria: (1) ≥ 50% reduction in pain "by standard pain rating methods", (2) did not increase their analgesic medication dosage, and (3) had improved physical activity proportionate to their neurological status and age.

Turner 2010: success criteria NR, determined by the treating physician

‡ Permanent SCS implantation - devices used:

Kemler 2001, 2004, 2008: electrode (model 3487A, Medtronic): placed in thoracic (for hand) or lumbar (for foot) spine so the patient experienced paresthesia over the entire region of pain upon stimulation; pulse generator (Itrell III, model 7425, Medtronic): implanted in the left lower abdominal wall; tunneled extension lead (model 7495-51/66, Medtronic); programmer (model 7434-NL, Medtronic); generator specifications: rate: 85 Hz, pulse width: 210usec, amplitude (adjusted by patient): 0–10 V.

Kumar 2007: implantable neurostimulation system (Synergy System, Medtronic)

North 2005: electrode (3487A-56 or 3587A Resume Electrode, Medtronic): no details given regarding placement; generator (X-trel or Itrel pulse generator, Medtronic): no details given.

Turner 2010: device details NR, devices used determined by the treating physician.

Appendix Table G5. Demographics, Non-randomized Studies for Interventions

Author (year), Study Period, Country	Condition and pain duration	Population	SCS Intervention	Comparator Intervention	Follow-up (% followed)	Crossover	Funding/COI
Turner 2010 December 2004 to June 2006 USA	FBSS (100%) Duration of chronic pain (median): 165 weeks	N=159 Mean age (range): 44.1 years (NR) Female: 33% White: NR Black: NR Hispanic/ Latino: NR Asian: NR Other: NR	SCS (n=52) Trial stimulation duration NR • Successful: 27/51 patients (53%), went on to receive permanent SCS implant. • Unsuccessful: 24/51 (47%) patients. Unclear if they dropped out. Permanent SCS specifications: • Device NR* • Rate: NR • Pulse width: NR • Amplitude NR	Pain clinic (n=51) Decisions for treatment were determined by the treating physician. Usual care (n=56) Treatment details NR	104 weeks SCS: n=43 Pain clinic: n=34 Usual care: n=61†	Patients were allowed to crossover shortly after enrollment SCS Crossover: from UC: +3 from PC: +1 Pain clinic Crossover: from UC: +4 from SCS:+2 Usual care Crossover: from PC: +16 from SCS: +3	Funded by Washington State Department of Labor and Industries COI: None
Perez 2021 Patients assessed between 2011 and 2015 to complete 24-month observational period. Spain	FBSS (100%) Mean symptom duration: 8.7 years	N=85 Mean age (range): 57 years (NR) Female: 68% White: NR Black: NR Hispanic/ Latino: NR Asian: NR Other: NR	SCS (n=39) Patients did 1 or 2 week trial, and permanently implanted if reporting ≥50% pain reduction. • Device NR • Rate: 83% of patients received 40-70 Hz; 17% received 1000 Hz • Pulse width: 83% received 280 to 420 microsec; 17% received 200 microsec • Amplitude: 83% received 3.8 to 6 mA; 17% received 2 mA	CMM (n=46) Included oral and intravenous pharmacological treatment (NSAIDs, opioids, muscle relaxants, anticonvulsants, and dual or tricyclic antidepressants), physical therapy, nerve block and trigger point block, epiduroscopy, radiofrequency,	12 weeks: 86% (73/85) 26 weeks: 79% (67/85) 52 weeks: 72% (61/85) 78 weeks: 64% (54/85) 104 weeks: 64% (54/85)	NR	Funding from Boston Scientific Iberica S.A. COI: None

Author (year), Study Period, Country	Condition and pain duration	Population	SCS Intervention	Comparator Intervention	Follow-up (% followed)	Crossover	Funding/COI
			All tonic patients added simultaneous subthreshold stimulation programs (Burst (6 pulses) and/or high frequency. All SCS patients were also offered pharmacological treatment, which was monitored during the trial period.	epidural procedures, and oxygen-ozone therapy.			
Dhruva 2023 Data analyzed‡ from February 1 2021 to August 31 2022 USA	FBSS (71%), chronic pain (26%), CRPS (10%) Symptom duration NR	N=7560§ Mean age (range): 64 years (NR) Female: 59% White: 77.9% Black: 11.9% Hispanic/ Latino: 6.4% Asian: 0.7% Other: 3.1%	SCS (n=1260) Patients only included if they had been a permanent SCS** Permanent SCS specifications: • Device NR • Rate: NR • Pulse width: NR • Amplitude NR	CMM (n=6300)§ Consisted of pain medications, spine surgery, radio-frequency ablation, epidural and facet corticosteroid injections, and conservative nonpharmacologic therapies such as physical therapy, chiropractic treatment, and acupuncture.	Unclear	NR	Supported by Arnold Ventures One authors reported other grants from the study funder, as well as various government agencies, and serves on the Institute for Clinical and Economic Review California Technology Assessment Forum. 5 authors report being employees of and owning stock in various

Author (year), Study Period, Country	Condition and pain duration	Population	SCS Intervention	Comparator Intervention	Follow-up (% followed)	Crossover	Funding/COI
							industry companies.
Vu 2022 Patients treated between December 2015 to May 2021 USA	FBSS (100%)	N=552937[††] Median age (IQR): 60 (51 to 69) Female: 55% White: 90.4% Black: 9.3% Hispanic/ Latino: 0% Asian: 0.3% Other: 0%	SCS (n=26179) Patients only included if they had been a permanent SCS[‡‡] Permanent SCS specifications: • Device NR • Rate: NR • Pulse width: NR • Amplitude NR	No SCS (n=526758) [††] Patients included in the control group if they were 18 years or older, remained within a participating health care organization between 12 before and 15 months after index date, and did not receive an SCS. Further details NR.	12 to 65 weeks 100% (552937/552937)	NR	Study funded by grant from MIRROR, Uniformed Services University of the Health Sciences, US Department of Defense One author reported receiving personal fees from SPR Therapeutics. No other COIs reported.
Lad 2014 Patient records from 2000 to 2009 USA	FBSS (100%)	N=16455 Mean age (range): 54 (NR) Female: (SCS) 63.8% vs. (reoperation) 55.3% White: NR	SCS (n=395) Patients only included if they had been a permanent SCS[§§] Permanent SCS specifications: • Device NR • Rate: NR • Pulse width: NR • Amplitude NR 104 weeks continuous enrollment cohort (n=111)	Reoperation (n=16060) Patients with inpatient stays coded from ICD-9 for lumbar surgery. 104 weeks continuous enrollment cohort (n=6386)	104 weeks 39% (6497/16455) patients with 104 weeks of post-operative continuous enrollment.	NR	No funding COI: NR

Author (year), Study Period, Country	Condition and pain duration	Population	SCS Intervention	Comparator Intervention	Follow-up (% followed)	Crossover	Funding/COI
		Black: NR Hispanic/ Latino: NR Asian: NR Other: NR					

CMM = conventional medical management; COI = conflict of interest; CRPS = complex regional pain syndrome; CTP-4 = Current Procedural Terminology, Fourth Edition; FBSS = failed back surgery syndrome; ICD-9 = International Classification of Disease, Ninth Revision; IQR = interquartile range; NR = not reported; NRSI = non-randomized studies of intervention; PC = pain clinic; SCS = spinal cord stimulation; UC = usual care.

*Decisions on procedures and equipment were determined by physicians.

† Unclear how many original patients were left in the group due to crossover effects.

‡ The cohort entry date was defined as the first diagnosis claim meeting any of these criteria after a diagnosis-free clean period of 6 months. If individuals had more than 1 qualifying diagnosis, cohort entry diagnosis and date was based on the following hierarchy: (1) failed back surgery syndrome, (2) complex regional pain syndrome, (3) chronic pain syndrome, and (4) other chronic postsurgical back and extremity pain.

§ Data comes from administrative claims data, including longitudinal medical and pharmacy claims, from US commercial and Medicare Advantage enrollees 18 years or older in Optum Labs Data Warehouse. Patients with incident diagnosis codes for failed back surgery syndrome, complex regional pain syndrome, chronic pain syndrome, and other chronic postsurgical back and extremity pain

** Individuals who received both SCS and CMM in the 52 weeks after cohort entry were assigned to the SCS group and baseline use of CMM treatments were evaluated as binary covariates. Only 6.3% (80/1260) did not receive any elements of the CMM treatments during the 6-month baseline period.

†† Data identified using the TriNetx Diamond Network.

‡‡ Patients included based on ICD-9 and ICD-10 codes, with the defined index date as the date of SCS implantation. Patients included those 18 years or older who remained within a participating health care organization for 52 weeks prior and 15 months after index date.

§§ Patients included from MarketScan commercial Claims and Encounters, Medicare Supplemental and Medicare database records. Patients were cases of FBSS or post laminectomy pain syndrome from IDC-9 and CPT-4 with codes for laminectomy or hemilaminectomy with or without simultaneous facetectomy or foraminotomy, as well as patients with lumbar fusion. Cases of SCS were coded for implantation or replacement of spinal neurostimulator lead with insertion or replacement of SCS system.

Appendix Table G6. Summary Characteristics for Crossover Trials

	Study, year			
	Al-Kaisy 2018	Hara 2022	Sokal 2020	Kriek 2016
Screening	Yes (NOS)	Yes (NOS)	Yes (NOS)	Unclear
N enrolled	53	65	23*	43
N, SCS trial completed	36	61	16*	40
Trial success threshold	≥50% pain reduction	≥2 point NRS reduction -leg pain	≥50% reduction	≥50% reduction or patient stated much improved

N permanent implant	92% (33/36)	50	18[*]	35
Same device, parameters, trial and permanent	Unclear	No[†]	Unclear	Yes[‡]
N randomized	30	50	18[*]	33
N analyzed	24	42	18	29
Mean age	48	50	57	43
Sex (female)	33%	54%	48%	14%
Comorbidities (any relevant)	NR	64%	NR	NR
Condition, diagnosis	FBSS (NOS)	Prior lumbar surgery, chronic radicular pain	FBSS 78% CRPS 22%	CRPS
Prior surgery	Yes, (NOS)	Median: 2 (1-3) diskectomy 76% Fusion 26% Decompression 22%	Yes (FBSS, NOS)	NA
Active Treatments	- RestoreSensor system - 1200 Hz @180 µsec, 3030 Hz@60 µsec, 5882 Hz @30 µsec - Dual octopolar leads placed between T7 and T10, using maximum of three active contacts. IPG placed subcutaneously in the abdomen or gluteal region. - Prophylaxis NR	- Precision Novi - Burst- 40 HZ, 4 spikes per burst, amplitude, 50% to 70% paresthesia perception threshold - Single 16-contact lead or two 8-contact leads implanted at L1/L2or L2/L3 and placed in epidural space at T9/T10 level under fluoroscopic guidance. - IPG placed subcutaneously on the upper buttock or abdomen. - Prophylaxis NR	- Precision Novi or Montage[§] - LF: 40-60 Hz, HF (1000 Hz), cluster tonic - Single 8-contact or dual 16-contact leads implanted between T7 and T10. - Permanent IPG location NR - Five patients who could not undergo percutaneous implantation were implanted with a surgical paddle electrode with central flavectomy	- Eon - 40 Hz SCS, 500 Hz SCS, 1200 Hz SCS, Burst SCS - Single 8-contact lead (location NR) under fluoroscopy. - IPG placed either in the lower abdomen or in the gluteal area. - Antibiotic prophylaxis.

			on the thoracic level and the IPG was implanted in the subcutaneous pocket. - Prophylaxis NR	
Sham	Generator discharging, no electrical transmission to leads	No stimulation	IPG deactivated	IPG switched off
Number Tx periods	4	4	4	5
Period length	3 weeks	12 weeks	2 weeks	2 weeks
Washout period between phases	No	Unclear/No	No	2 days
Check period effects	Yes	No	No	No
Repeated measures analysis	Yes	Yes	Yes	Yes
1st Phase data	NR	NR	NR	No
Co-intervention, medications	NR	Daily pain meds (baseline) Overall: 64% (32/50) Opioids: 36% Gabapentinoids: 34% Acetaminophen: 34% NSAIDs: 10% Antidepressants: 6%	Model estimates, Timing NR: Opioids: 49% NSAIDS: 72%	NR**
Funding	Industry	Non-industry	None	Industry
Notes	NR	NR	NR	NR

CRPS = complex regional pain syndrome; FBSS = failed back surgery syndrome; HF=high frequency; Hz = hertz; IPG = implanted pulse generator; LF= low frequency; NA = not applicable; NOS = not otherwise specified; NR = not reported; NRS = numerical rating scale; NSAIDs = non-steroid inflammatory drugs; RCT = randomized control trial; SCS = spinal cord stimulator; Tx = treatment; µsec = microsecond.

