

Spinal Cord Stimulation for Intractable Visceral Pain Originating from the Pelvic and Abdominal Region: A Narrative Review on a Possible New Indication for Patients with Therapy-Resistant Pain

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Aim: Visceral pain, characterized by pain that is diffuse and challenging to localize, occurs frequently and is difficult to treat. In cases where the pain becomes intractable despite optimal medical management, it can affect patients' Quality of Life (QoL). Spinal Cord Stimulation (SCS) has emerged as a potential solution for intractable visceral pain.

Purpose: In this narrative review, we collected all evidence regarding the efficacy of SCS for visceral pain across various underlying conditions.

Methods: A comprehensive literature search was conducted in PubMed, Embase, and Web of Science in which articles published from October 1st, 1963 up to March 7th, 2023 were identified.

Results: Seventy articles were included in this review of which most were retrospective cohort studies, case series and case reports. The studies, often with a small number of participants, reported on SCS for chronic pancreatitis, anorectal pain and bowel disorders, gynaecological diagnoses, visceral pelvic pain, urological disorders and finally general visceral pain. They found positive effects on pain and/or symptom relief, opioid consumption, anxiety and depression and QoL. Complications occurred frequently but were often minor and reversible.

Conclusion: Better screening and selection criteria need to be established to optimally evaluate eligible patients who might benefit from SCS. A positive outcome of a sympathetic nerve block appears to be a potential indicator of SCS effectiveness. Additionally, women receiving SCS for endometriosis had a better outcome compared to other indications. Finally, SCS could also relieve functional symptoms such as voiding problems and gastroparesis. Complications could often be resolved with revision surgery. Since SCS is expensive and not always covered by standard health insurance, the incorporation of cost-analyses is recommended. In order to establish a comprehensive treatment plan, including selection criteria for SCS, rigorous prospective, possibly randomized and controlled studies that are diagnosis-oriented, with substantial follow-up and adequate sample sizes, are needed.

Keywords: neuromodulation, SCS, spinal cord stimulation, visceral pain, chronic pelvic pain, chronic pain

Introduction

Visceral pain is characterized by pain that is diffuse and challenging to localize, frequently originating from the midline of the body, the lower sternum or upper abdomen. It is thought that the prevalence of visceral pain exceeds 20% of the global population.¹ In 2016, visceral pain from the chest, abdomen or pelvis accounted for more than 25 million emergency room visits and 2.5 million hospitalizations in the United States.² Visceral pain can be referred, where pain from visceral organs can be perceived in areas other than their source. For example, pain originating from the bladder can radiate to the perineal area and is caused by visceros-somatic convergence in the spinal cord.^{3–5} Visceral pain results from activation of nociceptors of the thoracic, pelvic, or abdominal visceral organs and typically originates from inflammation, distention, and ischaemia. Pain is induced when nociceptors surrounding visceral organs are stimulated as a result of inflammation and recurrent distention. When it occurs suddenly, visceral pain is frequently associated with clinical conditions such as appendicitis, cholecystitis, or ulcers. When occurring chronically, it is generally associated with clinical conditions such as endometriosis, pancreatitis or chronic pain originating from the bladder or bowel. Some cases may have no identifiable substrate and are considered idiopathic or functional visceral pain.¹ The sympathetic (thoracolumbar) and parasympathetic (craniosacral) nervous system innervates all thoracic and abdominal organs, other than the pancreas. The viscera are innervated through a complex network of two sets of nerves, either through vagal and spinal nerves, or through two anatomically distinct sets of spinal nerves.⁶

Management of visceral pain presents significant challenges. While prioritizing the resolution of the underlying (chronic) inflammation or distention is crucial, the need for pain management becomes necessary in many cases. The effectiveness of combining paracetamol with Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) for pain treatment in reducing visceral discomfort has been established.^{7,8} Opioids may be administered as needed, although their dosage requires caution due to the risk of opioid induced hyperalgesia – namely abnormal sensitivity to pain – which can mimic pain associated with progression of the underlying pathology. Consequently, this can result in the worsening of visceral pain. In addition, the concomitant administration of antidepressants or anti-epileptic medication with opioids may reduce visceral pain.⁸ Finally, neurolytic blocks such as a plexus hypogastricus block, plexus coeliacus block, or splanchnic nerves block, along with radiofrequency ablation, can aid in the reduction of visceral pain.⁹ Despite the implementation of optimal medical interventions, chronic visceral pain has the potential to become refractory, thereby exerting a negative impact on the overall quality of life (QoL) experienced by the affected individuals. A treatment that might offer a solution is Spinal Cord Stimulation (SCS). First introduced in 1967 for chronic intractable cancer pain, SCS is a minimally invasive therapy offering pain relief for a growing number of conditions.¹⁰ In SCS, electric fields are created between metal contacts which are placed in the epidural space. These applied fields can, based on tissue properties near the electrode, change the electrical potential across membranes. The electrodes are typically placed in close proximity to the physiological midline of the dorsal columns. The electrical stimuli activate dorsal column axons, resulting in orthodromic and antidromic transmission of action potentials. These action potentials generate segmental and supraspinal effects, resulting in pain relief. The electrical stimuli can be administered via various wave forms, which can be characterized based on pulse amplitude, frequency, width and electrodes activation sequence.^{11,12} For visceral pain, SCS can block the sympathetic pain pathway that carries nociceptive information in small fibres, thereby preventing the pain signal to arrive in the thalamus and cerebral cortex and thus removing the pain.^{13,14}

In the Netherlands, the number of diagnoses for which SCS is covered by health insurance is limited. Insurance companies cover expenses in cases solely associated with chronic pain caused by Persistent Spinal Pain Syndrome (PSPS) Type 2, Failed Neck Surgery Syndrome (FNSS), Complex Regional Pain Syndrome (CRPS), Diabetic Polyneuropathy with Small Fibre Neuropathy, or medically refractory Chronic Cluster Headache.¹⁵ Although several studies have suggested that SCS is effective in reducing visceral pain, SCS is not yet covered in the Netherlands for this indication by any Dutch health insurer. This because SCS for visceral pain currently does not comply with the state of research and practice, as determined by the Dutch healthcare institute. Only indications that comply with the determination of the healthcare institute, are covered by healthcare insurance. However, according to the systematic review by Woodroffe et al¹⁶ SCS has been successfully used for pain associated with chronic gastrointestinal (GI) motility disorders such as irritable bowel syndrome (IBS) or gastroparesis and post-surgical visceral hyperalgesia (for example status post Nissen fundoplication, gastric bypass, bowel resection, post-cholecystectomy, among others). For the male patient population, SCS has been successfully applied for chronic orchialgia (testicular pain) which, for example, can be caused by prostate carcinoma or a ruptured epididymis. For the female patient

population, it has been successfully applied for chronic pelvic pain that can be caused, among other things, by long-standing endometriosis. The authors noted that recent studies suggest it might be very effective in treating visceral pain. However, scientific evidence supporting this inference is limited.¹⁶

In this narrative review, our primary aim is to provide a comprehensive overview of the existing literature on the efficacy of SCS in treating visceral pain. By analyzing the current literature, we aim to contribute to the understanding of SCS as a potential therapeutic option for various visceral pain conditions and to identify the existing gaps in scientific evidence.

Methods

This narrative review was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). The narrative review was retrospectively registered in the PROSPERO international prospective register of systematic reviews (CRD42023448103; registration date 13th of July 2023).

To identify all relevant publications, we conducted systematic searches in the bibliographic databases PubMed, Embase.com and Web of Science (core collection). Articles published between October 1st 1963 until March 7th, 2023 were found. The systematic search was conducted in collaboration with a medical librarian. The references of the identified articles were searched to ensure that no relevant literature was excluded. Duplicate articles were excluded by a medical information specialist using Endnote X20.0.1 (Clarivate™), following the Amsterdam Efficient Deduplication (AED)-method¹⁷ and the Bramer-method.¹⁸ Full search strategies for all databases can be found in [Appendix A](#).

Three reviewers (MB, JWK and AHA) independently screened all potentially relevant titles and abstracts for eligibility. Full texts were screened when articles were considered eligible for inclusion based on the title and abstract. When there was a difference in judgement between the three reviewers, a consensus procedure was performed by discussing the article, its outcome measures and the reasoning behind the different opinions. This was done until consensus was reached. There are considerable difficulties in studying patients with refractory chronic pain and SCS: the patient group is small and heterogeneous, SCS is expensive and not readily available. These circumstances demand a wide inclusion of studies with various designs. Therefore, reports describing adult patients with all causes of visceral pain employing SCS from 1967 until March 7th, 2023 were included in this narrative review. Clinical trials were ranked highest, followed by cohort studies and finally, case series or reports. Comparative studies and non-comparative proof of concept and feasibility studies were also included. We included articles in Dutch and English. Technical reports, anatomical descriptions, dose finding studies, studies comparing neurostimulator modalities, and studies comparing various approaches were excluded. We focused on the population of patients with chronic refractory abdominal and pelvic visceral pain in whom SCS was employed to treat chronic pain. All articles were reviewed for the following outcomes: effectiveness (pain scores, pain reduction, reduced demand for systemic analgesic drugs, and patient satisfaction); complications (for example nerve injury, lead migration and malfunction, infection); functional recovery (for example gastroparesis, bladder function and voiding) and QoL. Other relevant findings (for example medical costs) were also recorded and summarized. ([Figure 1](#)).

Results

The literature search generated a total of 10,854 references. After removing duplicates, 7460 references remained (Flowchart [Figure 1](#)). A total of 56 reports were included from the primary search, and 14 were added after thorough examination of the reference lists of included studies. An overview per study can be found in [Table 1](#). The results are summarized according to diagnosis. We identified several randomized controlled trials. However the majority of the included studies were observational studies, case series and case reports, with low to very low quality evidence. Therefore, in addition to the heterogeneity of study outcomes, the results could not be compared quantitatively in a meta-analysis.

Spinal Cord Stimulation for Chronic Pancreatitis, [Table 2](#)

Chronic pancreatitis often results in chronic pain, which intensifies during episodes of active inflammation, while normal pancreatic function further deteriorates.⁸⁷ SCS is rarely used in patients with chronic pancreatitis and is currently not

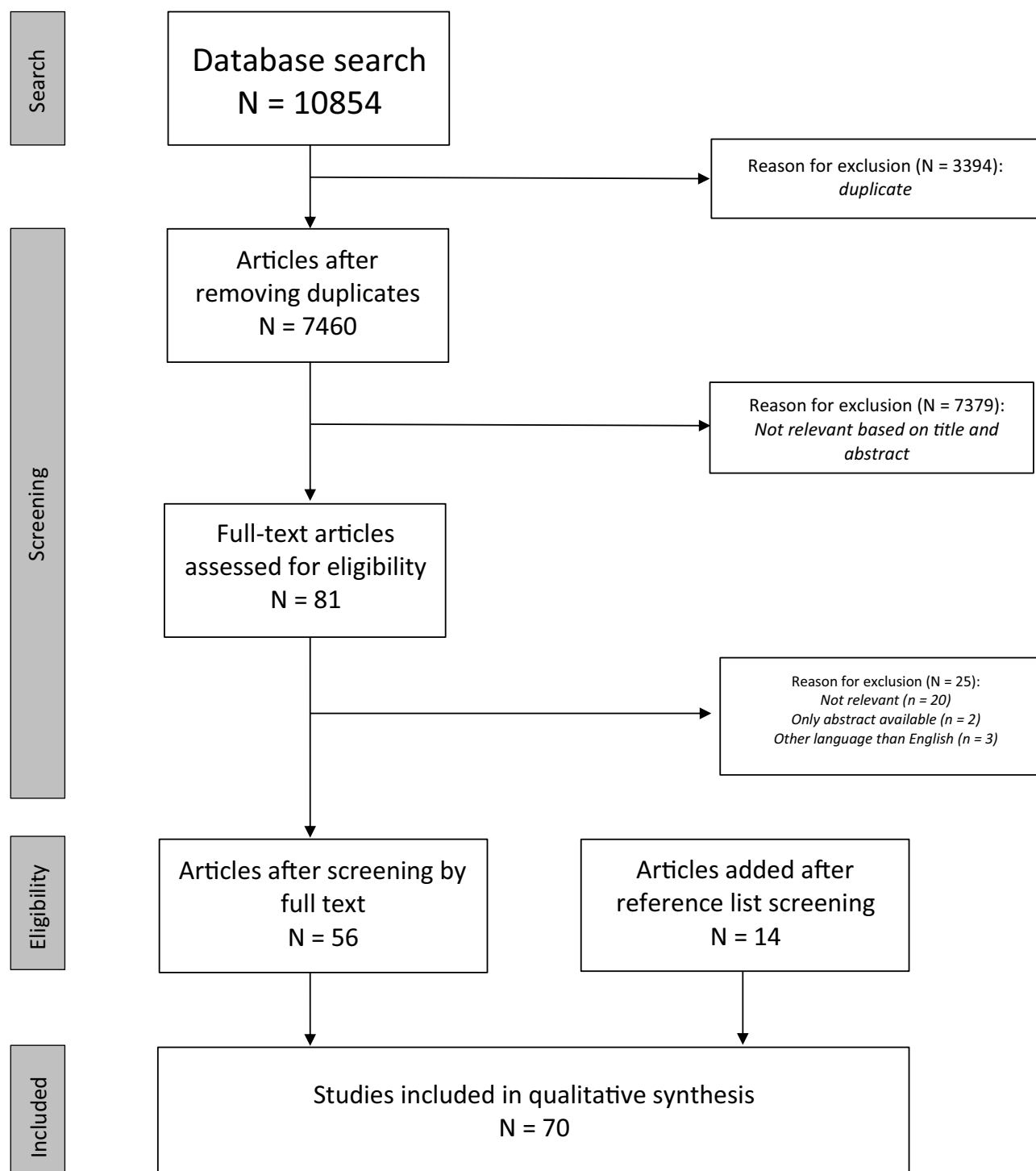


Figure I Results of the literature search and flowchart of all included articles.

recommended. However, studies performed on patients receiving permanent SCS for chronic pancreatitis concluded that pain scores decreased significantly, Pain Disability Indices (PDI) improved, opioid consumption was reduced, and ADLs improved.^{13,19–24,86} Complications that were observed included infection and lead migration, both of which necessitated the revision or removal of the device. Therefore, it could be concluded that when chronic pain from pancreatitis is drug therapy resistant and when management becomes intractable SCS can be a beneficial minimally invasive strategy prior to contemplating a surgical intervention.⁸⁸ The same can be considered for retractable pain associated with Sphincter of

Table 1 All Included Studies

Author	Design	Patients	Permanent Implantation	Outcome	Complications	Follow-up
Pancreatitis						
L. Kapural 2011 ¹⁹	Retrospective cohort	N=30	24/30 at T4-T6	VAS scores baseline (follow-up): average 8.0 ± 1.6 versus 3.7 ± 2.0 at end of trial period ($p=0.001$), 3.6 ± 2.0 at 1 year ($p < 0.001$). Opioid use baseline (follow-up): average 165 ± 120 mg MSE versus 105 ± 101 mg at end of trial period, 48.6 ± 58 mg MSE at 1 year ($p = 0.016$).	2 infection 1 lead migration	1 year (20/24)
Y.N. Khan 2005 ²⁰	Case series	n=5 pancreatitis n=4 other abdominal pain	9/9 T5-T10	VAS scores baseline (follow-up): 10, 7, 9, 7 and 6 versus 5, 3, 4, 3, and 2 at end of follow-up. Narcotic intake: 50%, 30%, 40%, 50%, 20% of intake at baseline.	1 lead migration	6–8 months
L. Kapural 2008 ²¹	Case report	N=1	1/1 at T5-T6	VAS scores baseline (follow-up): epigastric pain ranging 5–10 versus 1 during trial and 1 at 3 months. PDI score: score 62 at baseline, score 14 during trial period, score 15 after 3 months.	No complications	3 months
J.K. Kim 2009 ¹³	Case report	N=1	1/1 at T7-T8	VAS scores baseline (follow-up): score 10 versus 5 at 14 months. Opioid use 'reduced': baseline ~440mg MME to ~45mg (no clear data).	No complications	14 months
F. Vergani 2014 ²²	Case reports	N=2	2/2 at T8-T10	VAS scores baseline (follow-up): 10 and 9 versus 2 and 1 at end of follow-up. Daily opioid intake baseline (follow-up): morphine 60mg (0 mg); methadone 75 mg (0 mg).	No complications	7 years
K.H. Lee 2015 ²³	Case report	N=1	1/1 at T5-T7	VAS scores baseline (follow-up): baseline 8–9, versus 2–3 at 6 months. Opioid use 'reduced' (no clear data).	No complications	6 months
L. Delange 2019 ²⁴	Case report	N=1	1/1 at T5 burst	VAS scores baseline (follow-up): baseline constant 7–8, with breakthrough pains at ingestion, versus 2 and "no pain attacks" at 6 months. Opioid use baseline 300mg MME, at 6 months 125mg. Satisfaction scale: 2.	No complications	6 months

(Continued)

Table 1 (Continued).

