

Table 2. Characteristics of included studies – Behandelings Persistent Spinal Pain Syndrome type 2 (PSPS-2) - Neuromodulatie

Study	Participants	Intervention	Control	Outcomes	Comments	Risk of bias *
High versus low frequency						
De Andres 2017 <i>Spain, Multidisciplinary Pain Management Department of a hospital</i>	<u>N</u> I: 26 C: 29 <u>Sex (% female)</u> I: 42.3 C: 62.1 <u>Age (mean ± SD)</u> I: 53.8 ± 11.5 C: 51.6 ± 9.3 <u>NRS (mean ± SD)</u> I: 7.69 ± 1.17 C: 7.60 ± 1.06 <u>ODI (mean ± SD)</u>	High frequency SCS - initial pulse width 30 µs - initial amplitude 1.5 mA (max 5 mA) - frequency: 10.000 Hz	Low frequency SCS stimulation patterns tested for optimal overlap between paresthesia and the region of the subjects' back and leg pain covering the entire area of pain. - max amplitude 8 volts - initial pulse width 300 µs (max 450 µs) - initial frequency 40 Hz	<i>After 12 months:</i> Pain (NRS) Quality of Life (SF-12, HAD) Function (ODI) Adverse events (device related AEs)	Excluded patients from trial and analysis that had an unsuccessful trial phase (<50% NRS improvement)	LOW Pain, Quality of Life, Function, LOW Adverse events

Study	Participants	Intervention	Control	Outcomes	Comments	Risk of bias *
	I: 26.96 ± 5.18 C: 27.18 ± 5.21					
SENZA (Amirdelfan 2018, Kapural 2015 and 2016) United States, multicenter (mainly pain centers).	<u>N</u> I: 92 C: 87 <u>Sex (% female)</u> I: 62.0 C: 58.6 <u>Age (mean ± SD)</u> I: 54.6 ± 12.4 C: 55.2 ± 13.4 <u>Duration of pain (years; mean ± SD)</u> I: 13.0 ± 10.4 C: 14.2 ± 12.2 <u>FBSS (%)</u> I: 79.3 C: 74.7	High frequency SCS - 30 μs pulses delivered at 10,000 Hz with amplitude adjusted to optimal analgesic response (min, max ±SD: 1.6 ± 1.1, 3.8 ± 3.4 mA). No intraoperative testing Adjusted as needed based on patient feedback	Low frequency SCS. Adjusted to optimally overlap paresthesia with the region of the subject's back and leg pain. (min, max ±SD: 39.2 ± 15.0, 77.3 ± 133.5 Hz; amplitude 3.6 ± 2.8, 8.5 ± 4.0 mA; pulse width 347 ± 148, 591 ± 214 μ) Intraoperative testing Adjusted as needed based on patient feedback	<i>After 12 and 24 months:</i> Pain (>50%VAS improvement, VAS leg and back) Function (ODI) Quality of Life (PSQI, SF-12) Adverse Events	Excluded subjects with unsuccessful trial phase: only patients with ≥50% or greater back pain reduction from baseline were eligible to proceed to permanent implantation.	HIGH

Table 2. Characteristics of included studies – Behandeling Persistent Spinal Pain Syndrome type 2 (PSPS-2) - Neuromodulatie Richtlijn Wervelkolomgerelateerde pijnklachten lage rug 2026

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	<u>Previous back surgery (n,%)</u> I: 87.0 C: 86.2 <u>VAS (mm, mean ± SD)</u> <i>back pain</i> I: 7.4 ± 1.2 C: 7.8 ± 1.2 <i>Leg pain</i> I: 7.1 ± 1.5 C: 7.6 ± 1.4					
Differential Target Multiplexed (DTM)						
Fishman, 2021 <i>United States, 12 'investigational sites</i>	<u>N</u> I: 67 C: 61 <u>Sex (% female)</u> I: 50.7 C: 55.7 <u>Age (mean ± SD)</u>	DTM SCS 4 possible programs, intensity adjusted for optimal use. Possible settings: - 50 Hz 200 µs - 300 Hz 170 µs	Traditional SCS <i>"subjects were programmed according to the labeling/manual"</i>	<i>After 12 months:</i> Pain (NRS) Quality of Life (PROMIS) Function (ODI)	Included patients in ITT analysis that had an unsuccessful trial phase (<40% VAS improvement)	HIGH

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	<p>I: 61.28 ± 12.16 C: 60.66 ± 11.77</p> <p><u>VAS (mean ± SD)</u></p> <p><i>Back pain</i></p> <p>I: 7.3 ± 1.5 C: 7.4 ± 1.3</p> <p><i>Leg pain</i></p> <p>I: 6.2 ± 2.6 C: 6.6 ± 2.1</p> <p><u>Spine surgeries (mean ± SD)</u></p> <p>I: 1.5 ± 1.3 C: 1.4 ± 1.1</p> <p><u>Years since onset symptoms (mean ± SD)</u></p> <p>I: 12.64 ± 13.05 C: 12.89 ± 11.25</p>	Subjects could adjust stimulation intensity and selected DTM SCS options based on optimal pain relief.		Adverse events		

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Closed-loop SCS						
EVOKE (Mekhail 2020 and 2022) <i>United States, 12 sites: specialist clinics, academic centers and hospitals</i>	<u>N</u> I: 67 C: 67 <u>Sex (% female)</u> I: 48 C: 49 <u>Age (mean ± SD)</u> I: 55.9 ± 11.6 C: 54.6 ± 9.7 <u>Duration of pain (years; mean ± SD)</u> I: 11.2 ± 9.9 C: 13.6 ± 9.6 <u>FBSS (n (%))</u> I: 41 (61) C: 38 (57)	Fixed-output, open-loop SCS	Closed-loop SCS	<i>After 12 months:</i> Pain (≥50% improvement in VAS*, VAS) Quality of Life (EQ-5d-5L*, SF 12*) Function (ODI*, PSQI*) Adverse events (AE serious/ non serious) Use of pain medication (daily morphine equivalents)	(1) Previous surgery was not an inclusion criterium (not adhering fully to PICO) (2) Excluded highest functioning patients (ODI 41-80) (3) Included patients in analysis that had an unsuccessful trial phase (<50% VAS improvement). However, the study excluded patients that withdrew voluntarily, unrelated to device.	HIGH

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Study	Participants	Intervention	Control	Outcomes	Comments	Risk of bias *
	<p><u>Previous back surgery (n,%)</u></p> <p>I: 41 (61) C: 39 (58)</p> <p><u>VAS (mm, mean ± SD)</u></p> <p><i>Overall</i></p> <p>I: 82.3 ± 8.8 C: 81.9 ± 10.6</p> <p><i>Back pain</i></p> <p>I: 80.4 ± 11.2 C: 81.4 ± 10.2</p> <p><i>Leg pain</i></p> <p>I: 80.0 ± 9.9 C: 82.2 ± 8.8</p>			<p><i>*also change scores after 24 months</i></p>		
<p>Abbreviations: C- control; DTM SCS - Differential Target Multiplexed spinal cord stimulation; FBSS – failed back surgery syndrome; HAD – Hospital Anxiety and Depression Scale – intervention; NRS numeric rating scale; ODI – Oswestry Disability Index; SCS spinal cord stimulation; SF-12- 12-Item Short Form Survey; VAS – visual analogue scale</p>						

****For further details, see risk of bias table in the appendix***

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