* 1 patient did not achieve satisfactory pain relief, 2 did not agree to further evaluation, 1 patient's responses considered irrelevant, unreliable. 17 patients underwent trial stimulation; 13 patients from trial received permanent implant. An additional 5 patients (as well as another 1 that did not agree to further evaluation and dropped out) who had not undergone trial stimulation were added for a total of 18 randomized.

† Trial: External neurostim device with programming to optimize tonic conventional stim, determine paresthesia thresholds. Permanent: non-rechargeable implantable pulse generator

‡ Conventional SCS was used for both the trial and permanent SCS, however RCT interventions included burst and higher frequency stimulation.

§ Only one patient received the Montage IPG. All others were implanted with the Precision Novi.
** The protocol for this trial reports that medication consumption would be assessed at all time points, stratified into medication groups, and that the sum dosage of various pain medication groups would be calculated. This was not reported in the final publication.

Appendix Table G7. Characteristics of Parallel Trials in Patients with Chronic Low Back Pain

	Study, year					
	Kumar, 2007 PROCESS trial		Rigoard, 2019 PROMISE		Kapural, 2022	
	SCS (+ CMM)	CMM	SCS (+ CMM)	CMM	SCS (+ CMM)	CMM
Diagnosis	FBSS		FBSS		NSRBP	
Screening done	Yes (inclusion criteria)		Yes (exclusion criteria)		Yes (exclusion criteria)	
N enrolled	52	48	278		211	
N randomized	52	48	110	108	83	76
N analyzed	50	44	110	108	65	75
N, SCS trial completed	52	n/a	102	n/a	80	n/a
N SCS trial successful	82% (43/52)	n/a	80% (82/102)	n/a	93% (74/80)	n/a
Trial success threshold	≥80% overlap oftheir pain with stimulation-induced paresthesia and ≥ 50% leg pain relief	n/a	Subject finds paresthesia acceptable and adequate LBP relief with usual activity and appropriate analgesia as assessed by the investigator	n/a	≥50% pain relief on VAS	n/a
N permanent implant	92% (48/52)*	n/a	80% (82/102)	n/a	86% (69/80)	n/a
Was (were) same device, parameters, for trial and permanent	NR	n/a	NR	n/a	NR	n/a
N crossover (timing)	10.0% (5/50) (6 months)	72.7% (32/44) (6 months)	2.4% (2/83) (6 months)	73% (77/106 (6 months)	0% (6 months)	89% (67/75) (6 months)
Mean age	49 years	52 years	53	55	Median 53	Median 59

	Study, year					
	Kumar, 2007 PROCESS trial		Rigoard, 2019 PROMISE		Kapural, 2022	
Sex (female)	42%	56%	62%	59%	60%	53%
Comorbidities (any relevant)	NR	NR	NR	NR	NR; nonsurgical candidates due to underlying pathology or presentation (78%) or comorbidity (7%)	NR; nonsurgical candidates due to underlying pathology or presentation (80%) or comorbidity (7%)
Symptom duration	≥6 months	≥6 months	6.4 years	7.0 years	8.5 years	8.0 years
Prior CMM	NR	NR	100%	100%	100%	100%
FBSS diagnostic criteria described	Yes[†]	Yes	Yes[‡]	Yes	n/a	n/a
Prior surgery For FBSS – time since last surgery	4.7 years	4.6 years	5.3 years	5.6 years	n/a	n/a
Number of back surgeries	>1 surgery: 54%	>1 surgery: 46%	Mean 1.9	Mean 2.0	n/a	n/a
SCS characteristics	-Synergy™ system -LF: mean 49 ± 16.4 Hz -Pulse width: mean 350 ± 95.5 µs -Amplitude: 45% required ≥4 V -Burst or tonic: NR, assume tonic -Lead number and type: NR -antibiotic prophylaxis: NR		-Medtronic pulse generator (rechargeable or primary cell) -LF: 20-1200 Hz -Specify® 5-6-5 surgical lead (multicolumn) -other device specifics NR -Burst or tonic: NR, assume tonic -antibiotic prophylaxis: NR		-SENZA device -HF: 10 kHz -pulse width: 30 µsec -amplitude: adjusted to maximize pain relief -Burst or tonic: NR, assume tonic -2 percutaneous leads with 8 contacts each, placed epidurally (fluoroscopic guidance) between T8 and T11 -antibiotic prophylaxis: NR	
Comparator (definition, components)	Oral medications (i.e., opioid, NSAIDs, antidepressant, anticonvulsant/ antiepileptic, other analgesic therapies), nerve blocks, epidural corticosteroids, physical and psychological rehabilitative therapy, and/or chiropractic care		Individualized treatment plan that could include: 1) Pharmacological agents (e.g., antidepressants, opioids or tramadol, antiepileptics), 2) noninvasive treatments (e.g., acupuncture, psychological/ behavioral therapy, and		Best standard of care determined by study investigator, generally consistent with American College of Physicians and American Pain Society guidelines	

	Study, year			
	Kumar, 2007 PROCESS trial		Rigoard, 2019 PROMISE	Kapural, 2022
			physiotherapy), and/or 3) invasive treatments (e.g., spinal injections/blocks, epidural adhesiolysis, and neurotomies). Excluded: intrathecal drug delivery, peripheral nerve stimulation, back surgery, and experimental therapies	
Co-interventions, Medications at baseline	-Opioids: 29% -NSAIDs: 29% -Antidepressants: 37% -Physical rehabilitation: 2% -Psychological rehabilitation: 2% -Acupuncture: 4% -Massage: 0% -TENS: 6%	-Opioids: 48% -NSAIDs: 48% -Antidepressants: 40% -Physical rehabilitation: 4% -Psychological rehabilitation: 4% -Acupuncture: 2% -Massage: 4% -TENS: 10%	Opioid use (as treated group only): 73.5%	Opioid use (PP group only): 52.1%
Follow-up	3, 6, 12 and 24 months		6, 12, 24 months	3, 6, 12 months
Funding	Industry (Medtronic)		Industry (Medtronic)	Industry (Nevro Corp.)

CMM = Conventional medical management; FBSS = Failed Back Surgery Syndrome; HF = High frequency; Hz = Hertz; IPG = Implantable pulse generator; kHz = Kilohertz; LF = Low frequency; NR = Not reported; NSAIDs = Non-steroid anti-inflammatory drugs; NSRBP = Non-surgical back pain; PP = Per protocol; SCS = Spinal cord stimulator; TENS = transcutaneous electrical nerve stimulation; VAS = Visual analogue scale; µsec = microseconds

* 5 patients who failed requested to be implanted with device.

† Neuropathic pain of radicular origin predominantly in the legs (exceeding back pain), of an intensity of at least 50 mm on a visual analogue scale (0-100 mm) for at least 6 months after a minimum of one anatomically successful surgery for a herniated disc. Thus all patients had a documented history of nerve injury, i.e. root compression by herniated disc, competent to explain the complaint of radiating pain.

‡ For the purposes of this study, FBSS is defined as persistent or recurrent low back and leg pain of at least 6 months duration, following at least one decompression and/or fusion procedure.

Appendix Table G8. Characteristics of Parallel Trials in Patients with Failed Back Surgery Syndrome.

	Study, Year	
	North, 2005	
	SCS	Reoperation
Screening done	Yes (Inclusion and exclusion criteria)	
N enrolled	99	
N randomized	30	30
N analyzed	19	26
N, SCS trial completed	24	n/a
N SCS trial success	79% (19/24)	n/a
Trial success threshold	>=50% pain relief and stable or improved analgesic intake with improved physical activity commensurate with neurological status and age	n/a
N permanent implant	19	n/a
Was (were) same device, parameters, for trial and permanent	No	n/a
N crossover (timing)	21% (5/24) (immediate upon trial failure)	53.8% (14/26) (6 months)
Mean age	52 years	
% female	52%	
Comorbidities	NR	NR
Symptom duration	NR	NR
Prior CMM	100%	100%
FBSS diagnostic criteria described	Yes*	Yes
Prior surgery **For FBSS – time since last surgery**	NR	NR
Number of back surgeries	2.5 ± 1.1	
SCS characteristics	-3487A-56 or 3587A Resume electrode, X-trel or Itrel pulse generator (Medtronic, Inc.) -other device specifics NR -antibiotic prophylaxis: NR	

Comparator (definition, components)	Laminectomy and/or foraminotomy and/or discectomy in all patients with or without fusion, with or without instrumentation	
Co-interventions, Medications at baseline	NR	NR
Follow-up	Mean 2.9 ± 1.1 years (range, 1.8- 5.7 years)	
Funding	Industry (Medtronic)	

LF= low frequency; HF=high frequency; IPG = implanted pulse generator; FBSS = Failed Back Surgery Syndrome; NR = Not reported; SCS = Spinal cord stimulator.
* Surgically remediable nerve root compression and concordant complaints of persistent or recurrent radicular pain, with or without low back pain, after one or more lumbosacral spine surgeries.

Appendix Table G9. Summary Characteristics of Parallel Trials in Patients with Painful Diabetic Neuropathy

	Study, Year					
	De Vos, 2014 (index), Duarte 2016		Slangen, 2014 (index), van Beek, 2015		Petersen, 2021 (index), Petersen, 2022 SENZA-PDN trial	
	SCS	CMM	SCS	CMM	SCS	CMM
Screening done	Yes (Exclusion criteria)		Yes (Exclusion criteria)		Yes (Exclusion criteria)	
N enrolled	40	20	22	14	113	103
N randomized	40	20	22	14	113	103
N analyzed	40	20	22	14	113	103
N SCS trial completed	40	-	22	-	104	-
N SCS trial successful	93% (37/40)		82% (18/22)		94% (98/104)	-
Trial success threshold	NR	-	VAS ≤50% of baseline or ≥6 on PGIC	-	VAS ≤50% of baseline	-
N permanent implant	93% (37/40)	-	77% (17/22)*	-	87% (90/104)	-
Was (were) same device, parameters, for	No; parameters unclear	-	No; parameters unclear	-	Unclear	-

trial and permanent						
N crossover (timing)	-	78% (6 months)[†]	-	93% (6 months)	0% (6 months)[‡]	82% (6 months)[‡]
Mean age	58	61	57	57	61	61
Sex (female)	38%	20%	32%	36%	38%	36%
Comorbidities (any relevant)	NR	NR	NR	NR	NR	NR
Type II diabetes	75%	75%	86%	93%	93%	97%
Diabetes duration	16 (11) years	17 (12) years	12.7 (10.1)	12.6 (7.2)	12.9 (8.5) years	12.2 (8.5) years
Symptom duration	7 (6) years	7 (6) years	6.0 (5.1) years	4.9 (3.6) years	7.4 (5.7) years	7.1 (5.1) years
Prior surgery	NR	NR	NR	NR	NR	NR
Prior CMT	100%[§]	100%[§]	100%	100%	NR	NR
Co-interventions, Medications at baseline	Opioids: 45% NSAIDs: 15% Antidepressants: 35% Anticonvulsants: 58% Acetaminophen: 30%	Opioids: 55% NSAIDs: 10% Antidepressants: 45% Anticonvulsants: 35% Acetaminophen: 30%	Pain medications (% NR)	Pain medications (% NR)	Opioids: 44% Anticonvulsants: 78% Antidepressants: 31% Topicals: 10%	Opioids: 43% Anticonvulsants: 77% Antidepressants: 42% Topicals: 9%
SCS characteristics	- EonC, Eon, or Eon mini systems - Tonic, LF (2-1200 Hz) - Pulse width: 50-500 µsec - Amplitude: 0-25.5 mA -1 lead, placed epidurally between T9 and T12 -IPG subcutaneously implanted in anterior abdominal wall or upper buttock -antibiotic prophylaxis		- Synergy Versitrel or PrimeAdvanced systems - LF (3-130 Hz) - Pulse width: 60-450 µsec - Amplitude: 0-10.5 mA -1 lead, placed epidurally (fluoroscopic guidance) over thoracic level (NR) -IPG subcutaneously implanted in anterior abdominal wall or upper buttock -antibiotic prophylaxis		- Senza system - HF: 10k Hz - Pulse width: 30 µsec - Amplitude: 0.5-3.5 mA -2 percutaneous leads, placed epidurally along T8 to T11 -IPG implanted in low back -antibiotic prophylaxis - Lead (Octrode or S8 Lamitrode; St Jude Medical, Plano, Tex) was implanted in the epidural space and positioned where the patient reported optimal overlap between paresthesia and the painful area, generally over the physiological midline, with the tip of the electrode lead between vertebral level T9 and T12.	