Author	Design	Patients	Permanent Implantation	Outcome	Complications	Follow-up
J.C.Mamaril-Davis 2021²⁵	Case report	N=1	I/I at T4-T6	VAS scores baseline (follow-up): score 8–9 at baseline. 90% relief at end of follow-up. Additionally improvement in QoL, able to return to daily life at end of follow-up.	No complications	18 months
Pelvic Pain I: anorectal pain and bowel disorders						
J. Fassov 2014²⁶	Blinded crossover trial, ON/OFF	N=21	S3-S4	Pain (GSRS-IBS questionnaire) baseline (follow-up): median change 12 (range –22 to 44) in when neuromodulator was switched on immediately (ON/OFF) for one month, after which it was switched off for 1 month, versus –17.5 (–48 to –1) when neuromodulation was switched on after 1 month (OFF/ON)(P=0.0009). At 1 year follow-up GSRS-IBS score of 25, versus 62 at baseline (P=0.0001). QoL baseline (follow-up): median change 16 (range –24 to 69) in ON-OFF group, versus –42.5 (range –77 to 0) in OFF-ON group (P=0.0003). At 1 year follow up score of 52, versus score of 135 at baseline (P=0.0001).	7 total: 4 pain at implant site, of which 3 persistent needing relocation, 2 suspected migration, 1 recurrent cystitis	1 year
G. Lind 2015²⁷	Randomised crossover pilot study, ON/OFF	N=10	T6 – T8	VAS baseline (follow-up): median pain 7 (range 4–8) at baseline, VAS 3 (range 2.5–7) after 6 weeks (P<0.03) when neurostimulation was switched on immediately (ON/OFF) and VAS 4 (2–6) when neuromodulation was switched on after 6 weeks (OFF/ON) (P<0.04). Significantly reduced pain intensity for ON/OFF group (P<0.03) OFF/ON group (P<0.04). Significant reduction in number of pain attacks at 15–20 week follow up and 21–26 week follow up (P<0.04).	No complications	28 weeks
E.Falletto 2009²⁸	Prospective cohort	n=24	12/24 at S2-S4	VAS scores baseline (follow-up): average 8.2 ± 1.7 SD versus 2.2 ± 1.3 at 1 year. Opioid use: no data available SF-36 questionnaire improved: the physical component (26.3 ± 5.7 vs 39.0 ± 9.1 p <0.02). The mental component (32.6 ± 9.2 vs 38.3 ± 9.23 p =0.24).	1 infection 1 device failure 1 pain at implant site	15 months

E.Duchalais 2021²⁹	Prospective cohort study	N=423	284/423 at S2-S4	SNS for fecal incontinence (n=256): CCIS significantly improved (14.6 vs 9.9, P<0.001). FiQoL increased average of 0.67 points (2.08 vs 2.75, p<0.001). SNS for solitary rectal ulcer syndrome (n=5): 5/5 pts ≥50% improvement) at 6 year follow up. SNS for IBS (n=10): 5/10 pts ≥50% improvement at 4.5 year follow up. SNS for anterior resection syndrome (n=10): 8/10 pts decrease ≥50% in LARS at 20 month ¹ follow up.	31 total: 5 infections, 2 pain at implant site, 24 loss of efficacy	55 months
E.Krames 2004³⁰	Case report	N=1	1/1 at T8	VAS scores baseline (follow-up): score 9–10, versus 2–3 at 6 months. Regulated (disabling) gastrointestinal symptoms. Daily opioid use: baseline 360mg to 90mg at 6 months, increasing to 300mg.	Gradual loss of efficacy on pain	>6 months
T.C.Dudding 2007³¹	Case report	N=1	1/1 at S3	VAS scores baseline (follow-up): score 10, versus 0 at 1 year. Opioid use: no data.	No complications	1 year
B.Govaert 2010³²	Case series	N=9	4/9 at S3	VAS scores baseline (follow-up): scores of 9, 9, 7, and 6 at baseline versus 0, 1, 2 and 1 at end of follow-up Opioid use: no data GPE: completely recovered (1), much improved (3).	1 infection 2 pain at implant site	2 years
T.C.Dudding 2013³³	Case series	N=6	3/6 at S3	Effectiveness: 2/3 reported no effect and had it removed or turned off. 1/3 experienced subsequent good pain relief at 12 months follow-up, maintained until 5 year follow-up.	1 pain at implant site 1 dislodgement after fall	5 years
M.V.Rana 2013³⁴	Case report	N=1	1/1 at T8	VAS scores baseline (follow-up): score 8–10, versus 3 at 1 year. Regulated gastrointestinal symptoms. Opioid use: yes, no quantitative data. IBS-Severity score: baseline 410/500, at 1 year 180/500.	No complications	1 year
B. Richter 2020³⁵	Case series	N=3	3/3 at T6-T8 (burstDR)	VAS scores baseline (follow-up): score 5, 9 and 9 versus 4, 0 and 0 at end of follow-up. Regulated gastrointestinal symptoms. Opioid use baseline (follow-up): 60mg (0); 22,5mg (12, 5mg); 0mg (0) PGIC: 6, 7, 7	No complications	2 year or more

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Table I (Continued).

Author	Design	Patients	Permanent Implantation	Outcome	Complications	Follow-up
Pelvic Pain II: gynaecological						
S. Siegel 2001 ³⁶	Prospective, non-randomised study	N=10	S3-S4	VAS baseline (follow-up): average pain score 9.7 (scale 0–10) versus 4.4 at long-term follow-up (6–74 months).VAS worst pain baseline (follow-up): score 4.7 versus 2.2 at long-term follow-up in 9/10 patients.VAS least pain baseline (follow-up): 2.4 versus 1.2 at long-term follow-up in 7/10 patients.Hours without pain per day baseline (follow-up): 3.6 hours versus 13 hours at long-term follow-up.BDI baseline (follow-up): 6/10 patients reported improved scores at long-term follow-up (19 months).	27 total: 6 local wound infections, 4 pain at implant site, 1 wound infection needing explantation, later successful re-implantation.	6–74 months
J. Tate 2021 ³⁷	Prospective, single-arm pilot study	N=21	13/21 at T8-T12	VAS baseline (follow-up): score 8.1 versus 2.3cm at 12 month follow-up. Pain remission (VAS ≤ 3.0cm) was reported by 8/13 pts (62%). SF-MPQ-2 baseline (follow-up): mean total score of 4.1 versus 1.3 at 12 month follow-up. PDI baseline (follow-up): score 45.2 versus 16.2 at 12 month follow-up. Patient satisfaction: 69% of patients reported being satisfied or very satisfied with treatment at 3 month follow-up, increasing to 85% at 12 month follow-up.	No complications	12 months
J.Martellucci 2011 ³⁸	Prospective observational study	N=17	8/17 at S3-S4	VAS baseline (follow-up): 8.2 ± 0.9 pre-operatively versus 1.9 ± 1.2 at 6 month follow-up (reported by 8 pts) (p<0.0001), to 2.1 ± 1.3 at 12 month follow-up (reported by 7 pts), 2.0 ± 1.4 at 24 month follow-up (reported by 5 pts) and 1.8 ± 1.5 at 36 month follow-up (reported by 4 pts). QoL (in SF-36) baseline (follow-up): improvement in all eight domains from baseline to 6 month follow-up (P<0.05).	No complications	39 months

A.Polushkin 2019³⁹	Prospective cohort study SCS; SNS or pudendal NS	N=32	27/32 at Th10- Th12	VAS baseline (follow-up): mean score 8.61 ± 0.91 versus 3.53 ± 1.20 at 12 month follow-up. Pain medication baseline (follow-up): all patients were able to completely abandon drugs at 12 month follow up. QoL (in PQLS) baseline (follow-up): 8.59 ± 1.16 versus 5.44 ± 1.60 at 12 month follow up ($P < 0.05$). HADS scale baseline (follow-up): 14.03 ± 3.53 versus 8.80 ± 2.60 at 12 month follow up ($P < 0.05$).	5 electrode migration needing surgical correction, with restoration of effective neurostimulation	12 months
T.Vancaillie 2018⁴⁰	Retrospective cohort	n=64	52/64 at S2-S4 1 hypogastric lead	43/52 patients completed the questionnaire- VAS baseline (follow-up): mean score 8.3 versus 4.9 (95% CI: 2.60–4.27), after implantation ($P < 0.001$). QoL improved (35/43) Pain scores improved (32/43) Bowel function improved (15/43) Bladder function improved (10/43) Sexual function improved (10/43)	10 total: infection, pain at implant site, device failure, need for MRI, excess granulation tissue, allergy. Gradual loss of efficacy	Not described
M.Agnello 2020⁴¹	Retrospective cohort study	N=13	9/13 at S3 SNM Interstim	VAS baseline (follow-up): mean score 7.5 versus 4.0 after SNM implant. 1/9 participants improvement of intestinal constipation, with regularization of defecatory habits. 1/9 participants almost total resolution of anal and pelvic pain (VAS 8 at baseline versus VAS 2 after SNM implant).	No complications	Not mentioned
A.Zegrea 2020⁴²	Retrospective cohort	n=51 n=16 endometriosis	28/51 at S3-S4	VAS baseline (follow-up): median score 7.4 versus median score 2.2 during test trial. No data on long term follow-up. Opioid use: no data available Specifically good results for endometriosis (12/14).	1 infection 1 broken lead 1 lead migration device failure pain of the device	0.3–98.9 months
D.Abejón 2010⁴³	Observational study	N=20	S3	VAS baseline (follow-up): pain relief $73.57 \pm 13.7\%$ after the test period. Pain relief between 61.4% and 77.5%; pain area coverage 90%. SNS pain relief on scale 0–10, baseline (follow-up): average 8.6 ± 0.8 versus 3.8 ± 1.1 after test period ($P=0.03$). Satisfaction: 75% of participants 3–4 grade satisfaction at 3 and 4 month follow up, 83% of participants maintained this satisfaction at 6 month follow-up.	No complications	6 months

(Continued)

Table 1 (Continued).

Author	Design	Patients	Permanent Implantation	Outcome	Complications	Follow-up
C. Hunter 2013⁴⁴	Case series	n=5	4/5 at T7-T8	VAS baseline (follow-up): unknown, >50% reduction, >50% reduction, 5 (1). Opioid use baseline (follow-up): unknown, decreased, 5mg (2, 5mg), decreased. Decreased chronic headaches.	No complications	3–10 months
P. Sokal 2015⁴⁵	Case series	N=9	Th12-L1 and S2-S4	VAS baseline (follow-up): median score 9 versus score 2 after implantation (P=0.001). Score 3 at 6 month follow-up (P=0.043). Score 6 at 12 month follow up. Use of analgesics: 8/9 patients reduced analgesics.	5 total: 3 infections, 2 migration of electrodes	12 months
C. Hunter 2019⁴⁶	Case series	n=7	4/7 L1-S2 DRGS	VAS baseline (follow-up): 9, 9, 6 and 4 versus 2, 0, 2, 1 at end of follow-up. Opioid use baseline (follow-up): no exact data Improved sleep	No complications	1 year or more
J.M.Tiede 2006⁴⁷	Case report	n=2	2/2 at T2	VAS baseline (follow-up): score 10 and 10 versus 2 and 2–3 at end of follow-up. Opioid use baseline (follow-up): no dosage known and 240mg versus no opioid use and 160mg at end of follow-up.	1 lead migration	At least 3 and 4 months
M.Lavonius 2017⁴⁸	Case report	N=4	3/4 at S3-S4	Abdominal or pelvic pain: score 3 to 4 at 6 month follow-up, score 4 to 5 at 2.5 years follow-up. Dyspareunia: score 4 at 6 month follow-up, score 3 to 4 at 2.5 years follow-up. Dyschezia: score 4 to 5 at 6 month follow-up, score 4 at 2.5 years follow-up. Constipation: score 4 to 5 at 6 month follow-up, score 3 to 5 at 2.5 years follow-up. Anal incontinence: score 4 to 5 at 6 month follow-up, score 3 to 4 at 2.5 years follow-up. Dysuria: score 4 at 6 month follow-up, score 5 at 2.5 years follow-up. Voiding dysfunction: score 4 6 month follow-up, score 2 at 2.5 years follow-up. Urinary dysfunction: score 4 at 6 month follow-up, score 2 to 4 at 2.5 years follow-up. Satisfaction NRS between 8 and 9 at 6 month follow-up, NRS between 8 and 10 at 2.5 years follow up. 1: worse; 2: no change; 3: somewhat improved; 4 much improved; 5: excellent improvement	No complications	2.5 years

E.Samaniego 2020⁴⁹	Case report	N=2	2/2 at S2	<p><i>NRS pelvic pain baseline (follow-up):</i> score 10/10 versus 2/10 at 18 month follow up in first case. Score of 10/10 versus 2/10 at 10 month follow up in second case.</p> <p><i>QoL (in SF-36) baseline (follow-up):</i> improvement in QoL scores in both cases.</p> <p><i>ODI score baseline (follow-up):</i> score 52 versus 26 at 18 month follow up in the first case. Score 52 versus 26 at 18 month follow up in the second case.</p> <p><i>Pain medication baseline (follow-up):</i> Ketorolac 10mg 4x per day, acetaminophen 1gr 3x per day, diazepam 10mg a.n., amitriptyline 50 mg a.n., gabapentin 1800mg daily, tramadol 600mg daily at baseline versus acetaminophen 1gr daily at 18 month follow up in first case. Celecoxib 200mg twice per day, acetaminophen 1gr 3x per day, Duloxetine 120mg daily, pregabalin 300mg twice per day, Clonazepam 1mg a.n.</p>	No complications	18 months
Pelvic Pain III: urological disorders						
K.Everaert 2004⁵⁰	RCT 1 stage 2 stage	N=114	42/114 at S3	Failures more frequent in 1-stage versus 2-stage group (7 versus 3, P=0.02).	<p>23 revisions (17 failure; 2 repositioning leads; 4 pain)</p> <p>3 infection</p> <p>4 pain of the device</p> <p>2 pain of stimulation</p> <p>6 explants (3 failure; 3 infection)</p>	24 months
K.M.Peters 2007⁵¹	Randomized crossover trial	N=22	13/17 PNS 4/17 SNS	<p><i>VAS baseline (follow-up):</i> score 4.5 versus 3.2 at end of follow-up for PNS. Score 7.9 versus 4.0 at end of follow-up for SNS.</p> <p><i>Symptom reduction baseline (follow-up):</i> 59% for PNS and 44% for SNS (P=0.05).</p> <p><i>Voiding symptoms baseline (follow-up):</i> 41% improved for PNS and 33% for SNS.</p> <p><i>Mean voided volume baseline (follow-up):</i> increased by 95% for PNS and 21% for SNS.</p>	2 seroma formation	6 months

(Continued)

Table 1 (Continued).