Comparator (definition, components)	Medication adjustments and other conventional pain treatments, such as physical therapy, were allowed at any time during the study, if needed	CMT according to the international guidelines and the treatment algorithm of Jensen et al; Invasive therapy, such as intrathecal drug delivery, was not allowed	Included variety of non-invasive or minimally invasive treatments that comprise the SOC for neuropathic limb pain. Treatments include, but are not limited to, pharmacological agents, physical therapy, cognitive therapy, chiropractic care, nerve blocks, and other non-invasive or minimally invasive therapies.
Follow-up	6 months	3, 6, 12 and 24 months	6 and 12 months
Funding	Industry (St. Jude Medical)	Industry (Medtronic)	Industry

CMM = Conventional medical management; IPG = Implanted pulse generator; LF= Low frequency; HF = High frequency; NR = Not reported; PGIC = Patient Global Impression of Change; PND = Painful diabetic neuropathy; RCT = Randomized control trial; SCS = Spinal cord stimulation; VAS = Visual analogue scale.
*1 patient did not fail, but instead died before trial stimulation was complete.
† Out of 18 still using; as reported in Duarte 2016.
‡ Patients could opt to cross over to the other treatment arm at 6 months if they had insufficient pain relief (less than 50% improvement), were dissatisfied with treatment, and were appropriate to proceed as determined by their physician.
§ All patients had tried CMT, but had failed, and were unable to be further referred by their physicians. Further details not reported.

Appendix Table G10. Characteristics of parallel trials in patients with complex regional pain syndrome.

	Study, Year				
	Kemler, 2000		Canos-Verdecho, 2021		
	SCS + PT	**PT**	**LF-SCS**	**HF-SCS**	**CMM**
Screening done	Yes (Inclusion/Exclusion)		Yes (inclusion criteria)		
N enrolled	36	18	60		
N randomized	36	18	14	11	25
N analyzed	24	18	12	10	19
N, SCS trial completed	36	n/a	14	11	n/a
N SCS trial successful	67% (24/36)	n/a	86% (12/14)	91% (10/11)	n/a
Trial success threshold	≥50% reduction in VAS pain during last 4 days of treatment OR ≥6 on global perceived effect of treatment scale	n/a	≥50% improvement in symptoms OR ≥2 point decrease in VAS pain	≥50% improvement in symptoms OR ≥2 point decrease in VAS pain	n/a
N permanent implant	67% (24/36)	n/a	86% (12/14)	91% (10/11)	n/a
Was (were) same device, parameters, for trial and permanent	No	n/a	NR	NR	n/a
Mean age	40	35	49	46	51
Sex (female)	61%	83%	67%	70%	90%

Comorbidities (any relevant)	NR	NR	NR	NR	NR
Symptom duration	3.3 years	2.8 years	1.8 (range, 1-3) years	4.7 (range, 1-19) years	2.3 (range, 2-3) years
Prior CMM	100%	100%	100%	100%	100%
CRPS cause and location	Trauma (48%), Surgery (44%), Spontaneous (7%); Hand (61%), Foot (39%)		Trauma (42%), Surgery (58%), Spontaneous (0%); Upper limb only	Trauma (70%), Surgery (10%), Spontaneous (20%); Upper limb only	Trauma (68%), Surgery (32%), Spontaneous (0%); Upper limb only
SCS characteristics	-Itrel III IPG device, implanted subcutaneously in left lower abdomen wall -LF: 85 Hz -Pulse width: 210 µsec -Amplitude: 0 to 10 V, patient controlled -Lead number and type: NR -Electrode placed over thoracic spine if hand affected or lumbar spine if foot affected -antibiotic prophylaxis		-RestoreSensor device -LF: 40-60 Hz -Pulse: 250-400 MCS -Tonic -8-pole electrode for unilateral, 2 electrodes for bilateral; C3, C4 or C5 placement -antibiotic prophylaxis NR	-SenzaR device, subcutaneously implanted in abdominal wall or gluteal region -HF: 10 kHz -1 electrode at C2 and 1 electrode at C3 -antibiotic prophylaxis NR	n/a
Comparator (definition, components)	Standardized program of graded exercises designed to improve strength, mobility, and function. Total duration 6 months; 30-minute sessions, twice weekly, with ≥2 days between sessions; delivered by trained physical therapists		Pharmacological, physical, and blockages		
Co-interventions, Medications at baseline	NR	NR	NR	NR	NR
Follow-up	6, 24, 60 months		3, 6, 12 months		
Funding	Government		None		

CMM = Conventional medical management; CRPS = Complex regional pain syndrome; HF = High frequency; Hz = Hertz; IPG = implanted pulse generator; LF = Low frequency; MCS = Microseconds; NR = Not reported; PT = Physical therapy; SCS = Spinal cord stimulator.

Appendix Table G11. Inclusion and Exclusion Criteria for Crossover Trials

Author (year),	Inclusion	Exclusion
Al-Kaisy 2018	≥18 years old; informed consent; comprehends English; comply with study procedures; on stable dose (no new, discontinues, or changes) of all prescribed medications for ≥4 weeks prior to screening and willing to maintain or decrease through end of final visit; has tried CMT; not indicated for additional surgical treatment; has undergone previous spinal surgery; diagnoses with FBSS with VAS back pain ≥6 for at least 6 months and leg pain lower less than back; two 1x8 compact leads can be placed and leads not to be placed above T1 or below S2; able to use recharging equipment and willing to recharge up to 2 times per day	Active implanted device or current signs of systemic infection; pregnant, lactating, inadequate birth control, or possibility of pregnancy during study; untreated major psychiatric comorbidity; serious drug-related behavioral issues; neurological abnormalities unrelated to FBSS; Raynaud disease; Fibromyalgia; active malignancy or been diagnosed with cancer and has not been in remission for ≥1 year prior to screening; secondary gains which may interfere in the study; participating in another clinical trial; close contacts involved in the study; average VAS back pain <6, requires amplitude ≥3 V in the supine position during device trial.
Hara 2022	≥18 years old; undergone at least 1 decompressive or fusion procedure for degenerative lumbar spine disease; experienced postoperative chronic radicular pain refractory to non-surgical treatment for ≥6 months; reported average pain intensity with ≥5 VAS leg pain; no additional spine surgery or pharmacological treatment assumed to be beneficial.	Previously treated with spinal cord stimulation or subcutaneous nerve stimulation; abnormal pain behavior; unresolved psychiatric illness, unresolved issues of possible secondary gain; inappropriate medication use.
Sokal 2020	Patients with FBSS or CRPS with neuropathic and mixed pain in the low-back and/or legs that is refractory to conservative therapy; chronic pain reported for at least 6 months; 18 to 80 years of age.	Active malignancy; addition to alcohol and/or medication; evidence of an active disruptive psychiatric disorder; local infection at the site of surgical incision; pregnancy.
Kriek 2016	Diagnoses with CRPS that is in accordance with the endorsed IASP criteria; mean pain intensity of ≥5 on VAS scale; CRPS duration of ≥12 months; no lasting success or complications with conventional therapy; CRPS in one extremity only. Further inclusion <u>Primary implantation group:</u> chronic CRPS who are unresponsive to convectional therapies.	Anticoagulant drug therapy or disturbed coagulation; age <18 years; pregnancy; ICD or pacemaker; life expectancy <1 year; lack of cooperation; drugs, medication, or alcohol addiction; immune-compromised patients.

Author (year),	Inclusion	Exclusion
	Re-implantation group: patients who already had SCS therapy, or were treated with SCS in the past but with loss of therapeutic effect over time.	

CMT = conventional medical therapy; CRPS = complex regional pain syndrome; FBSS = failed back surgery syndrome; HF = high=frequency; IASP = International Association for the Study of Pain; ICD = implantable cardioverter defibrillator; LF = low-frequency; NR = not reported; PDN = painful diabetic neuropathy; SCS = spinal cord stimulator; VAS = visual analogue scale.

Appendix Table G12. Inclusion and Exclusion Criteria for Parallel Trials

Author (year),	Inclusion	Exclusion
Kemler, 2000	18 to 65 years old; met the diagnostic criteria for reflex sympathetic dystrophy established by the International Association for the Study of Pain with impaired function and symptoms beyond the area of trauma; disease that was clinically restricted to one hand or foot and affected the entire hand or foot, that had lasted for at least six months, and that did not have a sustained response to standard therapy (six months of physical therapy, sympathetic blockade, transcutaneous electrical nerve stimulation, and pain medication), with a mean pain intensity of at least 5 cm on a visual-analogue scale from 0 cm (no pain) to 10 cm (very severe pain)	Presence of Raynaud's disease; current or previous neurologic abnormalities unrelated to reflex sympathetic dystrophy; another condition affecting the function of the diseased or contralateral extremity; blood-clotting disorder or use of an anticoagulant drug; use of a cardiac pacemaker
Canos-Verdecho, 2021	Diagnosed with CRPS with upper limb involvement according to the Budapest criteria and with a Douleur Neuropathique 4 questions pain questionnaire (DN4) score ≥ 4 (this is included in order to be able to utilize DN4 as an outcome measure given that its sensitivity for CRPS is only 88%); lack of response, defined as no significant patient-reported pain reduction or improved functionality, to conventional treatment and minimally invasive techniques (physiotherapy, intravenous phentolamine, peripheral nerve block, radiofrequency and/or sympathetic blocks at the stellate ganglion level); according to the patient selection protocol, patient is a candidate for SCS; patient is between 18 and 75 years old at the time of inclusion; patient accepted a trial period according to	Immunosuppressed patient; patient with spinal cord injury, subarachnoid space obstruction, tumors, or abnormalities on CT/MRI myelography, which may prevent correct electrode placement; patient with a history of cancer who required active treatment during the last six months; patient with documented history of substance abuse (narcotics, alcohol, etc.) or substance dependence within the past six months; patient with systemic infection; patients with a life expectancy of less than two years; pregnant women or women who may become pregnant and are not using adequate contraception, according to the researcher; patients who cannot comply with the follow-up program; patients with cognitive impairment or difficulty understanding spinal stimulation

Author (year),	Inclusion	Exclusion
	hospital protocol; patient is able and willing to comply with all study requirements	therapy; and patients already participating in other clinical research with an active treatment group
Kapural, 2022	Diagnosed with chronic, refractory axial low back pain and not a candidate for surgery based on a spine surgeons' assessment; pain should have a predominant neuropathic component as per the investigator's clinical assessment; have not had any surgery for back or leg pain, or any surgery resulting in back or leg pain; considering daily activity and rest, have average back pain intensity of ≥ 5 out of 10 cm on the Visual Analog Scale (VAS) at enrollment; be on no or stable pain medications, as determined by the investigator, for at least 28 days prior to enrolling in this study; be 18 years of age or older at the time of enrollment; willing and capable of giving informed consent; willing and able to comply with study-related requirements, procedures, and visits; be capable of subjective evaluation, able to read and understand written questionnaires in the local language and are able to read, understand and sign the written inform consent	Diagnosed back condition with inflammatory causes of back pain (e.g., ankylosing spondylitis or diseases of the viscera); medical condition or pain in other area(s), not intended to be treated with SCS, that could interfere with study procedures, accurate pain reporting, and/or confound evaluation of study endpoints, as determined by the investigator; evidence of an active disruptive psychological or psychiatric disorder identified as the primary condition or other known condition significant enough to impact perception of pain, compliance of intervention and/or ability to evaluate treatment outcome, as determined by the investigator in consultation with a psychologist; current diagnosis of a progressive neurological disease, spinal cord tumor, or severe/critical spinal stenosis; current diagnosis of a coagulation disorder, bleeding diathesis, progressive peripheral vascular disease or uncontrolled diabetes mellitus that would add unacceptable risk to the procedure; benefitting within 30 days prior to enrollment from an interventional procedure to treat back and/or leg pain; opioid addiction or drug seeking behavior as determined by the investigator; existing drug pump and/or SCS system or another active implantable device such as a pacemaker; prior experience with neuromodulation devices (SCS, PNS, DRG, multifidus muscle stimulation); condition currently requiring or likely to require the use of diathermy or MRI that is inconsistent with Senza system guideline in the Physician's Manual; metastatic malignant disease or active local malignant disease; life expectancy of less than 1 year; active systemic or local infection; pregnant (participants of child-bearing potential that are sexually active must use a reliable form of birth control); significant untreated addiction to dependency producing medications or have been a substance abuser (including alcohol and illicit drugs) within 6 months of enrollment; concomitantly participating in another clinical study; involved in an injury claim under current litigation; pending or approved worker's compensation claim
Rigoard, 2019	FBSS diagnosis; no indication for further spine	NR