Author	Design	Patients	Permanent Implantation	Outcome	Complications	Follow-up
C.F.Maher 2001 ⁵²	Prospective cohort	n=15	11/15 at S3	VAS baseline (follow-up): mean score 8.9 versus 2.4 after test period. No data on long term follow-up. Voiding symptoms: improved SF-36: improvement on social functioning, bodily pain, general health. Opioid use: no data available	No complications	Not mentioned
S.Aboseif 2002 ⁵³	Prospective observational study	N=64	S3	Group 1 (frequency-, urgency- or urge incontinence, n=43): 33/43 pts (77%) >50% improvement in QoL and would recommend this therapy. Group 2 (idiopathic, non-obstructive chronic urinary retention, n=20): 18/20 pts (90%) >50% improvement in QoL and would recommend this therapy. Able to void spontaneously without catheterization. Group 3 (chronic pelvic pain, n=41): decrease in VAS; 5.8 pre-operative to 3.7 post-operative (P>0.05).	12 total: seroma formation at site of IPG; resolved spontaneously. 2 superficial wound infections treated with antibiotics. 1 deep infection needing IPG removal. 2 migration sacral wires needing revision. 2 device malfunction needing revision.	24 months
C.V.Comiter 2003 ⁵⁴	Prospective cohort	n=25	17/25 at S3	VAS baseline (follow-up): median score 5.8 versus 1.6 after implantation. No data on long term follow-up. Voiding symptoms: improved Opioid use: no data available Quadripolar lead more efficacious than unipolar.	No complications	2–28 months
K.M.Peters 2003 ⁵⁵	Prospective cohort	n=26	26/26	Moderate or marked improvement: Pelvic pain (71%) Pelvic pressure (67%) Quality of life (76%) Vaginal pain (60%)	3 revisions	
K.E. Whitmore 2003 ⁵⁶	Prospective cohort	n=33	23/33 positive test trial at sacral level	Test trial 23/33 positive (>50% pain reduction).	No complications	No data on permanent implantation

K.M.Peters 2015 ⁵⁷	Prospective cohort	n=13	13/13 at sacral level n=7 follow-up	CXCL-1 peptide and sIL-1 receptor antagonist positively associated with ICSP1 ($r = 0.43$, $P = 0.09$; $r = 0.50$, $P = 0.04$) and pain events ($r = 0.63$, $P = 0.009$; $r = 0.50$, $P = 0.04$). At 24 weeks SNM follow-up reduction in chemokines (MCP-1, sIL-1RA, and CCL5) and improvement ICSP1.	No data	24 weeks
K.M.Peters 2004 ⁵⁸	Retrospective cohort	n=21	21/21 at S3	General analgesic drug use: 4/21 stopped using Daily opioid use: baseline 82mg (follow-up 52mg) Pain score: 20/21 moderate or marked improvement.	No data	7.4–23.1 months
M. Elhilali 2005 ⁵⁹	Retrospective cohort	N=52	41/52 at S2-S4	<i>In group of urgency/frequency:</i> 17/22 pts long term use of IPG: 10 pts (45%) improvement in symptoms; 7 pts no improvement (32%). <i>In group of urge incontinence:</i> 1/6 pts reported improvement in frequency of incontinence episodes; 1 pt reported no improvement. <i>In chronic retention group:</i> 7/9 pts improvement in symptoms (78%). 1 pt chronic intermittent catheterization. <i>Interstitial cystitis:</i> 2/2 pts no improvement <i>Pelvic pain:</i> 1/2 reported improvement, the other one stopped using it.	5 removal 6 stopped using the device	Up to 13 years
T. Kessler 2006 ⁶⁰	Retrospective observational study	N=209	91/209 at S2-S4 84 lower urinary tract dysfunction, 7 CPP syndrome	<i>Success rate:</i> sacral neuromodulation was successful in 64/91 IPG implants (70%) <i>Leakages/24 hours baseline (follow up):</i> (A) 5 (2–10), 1 st follow up (B) 0 (0–2), last follow up (C) 0 (0–2) when urge incontinence. A vs B $P < 0.0001$. A vs C $P < 0.0001$. <i>Number of voids per day baseline (follow up):</i> (A) 10 (5–13), 1 st follow up (B) 6 (4–7), last follow up (C) 6 (4–8) when urge incontinence. A vs B $P < 0.0001$. A vs C $P < 0.0005$. (A) 3 (0–6), 1 st follow up (B) 6 (6–9), last follow up (C) 5 (5–6) when non-obstructive chronic urinary retention. A vs B $P = 0.25$. A vs C $P = 0.23$. <i>VAS baseline (follow up) when neuromodulation for CPP syndrome:</i> (A) 8 (8–9), 1 st follow up (B) 0 (0–1), last follow up (C) 2 (1–4). A vs B $p = 0.03$; A vs C $p = 0.03$. <i>Symptom improvement baseline (follow up) when neuromodulation for CPP syndrome:</i> B 100% (100–100%), C 65% (45–90%).	10 total: 2 lead migrations, 1 infection, 1 broken lead needing revision, 1 IPG migration, 1 IPG malfunction after MRI.	10–24 months

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Table 1 (Continued).

Author	Design	Patients	Permanent Implantation	Outcome	Complications	Follow-up
K.M.Peters 2008 ⁶¹	Retrospective cohort	n=87 n=16 chronic pain	No data	No data on the subgroup	No data	No data
J.B.Gajewski 2010 ⁶²	Retrospective cohort	n=78	46/78 at sacral level	Long term success implanted patients: 33/46 (72%) GRA scale (very good 70%, good 30%). Overall success rate 33/78 (43%).	13 removal: treatment failure painful stimulation 23 revisions: loss of efficacy local pain of the device painful stimulation battery replacement	33.8–89.2 months
C. Powell 2010 ⁶³	Retrospective cohort	N=39	22/39 at S3	<i>Symptom reduction:</i> 11/17 (64.7%) no more dysuria or pelvic pain. <i>Success rate:</i> 17/22 (77%) reported improvement >50%. <i>Analgesics use:</i> 6/13 (46.2%) dependent on amitriptyline stopped it completely, 54.5% (6/11) stopped hydroxyzine completely, 60.0% (9/15) stopped pentosane polysulfate completely, 60.0% (6/10) no longer needed DMSO, 20% (2/10) no longer needed narcotics.	9 replacements: 4 depleted batteries 1 loss of efficacy 1 infection 1 device malfunction 1 troublesome foot movement 1 device destruction after cardioversion	60 months
Y.Q.Ghazwani 2011 ⁶⁴	Retrospective cohort	N=21	11/21 at S3	VAS baseline (follow-up) in bladder pain: score 8.09 (1.1) versus 1.5 at 1 year-follow up ($P<0.001$). <i>Reduction in urgency baseline (follow-up):</i> 2.6 ± 0.6 versus 1.2 ± 0.7 at 1 year follow-up. <i>Reduction in day time frequency baseline (follow-up):</i> 12.8 ± 5 versus 6.1 ± 2.1 at 1 year follow-up. <i>Reduction in nycturia:</i> 6.5 ± 2.1 versus 3.8 ± 1.5 at 1 year follow-up. Improvements remained at last visit (± 5 years)	2 battery replacement 2 re-implantation of the device due to local pain	5 years
R.K.Leong 2011 ⁶⁵	Retrospective cohort questionnaire	N=207	Unknown	90% satisfaction Higher satisfaction: patient adjustability of the stimulation ($p<0.001$), patient still working ($p<0.001$) Less satisfaction with multiple pelvic floor comorbidities ($p=0.003$).	Decreased efficacy battery replacements need for MRI problems with reimbursement local pain of the device trouble with metal detectors in stores or when traveling	Not mentioned

S.P. Marinkovic 2011 ⁶⁶	Retrospective cohort	n=34	30/34 at sacral level	Mean pre-op/post-op pelvic pain and urgency/frequency scores: 21.61 ± 8.6 vs 9.22 ± 6.6 ($p < 0.01$). VAS baseline (follow-up): mean score 6.5 ± 2.9 versus 2.4 ± 1.1 at end of follow-up ($p < 0.01$).	5 lead migration 3 device erosions (after accidents)	6 years or more
M.H.Vaarala 2011 ⁶⁷	Retrospective cohort	n=180	74/180 n=7 PBS	Urinated volume (mL) baseline 141, follow-up 192 ($P=0.002$). Number of urinations baseline 13.1, follow-up 8.4 ($P<0.001$). Number of daily catheterization baseline 3.3, follow-up 0.2 ($P<0.001$). Younger patients with urinary retention are more likely to undergo permanent implantation (implanted 45 years vs tested 53 years) No results on subgroup with PBS.	15 revisions: loss of response, local pain of the device, device failure, infection	0–143 months
B. Kaaki 2020 ⁶⁸	Retrospective Cohort	N=66	55/66 at S2-S4	<i>Symptom improvement:</i> 40/55 (72.7%) pts experienced improvement of bladder symptoms from their own perspective. <i>Success rate:</i> SNS successful in 41/55 (74.5%) at 32 month follow-up.	3 pain 2 lead migration 1 IPG migration 1 infection 1 device malfunction 5 end of battery life (all replaced) 15 explants (5 decreased efficacy, 4 MRI, 3 pain, 2 end of life battery, 1 infection)	Median 24 months
A.Coguplugil 2021 ⁶⁹	Retrospective cohort	N=24	16/24 at sacral level	<i>Success rate:</i> Overall success rate for all indications was 87.5% after a mean follow-up of 42.3 months (100% for OAB, 100% for BPS/IC and 66.7% for IUR).	3 device failure 1 pain	Mean 42 months
G. Liu 2022 ⁷⁰	Prospective cohort	N=40 Control n=20 Intervention n=20	15/20 at sacral level	VAS score baseline (follow-up): score 8.8 ± 1.3 versus 4.5 ± 0.7 at 12 month follow-up. QoL baseline (follow-up): score 4.4 ± 0.7 versus 2.3 ± 0.4 at 12 month follow-up. O'Leary-sant score baseline (follow-up): 31.4 ± 5.8 versus 16.3 ± 3.0 at end 12 month follow-up. All $P<0.05$.	No complications	12 months
N.Moufarrij 2022 ⁷¹	Case Report	N=1	1/1 at T8-T10	<i>Symptom improvement:</i> at 6 month follow-up no low back pain, sciatica or interstitial cystitis pain, urinary urgency and frequency from interstitial cystitis. <i>Satisfaction score:</i> at 6 month follow-up score 10/10.	No complication	6 months

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Table 1 (Continued).

Author	Design	Patients	Permanent Implantation	Outcome	Complications	Follow-up
Visceral Pain: various causes						
J.L. Tate 2021³⁷	Prospective pilot study	n=21	13/21 at T8-T12 high frequency	VAS baseline (follow-up): score 8.2 versus 2.3 at the end of follow-up. SF-MPQ-2 (follow-up): total score of 4.1 versus 1.6 at 3 months and 1.3 at end of follow-up. PDI score baseline (follow-up): score of 45.2 versus 18.3 at 3 months follow-up and 16.2 at end of follow-up. Patient satisfaction: at 3 months follow-up 69% of participants were satisfied or very satisfied, increasing to 85% at the end of follow-up.	Device dislocation pain at site of the device light headedness infection	1 year
J.Martellucci 2012³⁸	Prospective cohort	n=27	16/27 at sacral level (SNM)	VAS baseline (follow-up): score 8.2 ± 0.9 versus 1.9 ± 1.2 at 6 month follow up (P<0.0001), 2.1 ± 1.3 at 12 months follow-up, 2.0 ± 1.4 at 24 months follow-up and 1.8 ± 1.5 at 36 month follow-up. QoL baseline (follow-up): improvement in all eight domains from baseline to 6 months follow-up (P<0.05).	No complications	12–71 months
N. Zabihi 2008⁷²	Prospective cohort	n=30	23/30 at S2-S4 (bilateral SNM)	VAS baseline (follow-up): improvement of 40% at end of follow-up. P=0.04. ICSI score baseline (follow-up): improvement of 35% at end of follow-up. P=0.005. ICPI score baseline (follow-up): improvement of 38% at end of follow-up. P=0.007. UDI score baseline (follow-up): improvement of 26% at end of follow-up. P=0.05.	5 removals: 4 device failure 1 infection 4 revisions: 3 infection 1 device failure	6–15 months
D. Guner 2022⁷³	Retrospective study	N=23	T9-T10 for LBP, T10-T11 for leg pain	VAS baseline (follow-up): 9 (8–10) versus 4 (4–6) at 3 month follow up and 3 (2–4) at 6 month follow-up (P<0.001). LANSS baseline (follow-up): median scores 19 (16–24) versus 16 (11–19) at 3 month follow-up and 11 (9–14) at 6 month follow-up (P<0.001). QoL (in SF-36) baseline (follow-up): mean value of 25 versus 62.5 at 3 month follow-up and 62.5 at 6 month follow-up (P<0.001). ODI score when receiving thoracic SCS baseline (follow-up): score of 76 (72–82) at baseline versus 32 (30–40) at 3 month follow-up and 30 (26–32) at 6 month follow-up (P<0.001).	No complications	6 months

C.Bridger 2021⁷⁴	Retrospective cohort	n=153	11/153 (various modalities)	<i>NRS baseline (follow-up):</i> score of 6.63 ± 0.45 versus score of 4.91 ± 0.93 at end of follow up. $P=0.11$.	No data	1–7 years
D.Hernandez-Hernandez 2021⁷⁵	Retrospective observational study	N=106	64/106	<i>Neuromodulation for OAB:</i> GRA between 50% and 75%. Significant reduction in ICIQ-SF questionnaire (mean 15.69 ± 4.79 pre-SNS vs 2.69 ± 3.01 post-SNS). <i>Neuromodulation for BPS/IC:</i> GRA between 50% and 75%. 16.6% reported complete resolution of symptoms. Significant reduction in NRS (-5.85 points, $P<0.0001$). <i>Neuromodulation for FI:</i> improvement between 50% and 75%. 14.3% reported complete resolution of symptoms. <i>Neuromodulation for UR:</i> mean number of catheterizations per day from 4.45 ± 1.98 at baseline, versus 1.97 ± 2.40 after implantation. <i>Neuromodulation for DI:</i> significant reduction in average pad use with mean 5.0 ± 2.71 at baseline versus 1.71 ± 0.76 after implantation. Significant reduction in ICIQ-SF scores with mean 15.50 ± 2.12 at baseline versus 1.50 ± 2.21 after implantation.	40.63% reported complications. 25 pain at implantation site 5 loss of efficacy 1 local infection needing explantation Overall explantation rate of 9.4% because of loss of efficacy (5/6) and need for repeat MRI (1/6).	14–220 months
T.Simopoulos 2018⁷⁶	Case series	n=3	3/3 at T8-T9 high frequency	<i>VAS baseline (follow-up):</i> CASE 1 average pain score 8.2 versus score of 4.0 at end of follow-up. CASE 2 average pain score 8.3 versus score of 3.3 at end of follow-up. CASE 3 average pain score 7.5 versus score of 4.1 at end of follow-up. <i>Analgesics use baseline (follow-up):</i> CASE 2 morphine 60mg twice daily, oxymorphone 15mg 4 times a day at baseline versus no more morphine and reduction oxymorphone 3 times daily at end of follow-up.	No complications	1 year
E.Romero-Serrano 2021⁷⁷	Case report	N=1	T8 and T9	<i>VAS baseline (follow-up):</i> score 7, increasing to 10 in movement versus score 3 at 18 month follow-up. <i>Analgesics use baseline (follow-up):</i> NSAID (celecoxib 600mg/day), Fluoxetine 30mg/day, gabapentin 1800mg/day, morphine 90mg/day at baseline. At 18 month follow-up several medications had been weaned off. <i>EQ-5D baseline (follow-up):</i> -0.0757 , meaning worse than death at baseline, versus $+0.6454$ at 18 month follow-up.	No complications	18 months

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Table 1 (Continued).

Author	Design	Patients	Permanent Implantation	Outcome	Complications	Follow-up
Table 7 Visceral pain II: general						
A. Levine 2016⁷⁸	Prospective cohort	n=32	15/32 3 SCS, 10 DNRS	VAS baseline (follow-up): score of 7.3 ± 1.3 versus 3.1 ± 2.8, 3.8 ± 2.4, and 4.2 ± 3.2 at 3, 6, and 12 months, respectively. MEDD baseline (follow-up): score of 175 ± 377 versus 77 ± 140 at 12 months follow-up. QoL in SF-36 baseline (follow-up): only graphic data shown, with 4/9 significant improvement SF-36 scoring.	3 infection 5 lead migration 1 CSF leak headache 15 revisions 2 removals (none responders)	1 year
L.Kapural 2020⁷⁹	Prospective, single-arm multicenter study	N=24	23/24 at T4 to T8	VAS baseline (follow-up): score 8.3(95% CI 7.5–9.5) versus 2.3 (95% CI 0.7–2.8) at 3 month follow up (P<0.001). These reductions maintained at 6 month and 12 months follow-up.PDI score baseline (follow-up): 48.5(95% CI 43.0–53.9) versus 21.0 (95% CI 14.3–27.7) at 12 months follow-up (P<0.001).SF-MPQ-2 baseline (follow-up): mean total score of 4.0 (95% CI 3.4–4.5) versus 1.5(95% CI 0.9–2.2) at 12 months follow-up (P<0.001).GAF score baseline (follow-up): score 36.0 versus 80.0 at 3 months follow-up and 90.0 at 12 months follow-up (P<0.001).Patient satisfaction: 19/22 pts were satisfied or very satisfied with treatment at 12 months follow-up.QoL (in SF-12) baseline (follow-up): improved physical and mental component. Physical score of 30.1 (95% CI 26.6–33.5) at baseline versus 39.9 (95% CI 35.8–44.0) at 12 months follow-up (P<0.001). Mental score of 43.8(95% CI 39.7–47.9) at baseline versus 50.5 (95% CI 46.8–54.2) at 12 months follow-up (P=0.02).		
B.A.Simpson 1991⁸⁰	Cohort	n=62 heterogeneous group	No data on subgroups	Improvement: 14 (23.3%) participants reported modest benefit, 28 (46.7%) participants reported significant benefit. 10 (16.7%) reported complete pain relief.	No data on subgroups	No data on subgroups

E.D. Hord 2003⁸¹	Retrospective cohort	n=23 heterogeneous group	15/23 at various levels	<p>When positive SB it was more likely there was positive SCS trial period: 13 patients with positive SB had good SCS trial periods, compared to 3/10 patients with negative SB (100% vs 30%, $P<0.001$).</p> <p>When positive SB it was more likely there was good pain relief at 1-month follow up: 100% of participants with positive SB had good pain relief, compared to 33% of participants with negative SB. $P=0.029$.</p>	No data	9 months
K. Kumar 2006⁸²	Cohort	n=410 200 FBS 6 perirectal pain	4/6 no data on subgroups	Success rate: 4/6 (66.7%) success, 3/6 (50%) long-term success	No data on subgroups	No data on subgroups
G. Baranidharan 2014⁸³	Retrospective cohort	n=26	26/26 ventral or dorsal SCS	<p>VAS baseline (follow-up): median score 9 versus 4 at 26 months follow-up ($p\leq 0.05$).</p> <p>Analgesics use baseline (follow-up): median dosage oral morphine of 160mg versus 26mg at 26 months follow-up ($p<0.001$). Overall reduction of 75% in anti-neuropathic drug such as amitriptyline, gabapentin, pregabalin consumption post-implant. 9/15 pts stopped all anti-neuropathic drugs.</p> <p>QoL baseline (follow-up): daily activities ($Z=-3.1$, $P<0.05$), mood ($Z=-2.3$, $p<0.05$) patient global impression of change ($Z = -5.2$, $P<0.05$), change in sleep ($Z=-1.8$, $P=0.06$).</p>	2 removals: infection device failure after accident	9–101 months

(Continued)

Table 1 (Continued).

Author	Design	Patients	Permanent Implantation	Outcome	Complications	Follow-up
B. Richter 2020³⁵	Retrospective review	N=3	3/3 at T6, T7 and T8 BurstDR stimulation	<p>VAS baseline (follow-up): CASE 1 score 5/10 without medication, with 30 monthly exacerbations with score 10/10 at baseline versus score $\leq 4/10$, decreasement exacerbations with 30% at end of follow-up.</p> <p>CASE 2 score 9/10 without medication, with 4 monthly exacerbations with score 10/10 at baseline versus score 0/10 at baseline without exacerbations at end of follow-up.</p> <p>CASE 3 score 9/10 without medication, with 8 monthly exacerbations with score 10/10 at baseline versus score 0/10 at baseline with single exacerbation per month (pain score 6/10) at most at end of follow-up.</p> <p>Analgesics use baseline (follow-up): CASE 1 morphine equivalent dosing of 60mg at baseline versus no morphine at end of follow-up. CASE 2 morphine equivalent dosing of 22.5mg at baseline versus 12.5mg at end of follow-up. CASE 3 use of gabapentin, celecoxib and methocarbamol at baseline versus use of gabapentin and celecoxib at end of follow-up.</p>	No complications	27–28 months
L.Kapural 2022⁸⁴	Retrospective chart review	N=26	23/26 at T4 and T5	<p>VAS baseline (follow-up): 8.7 ± 1.3 versus 3.0 ± 3.0 at 6 month follow-up ($P < 0.001$) and 3.2 ± 3.1 at last follow-up visit ($P < 0.001$).</p> <p>Analgesics use baseline (follow-up): average of 57.7mg (95% CI 34.3–81.0) MSO₄ versus average of 24.3mg (95% CI 8.9–39.7) at 6 months follow-up and 28.0mg (95% CI 12.3–43.8) at last follow-up visit ($P < 0.006$ vs baseline).</p> <p>Nausea baseline (follow-up): 20/23 pts daily nausea versus 8/23 pts (35%) at 6 months follow-up ($P = 0.001$), and 7/23 pts (30%) at last follow-up visit ($P < 0.001$).</p> <p>Patient satisfaction: 87% of pts satisfied with their therapy. 15 highest level of satisfaction, 2 pts lowest level. 20/23 would recommend this therapy.</p>	No complications	41 months

L.Kapural 2006⁸⁵	Case series	n=6	6/6 at T11-L1	VAS baseline (follow-up): score 9.0 ± 0.89 versus 2.3 ± 1.6 at end of follow-up. PDI baseline (follow-up): average 58 versus 19.7 at end of follow-up. Analgesics use baseline (follow-up): average 22.5mg of MSO ₄ versus 6.6mg at end of follow-up.	2 revisions: lead migration	10–70 months
L.Kapural 2010⁸⁶	Retrospective cohort	n=35	T5-T6 and T11-T12	VAS baseline (follow-up): average score of 8.2 ± 1.6 versus 3.1 ± 1.6 at end of trial period ($p < 0.001$), 3.8 ± 1.9 at 1 year follow-up ($p < 0.001$). Analgesics use baseline (follow-up): 110.0 ± 119.0 MSE versus 70.0 ± 68 mg MSE at end of trial period ($p = 0.212$), 38 ± 48 mg MSE at 1 year follow-up (0.089).	4 removals: 3 infection 1 lead migration	1 year
J. Tiede 2006⁴⁷	Case report	N=2	2/2 at T2	VAS baseline (follow-up): CASE 1 score 10/10 versus 2/10 at end of follow-up. CASE 2 score 8/10 versus 2–3/10 at end of follow-up. Analgesics use baseline (follow-up): CASE 1 usage of gabapentin, fentanyl, diazepam, promethazine, tegaserod maleate versus no opioid use at end of follow-up. CASE 2 usage of morphine 60mg every 8 hours, hydromorphone 4mg every 4 hours as needed, promethazine versus discontinuation hydromorphone and decrease of morphine by 33% at end of follow-up.	1 migration lead	Case 1: unknown Case 2: 3 months

Abbreviations: VAS, Visual Analogue Scale (scale 0–10cm); MSE, Morphine Sulfate Equivalents; PDI, Patient Disability Index (range 0–70); QoL, Quality of Life; GSRS-IBS questionnaire, Gastrointestinal Symptom Rating Scale – Irritable Bowel Syndrome questionnaire (7-Point Likert scale); SF-36 questionnaire, Short Form-36 questionnaire (range 0–100); SNS, Sacral Neurostimulation; CCIS, Cleveland Clinic Incontinence Scale (range 0–20); FiQoL, Fecal incontinence Quality of Life (scale 1–4); IBS, Irritable Bowel Syndrome; LARS, Low Anterior Resection Syndrome; GPE, Global Perceived Effect (0–10); PGIC, Patients Global Impression of Change (scale 1–7); BDI, Beck Depression Inventory (range 0–63); SF-MPQ-2, mean short-form McGill Pain Questionnaire 2 (range 0–78); PQLS, Patient Quality of Life Card questionnaire (range unknown); HADS, Hospital Anxiety and Depression Scale (range 0–21); SNM, Sacral Nerve Modulation; DRGS, Dorsal Root Ganglion Stimulation; NRS, Numeric Rating Scale (scale 0–10); ODI, Oswestry Disability Index (range 0–100); PNS, Peripheral Neurostimulation; SNS, Sacral Neurostimulation; IPG, Internal Pulse Generator; ICSPI, Interstitial Cystitis Symptom Problem Index (range 0–20); GRA, Global Response Assessment (scale 0–3); DMSO, Dimethylsulfoxide; PBS, Painful Bladder Syndrome; OAB, Overactive Bladder; BPS/IC, Bladder Pain Syndrome/Interstitial Cystitis; IUR, Idiopathic non-obstructive Urinary Retention; ICSI, Interstitial Cystitis Symptom Index (range 0–20); ICPI, Interstitial Cystitis Problem Index (range 0–16); UDI, Urogenital Distress Inventory (range 0–300); LPB, Low Back Pain; LANSS, Leeds Assessment of Neuropathic Symptoms and Signs (range 0–24); SCS, Spinal Cord Stimulation; ICIQ-SF, International Consultation on Incontinence Questionnaire – Short Form (range 0–21); FI, Fecal Incontinence; UR, Urinary retention; DI, Double incontinence; EQ-5D, EuroQoL-5D (scale 0–100); DNRS, Dorsal Nerve Root Stimulation; MEDD, Morphine Equivalent Daily Dose; GAF, Global Assessment of Functioning (range 0–100); SF-12, Short Form-12 questionnaire (range 0–100); SB, Sympathetic block; MSO₄, magnesium sulfate.

Table 2 Pancreatitis

Author	Design	Patients	Permanent Implantation	Outcome	Complications	Follow-up
L.Kapural 2011 ¹⁹	Retrospective cohort	n=30	24/30 at T4-T6	VAS scores baseline (follow-up): average 8.0 ± 1.6 versus 3.7 ± 2.0 at end of trial period ($p,0.001$), 3.6 ± 2.0 at 1 year ($p <0.001$). Opioid use baseline (follow-up): average 165 ± 120 mg MSE versus 105 ± 101 mg at end of trial period, 48.6 ± 58 mg MSE at 1 year ($p = 0.016$).	2 infection 1 lead migration	1 year (20/24)
Y.N.Khan 2005 ²⁰	Case series	n=5	5/5 T5-T6	VAS scores baseline (follow-up): 10, 7, 9, 7 and 6 versus 5, 3, 4, 3, and 2 at end of follow-up. Narcotic intake: 50%, 30%, 40%, 50%, 20% of intake at baseline.	1 lead migration	6–8 months
L.Kapural 2008 ²¹	Case report	N=1	1/1 at T5-T6	VAS scores baseline (follow-up): epigastric pain ranging 5–10 versus 1 during trial and 1 at 3 months. PDI score: score 62 at baseline, score 14 during trial period, score 15 after 3 months.	No complications	3 months
J.K. Kim 2009 ¹³	Case report	n=1	1/1 at T7-T8	VAS scores baseline (follow-up): score 10 versus 5 at 14 months. Opioid use 'reduced': baseline ~440mg MME to ~45mg (no clear data).	No complications	14 months
F.Vergani 2014 ²²	Case report	n=2	2/2 at T8-T10	VAS scores baseline (follow-up): 10 and 9 versus 2 and 1 at end of follow-up. Daily opioid intake baseline (follow-up): morphine 60mg (0 mg); methadone 75 mg (0 mg).	No complications	10 and 4 years
K.H. Lee 2015 ²³	Case report	n=1	1/1 at T5-T7	VAS scores baseline (follow-up): baseline 8–9, versus 2–3 at 6 months. Opioid use 'reduced' (no clear data).	No complications	6 months
L.Delange 2019 ²⁴	Case report	n=1	1/1 at T5 burst	VAS scores baseline (follow-up): baseline constant 7–8, with breakthrough pains at ingestion, versus 2 and "no pain attacks" at 6 months. Opioid use baseline 300mg MME, at 6 months 125mg. Satisfaction scale 1 (fully satisfied) to 5 (unsatisfied): 2.	No complications	6 months
Mamaril-Davis 2021 ²⁵	Case report	N=1	1/1 at T4-T6	VAS scores baseline (follow-up): score 8–9 at baseline. 90% relief at end of follow-up. Additionally improvement in QoL, able to return to daily life at end of follow-up.	No complications	18 months

Abbreviations: VAS, Visual Analogue Scale (scale 0–10cm); MSE, Morphine Sulfate Equivalents; PDI, Patient Disability Index (range 0–70); MME, Morphine Milligram Equivalents; QoL, Quality of Life.

Oddi dysfunction, described in a case report by Mamaril-Davis et al.²⁵ They found that pain scores, QoL, sleep and appetite improved after implantation of sacral neuromodulation (SNM), with 90% pain relief at 18 months follow-up. No complications were reported.