Author (year),	Inclusion	Exclusion
	surgery; average lower back pain score of >=5 on the 7-day pain diary completed twice daily (morning and evening) at home using the Numeric Pain Rating Scale (NPRS); average leg pain less than mean back pain; candidates for SCS using the studied surgical lead	
Kumar, 2007	18 years of age; suffered from neuropathic pain of radicular origin (radiating in dermatomal segments L4 and/or L5 and/or S1) predominantly in the legs (exceeding back pain), at least 50 mm on a visual analogue scale (VAS: 0 to 100 mm) for at least 6 months after a minimum of one anatomically successful surgery for a herniated disc; documented history of nerve injury (i.e. root compression by herniated disc, competent to explain the complaint of radiating pain); neuropathic nature of pain was checked as per routine practice at the center (i.e. by clinical investigation of pain distribution, examination of sensory/motor/reflex change, with supporting tests such as X-ray, MRI and EMG); some patients had undergone additional procedures, namely repeat lumbar disc operations, laminectomies with or without foraminotomies or spinal fusion	Another clinically significant or disabling chronic pain condition; expected inability to receive or operate the SCS system; history of a coagulation disorder, lupus erythematosus, diabetic neuropathy, rheumatoid arthritis, or ankylosing spondylitis; evidence of an active psychiatric disorder; inability to evaluate treatment outcome as determined by the principal investigator; life expectancy of less than 1 year; existing or planned pregnancy
North, 2005	Surgically remediable nerve root compression and concordant complaints of persistent or recurrent radicular pain, with or without low back pain, after one or more lumbosacral spine surgeries; pain refractory to conservative care, with concordant neurological, tension, and/or mechanical signs and imaging findings of neural compression	Disabling neurological deficit (e.g., foot drop, neurogenic bladder) in the distribution of a nerve root or roots caused by surgically remediable compression; radiographically demonstrated (by myelographic block or its magnetic resonance imaging equivalent) critical cauda equina compression; radiographic evidence of gross instability (spondylolisthesis or abnormal subluxation) necessitating fusion; significant untreated dependency on prescription narcotic analgesics or benzodiazepines; major untreated psychiatric comorbidity; unresolved issues of secondary gain; concurrent clinically significant or disabling chronic pain problem; chief complaint of axial (low back) pain exceeding radicular (hip, buttock, and leg) pain
De Vos, 2014	At least 18 years of age and had refractory diabetic neuropathic pain in the lower extremities for more than 1 year; all conventional pain treatments had been tried, and the patients could not be treated any further according to their	Pain due to atherosclerotic lesions were excluded to avoid doubt regarding which pain etiology was being treated; infection; neuropathic pain in upper extremities (VAS score of more than 20 while at rest); received

Author (year),	Inclusion	Exclusion
	referring medical specialist; average pain score on a visual analogue scale (VAS) of at least 50	anticoagulant medication or had known coagulation irregularities; psychiatric problems (eg, depression) requiring treatment; addiction to drugs or alcohol; incapable of cooperation
Slangen, 2014	18 to 80 years of age, suffering from moderate to severe painful diabetic peripheral neuropathy present in the lower limbs according to the Michigan Diabetic Neuropathy Score (MDNS); insufficient pain relief and/or unacceptable side effects with drug treatment according to the guidelines and the algorithm described for painful diabetic peripheral neuropathy including antidepressants, antiepileptic drugs, opioids, or a combination of these therapies; pain present for >12 months, with a mean pain intensity during daytime or nighttime on a numeric rating scale (NRS) of 5 or higher	Neuropathic pain most prevalent in the upper limbs (NRS >3); neuropathy or chronic pain of other origin than diabetes mellitus; recent neuromodulation therapy (<1 month before the intake-visit); drug, medication, or alcohol (>5 units/day) abuse; insufficient cooperation from the patient (little motivation, understanding, or communication); blood clotting disorder; immune deficiency; peripheral vascular disease with no palpable foot pulses at both feet (inclusion was possible if pulses were absent, but Doppler ankle-brachial index was between 0.7 and 1.2 in both feet); active foot ulceration; life expectancy <1 year; pacemaker; local infection or other skin disorders at site of incision; psychiatric problems potentially interfering with cooperation in the study; pregnancy; severe cardiac or pulmonary failure (>New York Heart Association classification II); unstable blood glucose control (change in hemoglobin A1c [HbA1c] >1.0% in the 3 months preceding the trial); use of oral anticoagulation that could not be stopped for a period of 10 days around the implantation procedure
Petersen, 2021	Clinically diagnosed with diabetes, according to the American Diabetes Association guidelines, as well as painful diabetic neuropathy (PDN) of the lower limbs, and are symptomatic despite conservative therapy for a minimum of 12 months, have tried pregabalin (Lyrica®) OR gabapentin (Neurontin®, Gralise®, etc.) administered at an adequate dose and for an appropriate duration, in the investigator's judgement, have tried at least one other class of analgesic medication in addition to pregabalin/gabapentin, are on a stable dosage of analgesic medications for at least 30 days; average pain intensity of >= 5 out of 10 cm on the VAS in the lower extremities at enrollment; stable neurological status measured by motor, sensory and reflex function as determined by the investigator; on a stable analgesic regimen, as determined by the investigator, for at least 30 days prior to	Diagnosis of a lower limb mononeuropathy (e.g., causalgia and tibial or peroneal neuropathies); lower limb amputation other than toes due to diabetes; large (≥3 cm) and/or gangrenous ulcers of the lower limbs; average pain intensity of >=3 out of 10 cm on the Visual Analog Scale (VAS) in the upper extremities due to diabetic neuropathy at enrollment; hemoglobin A1c (HbA1c) > 10%; BMI > 45; currently prescribed a daily opioid dosage >120mg morphine equivalents; medical condition or pain in other area(s), not intended to be treated in this study, that could interfere with study procedures, accurate pain reporting, and/or confound evaluation of study endpoints, as determined by the investigator (such as primary headache, fibromyalgia, post-herpetic neuralgia, osteoarthritis, peripheral vascular disease, or small vessel disease); current

Author (year),	Inclusion	Exclusion
	assessing pain intensity and willing to stay on those medications with no dose adjustments until activation of the permanently implanted SCS device (HF10 therapy group) or baseline assessment (CMM only group); 22 years of age or older at the time of enrollment; appropriate candidate for the surgical procedures required in this study based on the clinical judgment of the implanting physician; capable of subjective evaluation, able to read and understand English-written questionnaires, and able to read, understand and sign the written informed consent in English; willing and capable of giving informed consent; willing and able to comply with study-related requirements, procedures, and scheduled visits; adequate cognitive ability to use a patient programmer and recharger as determined by the investigator	diagnosis of a progressive neurological disease such a multiple sclerosis, chronic inflammatory demyelinating polyneuropathy, rapidly progressive arachnoiditis, brain or spinal cord tumor, central deafferentation syndrome, Complex Regional Pain Syndrome, acute herniating disc, severe spinal stenosis and brachial plexus injury, as determined by the investigator; current diagnosis or condition such as a coagulation disorder, bleeding diathesis, platelet dysfunction, low platelet count, severely diminished functional capacity due to underlying cardiac/pulmonary disease, symptomatic uncontrolled hypertension, progressive peripheral vascular disease or uncontrolled diabetes mellitus that presents excess risk for performing the procedure, as determined clinically by the investigator; prior experience with SCS, dorsal root ganglion (DRG) stimulation, peripheral nerve field stimulation (PNfS), or peripheral nerve stimulation (PNS) for chronic intractable pain; significant spinal stenosis, objective evidence of epidural scarring and/or any signs or symptoms of myelopathy as determined by the investigator based on MRI conducted within the past 12 months; any previous history of surgery on the posterior elements (laminectomy, posterior fusion) resulting in a compromised epidural space, as determined by the investigator; benefitting from an interventional procedure and/or surgery to treat lower limb pain (subjects should be enrolled at least 30 days from last benefit); existing drug pump and/or another active implantable device such as a pacemaker; condition currently requiring or likely to require the use of diathermy or MRI that is inconsistent with Senza system guidelines in the Physician's Manual; metastatic malignant neoplasm or untreated local malignant neoplasm; life expectancy of less than one year; local infection at the anticipated surgical entry site or an active systemic infection; pregnant or planning to become pregnant during the study (women of childbearing potential who are sexually active must use a reliable form of birth control, be surgically sterile, or be at least 2 years post-menopausal); significant untreated addiction to dependency producing medications, alcohol or illicit drugs within 6 months of enrollment; concomitantly participating in another

Author (year),	Inclusion	Exclusion
		clinical study; involved in an injury claim under current litigation; receiving temporary Social Security Disability Insurance (SSDI) benefits due to chronic pain; pending or approved worker's compensation claim; evidence of an active disruptive psychological or psychiatric disorder or other known condition significant enough to impact perception of pain, compliance with intervention and/or ability to evaluate treatment outcome, as determined by a psychologist in the last 12 months.

BMI: Body mass index, CMM: Conventional medical management, CRPS: Complex Regional Pain Syndrome, CT: Computed topography, DRG: Dorsal root ganglion, EMG: Electromyography, FBSS: Failed Back Surgery Syndrome, MRI: Magnetic Resonance Imaging, NR: Not reported, PNS: Peripheral nerve stimulator, SCS: Spinal cord stimulator, VAS: Visual analog scale

Appendix Table G13. Inclusion and Exclusion Criteria for NRSI

Author (year),	Inclusion	Exclusion
Turner, 2010	Open Washington State workers' compensation claim of any duration for a back injury and to be receiving work time loss compensation due to temporary total inability to work because of the injury; pain radiating into one or both legs for more than 6 months; radicular pain greater than axial pain; average leg pain in the last month rated 6 or greater on a 0–10 scale; no previous SCS surgery; no current diagnosis of diabetes or cancer; and ability to speak English or Spanish; age 18 to 60 years; and 1 to 3 previous open lumbar spine operations during the claim	NR
Dhruva, 2023	18 years or older; incident diagnosis of failed back surgery syndrome, complex regional pain syndrome, chronic pain syndrome, and other chronic postsurgical back and extremity pain (for the latter diagnosis, history of spine surgery within 6 months of diagnosis was required) between April 1, 2016, and August 31, 2019	Individuals without 6 months of contiguous pharmacy and medical coverage before and 12 months after cohort entry
Vu, 2022	At least 18 years of age at the time of SCS implant and those who remained within a participating health care organization for 12 months prior and 15 months after the index date	patients who underwent SCS prior to their PLS diagnosis and those who underwent spine surgery within the range of 12 months before and 15 months after the index date; patients who received an SCS over 18 months after a PLS diagnosis
Lad, 2014	All inpatient stays for patients receiving a laminectomy or hemilaminectomy with or without simultaneous facetectomy or foraminotomy (ICD-9-CM: 03.09; CPT-4: 63005, 63012, 63030,	Younger than 18 years old

Author (year),	Inclusion	Exclusion
	63042, 63044, 63047, 63056, 63035, 63048, and 63057); patients who received a lumbar fusion (ICD-9-CM: 81.06, 81.07, and 81.08; CPT-4: 22558, 22630, and 22612). For implantation or replacement of spinal neurostimulator lead, we used ICD-9-CM code 03.93 and CPT-4 codes 63650 and 63655 with the insertion or replacement of single/dual/rechargeable/nonrechargeable neurostimulator generator (ICD-9-CM: 86.94–86.98; CPT-4: 63685). The diagnosis of FBSS was recognized by the ICD9-CM code 225.1 and postlaminectomy pain syndrome by ICD-9-CM code 722.83	
Perez, 2021	Aged ≥18; diagnosed with secondary pain related to FBSS; able to properly understand and speak the spanish language; patients newly sent to the Pain Unit.	Pain not related to FBSS; unable to answer the questions due to their educational level or to a psychiatric or neurological disorder; patients whose clinical data could not be obtained

FBSS = Failed back surgery syndrome; NR = Not reported; PLS = Primary lateral sclerosis; SCS = Spinal cord stimulator.

APPENDIX H. Clinical Guidelines Cited in Prior Report and in Public Comments from Current Report

Appendix Table H1: Clinical Guidelines Included in 2010 Report

Guideline	Year	Recommendation	Rating/Strength of Recommendation
American Society of Regional Anesthesia and Pain Medicine (ASRAPM)	2010	The organizational members and consultants "strongly agree" that SCS should be used for persistent radicular pain, and all agree that it should be used for other conditions, such as postherpetic neuralgia, postamputation pain, peripheral neuropathic pain, spinal cord injury, CRPS, cauda equina syndrome, and cervical root injury pain. In addition, all members and consultants "strongly agree" that a SCS trial should be performed prior to considering permanent implantation of a stimulation device	NR
American Pain Society (APS)	2009	The American Pain Society recommends that, for the treatment of persistent and disabling radicular pain following surgery for herniated disc (with no evidence of a persistently compressed nerve root), clinicians discuss the risks and benefits of SCS as a treatment option, and note the high rate of complications following SCS implantation.	Weak
American Society of Interventional Pain Physicians (ASIPP)	2009	The recommendation for clinical use of SCS for FBSS on a long-term basis is 1B or 1C, indicating a strong recommendation in which the benefits clearly outweigh the risk and burdens	Strong
Institute for Clinical Systems Improvement (ICSI)	2008	Regarding treatment of chronic pain, the ICSI18 considers placement of a SCS to be a level II treatment, which is only considered appropriate in patients who have failed more conservative (level I) treatment options (including transcutaneous nerve stimulation, drug therapies, physical rehabilitation, and behavioral techniques). SCS should be performed alongside a comprehensive treatment plan that includes pharmacologic, rehabilitative, and psychological interventions; if used alone, the evidence is limited in its success.	NR
National Institute for Health and Clinical Excellence (NICE)	2008	Included in Table 2 of full report	Included in Table 2 of full report
American College of Occupational and Environmental Medicine	2007	The use of SCS for acute, subacute, or chronic low back pain; radicular pain syndromes; or FBSS is not recommended based on insufficient evidence for an evidence-based recommendation due to high costs or high potential for harm to the patient.	Insufficient/irreconcilable evidence
European Federation of Neurological Societies (EFNS)	2007	The EFNS concluded that there was level B evidence for the effectiveness of SCS in FBSS and CRPS type I. Level B evidence indicates that SCS is probably effective.	Level B

		They also found positive evidence for SCS in the treatment of CRPS type II, peripheral nerve injury, diabetic neuropathy, post-herpetic neuralgia, brachial plexus lesion, stump pain, phantom lib pain, and partial spinal cord injury, but require confirmatory comparative trials for the unreserved recommendation of SCS use in these conditions.	
Reflex Sympathetic Dystrophy Syndrome Association (RSDSA)	2006	The RSDSA recommends that CRPS patients who are not progressing in the functional restoration/interdisciplinary algorithm to proceed in a stepwise progression from minimally invasive therapies (sympathetic nerve blocks, intravenous regional nerve blocks, and somatic nerve blocks) to more invasive therapies (neurostimulation, epidural and plexus catheter block(s), and intrathecal drug infusion), and finally to surgical and experimental therapies (sympathectomy and motor cortex stimulation) in order to facilitate the patient's functional improvement and pain control.	NR
Sanders et al., 2005	2005	Despite the growing number of studies and systematic reviews regarding the efficacy of SCS, the current guidelines do not recommend their use in chronic non-malignant pain syndrome patients given the continued absence of quality research.	NR

FBSS = Failed Back Surgery Syndrome; CRPS = Complex Regional Pain Syndrome; NR = Not reported; SCS = spinal cord stimulation.

Appendix Table H2: Clinical Guidelines from Public Comment

Author, Year	Specifically Requested to Add to Draft	Include/Exclude	Reason for Inclusion/Exclusion
American Society of Anesthesiologists Task Force on Chronic Pain Management, American Society of Regional Anesthesia and Pain Medicine, 2010	Yes	Include	Included in Appendix table H1 with other guidelines from 2010 report
British Pain Society, 2009	No	Exclude	Published before 2010 (exclusion criteria), not included in 2010 report
Chou, 2009	Yes	Include	Included in Appendix table H1 with other guidelines from 2010 report
Manchikanti, 2013	Yes	Exclude	Previously excluded at title abstract review
Neuromodulation Therapy Access Coalition, 2008	No	Exclude	Published before 2010 (exclusion criteria), not included in 2010 report
Premera Blue Cross, date NA (accessed 2023)	No	Exclude	Not a guideline, sufficient number of bellwether insurance payers already included
Shanthanna, 2023	No	Exclude	Focuses on SCS trial only, not permanent implant

HHS Best Practice Pain Management Inter-Agency Task Force, 2019	No	Exclude	Does not provide actual recommendation/guidelines on SCS

NA = not applicable; SCS = Spinal cord stimulator.

APPENDIX I. Economic Tables

Appendix Table I1. US-Based economic studies of SCS

Type 1 Studies:	Hollingworth 2011[2]	Patel 2022[3]
Population	**N=158** with FBSS, patients receiving workers' compensation in 3 groups: **1.** SCS w/ or w/o permanent device implant **(N=51)** **2.** pain clinic (PC) evaluation with or without treatment **(N=39)** **3.** usual care **(N=68)** 3 groups similar in age, sex, and other characteristics. Baseline: Leg pain mean score (0-10 scale): 7.7 for SCS group, 7.3 in PC group, and 7.2 in UC group. Leg pain median duration: 48 months for SCS, compared with 31 months in PC group and 36 months in UC group. Median Work time loss compensation: 39 months in SCS group, 24 months in PC group and 30 months in UC group. Pain-related to physical disability: score 21.1 in SCS group, vs 20.1 in the PC group and 20.0 in the UC group Legal representation: 49% in SCS group, vs 26% in PC group and 29% in the UC group.	**N=159 patients** with nonsurgical refractory back pain (NSRBP). **10-kHz SCS (n = 83):** 3.1% (69/83) had implant of permanent SCS System Female: 60.2% Avg Age (SD): 54.5 years old (12.1) BMI (SD): 31.9 kg/m2 (6.6) White: 90.4% Avg VAS (SD): 7.4 (1.15) ODI (SD): 47.2 (10.9) EQ-5D-5L (SD): 0.579 (0.121) Avg Opioid daily dose: 45.4 MME Degenerative disc disease: 72.3% **CMM (n = 76):** Female: 52.6% Avg Age (SD): 56.2 years old (11.6) BMI (SD): 30.8 kg/m2 (6.5) White: 96.1% Avg VAS (SD): 7.23 (1.02) ODI (SD): 47.4 (10.8) EQ-5D-5L(SD): 0.558 (0.130) Avg Opioid daily dose: 32.0 MME Degenerative disc disease: 68.4%
Intervention(s)	SCS (NOS)	SCS at 10 kHz
Comparator(s)	Pain clinic (PC) referral (with or without treatment provided) Usual care (UC),	UC for NSRBP
Country	United States	United States
Funding	Washington State Department of Labor and Industries	Nevro Corp. Multiple author-reported financial relationships
Study design	Cost-effectiveness	CUA

Type 1 Studies:	Hollingworth 2011[2]	Patel 2022[3]
Perspective	Payer	NR (health system assumed)
Time horizon	24 months	6 months (prior to cross-over) , 12 months
Analytic model	Cost-effectiveness analysis Bayesian methods Logistic regression Bootstrapping and bias-accelerated CI	CUA (modeling not specified)
Effectiveness outcome	Success Primary outcome: Composite measure of leg-pain intensity success (at least 50% reduction relative to baseline, VAS 0-10 scale), ≥2 point decrease on disability score (0-24) and less than daily opioid medication use; Success for pain and disability also evaluated separately	QALY
Effectiveness outcome components	VA Pain, Roland Morris Disability Questionnaire (RDQ)	EQ-5D 5-level QOL,
Source for effectiveness data	Prospective Cohort Study	Concurrent RCT
Costing year	2007	January 1, 2010, through October 31, 2020
Currency	USD	USD
Discounting	3%	NR
Components of cost data	Actual reimbursement costs: medical costs, cost of SCS implantation, revision, replacement, and removal procedures; physical therapy, back brace, corset, spinal injections. Productivity loss costs	Medication use, HCU: office visits (including primary care), pain management, injections (e.g., epidural injection, sacroiliac joint injection), emergency department visits, hospital admissions, medical tests, lead revision/reposition, IPG revision/reposition, IPG explant, lead explant.
Cost sources	Administrative databases Department of Labor & Industries	Medication cost estimates derived from WAAMP (from First Databank, Inc.) as of November 30, 2021. HCU estimation from PearlDiver database (PearlDiver Technologies) which uses payer data from commercial, Medicare, Medicaid, government, and cash pay sources.

Type 1 Studies:	Hollingworth 2011[2]	Patel 2022[3]
		.
Sensitivity analysis	Bootstrapping, adjusted cost-effectiveness acceptability curves; probability of cost-effectiveness. Description of cost drivers, evaluation of assumptions not explicitly described	NR
QHES	90/100	60/100
Results:		
Cost/ QALY (or other appropriate benefit measure)	NR	Cost/QALY for groups: NR Total Costs: HF-SCS 6 months: $3,507 (excludes device, trial, and procedure costs) EQ-5D QOL, Mean (SD) 6 months: 0.781 (0.111) QALY: 0.201
Cost / QALY(or other appropriate benefit measure) **of comparator(s)**	NR	Cost/QALY for groups: NR Total Costs: CMM 6 months: $3804 EQ-5D QOL, Mean (SD) 6 months: 0.515 (0.155) QALY : -0.042
ICER	Incremental cost per outcome at 24 months based on adjusted estimates (95% CrI) for primary composite outcome: All patients: SCS vs. PC: $131,146 (SCS dominates-$271,075) SCS vs. UC $334,704 (95% CrI, $142,203–489,243) SCS patients with permanent implant vs. PC, Incremental cost per outcome (95%CI):	SCS dominants −$2,236/QALY (1st 6 months) −$4,964/QALY (12 months) QALY: 0.201 HF-SCS (i.e., improvement in QALY over CMM (EQ-5D-5L index score change of 0.201 vs −0.042, p < 0.001) QALY : -0.042 CMM

Type 1 Studies:	Hollingworth 2011[2]	Patel 2022[3]
	Primary composite: $520,315 ($17,728 — PC dominates) Leg pain success: $436,512 ($24,405 — PC dominates) RDQ success: $140,049 ($236 — PC dominates)	
One-way SA	NR	NR
Other SA	Bootstrapping, CEAC <5% probability that SCS would be cost effective at any willingness to pay <7% probability SCS would be cost effective with higher response rates for pain, function. Probability that SCS is cost effective did not exceed 20% even at WTP of $250,000 for ≥2 point RDQ improvement	NR
Author's Conclusion	SCS not cost-effective vs. PC or UC; SCS costs were not counterbalanced by lower cost of subsequent care. Benefits and cost savings reported in RCTS may not be replicated in workers' compensation patients treated in a community setting.	10KHz SCS provides higher QOL at lower average cost per patient vs. CMM for patients with NSRBP; SCS was predicted to be cost-effective vs. CMM within 2.1 years of treatment.
Limitations	• Small sample size • Limited sensitivity analysis • Unclear applicability of findings outside of Worker's Compensation population	• Short time horizon and no long-term assessment of benefits for HCU and medication usage • Unclear modeling of HCU components and adverse events • No formal sensitivity analyses and limited analyses on potential drivers of cost but not on ICERs • Potential conflict of interest • Exclusion of cost of the SCS trial implant from HCU cost

CEAC= Cost-effectiveness acceptability curve; CMM = Conventional medical management; CrI =credibility interval; EQ-5D = EuroQol 5D; HCU = health care utilization; HF= high frequency; ICER = incremental cost-effectiveness ratio; NSRBP = nonsurgical refractory low back pain; ODI = Oswestry Disability Index; PC= pain clinic referral; QALY = Quality adjusted life years; RDQ = Roland-Morris Disability Questionnaire; SCS= spinal cord stimulation; UC= usual care; USD = US dollars.