Patient selection for treating pancreatitis with SCS is challenging, due to the absence of large RCTs and comprehensive inclusion- and exclusion criteria. Until these criteria are more firmly established, most clinics and studies continue to use a test trial period prior to permanent implantation. The PANACEA trial (NCT03595241), is the first randomized clinical trial evaluating the effectiveness of SCS for patients with chronic pancreatitis.^{25,89} They recently reported their four-month follow-up and found significant reduced pain scores when SCS was applied, compared to conservative medical management. However, we are still awaiting their definitive results.⁹⁰

Spinal Cord Stimulation for Pelvic Pain

Anorectal Pain and Bowel Disorders, Table 3

Functional anorectal pain disorder (also known as chronic idiopathic anal pain) is a diagnosis per exclusionem. It is diagnosed only after excluding all other causes of rectal pain with a structural cause such as active ischemia, fissure, inflammatory bowel disease, infection, haemorrhoids and tumours. In the limited studies with small sample sizes that are available, drastic improvement in pain scores and patient global perceived effect (PGPE) have been demonstrated.^{28,31,32} However, complications such as infection, lead migration, and discomfort at the stimulator site are frequently observed. The authors of these limited-scale studies acknowledge that this cohort of patients, similar to numerous patients with chronic pain, is not a one-size-fits-all category. Consequently, personalized approaches for patients, such as the use of spinal cord stimulation (SCS), are required when conventional treatment has been proven ineffective.³² The different treatment options were evaluated in a network meta-analysis by Byrnes et al⁹¹ that included 27 studies on the treatment of anorectal pain, of which six studies reported on treatment with sacral neuromodulation (SNM). They concluded that intramuscular injection of triamcinolone and SNM were likely to be clinically effective, with a surface under the cumulative ranking (SUCRA) score of 0.79 and 0.74, respectively. Compared to other treatment methods, SNM showed superior efficacy in reducing pain scores. However, it should be noted that the interpretation of these findings is limited due to the inclusion of low-quality research and the large contribution of the study by Rongqing et al who included 120 patients without implantation of a permanent device.⁹² A case series by Dudding et al permanently implanted three patients for idiopathic anal pain, which was beneficial in only one of their three patients.³³

Bowel disorders such as gastroparesis, irritable bowel syndrome and faecal incontinence might benefit from SCS, as is described in case reports of patients who suffered not only from intractable abdominal pain, but also from debilitating gastrointestinal symptoms.²⁹ All symptoms resolved following initiation of SCS.^{30,34} In patients with gastroparesis who were studied prospectively⁷⁹ and retrospectively,⁸⁴ both traditional tonic and 10 kHz subthreshold stimulation was not only effective in improving pain scores but also in reducing the occurrence of nausea and vomiting.^{79,84} However, significant improvements in pain scores, nausea and vomiting occurrence were achieved when 10 kHz SCS was used as opposed to low-frequency, traditional tonic stimulation. Pain severity scores in patients stimulated at 10 kHz (n=12) decreased from 8.4±1.2 cm at baseline to 2.6±3.2 cm at the latest patient visit (p<0.001), whereas the traditional SCS group (n=11) scores reduced from 8.9±1.4 cm at baseline to 3.8±3.0 cm (p=0.001). Similarly, the number of 'nausea days' per month showed a reduction of over 50% for both study groups, although 10 Hz was significantly better (p=0.035) regarding this metric.⁸⁴

Three studies have reported on the efficacy of SCS for IBS symptoms. Compared to the baseline scores, each study reported (often significant) improvement in pain (measured using VAS, scale 0–10cm), in pain frequency, in anorectal comfort, in IBS-specific symptom scores (measured by the Gastro-intestinal Syndrome Rating Scale), and finally in IBS-specific QoL.^{26,27,29} The reported complications included infection, lead migration, pain at the implantation site or loss of device efficacy. Given the current evidence on the “brain-gut axis”,^{93,94} it is plausible to propose neurostimulation as a treatment option for severe cases of irritable bowel syndrome, which is considered a dysregulation of the central nervous system.³⁰

Table 3 Pelvic Pain I - Anorectal Pain and Bowel Disorders

Author	Design	Patients	Permanent Implantation	Outcome	Complications	Follow-up
J. Fassov 2014²⁶	Blinded crossover trial, ON/OFF	N=21	S3-S4	<i>Pain (GSRS-IBS questionnaire) baseline (follow-up):</i> median change 12 (range -22 to 44) in when neuromodulator was switched on immediately (ON/OFF) for one month, after which it was switched off for 1 month, versus -17.5 (-48 to -1) when neuromodulation was switched on after 1 month (OFF/ON) (P=0.0009). At 1 year follow-up GSRS-IBS score of 25, versus 62 at baseline (P=0.0001). <i>QoL baseline (follow-up):</i> median change 16 (range -24 to 69) in ON-OFF group, versus -42.5 (range -77 to 0) in OFF-ON group (P=0.0003). At 1 year follow up score of 52, versus score of 135 at baseline (P=0.0001).	4 pain at implant site, of which 3 persistent needing relocation 2 suspected migration 1 recurrent cystitis	1 year
G. Lind 2015²⁷	Randomised crossover pilot study, ON/OFF	N=10	T6 – T8	<i>VAS baseline (follow-up):</i> median pain 7 (range 4–8) at baseline, VAS 3 (range 2.5–7) after 6 weeks (P<0.03) when neurostimulation was switched on immediately (ON/OFF) and VAS 4 (2–6) when neuromodulation was switched on after 6 weeks (OFF/ON) (P<0.04). Significantly reduced pain intensity for ON/OFF group (P<0.03) OFF/ON group (P<0.04). Significant reduction in number of pain attacks at 15–20 week follow up and 21–26 week follow up (P<0.04).	No complications	28 weeks
E.Falletto 2009²⁸	Prospective cohort	N=24	12/24 at S2-S4	<i>VAS scores baseline (follow-up):</i> average 8.2 ± 1.7 SD versus 2.2 ± 1.3 at 1 year. <i>Opioid use:</i> no data available <i>SF-36 questionnaire improved:</i> the physical component (26.3 ± 5.7 vs 39.0 ± 9.1 p <0.02). The mental component (32.6 ± 9.2 vs 38.3 ± 9.23 p =0.24).	1 infection 1 device failure 1 pain at implant site	Median 15 months (3–80 months)
E.Duchalais 2021²⁹	Prospective cohort study	N=423	284/423 at S2-S4	<i>SNS for fecal incontinence (n=256):</i> CCIS significantly improved (14.6 vs 9.9, P<0.001). FiQoL increased average of 0.67 points (2.08 vs 2.75, p<0.001). <i>SNS for solitary rectal ulcer syndrome (n=5):</i> 5/5 pts ≥50% improvement) at 6 year follow up. <i>SNS for IBS (n=10):</i> 5/10 pts ≥50% improvement at 4.5 year follow up. <i>SNS for anterior resection syndrome (n=10):</i> 8/10 pts decrease ≥50% in LARS) at 20 month' follow up.	5 infection 2 pain at implant site 24 loss of efficacy	55 months
E.Krames 2004³⁰	Case report	N=1	1/1 at T8	<i>VAS scores baseline (follow-up):</i> score 9–10, versus 2–3 at 6 months. Regulated (disabling) gastrointestinal symptoms. <i>Daily opioid use:</i> baseline 360mg to 90mg at 6 months, increasing to 300mg.	Gradual loss of efficacy on pain	> 6 months
T.C.Dudding 2007³¹	Case report	N=1	1/1 at S3	<i>VAS scores baseline (follow-up):</i> score 10, versus 0 at 1 year. <i>Opioid use:</i> no data.	No complications	1 year

B.Govaert 2010 ³²	Case series	N=9	4/9 at S3	VAS scores baseline (follow-up): scores of 9, 9, 7, and 6 at baseline versus 0, 1, 2 and 1 at end of follow-up Opioid use: no data GPE: completely recovered (1), much improved (3).	1 infection 2 pain at implant site	2 years
T.C.Dudding 2013 ³³	Case series	N=6	3/6 at S3	Effectiveness: 2/3 reported no effect and had it removed or turned off. 1/3 experienced subsequent good pain relief at 12 months follow-up, maintained until 5 year follow-up.	1 pain at implant site 1 dislodgement after fall	5 years
M.V.Rana 2013 ³⁴	Case report	N=1	1/1 at T8	VAS scores baseline (follow-up): score 8–10, versus 3 at 1 year. Regulated gastrointestinal symptoms. Opioid use: yes, no quantitative data. IBS-Severity score: baseline 410/500, at 1 year 180/500.	No complications	1 year
B. Richter 2020 ³⁵	Case series	N=3	3/3 at T6-T8 (burstDR)	VAS scores baseline (follow-up): score 5, 9 and 9 versus 4, 0 and 0 at end of follow-up. Regulated gastrointestinal symptoms. Opioid use baseline (follow-up): 60mg (0); 22,5mg (12,5mg); 0mg (0) PGIC: 6, 7, 7.	No complications	2 year or more

Abbreviations: GSRS-IBS questionnaire: Gastrointestinal Symptom Rating Scale – Irritable Bowel Syndrome questionnaire (7-Point Likert scale); QoL, Quality of Life; VAS, Visual Analogue Scale (scale 0–10cm); SF-36 questionnaire, Short Form-36 questionnaire (range 0–100); SNS, Sacral Neurostimulation; CCIS, Cleveland Clinic Incontinence Scale (range 0–20); FIQoL, Fecal incontinence Quality of Life (scale 1–4); IBS, Irritable Bowel Syndrome; LARS, Low Anterior Resection Syndrome; GPE, Global Perceived Effect (0–10); PGIC, Patients Global Impression of Change (scale 1–7).

Table 4 Pelvic Pain II – Gynaecological

Author	Design	Patients	Permanent Implantation	Outcome	Complications	Follow-up
S. Siegel 2001 ³⁶	Prospective, non-randomised study	N=10	S3-S4	VAS baseline (follow-up): average pain score 9.7 (scale 0–10) versus 4.4 at long-term follow-up (6–74 months). VAS worst pain baseline (follow-up): score 4.7 versus 2.2 at long-term follow-up in 9/10 patients. VAS least pain baseline (follow-up): 2.4 versus 1.2 at long-term follow-up in 7/10 patients. Hours without pain per day baseline (follow-up): 3.6 hours versus 13 hours at long-term follow-up. BDI baseline (follow-up): 6/10 patients reported improved scores at long-term follow-up (19 months).	27 complications, no serious adverse events. 6 local wound infections 4 pain at implant site 1 wound infection needing explantation, later successful re-implantation.	6–74 months
J. Tate 2021 ³⁷	Prospective, single-arm pilot study	N=21	13/21 at T8-T12	VAS baseline (follow-up): score 8.1 versus 2.3cm at 12 month follow-up. Pain remission (VAS ≤ 3.0cm) was reported by 8/13 pts (62%). SF-MPQ-2 baseline (follow-up): mean total score of 4.1 versus 1.3 at 12 month follow-up. PDI baseline (follow-up): score 45.2 versus 16.2 at 12 month follow-up. Patient satisfaction: 69% of patients reported being satisfied or very satisfied with treatment at 3 month follow-up, increasing to 85% at 12 month follow-up.	No complications	12 months
J.Martellucci 2011 ³⁸	Prospective observational study	N=17	8/17 at S3-S4	VAS baseline (follow-up): 8.2 ± 0.9 pre-operatively versus 1.9 ± 1.2 at 6 month follow-up (reported by 8 pts) (p<0.0001), to 2.1 ± 1.3 at 12 month follow-up (reported by 7 pts), 2.0 ± 1.4 at 24 month follow-up (reported by 5 pts) and 1.8 ± 1.5 at 36 month follow-up (reported by 4 pts). QoL (in SF-36) baseline (follow-up): improvement in all eight domains from baseline to 6 month follow-up (P<0.05).	No complications	39 months
A.Polushkin 2019 ³⁹	Prospective cohort study Spinal Cord Stimulation: sacral or pudendal neuro-stimulation	N=32	27/32	VAS baseline (follow-up): mean score 8.61 ± 0.91 versus 3.53 ± 1.20 at 12 month follow-up. Pain medication baseline (follow-up): all patients were able to completely abandon drugs at 12 month follow up. QoL (in PQLS) baseline (follow-up): 8.59 ± 1.16 versus 5.44 ± 1.60 at 12 month follow up (P<0.05). HADS scale baseline (follow-up): 14.03 ± 3.53 versus 8.80 ± 2.60 at 12 month follow up (P<0.05).	5 electrode migration needing surgical correction, with restoration of effective neurostimulation	12 months
T.Vancaillie 2018 ⁴⁰	Retrospective cohort	N=64	52/64 at S2-S4 1 hypogastric lead	43/52 patients completed the questionnaire- VAS baseline (follow-up): mean score 8.3 versus 4.9 (95% CI: 2.60–4.27), after implantation (P < 0.001). QoL improved (35/43) Pain scores improved (32/43) Bowel function improved (15/43) Bladder function improved (10/43) Sexual function improved (10/43)	24 in total (10 removals): infection, pain at implant site, device failure, need for MRI, excess granulation tissue, allergy, gradual loss of efficacy	Not described

M.Agnello 2020⁴¹	Retrospective cohort study	N=13	9/13 at S3 SNM Interstim	VAS baseline (follow-up): mean score 7.5 versus 4.0 after SNM implant. 1/9 participants improvement of intestinal constipation, with regularization of defecatory habits. 1/9 participants almost total resolution of anal and pelvic pain (VAS 8 at baseline versus VAS 2 after SNM implant).	No complications	Not mentioned
A.Zegrea 2020⁴²	Retrospective cohort	N=51	28/51 at S3-S4	VAS baseline (follow-up): median score 7.4 versus median score 2.2 during test trial. No data on long term follow-up. Opioid use: no data available Specifically good results for endometriosis (12/14).	1 infection 1 broken lead 1 lead migration device failure pain of the device	0.3–98.9 months
D.Abejón 2010⁴³	Observational study	N=20	S3	VAS baseline (follow-up): pain relief $73.57 \pm 13.7\%$ after the test period. Pain relief between 61.4% and 77.5%; pain area coverage 90%. SNS pain relief on scale 0–10, baseline (follow-up): average 8.6 ± 0.8 versus 3.8 ± 1.1 after test period ($P=0.03$). Satisfaction: 75% of participants 3–4 grade satisfaction at 3 and 4 month follow up, 83% of participants maintained this satisfaction at 6 month follow-up.	No complications	6 months
C. Hunter 2013⁴⁴	Case series	N=5	4/5 at T7-T8	VAS baseline (follow-up): unknown, >50% reduction, >50% reduction, 5 (1). Opioid use baseline (follow-up): unknown, decreased, 5mg (2,5mg), decreased. Decreased chronic headaches	Lead migration	3–10 months
P. Sokal 2015⁴⁵	Case series	N=9	Th12-L1 and S2-S4	VAS baseline (follow-up): median score 9 versus score 2 after implantation ($P=0.001$). Score 3 at 6 month follow-up ($P=0.043$). Score 6 at 12 month follow up. Use of analgesics: 8/9 patients reduced analgesics.	3 infections 2 migration of electrodes	12 months
C. Hunter 2019⁴⁶	Case series	N=7	4/7 L1-S2 DRGS	VAS baseline (follow-up): 9, 9, 6 and 4 versus 2, 0, 2, 1 at end of follow-up. Opioid use baseline (follow-up): no exact data Improved sleep	No complications	1 year or more
J.M.Tiede 2006⁴⁷	Case report	N=2	2/2 at T2	VAS baseline (follow-up): score 10 and 10 versus 2 and 2–3 at end of follow-up. Opioid use baseline (follow-up): no dosage known and 240mg versus no opioid use and 160mg at end of follow-up.	1 lead migration	> 3 months

(Continued)

Table 4 (Continued).

Author	Design	Patients	Permanent Implantation	Outcome	Complications	Follow-up
M.Lavonius 2017 ⁴⁸	Case report	N=4	3/4 at S3-S4	<i>Abdominal or pelvic pain:</i> score 3 to 4 at 6 month follow-up, score 4 to 5 at 2.5 years follow-up. <i>Dyspareunia:</i> score 4 at 6 month follow-up, score 3 to 4 at 2.5 years follow-up. <i>Dyschezia:</i> score 4 to 5 at 6 month follow-up, score 4 at 2.5 years follow-up. <i>Constipation:</i> score 4 to 5 at 6 month follow-up, score 3 to 5 at 2.5 years follow-up. <i>Anal incontinence:</i> score 4 to 5 at 6 month follow-up, score 3 to 4 at 2.5 years follow-up. <i>Dysuria:</i> score 4 at 6 month follow-up, score 5 at 2.5 years follow-up. <i>Voiding dysfunction:</i> score 4 6 month follow-up, score 2 at 2.5 years follow-up. <i>Urinary dysfunction:</i> score 4 at 6 month follow-up, score 2 to 4 at 2.5 years follow-up. Satisfaction NRS between 8 and 9 at 6 month follow-up, NRS between 8 and 10 at 2.5 years follow up. <i>1: worse; 2: no change; 3: somewhat improved; 4 much improved; 5: excellent improvement</i>	No complications	2.5 years
E.Samaniego 2020 ⁴⁹	Case report	N=2	2/2 at S2	<i>NRS pelvic pain baseline (follow-up):</i> score 10/10 versus 2/10 at 18 month follow up in first case. Score of 10/10 versus 2/10 at 10 month follow up in second case. <i>QoL (in SF-36) baseline (follow-up):</i> improvement in QoL scores in both cases. <i>ODI score baseline (follow-up):</i> score 52 versus 26 at 18 month follow up in the first case. Score 52 versus 26 at 18 month follow up in the second case. <i>Pain medication baseline (follow-up):</i> Ketorolac 10mg 4x per day, acetaminophen 1gr 3x per day, diazepam 10mg a.n., amitriptyline 50 mg a. n., gabapentin 1800mg daily, tramadol 600mg daily at baseline versus acetaminophen 1gr daily at 18 month follow up in first case. Celecoxib 200mg twice per day, acetaminophen 1gr 3x per day, Duloxetine 120mg daily, pregabalin 300mg twice per day, Clonazepam 1mg a.n.	No complications	18 months

Abbreviations: VAS, Visual Analogue Score (scale 0–10cm); BDI, Beck Depression Inventory (range 0–63); SF-MPQ-2, mean short-form McGill Pain Questionnaire 2 (range 0–78); PDI, Patient Disability Index (range 0–70); QoL, Quality of Life; SF-36 questionnaire, Short Form-36 questionnaire (range 0–100); PQLS, Patient Quality of Life Card questionnaire (range unknown); HADS, Hospital Anxiety and Depression Scale (range 0–21); SNS, Sacral Nerve Modulation; SNS, Simple Numeric Scale (scale 0–10); DRGS, Dorsal Root Ganglion Stimulation; NRS, Numeric Rating Scale (scale 0–10); ODI, Oswestry Disability Index Score (range 0–100).

Gynaecological, Table 4

Chronic Pelvic Pain (CPP) shares a similarity with the above-mentioned pain syndromes, as it is a diagnosis per exclusionem. Nonetheless, the condition is debilitating. Endometriosis is no diagnosis per exclusionem and is, apart from CPP, additionally associated with symptoms of dysmenorrhea, dyspareunia, dysuria and dyschezia. Because of their experienced pain, patients may undergo a hysterectomy or otherwise invasive surgery, which could be ineffective in removing all pain or might even result in an aggravation of pain.⁹⁵ CPP is a multifactorial condition that affects psychological, psychosocial, cultural, and economic factors. Furthermore, the pelvic region has a complex innervation and chronic pelvic pain may arise due to central sensitization. This condition is marked by the recurrent or extended stimulation of nociceptors, leading to a decreased threshold for activation. As a result, patients may experience pain even when there is no pain substrate,⁹⁶ thereby presenting a significant challenge in terms of treatment.⁹⁷ SCS can be effective in selected patients as it is minimal invasive, making it a viable option to consider before proceeding with a more permanent surgical or neurolytic procedure.^{44,46} After implantation of SCS, patients reported an improvement in QoL, pain severity scores, Pain Disability Index (PDI) scores, Beck Depression Inventory (BDI) scores, and functional symptoms. In addition, patients exhibited a high level of satisfaction, with some even expressing a profound level of contentment, in response to SCS treatment.^{36,38,40,45}

Also of note in this patient cohort there was a high incidence of complications. Some patients underwent explantation of the device due to infection, local pain, device failure, lead migration, a broken lead, excess granulation tissue, the need for an MRI for non-MRI compatible devices, allergy, and gradual loss of effect in the older wave form units. A Finnish national study confirmed this, where they found similar adverse events despite overall positive results. In their study, they determined that women with SCS for CPP related to endometriosis reported superior success rates compared to women with SCS for idiopathic CPP (75% vs 41% resp., $P=0.026$), with a high percentage of advancement to permanent implantation and strong symptom improvement following implantation. However, the IPG was removed in six of 50 participants (12%) due to loss of efficacy (4/6), pain (1/6) or infection (1/6).⁴² As was already stated in the Cochrane review in 2000:

Given the prevalence and the health care costs associated with chronic pelvic pain in women, randomised controlled trials of other medical, surgical and psychological interventions are urgently required.⁹⁸

Unfortunately, these are currently lacking in the literature.

Five previous studies determined that Sacral Nerve Stimulation (SNS), SCS and/or Peripheral Nerve Stimulation (PNS) were effective in reducing endometriosis-related pain symptoms such as CPP and dyspareunia, anal pain, and intestinal constipation. They also found high patient satisfaction, an improvement of QoL, a reduction in the use of pain medication, an improvement in Oswestry Disability Index (ODI) scores, Hospital Anxiety and Depression Scale (HADS) scores. Finally, they found improvements in social participation where women were able to work again, take part in social activities and travel.^{39,41,43,48,49} The complication most frequently reported was electrode migration. At present, there are three trials recruiting (in France, the Netherlands (NCT05558540) and Turkey) participants that are treated with SCS and suffer either from pelvic pain related to endometriosis or are suffering from CPP in general.

Urological Disorders, Table 5

Despite the number of studies being limited, most prospective studies on SCS for pelvic pain focus on urological disorders and universally conclude that well-selected patients respond favourably to SCS with improved pain severity scores, reduced CPP and improved voiding symptoms.^{52–56,58,60,61,66,69,71,99,100} Their results seem sustainable in the absence of complications, which is substantiated by studies with longer follow-up periods.^{62,64,66} Further, when comparing it to a control group with similar disease presentation, SCS improves pain severity scores and overall outcomes.⁷⁰ However, an older study by Elhilali et al demonstrated that not all functional urological problems are successfully treated with SNM and treatment can lose its efficacy over time.⁵⁹ However, this study was published in 2005, at a time when advanced wave forms were unavailable, so application to current clinical realities is questionable. Complication rates vary between studies, with revision rates being as high as 50%. These were primarily attributed to loss of efficacy, local pain at the implant site, painful stimulation, and the necessity for battery revisions. In some studies,

Table 5 Pelvic Pain III – Urological Disorders

Author	Design	Patients	Permanent Implantation	Outcome	Complications	Follow-up
K.Everaert 2004 ⁵⁰	RCT 1 stage 2 stage	N=114	42/114 at S3	Failures more frequent in 1-stage versus 2-stage group (7 versus 3, P=0.02).	23 revisions (17 failure; 2 repositioning leads; 4 pain) 3 infection 4 pain of the device 2 pain of stimulation 6 explants (3 failure; 3 infection)	24 months
K.M.Peters 2007 ⁵¹	Randomised crossover trial	N=22	13/17 PNS 4/17 SNS	VAS baseline (follow-up): score 4.5 versus 3.2 at end of follow-up for PNS. Score 7.9 versus 4.0 at end of follow-up for SNS. Symptom reduction baseline (follow-up): 59% for PNS and 44% for SNS (P=0.05). Voiding symptoms baseline (follow-up): 41% improved for PNS and 33% for SNS. Mean voided volume baseline (follow-up): increased by 95% for PNS and 21% for SNS.	2 seroma formation	6 months
C.F.Maher 2001 ⁵²	Prospective cohort	N=15	11/15 at S3	VAS baseline (follow-up): mean score 8.9 versus 2.4 after test period. No data on long term follow-up. Voiding symptoms: improved SF-36: improvement on social functioning, bodily pain, general health. Opioid use: no data available	No complications	No data
S.Aboseif 2002 ⁵³	Prospective observational study	N=64	S3	Group 1 (frequency-, urgency- or urge incontinence, n=43): 33/43 pts (77%) >50% improvement in QoL and would recommend this therapy. Group 2 (idiopathic, non-obstructive chronic urinary retention, n=20): 18/20 pts (90%) >50% improvement in QoL and would recommend this therapy. Able to void spontaneously without catheterization. Group 3 (chronic pelvic pain, n=41): decrease in VAS; 5.8 pre-operative to 3.7 post-operative (P>0.05).	12 complications. Seroma formation at site of IPG; resolved spontaneously. 2 superficial wound infections treated with antibiotics. 1 deep infection needing IPG removal. 2 migration sacral wires needing revision 2 device malfunction needing revision	24 months

C.V. Comiter 2003 ⁵⁴	Prospective cohort	N=25	17/25 at S3	VAS baseline (follow-up): median score 5.8 versus 1.6 after implantation. No data on long term follow-up. Voiding symptoms: improved Opioid use: no data available Quadripolar lead more efficacious than unipolar.	No complications	2–28 months
K.M.Peters 2003 ⁵⁵	Prospective cohort	N=26	26/26 at sacral level	Moderate or marked improvement: Pelvic pain (71%) Pelvic pressure (67%) Quality of life (76%) Vaginal pain (60%)	3 revisions	
K.E. Whitmore 2003 ⁵⁶	Prospective cohort	N=33	23/33 positive test trial at sacral level	Test trial 23/33 positive (>50% pain reduction).	No complications	No data on permanent implantation
K.M.Peters 2015 ⁵⁷	Prospective cohort	N=13	13/13 at sacral level n=7 follow-up	CXCL-1 peptide and sIL-1 receptor antagonist positively associated with ICSP1 ($r = 0.43$, $P = 0.09$; $r = 0.50$, $P = 0.04$) and pain events ($r = 0.63$, $P = 0.009$; $r = 0.50$, $P = 0.04$). At 24 weeks SNM follow-up reduction in chemokines (MCP-1, sIL-1RA, and CCL5) and improvement ICSP1.	No data	24 weeks
K.M.Peters 2004 ⁵⁸	Retrospective cohort	N=21	21/21 at S3	General analgesic drug use: 4/21 stopped using Daily opioid use: baseline 82mg (follow-up 52mg) Pain score: 20/21 moderate or marked improvement.	No data	7.4–23.1 months
M. Elhilali 2005 ⁵⁹	Retrospective cohort	N=52	41/52 at S2-S4	In group of urgency/frequency: 17/22 pts long term use of IPG: 10 pts (45%) improvement in symptoms; 7 pts no improvement (32%). In group of urge incontinence: 1/6 pts reported improvement in frequency of incontinence episodes; 1 pt reported no improvement. In chronic retention group: 7/9 pts improvement in symptoms (78%). 1 pt chronic intermittent catheterization. Interstitial cystitis: 2/2 pts no improvement Pelvic pain: 1/2 reported improvement, the other one stopped using it.	Urgency/frequency: 2 pts removal of implant, 3 pts stopped using it. Urge incontinence: 3 pts (50%) removal; 1 pt stopped using it. Chronic retention: 1 pt stopped using it. Pelvic pain: 1 pt stopped using it.	Up to 13 years

(Continued)

Table 5 (Continued).

Author	Design	Patients	Permanent Implantation	Outcome	Complications	Follow-up
T. Kessler 2006⁶⁰	Retrospective observational study	N=209	91/209 at S2-S4 84 lower urinary tract dysfunction, 7 CPP syndrome	<p>Success rate: sacral neuromodulation was successful in 64/91 IPG implants (70%)</p> <p>Leakages/24 hours baseline (follow up): (A) 5 (2–10), 1st follow up (B) 0 (0–2), last follow up (C) 0 (0–2) when urge incontinence. A vs B $P<0.0001$. A vs C $P<0.0001$.</p> <p>Number of voids per day baseline (follow up): (A) 10 (5–13), 1st follow up (B) 6 (4–7), last follow up (C) 6 (4–8) when urge incontinence. A vs B $P<0.0001$. A vs C $P<0.0005$. (A) 3 (0–6), 1st follow up (B) 6 (6–9), last follow up (C) 5 (5–6) when non-obstructive chronic urinary retention. A vs B $P=0.25$. A vs C $P=0.23$.</p> <p>VAS*¹ baseline (follow up) when neuromodulation for CPP syndrome: (A) 8 (8–9), 1st follow up (B) 0 (0–1), last follow up (C) 2 (1–4). A vs B $p=0.03$; A vs C $p=0.03$.</p> <p>Symptom improvement baseline (follow up) when neuromodulation for CPP syndrome: B 100% (100–100%), C 65% (45–90%).</p>	<p>10/91 adverse events. 6/91 needed revision because of:</p> <ul style="list-style-type: none"> 2 lead migrations 1 infection 1 broken lead needing revision 1 IPG migration 1 IPG malfunction after MRI. 	10–24 months
K.M.Peters 2008⁶¹	Retrospective cohort	N=87 n=16 chronic pain	No data	No data on the subgroup	No data	No data
J.B. Gajewski 2010⁶²	Retrospective cohort	N=78	46/78 at sacral level	<p>Long term success implanted patients: 33/46 (72%) GRA scale (very good 70%, good 30%).</p> <p>Overall success rate 33/78 (43%).</p>	<p>13 removal:</p> <ul style="list-style-type: none"> treatment failure painful stimulation <p>23 revisions:</p> <ul style="list-style-type: none"> loss of efficacy local pain of the device painful stimulation battery replacement 	Median 61.5 months (33.8–89.2 months)

C. Powell 2010 ⁶³	Retrospective cohort	N=39	22/39 at S3	<i>Symptom reduction:</i> 11/17 (64.7%) no more dysuria or pelvic pain. <i>Success rate:</i> 17/22 (77%) reported improvement >50%. <i>Analgesics use:</i> 6/13 (46.2%) dependent on amitriptyline stopped it completely, 54.5% (6/11) stopped hydroxyzine completely, 60.0% (9/15) stopped pentosane polysulfate completely, 60.0% (6/10) no longer needed DMSO, 20% (2/10) no longer needed narcotics.	9 replacements: 4 depleted batteries 1 loss of efficacy 1 infection 1 device malfunction 1 troublesome foot movement 1 device destruction after cardioversion	60 months
Y.Q. Ghazwani 2011 ⁶⁴	Retrospective cohort	N=21	11/21 at S3	<i>VAS baseline (follow-up) in bladder pain:</i> score 8.09 (1.1) versus 1.5 at 1 year follow up ($P<0.001$). <i>Reduction in urgency baseline (follow-up):</i> 2.6 ± 0.6 versus 1.2 ± 0.7 at 1 year follow-up. <i>Reduction in day time frequency baseline (follow-up):</i> 12.8 ± 5 versus 6.1 ± 2.1 at 1 year follow-up. <i>Reduction in nycturia:</i> 6.5 ± 2.1 versus 3.8 ± 1.5 at 1 year follow-up. Improvements remained at last visit (± 5 years)	2 battery replacement 2 re-implantation of the device due to local pain	5 years
R.K.Leong 2011 ⁶⁵	Retrospective cohort questionnaire	N=207	Unknown	90% satisfaction Higher satisfaction: patient adjustability of the stimulation ($p<0.001$), patient still working ($p<0.001$) Less satisfaction with multiple pelvic floor comorbidities ($p=0.003$).	Decreased efficacy, battery replacements, need for MRI, local pain of the device, trouble with metal detectors	Not mentioned
S.P. Marinkovic 2011 ⁶⁶	Retrospective cohort	N=34	30/34 at sacral level	Mean pre-op/post-op pelvic pain and urgency/frequency scores: 21.61 ± 8.6 vs 9.22 ± 6.6 ($p<0.01$). VAS baseline (follow-up): mean score 6.5 ± 2.9 versus 2.4 ± 1.1 at end of follow-up ($p<0.01$).	5 lead migration 3 device erosions (after accidents)	6 years or more
M.H. Vaarala 2011 ⁶⁷	Retrospective cohort	N=180	74/180 n=7 PBS ¹²	Urinated volume (mL) baseline 141, follow-up 192 ($P=0.002$). Number of urinations baseline 13.1, follow-up 8.4 ($P<0.001$). Number of daily catheterization baseline 3.3, follow-up 0.2 ($P<0.001$). Younger patients with urinary retention are more likely to undergo permanent implantation (implanted 45 years vs tested 53 years) No results on subgroup with PBS.	15 revisions: loss of response, local pain of the device, device failure, infection	mean 41 months (0–143 months)

(Continued)

Table 5 (Continued).