Appendix Table I2. Non-US economic studies of SCS: Back pain, FBSS

	Annemans 2014 [1]	Deloitte 2019 [2]	Rojo 2021 [3]
Population	**N=67** with FBSS patients (1 dropped): At enrollment: 91% predominant back pain **n=57 (86.4%):** SCS implantation <u>Baseline:</u> Male: 45% Mean age: 49.7 years old Responder rate at 6 months in SCS group: • 74% had >=50% pain reduction in VAS scores	Hypothetical cohort	**N=86** **n=46 (CMM patients)** EQ-VAS: 17.2 **n=39 (SCS+CMM patients) out of which:** -83% conventional SCS systems implantation (40-70 Hz SCS) -17% high frequency SCS implantation (1000 Hz) EQ-VAS: 21.36 >90% of neuropathic pain Age: 7.78 years younger on avg compared to the CMM group
Intervention(s)	HF 10 kHZ SCS	SCS	TR SCS (12 and 25 years of battery life) + CMM vs CMM
Comparator(s)	CMM, repeat spinal operation, and traditional SCS treatment in FBSS (i.e., TNR-SCS and TR-SCS)	UC w/reoperation for patients in FBSS	CMM
Country	United Kingdom	Australia	Spain
Funding	NR	Australian and New Zealand Neuromodulation Society Limited	Axentiva Solutions SL
Study design	CUA	CUA	CUA
Perspective	UK National Health Care System	Health care system and societal	Spain National Health Service
Time horizon	24 months	15 years	5 years
Analytic model	Decision tree model (first 6 months: SCS vs CMM) Markov model (3-month cycles) Simulated cohort of 1000 patients over 15 years	Decision tree Markov simulation model (1-year cycle)	Cost-utility analysis based on nonrandomized study
Effectiveness outcome	QALY	QALY	QALY

	Annemans 2014 [1]	Deloitte 2019 [2]	Rojo 2021 [3]
Effectiveness outcome components	EQ-5D utility scores, pain relief, and complications	EQ-5D utility scores, transition probabilities, pain relief	VAS, EQ-5D utility scores, neuropathic pain relief, EQ-VAS
Source for effectiveness data	Published Literature RCTs, 24-month prospective trial	Published Literature	SEFUDOCE study Published Literature (Lin method)
Costing year	NR	NR	2019
Currency	GBP	AUD	EUR
Discounting	3.5%	5%	3%
Components of cost data	Cost of SCS trial, SCS implantation, surgery, CMM costs, complication costs, medication and non-drug pain therapy costs, and cost related to patients' withdrawal	Trial stimulation cost: GP, specialist, neurosurgeon, psychologist consultations, imaging (CT scans, MRI scans, x-rays, myelograms), device costs, surgery costs (anesthesia costs, operating room), implantation cost, explantation cost, annual maintenance costs	Non-pharmacological and pharmacological treatments, primary care visits, specialists visits, non-referral specialists visits, diagnostic tests, hospitalizations, emergency room visits, ambulatory visits, implant/reoperation costs, medical tests
Cost sources	Published Literature Manufacturer	National Hospital Cost Data Collection Private Hospital Data Bureau annual report 2016-17 Australian refined diagnosis-related group Independent Hospital Pricing Authority Department of Health	Nonrandomized study. National Health Service Official taxes of Madrid Drug cost database
Sensitivity analysis	SA around loss to follow-up, response rate, device cost, device longevity	One-way SA with different time horizons (i.e., 2, 5 or 10 years), different discount rates (i.e., 3 or 7%), different ongoing cost levels of SCS/UC therapy, and different SCS device longevity (i.e., 5 or 7 years); cost of maintenance, return to work rates,	PSA using bootstrapping (10,000 bootstrap sub-samples: resampling with replacement)
QHES	81/100	90/100	73/100
Results:			
Cost / QALY Intervention	**H10 SCS:** Cost: £86,417,656; QALY: 5,151	**From health care system perspective:** -costs=AUD $958 / person per year; QALY = AUD 0.06 / year	**SCS:** Cost=24,790; QALY=2.46
Cost / QALY of comparator(s)	**CMM:** Cost: £80,605,788 QALY: 3,308	NR	CMM: Cost=€ 9,383; QALY=2.46

	Annemans 2014 [1]	Deloitte 2019 [2]	Rojo 2021 [3]
	Reoperation: Cost: £82,187,498 QALY: 3,565		
ICER	**H10 SCS vs CMM:** £3,153 / QALY gained **H10 SCS vs Reoperation:** £2,666 / QALY gained	**From health care system perspective:** AUD $15,070/QALY for FBSS **From societal perspective:** **-(**Minus) $11,902 AUD /QALY for FBSS SCS was considered dominant	€ 27,330 / QALY gained
One-way SA	Results show that device longevity and cost as driving parameters: -Range in the HF10 SCS therapy's ICER when changing device cost from lower limit to upper limit is: £0 to £13,000 / QALY -Range in the HF10 SCS therapy's ICER when changing device longevity from lower limit to upper limit is: <£1,000 to <£7,000 / QALY	Analysis results most sensitive to: time horizon, discount rate, ongoing costs of SCS/UC treatment, and device longevity. ICERs from a health system perspective ranged from a low of $7,335 AUD/QALY to $97,896 AUD/QALY	NR
Other SA	NR		Cost-effectiveness acceptability curves based on 10,000 bootstrapped samples: SCS+ CMM had 79% probability of being cost-effective vs. CMM at WTP of €30,000, and a 51.7% probability given a threshold of €20,000; Authors suggest that SCS and CMM remain cost effective up to 9.5 years.
Author's Conclusion	Evidence of cost effectiveness of HF10 SCS system vs CMM alone and reoperation	SCS devices estimated to be cost effective from perspective of health care system	Evidence of SCS of cost effectiveness of SCS system vs CMM alone (i.e., 79% probability)
Limitations	• Quality of clinical studies used is unclear • 15-year horizon but clinical/other data do not extend that far	• Information on relevant patient population not provided • No discussion of the impact of direction or magnitude of potential biases.	• Patients in the SCS+CMM group were on average 7.78 years younger than those in the SCS group and other base line differences were noted; how or if this was adjusted for in analyses and

	Annemans 2014 [1]	Deloitte 2019 [2]	Rojo 2021 [3]
		• Costing year missing	any potential impact on comparative results unclear. • Authors indicate differential loss to follow-up (more loss in the CMM group) at 12 and 24 months. It is unclear how this may impact the findings. • Modeling of device and implantation costs or of SCS trial is not evident. • No clear modeling of adverse events, need for device replacement or explant described. • No modeling of cost-drivers or evaluation of assumptions related to issues like device longevity, etc. • Time horizon (5 years and beyond) extended beyond reported clinical data (24 months). • No discussion of the impact of direction or magnitude of potential biases. • Potential conflict of interest as one of the authors is a member of Axentiva Solutions SL who funded this study • No demographic characteristics reported

AE = Adverse events; CEA = Cost-effectiveness analysis; CMM = Conventional medical management; CUA = Cost utility analysis; FBSS = Failed back surgery syndrome; HF10 SCS = 10 kHz high-frequency SCS; ICER = incremental cost-effectiveness ratio; ODI = Oswestry Disability Index; QALYs = quality adjusted life years; SCS = Spinal cord stimulation; SP = Spain; UK = United Kingdom; VAS = Visual analog score.

Appendix Table I3. Non-US economic studies of SCS: FBSS

	Kumar 2013 [4]
Population	**n=184 (SCS group: patients w/FBSS)** Mean age: 49 years old Male: 64% Baseline Mean VAS:8.2 Baseline EQ-5D:0.28 **n=49 (CMM)** Mean age: 50 years old Male: 61% Baseline Mean VAS:8.2 Baseline EQ-5D:0.29
Intervention(s)	SCS (rechargeable and non-rechargeable IPGs)
Comparator(s)	CMM alone
Country	Canada
Funding	Mitacs (not-for-profit org funded though CA federal and provincial governments
Study design	CUA
Perspective	CA provincial Ministry of Health
Time horizon	20 years
Analytic model	Markov simulation models (6-month cycles with a total of 40 treatment cycles) Long term complication rate: 19%
Effectiveness outcome	QALY
Effectiveness outcome components	EQ-5D utility scores
Source for effectiveness data	Case series
Costing year	2012 CAN $
Currency	CAD
Discounting	3.5%
Components of cost data	**SCS group:** -Pre-implant costs: evaluations/consultations costs (i.e., physicians, orthopedic surgeons, psychiatrists, social workers, neurologists, and neurosurgeons), diagnostic procedures (MRI, CT scanning, ultrasound, lumbar spine X-ray films. -Implant procedure costs: professional surgical and anesthesia fees, operating room fees, hospital stay, and equipment costs.

	Kumar 2013 [4]
	-Maintenance costs: nursing contact, physician consultations, medication, costs for complications, hospitalizations. -Therapy costs: acupuncture, physiotherapy, massage, and chiropractic therapy. -Pharmacotherapy costs: drug and dispensing costs. **CMM group:** -Evaluation costs by various healthcare providers: family physicians, orthopedic surgeons, psychiatrists, social workers, neurologists, and neurosurgeons. -Imaging costs: CT, MRI, X-ray, and ultrasound studies. -Cost of alternative therapies: epidural steroid blocks, trigger point injections, nerve blocks, physiotherapy, chiropractic treatments, massage therapy, and acupuncture. -Pharmacotherapy costs: drug and dispensing costs. -Costs of hospitalization.
Cost sources	Regina, Saskatchewan (Canada) province fee schedule Manufacturer
Sensitivity analysis	Probability sensitivity analyses over 20 years (50,000 Monte Carlo Simulation). Deterministic sensitivity analysis
QHES	86/100
Results:	
Cost / QALY Intervention	**FBSS (SCS+CMM):** Cost=CAN$ 166,439 QALY=4.84
Cost / QALY of comparator(s)	**FBSS (CMM):** Cost=CAN$ 153,522 QALY=3.45
ICER	FBSS: CAN$ 9,293 / QALY gained
One-way SA	Deterministic sensitivity analysis
Other SA	Deterministic and probabilistic sensitivity analyses
Author's Conclusion	SCS+CMM cost-effective vs CMM alone for patients with CRPS In patients w/ CRPS, SCS (over CMM) provides a positive incremental net monetary benefit at WTP thresholds >= CAN $7,000 / QALY gained 75% probability that SCS is cost-effective w/ WTP threshold of CAN $50,000/QALY

	Kumar 2013 [4]
Limitations	• Authors did not address selection bias and did not address any AEs or negative outcomes in the study • Case series data used. Lack of long-term head-to-head comparative data for modeling a 20-year time horizon. • Impact of complications (e.g., SCS revision/replacement, explant, and device lifetime unclear especially over the long term) • Potential sources of bias and impact on the cost-effectiveness of SCS vs. CMM not provided. Authors note that use of nonrandomized data may lead to treatment effect overestimation and selection bias. • Applicability of the findings to the U.S. healthcare system are unclear.

AE=Adverse events; CAN = Canada; CEA = Cost-effectiveness analysis; CMM = Conventional medical management; CUA = Cost utility analysis; FBSS = Failed back surgery syndrome; ICER = incremental cost-effectiveness ratio; PSA = Probabilistic Sensitivity Analysis; QALYs = Costs and quality adjusted life years; SA = Sensitivity analysis; SCS = Spinal cord stimulation; WTP = willingness to pay

Appendix Table I4. Non-US economic studies of SCS: Back pain, CRPS

	Kemler 2010 [1]	Kumar 2013 [2]	Deloitte 2019 [3]
Population	Male and female patients with CRPS type I. Age: 18 to 65 years old. **66.7%:** SCS implantation Leg/hand pain for at least 6 months Pain intensity: at least 5 cm on VAS scale from 0 mm to 100 mm	**n=42 (SCS group: patients w/ CRPS)** Mean age: 51 years old Male: 52% Baseline Mean VAS:8.1 Baseline EQ-5D:0.30 **n=11 (CMM)** Mean age: 50 years old Male: 56% Baseline Mean VAS:8.2 Baseline EQ-5D:0.32	NR
Intervention(s)	SCS	SCS (rechargeable and non-rechargeable IPGs)	SCS
Comparator(s)	CMM in CRPS patients, non-rechargeable vs rechargeable SCS IPGs	CMM alone in FBSS and CRPS patients	UC incl. ketamine infusions for CRPS
Country	United Kingdom	Canada	Australia
Funding	Medtronic, Inc.	Mitacs (not-for-profit org funded though CA federal and provincial governments)	NR (Australian and New Zealand Neuromodulation Society Limited)