Author	Design	Patients	Permanent Implantation	Outcome	Complications	Follow-up
B. Kaaki 2020⁶⁸	Retrospective cohort	N=66	55/66 at S2-S4	<i>Symptom improvement:</i> 40/55 (72.7%) pts experienced improvement of bladder symptoms from their own perspective. <i>Success rate:</i> SNS successful in 41/55 (74.5%) at 32 month follow-up.	3 pain 2 lead migration 1 IPG migration 1 infection 1 device malfunction 5 end of battery life (all replaced) 15 explants (5 decreased efficacy, 4 MRI, 3 pain, 2 end of life battery, 1 infection)	Median 24 months
A. Coguplugil 2021⁶⁹	Retrospective cohort	N=24	16/24 at sacral level	<i>Success rate:</i> Overall success rate for all indications was 87.5% after a mean follow-up of 42.3 months (100% for OAB, 100% for BPS/IC and 66.7% for IUR).	3 device failure 1 pain	Mean 42 months
G. Liu 2022⁷⁰	Prospective cohort	N=40 Control n=20 Intervention n=20	15/20 at sacral level	<i>VAS score baseline (follow-up):</i> score 8.8 ± 1.3 versus 4.5 ± 0.7 at 12 month follow-up. <i>QoL baseline (follow-up):</i> score 4.4 ± 0.7 versus 2.3 ± 0.4 at 12 month follow-up. <i>O'Leary-sant score baseline (follow-up):</i> 31.4 ± 5.8 versus 16.3 ± 3.0 at end 12 month follow-up. All $P < 0.05$.	No complications	12 months
N. Moufarrij 2022⁷¹	Case Report	N=1	1/1 at T8-T10	<i>Symptom improvement:</i> at 6 month follow-up no low back pain, sciatica or interstitial cystitis pain, urinary urgency and frequency from interstitial cystitis. <i>Satisfaction score:</i> at 6 month follow-up score 10/10.	No complication	6 months

Abbreviations: VAS, Visual Analogue Scale (scale 0–10cm); PNS, Peripheral Neurostimulation; SNS, Sacral Neurostimulation; SF-36 questionnaire, Short Form-36 questionnaire (range 0–100); QoL, Quality of Life; IPG, Internal Pulse Generator; ICSP, Interstitial Cystitis Symptom Problem Index (range 0–20); SNM, Sacral Nerve Modulation; CPP, Chronic Pelvic Pain; GRA, Global Response Assessment (scale 0–3); DMSO, Dimethylsulfoxide; PBS, Painful Bladder Syndrome; OAB, Overactive Bladder; BPS/IC, Bladder Pain Syndrome/Interstitial Cystitis; IUR, Idiopathic non-obstructive Urinary Retention.

the explant rate was as high as 27% and seems to be attributed to a more practical concern, namely the need for an MRI.⁶⁸ This challenge was not exclusive to SCS for urological disorders, but rather a recurring issue encountered in the context of any implanted device.¹⁰¹ However, the significance of this matter has diminished in light of the recent emergence of MRI-compatible technologies. Even though reported revision rates were relatively high, SNM should be considered prior to proceeding with any invasive surgical intervention.^{62,102}

Aiming to optimize SCS treatment, Everaert et al studied the 1-stage versus 2-stage SNS for bladder dysfunction where a lower rate of treatment failure was demonstrated in the 2-stage implant. Moreover, the trial procedure has been subject to innovation. According to Powell et al (2010) a greater number of patients have a successful trial with quadripolar lead placement compared to a single test lead. However, the benefit of long-term treatment was equal in both groups.^{50,63} In their study, Peters et al compared pudendal nerve stimulation to sacral neuromodulation and calculated that 77% of patients (13/17) chose pudendal nerve stimulation following blinded testing. Nevertheless, irrespective of the patients' preferences, long-term outcomes were comparable in both cohorts.⁵¹ A noteworthy observation is the association between higher pain scores, the Interstitial Cystitis Symptom Problem Index (ICSPI) scores and the levels of urine chemokines.⁵⁷ Follow-up after device implantation demonstrated a decrease in ICSPI with a concomitant decrease in urine chemokines, which implies a role of chemokines in neurophysiological signalling in bladder pain and -function.¹⁰³

A large retrospective cohort study examined the Finnish experience and collected data since the initiation of SCS in Finland in 1996. This study included the application of SCS for three diagnoses: urgency-frequency syndrome, urinary retention, and painful bladder syndrome/ interstitial cystitis (PBS/IC).⁶⁷ Although over 50% of their patients did not receive permanent implantation (74/180), all three groups experienced benefit from SCS with improvement in voiding symptoms, a reduction in the number of catheterizations and in pain severity. The results of the study furthermore suggested that younger patients are more likely to benefit from SCS. For some indications, alternative treatments may be more cost-efficient as financial costs of SCS are significant. However, research comparing health care utilization and cost-effectiveness associated with SCS to other therapies is strongly needed to understand relevant economic issues. For example, Botulinum A toxin is a more cost-effective alternative to SCS for patients with urge incontinence and should therefore be tried first.^{67,104}

Patients implanted with SCS reported a high rate of satisfaction (90%), despite the limitations and complications of the treatment. Satisfaction with SCS was positively correlated with the ability that the patient could personally adjust the device and whether the patient was still active and/or working. The presence of two or more pelvic floor comorbidities was negatively correlated with the patients' satisfaction with SCS.⁶⁵ Also, given that chronic pain and mental health are often intertwined, most medical institutions that implement SCS have established a close collaboration with the psychologic or psychiatric departments. For some, the coexistence of pain and depression is considered a contra-indication for implantation of a neuromodulator. Nevertheless, the use of SCS has shown potential in improving depression scores,^{71,105} raising a complex question regarding causality. Additionally, Killinger et al demonstrated that patients who manifested major depressive symptoms (PHQ-8 scores ≥ 10) did not display an inferior response to SCS.¹⁰⁶

Various Causes of Pelvic Pain, Table 6

Not all studies make a distinction between different causes of CPP. These studies include various patient cohorts, predominantly those who present cohorts with combined surgical, gynaecological and urological symptoms. Their results were similar to those mentioned in the previous sections: SCS resulted in reduced pain and improved functional symptoms. Patients with chronic pelvic pain following hysterectomy and those with only one pelvic comorbidity reported better results compared to other, or multiple pelvic comorbidities.^{73,107} One case report suggests that SCS may be effective in reducing CPP secondary to multiple Tarlov Cysts, which were previously worsened by surgical treatment as well as in reducing the use of analgesics.¹⁰⁸ Another case report suggested that SCS may be effective in reducing CPP secondary to multiple pelvic fractures.⁷⁷ Various pelvic disorders were combined in the study by Hernandez-Hernandez et al who demonstrated substantial improvements in pain severity scores, functional symptoms and QoL. However, complication rates were as high as 40.6%, which resulted in 5/64 patients undergoing device explantation.⁷⁵ This is relatively low compared to the study by Al-Kaisy et al, which identified explant rates of SNM devices of 17.8% after five years and of 25.2% after ten years, where explantation was performed because of various indications.¹⁰⁹ An attempt to

Table 6 Pelvic Pain III–Various Causes

Author	Design	Patients	Permanent Implantation	Outcome	Complications	Follow-up
J.L. Tate 2021 ³⁷	Prospective pilot study	n=21	13/21 at T8-T12 high frequency	VAS baseline (follow-up): score 8.2 versus 2.3 at the end of follow-up. SF-MPQ-2 (follow-up): total score of 4.1 versus 1.6 at 3 months and 1.3 at end of follow-up. PDI score baseline (follow-up): score of 45.2 versus 18.3 at 3 months follow-up and 16.2 at end of follow-up. Patient satisfaction: at 3 months follow-up 69% of participants were satisfied or very satisfied, increasing to 85% at the end of follow-up.	Device dislocation pain at site of the device light headedness infection	1 year
J.Martellucci 2012 ³⁸	Prospective cohort	n=27	16/27 at sacral level (SNM), S3-S4	VAS baseline (follow-up): score 8.2 ± 0.9 versus 1.9 ± 1.2 at 6 month follow up (P<0.0001), 2.1 ± 1.3 at 12 months follow-up, 2.0 ± 1.4 at 24 months follow-up and 1.8 ± 1.5 at 36 month follow-up. QoL baseline (follow-up): improvement in all eight domains from baseline to 6 months follow-up (P<0.05).	No complications	12–71 months
N. Zabihi 2008 ⁷²	Prospective cohort	n=30	23/30 at S2-S4 (bilateral SNM ⁴)	VAS baseline (follow-up): improvement of 40% at end of follow-up. P=0.04. ICSI score baseline (follow-up): improvement of 35% at end of follow-up. P=0.005. ICPI score baseline (follow-up): improvement of 38% at end of follow-up. P=0.007. UDI score baseline (follow-up): improvement of 26% at end of follow-up. P=0.05.	5 explants: 4 device failure 1 infection 4 revisions: 3 infection 1 device failure	6–15 months
D. Guner 2022 ⁷³	Retrospective study	N=23	T9-T10 for LBP, T10-T11 for leg pain	VAS baseline (follow-up): 9 (8–10) versus 4 (4–6) at 3 month follow up and 3 (2–4) at 6 month follow-up (P<0.001). LANSS baseline (follow-up): median scores 19 (16–24) versus 16 (11–19) at 3 month follow-up and 11 (9–14) at 6 month follow-up (P<0.001). QoL (in SF-36) baseline (follow-up): mean value of 25 versus 62.5 at 3 month follow-up and 62.5 at 6 month follow-up (P<0.001). ODI score when receiving thoracic SCS baseline (follow-up): score of 76 (72–82) at baseline versus 32 (30–40) at 3 month follow-up and 30 (26–32) at 6 month follow-up (P<0.001).	No complications	6 months
C.Bridger 2021 ⁷⁴	Retrospective cohort	N=153	11/153 (various modalities)	NRS baseline (follow-up): score of 6.63 (±0.45) versus score of 4.91 (±0.93) at end of follow up. P=0.11.	No data	1–7 years

D.Hernandez-Hernandez 2021 ⁷⁵	Retrospective observational study	N=106	64/106	<p><i>Neuromodulation for OAB:</i> GRA between 50% and 75%. Significant reduction in ICIQ-SF questionnaire (mean 15.69±4.79 pre-SNS vs 2.69 ±3.01 post-SNS).</p> <p><i>Neuromodulation for BPS/IC:</i> GRA between 50% and 75%. 16.6% reported complete resolution of symptoms. Significant reduction in NRS (−5.85 points, P<0.0001).</p> <p><i>Neuromodulation for FI:</i> improvement between 50% and 75%. 14.3% reported complete resolution of symptoms.</p> <p><i>Neuromodulation for UR:</i> mean number of catheterizations per day from 4.45 (±1.98) at baseline, versus 1.97 (±2.40) after implantation.</p> <p><i>Neuromodulation for DI:</i> significant reduction in average pad use with mean 5 (±2.71) at baseline versus 1.71 (±0.76) after implantation. Significant reduction in ICIQ-SF scores with mean 15.50 (±2.12) at baseline versus 1.50 (±2.21) after implantation.</p>	<p>40.63% reported complications.</p> <p>25 pain at implantation site</p> <p>5 loss of efficacy</p> <p>1 local infection needing explantation</p> <p>Overall explantation rate of 9.4% because of loss of efficacy (5/6) and need for repeat MRI (1/6)</p>	14–220 months
T.Simopoulos 2018 ⁷⁶	Case series	N=3	3/3 at T8-T9 high frequency	<p><i>VAS baseline (follow-up):</i> CASE 1 average pain score 8.2 versus score of 4.0 at end of follow-up.</p> <p>CASE 2 average pain score 8.3 versus score of 3.3 at end of follow-up.</p> <p>CASE 3 average pain score 7.5 versus score of 4.1 at end of follow-up.</p> <p><i>Analgesics use baseline (follow-up):</i> CASE 2 morphine 60mg twice daily, oxymorphone 15mg 4 times a day at baseline versus no more morphine and reduction oxymorphone 3 times daily at end of follow-up.</p>	No complications	
E.Romero-Serrano 2021 ⁷⁷	Case report	N=1	T8 and T9	<p><i>VAS baseline (follow-up):</i> score 7, increasing to 10 in movement versus score 3 at 18 month follow-up.</p> <p><i>Analgesics use baseline (follow-up):</i> NSAID (celecoxib 600mg/day), Fluoxetine 30mg/day, gabapentin 1800mg/day, morphine 90mg/day at baseline. At 18 month follow-up several medications had been weaned off.</p> <p><i>EQ-5D baseline (follow-up):</i> −0.0757, meaning worse than death at baseline, versus +0.6454 at 18 month follow-up.</p>	No complications	18 months

Abbreviations: VAS, Visual Analogue Scale (scale 0–10cm); SF-MPQ-2, Short-form McGill Pain Questionnaire 2 (range 0–78); PDI, Patient Disability Index (range 0–70); SNM, Sacral Neuromodulation; QoL, Quality of Life; ICSI, Interstitial Cystitis Symptom Index (range 0–20); ICPI, Interstitial Cystitis Problem Index (range 0–16); UDI, Urogenital Distress Inventory (range 0–300); LANSS, Leeds Assessment of Neuropathic Symptoms and Signs (range 0–24); SF-36 questionnaire, Short Form-36 questionnaire (range 0–100); ODI, Oswestry Disability Index Score (range 0–100); SCS, Spinal Cord Stimulation; NRS, Numeric Rating Scale (scale 0–10); OAB, Overactive Bladder; ICIQ-SF, International Consultation on Incontinence Questionnaire – Short Form (range 0–21); SNS, Spinal Neurostimulation; BPS/IC, Bladder Pain Syndrome/Interstitial Cystitis; GRA, Global Response Assessment (scale 0–3); FI, Fecal Incontinence; UR, Urinary retention; DI, Double incontinence; EQ-5D, EuroQoL-5D (scale 0–100).

develop a management algorithm for patients with CPP was published by Bridger et al in 2021.⁷⁴ Over the course of seven years, 233 patients with CPP were referred, 153 were included in the protocol, and only eleven underwent SCS. These patients experienced neuropathic pain, penile pain, painful bladder syndrome, small fibre neuropathy, and neuralgia. The authors intended to compare the SCS group to the non-SCS group, but patient numbers were too small to allow a comparison. Nevertheless, it appeared that SCS was more effective in treating neuropathic pain compared to other treatment options.⁷⁴

A pilot study across multiple etiologies for chronic pelvic pain (predominantly post-surgical CPP, post-partum CPP, and interstitial cystitis) reported effective use of high frequency SCS³⁷ for patients with CPP, with 10/14 (71%) patients who received a permanent implant reporting $\geq 50\%$ pain relief at twelve months. This high-frequency 10-kHz therapy is paraesthesia-free, although it requires dedication to uncover the optimal programming. In addition, there frequently is a delay in analgesic onset (12–48 hours or longer), which is distinctly different from low-frequency therapy.^{76,110} In their study, Kapural et al studied the efficacy of high-frequency therapy in providing pain relief and compared it to low-frequency spinal cord stimulation (SCS). Their findings indicated that high-frequency therapy may be more successful than low-frequency SCS in alleviating pain, not only in patients with chronic back and/or leg pain, but also in those experiencing chronic abdomen pain. In the examined patient cohort no paraesthesia was reported.^{79,111–114} Although high-frequency therapy is not universally implemented in all European countries, it is implemented in the Netherlands. A study from the Netherlands concluded that the use of bilateral stimulation over multiple levels could be more effective because chronic pain can result in recruitment and upregulation of additional fibers.⁷²

Visceral Pain in General, Table 7

In some studies, SCS for visceral pain in general was the terminus a quo, thereby including a wide range of underlying conditions. These conditions included postsurgical pain, post-childbirth, interstitial cystitis, pancreatitis, inflammatory bowel disease, endometriosis, renal calculi, liver pathology, trauma, pudendal neuralgia and post infection chronic pain. Overall, all studies reported improved pain severity scores and PDI, decreased analgesia consumption and improvement in PGIC, QoL, SF-MPQ-2 scores, GAF scores, daily activities and mood.^{35,47,78–80,83–86} The initial prospective SCS study for chronic and refractory abdominal pain that received IDE approval from the FDA was performed by Kapural et al and used a 10 kHz SCS. The authors documented an improvement in pain severity scores (in VAS, scale 0–10cm) of 6cm from baseline, a reduction in PDI and opioid usage and finally a profound improvement in patient satisfaction twelve months after implantation.⁷⁹ Despite these excellent prospects of SCS, no standard approach to chronic abdominal pain is currently governed.¹⁶ Both ventral and dorsal horn implantation were effectively applied. However, ventral stimulation was preferred by four patients with dual leads and was lower for ventral stimulation. This was likely due to the cerebrospinal thickness in the dorsal and ventral space.⁸³ However, recent studies did not confirm this finding. For dorsal column stimulation, a “sweet spot” for treatment of visceral pelvic pain is suggested at the level of T12 due to the segmental suppression of sympathetic outflow to the pelvis via the hypogastric plexus.⁸⁵ Kapural et al also observed that the efficacy of sympathetic nerve blocks may serve as a potential indicator for the success of SCS. Six patients who failed the trial period and one patient who had the device removed because of ineffectiveness shared a poor response to the preceding sympathetic nerve block.⁸⁵ This was supported by the study by Hord et al who treated CRPS with SCS. They found that twelve patients with a positive sympathetic nerve block experienced strong and long-lasting pain relief, whereas only one (33.3%) out of three patients with a negative response to the nerve block reported substantial pain relief.⁸¹ Therefore, caution is advised when implanting patients subsequent to a failed sympathetic nerve block.