	Kemler 2010 [1]	Kumar 2013 [2]	Deloitte 2019 [3]
Study design	CEA	CUA	CUA, cost-benefit analysis
Perspective	UK National Health Care System	CA provincial Ministry of Health	Health care system and societal
Time horizon	15 years	20 years	15 years
Analytic model	2-stage decision tree model Markov simulation model (3-month cycles over 15-year time horizon)	Markov simulation models (6-month cycles with a total of 40 treatment cycles) Long term complication rate: 19%	Decision tree Markov simulation model (1-year cycle)
Effectiveness outcome	QALY	QALY	QALY
Effectiveness outcome components	EQ-5D utility scores, pain relief	EQ-5D utility scores	EQ-5D utility scores, transition probabilities, pain relief
Source for effectiveness data	Published Literature UK population weights	Case series	Published Literature
Costing year	2008 GBP	2012 CAN $	NR
Currency	GBP	CAD	AUD
Discounting	3.5% (where £1.00 = US$ 1.62)	3.5%	5%
Components of cost data	cost of SCS implantation, surgery, CMM costs, complication costs	**SCS group:** -Pre-implant costs: evaluations/consultations costs (i.e., physicians, orthopedic surgeons, psychiatrists, social workers, neurologists, and neurosurgeons), diagnostic procedures (MRI, CT scanning, ultrasound, lumbar spine X-ray films. -Implant procedure costs: professional surgical and anesthesia fees, operating room fees, hospital stay, and equipment costs. -Maintenance costs: nursing contact, physician consultations, medication, costs for complications, hospitalizations. -Therapy costs: acupuncture, physiotherapy, massage, and chiropractic therapy.	Trial stimulation cost: GP, specialist, neurosurgeon, psychologist consultations, imaging (CT scans, MRI scans, x-rays, myelograms), device costs, surgery costs (anesthesia costs, operating room), implantation cost, explantation cost, annual maintenance costs

	Kemler 2010 [1]	Kumar 2013 [2]	Deloitte 2019 [3]
		-Pharmacotherapy costs: drug and dispensing costs. **CMM group:** -Evaluation costs by various healthcare providers: family physicians, orthopedic surgeons, psychiatrists, social workers, neurologists, and neurosurgeons. -Imaging costs: CT, MRI, X-ray, and ultrasound studies. -Cost of alternative therapies: epidural steroid blocks, trigger point injections, nerve blocks, physiotherapy, chiropractic treatments, massage therapy, and acupuncture. -Pharmacotherapy costs: drug and dispensing costs. -Costs of hospitalization.	
Cost sources	Published Literature Manufacturer PROCESS study	Regina, Saskatchewan (Canada) province fee schedule Manufacturer	National Hospital Cost Data Collection Private Hospital Data Bureau annual report 2016-17 Australian refined diagnosis-related group Independent Hospital Pricing Authority Department of Health
Sensitivity analysis	PSA over 15 years (1,000 Monte Carlo Simulation).	PSA over 20 years (50,000 Monte Carlo Simulations). Deterministic and probabilistic sensitivity analysis	sensitive to time horizon (2, 5 and 10 years), discount rate (3 and 7%), ongoing costs of SCS/UC treatment, and device longevity: -SCS cost-effective in CRPS patients if time horizon>5 years
QHES	94/100	87/100	90/100
Results:			

	Kemler 2010 [1]	Kumar 2013 [2]	Deloitte 2019 [3]
Cost / QALY Intervention	**SCS:** Cost= £86,770 QALY=4.84	**CRPS (SCS+CMM):** Cost=CAN$ 172,577 QALY=4.24	**From health care system perspective:** Costs=AUD $188 for CRPS; QALY=AUD 0.08 for CRPS
Cost / QALY of comparator(s)	**CMM:** Cost= £79,775 QALY=2.88	**CRPS (CMM):** Cost=CAN$ 148,799 QALY=2.12	NR
ICER	**SCS vs CMM:** £3,562 / QALY gained	**SCS+CMM:** CAN$ 11,216 / QALY gained	**From health care system perspective:** -AUD $2,321/QALY gained **From societal perspective:** -Minus AUD $18,868/QALY gained
One-way SA	One-way SA. Cost-effectiveness of SCS increases as: - cost of drug pain therapy for SCS patients decreases, - time before IPG replacement increases, - cost of drug pain therapy in CMM patients increases, - annual probability of no pain relief with SCS decreases	One-way SA.	One-way SA performed considering different time horizons (i.e., 2, 5 or 10 years), different discount rates (i.e., 3 or 7%), different ongoing cost levels of SCS/UC therapy, and different SCS device longevity (i.e., 5 or 7 years).
Other SA	PSA using probabilities of clinical success, reoperation, and death, probabilities of achieving optimal and suboptimal pain reliefs, complication rates, costs and drug treatments, utilities of health states, and SCS failure rates over time	Deterministic and probabilistic sensitivity analyses	NR
Author's Conclusion	74% probability that SCS is cost-effective with a WTP threshold of £20,000/QALY 87% probability that SCS is cost-effective with a WTP threshold of £30,000/QALY	SCS+CMM cost-effective vs CMM alone for CRPS In CRPS, SCS (over CMM) provides a positive incremental net monetary benefit at WTP thresholds >= CAN $7,000 / QALY gained 87% probability for SCS cost-effectiveness given CAN $30,000 WTP threshold	SCS devices estimated to be cost effective from perspective of health care system

	Kemler 2010 [1]	Kumar 2013 [2]	Deloitte 2019 [3]
Limitations	• Some data from trial in FBSS patients rather than CRPS patients • All cost data from published literature and other studies • 15-year time horizon and lack of long-term outcome data • Limited discussion of potential sources of bias and possible impact on findings. • The applicability of the findings to the U.S. healthcare system are unclear.	• Use of case series data from a single institution • 20-year time horizon and lack of long-term outcome data • The applicability of the findings to the U.S. healthcare system are unclear. • Limited discussion of potential sources of bias and possible impact on findings.	• Demographics information missing • Costing year missing • Authors do not discuss limitations of the analyses such as potential sources of bias and possible impact of these on the direction and magnitude of their findings • The applicability of the findings to the U.S. healthcare system are unclear.

AE=Adverse events; CA = Canada; CEA = Cost-effectiveness analysis; CMM = Conventional medical management; CRPS = Complex regional pain syndrome; CUA = Cost utility analysis; FBSS = Failed back surgery syndrome; HF10 SCS = 10 kHz high-frequency SCS; ICER = incremental cost-effectiveness ratio; IPGs = Implanted pulse generators; NR = Non-rechargeable; PSA = Probabilistic Sensitivity Analysis; QALYs = Costs and quality adjusted life years; SA = Sensitivity analysis; SCS = Spinal cord stimulation; SR = Systematic review; TNR-SCS = traditional non-rechargeable spinal cord stimulation; TR-SCS = traditional rechargeable spinal cord stimulation; UC = Usual care; VAS = Visual analog score; WTP = willingness to pay

Appendix Table I5. Non-US economic studies of SCS: Back pain, PDN

	Slangen 2016[1]
Population	**N=36** (i.e., PDN patients) Pain> 12 months; Pain intensity >=5 (NRS scale) **n=22 (61%)** patients in SCS group (1 death, 1 withdrawal, 5 complications during follow-up) Mean age (SD): 57.1 years old (12.4); Male: 68% Diabetes Mellitus: I (14%) / II (86%) MDNS 0: 13.6% MDNS 1: 18.2% MDNS 2: 40.9% MDNS 3: 27.3% Employment status: Retired: 31.8% Employed: 40.9% Unemployed: 0% Incapacitated: 22.7% Domestic Work: 4.6% EQ-5D (pooled mean): 0.25

	Slangen 2016[1]
	n=14 (39%) patients in best medical therapy (BMT) group Mean age (SD): 56.5 years old (8); Male: 64% Diabetes Mellitus: I (7%) / II (93% MDNS 0: 21.4% MDNS 1: 21.4% MDNS 2: 35.8% MDNS 3: 21.4% Employment status: Retired: 21.4% Employed: 21.4% Unemployed: 7.1% Incapacitated: 21.4% Domestic Work: 28.6% EQ-5D (pooled mean): 0.33
Intervention(s)	SCS
Comparator(s)	BMT
Country	Netherlands
Funding	Medtronic, Inc.
Study design	CUA
Perspective	Societal and healthcare
Time horizon	12 months for SCS 6 months for BMT
Analytic model	Non-parametric bootstrap analysis (1000 replications) Sensitivity analyses
Effectiveness outcome	QALY
Effectiveness outcome components	EQ-5D utility scores, pain relief
Source for effectiveness data	Dutch Tariff
Costing year	2012
Currency	GBP
Discounting	4% for costs and 1.5% for utilities
Components of cost data	Healthcare costs, non-healthcare costs, and societal costs (i.e., diagnostic procedures and tests, treatment procedure, hospitalization, clinic visits, phone consultations, general practitioners' visits and consultations, diabetes nurse, home care, emergency admissions, visits to diabetologist, neurologist, pain specialist, PT, ergo

	Slangen 2016[1]
	therapy, podiatrist, pedicure, medication, devices, orthopedic shoes, non-healthcare related costs (domestic help, productivity loss, loss of daily activities))
Cost sources	Hospital information system Dutch manual Maastricht University Medical Centre Medication and Aid Information Project Database
Sensitivity analysis	Bootstrapping analyses to adjust cost imbalance between two groups at baseline Sensitivity analyses to account for longer depreciation period of SCS device
QHES	81/100
Results:	
Cost / QALY	**SCS:** Total societal costs/patient = €26,539 QALY = 0.58 (after adj. for baseline imbalance in utility scores) -Healthcare costs: €18,742 -Non-healthcare costs: €7,797
Cost / QALY of comparator(s)	**BMT:** Total societal costs/patient = €5,313 QALY = 0.36 (after adj. for baseline imbalance in utility scores) -Healthcare costs: €2,173 -Non-healthcare costs: €3,140
ICER	**SCS (Societal perspective):** € 94,160 / QALY gained at 12 months € 117,815 / QALY gained at 6 months **SCS (Health Care perspective):** € 34,519 / QALY gained at 12 months
One-way SA	NR
Other SA	Reduced ICERs from a societal perspective after bootstrapping analyses and sensitivity analyses (4-year SCS cost depreciation period and extrapolation of results to 4 years): ICER: €62,775 / QALY gained at 1 year ICER: €52,252 / QALY gained at 4 years Authors state that after correcting for baseline differences in costs and extending the depreciation of SCS to 4 years there was a considerable drop in ICER.
Author's Conclusion	SCS (vs BMT) not cost-effective at 12 months follow-up due to the high initial costs of SCS;
Limitations	• Baseline cost imbalance between the 2 groups.

	Slangen 2016[1]
	• Imputation of missing data in both groups (e.g., by linear extrapolation in BMT group up to 12 months and assuming no changes between 6th and 12th month of follow up) • Potential conflict of interest • Basis for the time horizon was life battery of SCS assumed to be 4 years; shorter term data were extrapolated to 4 years • The applicability of the findings to the U.S. healthcare system are unclear.

AE=Adverse events; BMT = Best medical treatment; CMM = Conventional medical management; CRPS = Complex regional pain syndrome; CUA = Cost utility analysis; FBSS = Failed back surgery syndrome; HF10 SCS = 10 kHz high-frequency SCS; ICER = incremental cost-effectiveness ratio; IPGs = Implanted pulse generators; MSDN = Michigan Diabetic Neuropathy Score; NRS = Numeric rating scale; PDPN = Painful diabetic peripheral neuropathy; PSA = Probabilistic Sensitivity Analysis; PT = Physical therapy; QALYs = Costs and quality adjusted life years; SA = Sensitivity analysis; SCS = Spinal cord stimulation; SR = Systematic review; TNR-SCS = traditional nonrechargeable spinal cord stimulation; TR-SCS = traditional rechargeable spinal cord stimulation; VAS = Visual analog score; WTP = willingness to pay.

APPENDIX J. Definitions for Magnitude of Effects

Appendix Table J1. Definitions for Magnitude of Effects, Based on Mean Between-Group Differences

Slight/Small	Moderate	Large/Substantial
Pain		
5–10 points on a 0-to 100-point VAS or the equivalent 0.5–1.0 points on a 0-to 10-point numerical rating scale or the equivalent	>10–20 points on a 0-to 100-point VAS or the equivalent >1–2 points on a 0-to 10-point numerical rating scale or the equivalent	>20 points on a 0-to 100-point VAS or the equivalent >2 points on a 0-to 10-point numerical rating scale or the equivalent
Function		
4.8–9.6 points on the WOMAC	>9.6–19.2 points on the WOMAC	>19.2 points on the WOMAC
3.4-6.8 points on the WOMAC PF	>6.8-13.6 points on the WOMAC PF	>13.6 points on the WOMAC PF
1-2 points on the WOMAC pain	2-4 points on the WOMAC pain	>4 points on the WOMAC pain
5–10 points on the KOOS	>10–20 points on the KOOS	>20 points on the KOOS
5-10 points on the KSS	>10–20 points on the KSS	>20 points on the KSS
5-10 points on the IKDC	>10–20 points on the IKDC	>20 points on the IKDC
1-2 points on Lequesne Index	>2-5 points on the Lequesne Index	5 points on the Lequesne Index
5-10 points on the SF-36	>10-20 on the SF-36	>20 points on the SF-36
5-10 points on the EQ-VAS	>10-20 on the EQ-VAS	>20 points on the EQ-VAS
Pain or function		
0.2–0.5 SMD	>0.5–0.8 SMD	>0.8 SMD

FIQ = Fibromyalgia Impact Questionnaire; IKDC = International Knee Documentation Committee; KOOS=Knee Injury and Osteoarthritis Outcome Score; KSS = Knee Society Score; PF = physical function; SF-36 = 36-item Short Form Survery; SMD = standardized mean difference; EQ-VAS = EuroQol visual analogue scale; WOMAC = Western Ontario and Mc Maters Universities Osteoarthritis index;

Appendix Table J2. Definitions of effect sizes

Effect Size	Definition
Small effect	• MD 0.5 to 1.0 points on a 0 to 10-point scale, 5 to 10 points on a 0 to 100-point scale • SMD 0.2 to 0.5 • RR/OR 1.2 to 1.4
Moderate effect	• MD >1 to 2 points on a 0 to10-point scale, >10 to 20 points on a 0 to 100-point scale • SMD >0.5 to 0.8 • RR/OR 1.5 to 1.9
Large effect	• MD >2 points on a 0 to10-point scale, >20 points on a 0 to 100-point scale • SMD >0.8 • RR/OR ≥2.0

MD = mean difference; OR = odds ratio; RR = relative risk; SMD = standardized mean difference.

APPENDIX K. FDA Approved SCS Devices

Appendix Table K1: Spinal Cord Stimulators approved by the FDA

Manufacturer FDA Number (year)	Device Name	Details	Indications	Contraindications
Boston Scientific PMA: P030017 (2004)	Precision Montage™ Precision™ Plus, Precision Spectra™ Precision Novi™ Spectra WaveWriter™ WaveWriter Alpha™	Rate: 2 to 1200 Hz Pulse width: 20 to 1000 µsec Amplitude: 0 to 25.5 mA	Management of chronic intractable pain of the trunk and/or limbs including unilateral or bilateral pain associated with the following: FBSS; CRPS Types I and II; intractable low back pain and leg pain, painful diabetic neuropathy.	Patients unable to operate the SCS system; have failed trial stimulation by failing to receive effective pain relief; are poor surgical risks; are pregnant
Medtronic PMA: P840001 (1984)	Vanta™ Intellis™ Itrel™ Synergy Versitrel™ Restore™ Family of Neurostimulators*	Frequency: 40-1000 Hz Pulse width: NR Amplitude: NR	Management of chronic, intractable pain of the trunk and/or limbs-including unilateral or bilateral pain, pain resulting from peripheral neuropathy.	Diathermy.
	PrimeAdvanced™ SureScan™ MRI	Rate: 2 to 130 Hz Pulse width: 60 to 450 µsec Amplitude: 0 to 10.5 mA	FBSS or low back syndrome or failed back; radicular pain syndrome or radiculopathies resulting in pain secondary to FBSS or herniated disk; Post laminectomy pain; Multiple back operations; unsuccessful disk	Diathermy.

Manufacturer FDA Number (year)	Device Name	Details	Indications	Contraindications
			surgery; degenerative disk disease; herniated disk pain refractory to conservative and surgical interventions; peripheral causalgia; epidural fibrosis; arachnoiditis or lumbar adhesive arachnoiditis; CRPS, reflex sympathetic dystrophy, or causalgia, pain resulting from peripheral neuropathy.	
Saluda Medical PMA: P190002 (2022)	Evoke™ SCS system	Rate: 10 to 1500 Hz Pulse width: 20 to 1000 µsec Amplitude: 1 to 50 mA	Manage chronic pain in the trunk or limbs, including one-sided or two-sided pain associated with FBSS; intractable low back pain, or leg pain.	Cannot operate the SCS system; have not received effective pain relief during trial stimulation; are poor SCS surgical candidates.
Nevro Corp PMA: P130022 (2015)	Senza™ Senza™ II Omnia™	Rate: 1200 to 10000 Hz Pulse width: 40 µsec Amplitude 0.5 to 3.5 mA	Management of chronic intractable pain of the trunk and/or limbs, including unilateral or bilateral pain associated with the following: FBSS; intractable low back pain, or leg pain. When programmed to include a frequency of 10000 Hz, are	Poor surgical candidates, including those with poor glycemic control in whom the safety of the device has not yet been characterized; fail to receive effective pain relief during trial stimulation; unable to operate the SCS system.

Manufacturer FDA Number (year)	Device Name	Details	Indications	Contraindications
			indicated as aids in the management of chronic intractable pain of the lower limbs, including unilateral or bilateral pain, associated with diabetic neuropathy.	
Abbott[†] PMA: P010032 (2001)	Proclaim™ XR Proclaim™ Plus Prodigy™ MRI Eterna™ Eon™ EonC™ Eon™ Mini	Rate: 2 to 1200 Hz Pulse width: 20 to 1000 µsec Amplitude: 0 to 25.5 mA	Management of chronic, intractable pain of the trunk and/or limbs, including unilateral or bilateral pain associated with the following: FBSS and intractable low back, or leg pain, diabetic neuropathy.	Unable to operate the SCS system; failed to receive pain relief during trial stimulation.
Biotronik PMA: P210037 (2023)	Prospera™	Rate: 2 to 1400 Hz Pulse width: 30 to 1000 µsec Amplitude: up to 20 mA	Failed back syndrome or low back syndrome or failed back; radicular pain syndrome or radiculopathies resulting in pain secondary to failed back syndrome or herniated disk; post-laminectomy pain; multiple back operations; unsuccessful disk surgery; degenerative disk disease or herniated disk pain	Unable to operate the SCS system; failed to receive effective pain relief during SCS trial stimulation; patients who are poor SCS candidates based on presentation and underlying pathology.

Manufacturer FDA Number (year)	Device Name	Details	Indications	Contraindications
			refractory to conservative and surgical interventions; peripheral causalgia; epidural fibrosis; arachnoiditis or lumbar adhesive arachnoiditis; CRPS; reflex sympathetic dystrophy, or causalgia.	

CRPS = Complex Regional Pain Syndrome; ECAP = Evoked Compound Action Potentials; FBSS = Failed Back Surgery Syndrome; FDA = Food and Drug Administration; Hz = hertz; mA = milliamp; MRI = Magnetic resonance imaging; NR = Not reported; PMA = Premarket approval; SCS = spinal cord stimulator; µsec = microsecond.
* Includes RestoreUltra™, SureScan™ MRI, RestoreSensor™ SureScan™, RestoreAdvanced™ SureScan™ MRI. Some of these devices have been recalled due to issues with the battery and software.
† Formerly St. Judes Medical.

APPENDIX L. List of on-going studies

Title	Conditions	Interventions / Control	Study Design	N	Trial Number
Efficacy of different spinal cord stimulation paradigms for the treatment of chronic neuropathic pain (PARS-trial): study protocol for a double-blinded, randomized, and placebo-controlled crossover trial.	Neuropathic leg pain	SCS / Placebo	Crossover RCT	60	DRKS00018929
Multicentre, double-blind, randomised, sham-controlled trial of 10 khz high-frequency spinal cord stimulation for chronic neuropathic low back pain (MODULATE-LBP): a trial protocol.	CLBP	HF-SCS / Sham	RCT	96	NCT87648175
Spinal cord stimulation vs. medical management for low back pain (DISTINCT)	CLBP	SCS / CMM	RCT	270	NCT04479787
A Multi-Center, Prospective, Pragmatic, Randomized, Controlled Clinical Trial to Compare HF10 Therapy to Conventional Medical Management in the Treatment of Non-Surgical Refractory Back Pain	CLBP	HF-SCS / CMM	RCT	211	NCT03680846
An evaluation of spinal cord stimulation for the treatment of chronic pain, also its effect on mood, sleep, physical activity and analgesic medicine requirements.	CLBP	SCS / Sham	Crossover RCT	NR	ACTRN12620000720910
Comparison of spinal cord stimulation in combination with standard pain treatment versus standard pain treatment only in patients with intractable chronic back pain without previous history of spine surgery	CLBP	SCS / CMM	RCT	115	ISRCTN10663814
The Efficacy of Spinal Cord Stimulation in Patients With a Failed Back Surgery Syndrome.	FBSS	High Density SCS / SCS / Sham	Crossover RCT	10	NCT03462147
Spinal Cord Burst Stimulation for Chronic Radicular Pain Following Lumbar Spine Surgery: A Randomized Double-blind Sham-controlled Crossover Trial	FBSS	Burst SCS / Sham	Crossover RCT	50	NCT03546738

Comparing Long-Term Effectiveness of High Frequency and Burst Spinal Cord Stimulation	CLBP	HF-SCS / Burst SCS	Randomized (open label)	160	NCT03681262
Clinical Characterization of Burst Spinal Cord Stimulation for Chronic Pain Management	FBSS, intractable low back and leg pain	Burst SCS / Sham SCS	Crossover RCT	20	NCT03718325
A Randomised Sham-controlled Double-blinded Study of Burst Spinal Cord Stimulation for Chronic Peripheral Neuropathic Pain	Chronic peripheral neuropathic pain	Burst SCS / Sham SCS	Crossover RCT	10	NCT03733886
Spinal Cord Stimulation System in the Treatment of Chronic Pain	Chronic, intractable trunk/limb pain	SCS / Sham SCS	Crossover RCT	54	NCT03858790
A Randomized Controlled Study to Evaluate the Safety and Effectiveness of Boston Scientific Spinal Cord Stimulation (SCS) Systems in the Treatment of Chronic Low Back and/or Leg Pain With No Prior Surgeries	CLBP	SCS / CMM	RCT	241	NCT04676022
Prospective Single-center, Double-blind, Randomised Study to Evaluate the Effect of Spinal Cord Stimulation Frequency on wash-in/Wash-out Time and Clinical Outcomes in Subjects Using Fast-Acting Sub-perception Therapy (FAST) for Chronic Pain	CLBP	SCS / Other SCS	Crossover RCT	20	NCT04943770
Effects of Active Versus Passive Recharge Burst Spinal Cord Stimulation on Pain Experience in Persistent Spinal Pain Syndrome Type 2: A Multicenter Randomized Trial (BURST-RAP Study)	FBSS	Active Recharge Burst SCS / Passive Recharge Burst SCS	RCT	96	NCT05421273
Spinal cord stimulation compared with Lumbar Instrumentation for Low Back Pain After Previous Lumbar Decompression (PROMISE): a Prospective Randomized Controlled Study	FBSS	SCS / Fusion Surgery	RCT	84	NCT05466110
The Teaspoon Study - Telefitting Spinal Cord Stimulation for Pain	CLBP / Radiculopathy	Different SCS forms	Crossover	15	NCT05741788
PDN-SENSORY: A Multi-Center Randomized Controlled Trial to Evaluate Pain and Neurological Function With 10 kHz SCS in Treatment of Painful Diabetic Neuropath	PDN	HF-SCS / CMM	RCT	236	NCT05777317
Pain Medication Tapering for Patients With Persistent Spinal Pain Syndrome Type 2, Treated With Spinal Cord Stimulation	FBSS	SCS + Standard pain tapering / SCS + Personalized pain tapering / Usual care	RCT	195	NCT05861609
Treatment of Neuropathic Pain With Spinal Cord Stimulation and Physiotherapy for More Effective Pain	Neuropathic pain	SCS + Physiotherapy / Physiotherapy	RCT	160	NCT03740763

Relief, Increased Physical Activity and Improved Health Related Quality of Life					

CLBP = Chronic low back pain; CMM = Conventional medical management; FBSS = Failed back surgery syndrome; HF = High frequency; kHz = Kilohertz; PDN = Painful diabetic neuropathy; RCT = Randomized control trial; SCS = Spinal cord stimulator.

APPENDIX M. Clinical Expert Peer Review

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Professor of Medicine – School of Medicine
Director – Pacific Northwest Evidence-based Practice Center
Director of Medical Informatics and Clinical Epidemiology – School of Medicine
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APPENDIX N. Appendix References

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