There is a potential oversight of patients with visceral pain in our narrative review, since certain cases may be obscured within studies encompassing diverse patient cohorts. Individual patients are often lost in a large group, as no details are provided per subgroup. For example, the series by Kumar et al reported on 410 patients treated with SCS for various underlying chronic pain conditions. Over 200 patients were treated with SCS for Persistent Spinal Pain Syndrome (PSPS) Type 2 in addition to six patients with perirectal pain. Of these patients, four ultimately received a permanent SCS implant with long term success.⁸² No further mention was made regarding this subgroup. The authors

Table 7 Visceral Pain – General

Author	Design	Patients	Permanent Implantation	Outcome	Complications	Follow-Up
A. Levine 2016 ⁷⁸	Open label, prospective	N=32	32/15 at	VAS baseline (follow-up): score of 7.3 ± 1.3 versus 3.1 ± 2.8 , 3.8 ± 2.4 , and 4.2 ± 3.2 at 3, 6, and 12 months, respectively. MEDD baseline (follow-up): score of 175 ± 377 versus 77 ± 140 at 12 months follow-up. QoL in SF-36 baseline (follow-up): only graphic data shown, with 4/9 significant improvement SF-36 scoring.	3 superficial skin infection 5 lead migration 1 cerebrospinal fluid leak headache During follow-up: 15 revision operations for lead migration (9/15), lead fracture (1/15), improvement of paraesthesia (3/15), device removals (2/15).	12 months
L.Kapural 2020 ⁷⁹	Prospective, single-arm multicenter study	N=24	23/24 at T4 to T8	VAS baseline (follow-up): score 8.3 (95% CI 7.5–9.5) versus 2.3 (95% CI 0.7–2.8) at 3 month follow up ($P<0.001$). These reductions maintained at 6 month and 12 months follow-up. PDI score baseline (follow-up): 48.5 (95% CI 43.0–53.9) versus 21.0 (95% CI 14.3–27.7) at 12 months follow-up ($P<0.001$). SF-MPQ-2 baseline (follow-up): mean total score of 4.0 (95% CI 3.4–4.5) versus 1.5 (95% CI 0.9–2.2) at 12 months follow-up ($P<0.001$). GAF score baseline (follow-up): score 36.0 versus 80.0 at 3 months follow-up and 90.0 at 12 months follow-up ($P<0.001$). Patient satisfaction: 19/22 pts were satisfied or very satisfied with treatment at 12 months follow-up. QoL (in SF-12) baseline (follow-up): improved physical and mental component. Physical score of 30.1 (95% CI 26.6–33.5) at baseline versus 39.9 (95% CI 35.8–44.0) at 12 months follow-up ($P<0.001$). Mental score of 43.8 (95% CI 39.7–47.9) at baseline versus 50.5 (95% CI 46.8–54.2) at 12 months follow-up ($P=0.02$).	1 postoperative wound infection needing revision. 1 aspiration during implantation. 1 infection at 3 months follow-up needing explantation and discontinuation of the study	12 months
B.A.Simpson 1991 ⁸⁰	Cohort	n=62 heterogeneous group	No data on subgroups	Improvement: 14 (23.3%) participants reported modest benefit, 28 (46.7%) participants reported significant benefit. 10 (16.7%) reported complete pain relief.	No data on subgroups	No data on subgroups

(Continued)

Table 7 (Continued).

Author	Design	Patients	Permanent Implantation	Outcome	Complications	Follow-Up
E.D. Hord 2003⁸¹	Retrospective cohort	n=23 heterogeneous group	15/23 at various levels	<p>When positive SB it was more likely there was positive SCS trial period: 13 patients with positive SB had good SCS trial periods, compared to 3/10 patients with negative SB (100% vs 30%, $P<0.001$).</p> <p>When positive SB it was more likely there was good pain relief at 1-month follow up: 100% of participants with positive SB had good pain relief, compared to 33% of participants with negative SB. $P=0.029$.</p>	No data	9 months
K. Kumar 2006⁸²	Retrospective review	N=410	6/410 relevant for this review.	Success rate: 4/6 (66.7%) success, 3/6 (50%) long-term success	No data on subgroups	22 years
G. Baranidharan 2014⁸³	Retrospective review	N=26	22/26 at T10/11 – T11/12	<p>VAS baseline (follow-up): median score 9 versus 4 at 26 months follow-up ($p\leq0.05$).</p> <p>Analgesics use baseline (follow-up): median dosage oral morphine of 160mg versus 26mg at 26 months follow-up ($p<0.001$).</p> <p>Overall reduction of 75% in anti-neuropathic drug such as amitriptyline, gabapentin, pregabalin consumption post-implant. 9/15 pts stopped all anti-neuropathic drugs.</p> <p>QoL baseline (follow-up): daily activities ($Z=-3.1$, $P<0.05$), mood ($Z=-2.3$, $p<0.05$) patient global impression of change ($Z = -5.2$, $P<0.05$), change in sleep ($Z=-1.8$, $P=0.06$).</p>	1 infection 1 frequent falls causing device-related complications.	26 months
B. Richter 2020³⁵	Retrospective review	N=3	3/3 at T6, T7 and T8 BurstDR stimulation	<p>VAS baseline (follow-up): CASE 1 score 5/10 without medication, with 30 monthly exacerbations with score 10/10 at baseline versus score $\leq4/10$, decreasement exacerbations with 30% at end of follow-up.</p> <p>CASE 2 score 9/10 without medication, with 4 monthly exacerbations with score 10/10 at baseline versus score 0/10 at baseline without exacerbations at end of follow-up.</p> <p>CASE 3 score 9/10 without medication, with 8 monthly exacerbations with score 10/10 at baseline versus score 0/10 at baseline with single exacerbation per month (pain score 6/10) at most at end of follow-up.</p> <p>Analgesics use baseline (follow-up): CASE 1 morphine equivalent dosing of 60mg at baseline versus no morphine at end of follow-up.</p> <p>CASE 2 morphine equivalent dosing of 22.5mg at baseline versus 12.5mg at end of follow-up.</p> <p>CASE 3 use of gabapentin, celecoxib and methocarbamol at baseline versus use of gabapentin and celecoxib at end of follow-up.</p>	No complications	27–28 months

L.Kapural 2021⁸⁴	Retrospective review	N=26	23/26 at T4 and T5	<p>VAS baseline (follow-up): 8.7 ± 1.3 versus 3.0 ± 3.0 at 6 month follow-up ($P<0.001$) and 3.2 ± 3.1 at last follow-up visit ($P<0.001$).</p> <p>Analgesics use baseline (follow-up): average of 57.7mg (95% CI 34.3–81.0) MSO₄ versus average of 24.3mg (95% CI 8.9–39.7) at 6 months follow-up and 28.0mg (95% CI 12.3–43.8) at last follow-up visit ($P<0.006$ vs baseline).</p> <p>Nausea baseline (follow-up): 20/23 pts daily nausea versus 8/23 pts (35%) at 6 months follow-up ($P=0.001$), and 7/23 pts (30%) at last follow-up visit ($P<0.001$).</p> <p>Patient satisfaction: 87% of pts satisfied with their therapy. 15 highest level of satisfaction, 2 pts lowest level. 20/23 would recommend this therapy.</p>	No complications	41 months
L.Kapural 2006⁸⁵	Case series	N=6	6/6 at T11-T12. 2/6 compact leads, 4/6 quad leads	<p>VAS baseline (follow-up): score 9.0 ± 0.89 versus 2.3 ± 1.6 at end of follow-up.</p> <p>PDI baseline (follow-up): average 58 versus 19.7 at end of follow-up.</p> <p>Analgesics use baseline (follow-up): average 22.5mg of MSO₄ versus 6.6mg at end of follow-up.</p>	No complications	Average 30.6 months
L.Kapural 2010⁸⁶	Retrospective cohort	N=35	T5-T6 and T11-T12	<p>VAS baseline (follow-up): average score of 8.2 ± 1.6 versus 3.1 ± 1.6 at end of trial period ($p<0.001$), 3.8 ± 1.9 at 1 year follow-up ($p<0.001$).</p> <p>Analgesics use baseline (follow-up): 110.0 ± 119.0 MSE¹² versus 70.0 ± 68 mg MSE at end of trial period ($p=0.212$), 38 ± 48 mg MSE at 1 year follow-up (0.089).</p>	3 infection 1 migration lead	1 year
J. Tiede 2006⁴⁷	Case report	N=2	2/2 at T2	<p>VAS baseline (follow-up): CASE 1 score 10/10 versus 2/10 at end of follow-up.</p> <p>CASE 2 score 8/10 versus 2–3/10 at end of follow-up.</p> <p>Analgesics use baseline (follow-up): CASE 1 usage of gabapentin, fentanyl, diazepam, promethazine, tegaserod maleate versus no opioid use at end of follow-up.</p> <p>CASE 2 usage of morphine 60mg every 8 hours, hydromorphone 4mg every 4 hours as needed, promethazine versus discontinuation hydromorphone and decrease of morphine by 33% at end of follow-up.</p>	1 migration lead	Case 1: unknown Case 2: 3 months

Abbreviations: VAS, Visual Analogue Scale (scale 0–10cm); MEDD, Morphine Equivalent Daily Dose; QoL, Quality of Life; SF-36 questionnaire, Short Form-36 questionnaire (range 0–100); PDI, Patient Disability Index (range 0–70); SF-MPQ-2, Short-form McGill Pain Questionnaire 2 (range 0–78); GAF, Global Assessment of Functioning (range 0–100); SF-12, Short Form-12 questionnaire (range 0–100); SB, Sympathetic Block; SCS, Spinal Cord Stimulation; MSO₄, magnesium sulphate; MSE, Morphine Sulfate Equivalents.

strongly supported the use of SCS, as they noted its reversibility, minimal invasiveness, low complication rate, and effectiveness.

Conclusion

This narrative review provides an overview of the current evidence on SCS for visceral pain across a wide range of underlying conditions. Most studies we identified were of low quality, with many retrospective cohorts, case series and -reports. This review highlights the necessity for improved screening and selection criteria to evaluate eligible patients who will benefit most from treatment with SCS. Multidisciplinary involvement is essential for finding the best treatment option for each patient. A noteworthy observation from several studies is the potential of using preceding positive responses to sympathetic nerve block as the basis for selecting patients for SCS. Patients who do not experience a positive effect from sympathetic nerve blocks might not necessarily respond to SCS, even after a positive trial. Some general studies on SCS suggest a positive correlation with younger age and efficacy of SCS for urological disorders. Other studies indicate a negative correlation between a greater number or complex pelvic comorbidities and the efficacy of SCS. Patients with endometriosis might have more favourable results in comparison to individuals with other etiologies of CPP. Furthermore, SCS can successfully treat both chronic pelvic pain and functional symptoms. These include disabling bowel and voiding problems in a selected group of patients. However, high complication rates negatively affect the applicability of SCS, particularly with older units. Steps towards reducing these complication rates should be made, as these directly impact the quality of life of patients. Moreover, some studies suggest that the positive effects of SCS gradually decline over time. However, this concern appears to be mitigated with the introduction of more advanced waveforms. Finally, this review acknowledges that costs are a major concern, as SCS is expensive and not commonly covered by standard health insurance in the Netherlands and on a global level. We stress the need for sound, prospective, possibly randomized and controlled studies, with an adequate number of patients and substantial follow-up, to determine a pain treatment plan including selection criteria for SCS. It is recommended to incorporate cost analyses into future studies.

Disclosure

Matthanja Bieze and Annelotte Pauline van Haaps are co-first authors for this study. AH reports to have received a travel fee from Merck KgaA to visit the ESHRE 2022 congress in Milan. This is not related to this manuscript. LK reports to have received consulting fees from Avanos, FUS Mobile, Neuralace, Nevro, Xalud, Nalu Medical, Medtronic, Biotronik, SAOL Therapeutics, Gimer, Man and Science and Sollis. In addition, he reports to have received honoraria for lectures from Nevro, Avanos and Saluda. These are not related to this manuscript. LK also reports to participate in the Advisory Board of Avanos, Neuros, Neuralace, Biotronik, Presidio and PainTaq and finally reports to have stock options in Nalu Medical and Gamma Core. SL reports to have received consulting fees from Abbott, Avanos, Biotronik, Nalu Medical, Nevro, NeuraLace, Ethos Lab, PainTaq, Saluda, SPR Therapeutics and Vertos. In addition, he reports to have received honoraria from Averitas Pharma and Scilex Pharm. These are not related to this manuscript. SL also reports to previously have been president of the New Jersey Society of Interventional Pain Physicians, and is current treasurer of the American Society of Pain and Neuroscience. Finally, SL reports to have stock options in Nalu Medical and NeuroOne. KF reports to be part of the Education Committee Spine Intervention Society, of the Education Committee Neuromodulation Society, is a member of the Wisconsin Medical Board and is Vice President of Wisconsin American Society of Interventional Pain Management. MS reports to be a research consultant for Modoscript, Collegium and to have been an AdComm for Syneos Health. These are not related to this manuscript. VM reports to have received research grants from Guerbet, Merck KgaA and Ferring, which were made to the Amsterdam UMC. In addition, VM has received a lecture honorarium and payment from Guerbet for meeting attendance of the ESHRE 2022 congress in Milan. These are not related to this manuscript. JWK reports to have received consulting fees from Boston Scientific, Saluda, Nevro, Abbott and Medtronic. These are not related to this manuscript. He also reports to be a member of the Advisory Board of Boston Scientific, Saluda, Nevro, Abbott and Medtronic, and to be a board member of the BNS. The authors report no other conflicts of interest in this work.

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