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REVIEW

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Sacral neuromodulation in the management of chronic pelvic pain: A systematic review and meta-analysis

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Abstract

Introduction: Sacral neuromodulation (SNM) is a treatment approved for use in several conditions including refractory overactive bladder (OAB) and voiding dysfunction. Chronic pelvic pain (CPP) is a debilitating condition for which treatment is often challenging. SNM shows promising effect in patients with refractory CPP. However, there is a lack of clear evidence, especially in long-term outcomes. This systematic review will assess outcomes of SNM for treating CPP.

Methods: A systematic search of MEDLINE, Embase, Cochrane Central and clinical trial databases was completed from database inception until January 14, 2022. Studies using original data investigating SNM in an adult population with CPP which recorded pre and posttreatment pain scores were selected. Primary outcome was numerical change in pain score. Secondary outcomes were quality of life assessment and change in medication use and all-time complications of SNM. Risk of bias was assessed using the Newcastle Ottawa Tool for cohort studies.

Results: Twenty-six of 1026 identified articles were selected evaluating 853 patients with CPP. The implantation rate after test-phase success was 64.3%. Significant improvement of pain scores was reported in 13 studies; three studies reported no significant change. WMD in pain scores on a 10-point scale was −4.64 (95% confidence interval [CI] = −5.32 to −3.95, $p < 0.00001$) across 20 studies which were quantitatively synthesized: effects were maintained at long-term follow-up. Mean follow-up was 42.5 months (0–59). Quality of life was measured by RAND SF-36 and EQ-5D questionnaires and all studies reported improvement in quality of life. One hundred and eighty-nine complications were reported in 1555 patients (Clavien-Dindo Grade I-IIIb). Risk of bias ranged from low to high risk. Studies were case series and bias stemmed from selection bias and loss to follow-up.

Conclusion: Sacral Neuromodulation is a reasonably effective treatment of Chronic Pelvic Pain and significantly reduces pain and increases patients' quality of life with immediate to long-term effects.

KEYWORDS
interstitial cystitis, nerve stimulation, neuromodulation, pelvic pain, sacral nerve

1 | INTRODUCTION

Chronic pelvic pain (CPP) is defined as pain in the lower abdomen or pelvis lasting a minimum of 6 months and not associated exclusively with menstruation or related to pregnancy.[1] CPP affects both males and females and may be localized to a single organ or generalized to the anatomical pelvis. Prevalence in reproductive-age women in the United Kingdom is 24%, comparable to migraine and back pain.[2] Despite this, CPP remains poorly understood. Commonly, pain presents alongside symptoms related to the organ system involved such as voiding, sexual or bowel dysfunction. CPP has a debilitating effect on quality of life (QoL) and is associated with psychological comorbidity including depression, anxiety and sleep disorders.[3] Treatment options for CPP include pharmacological, physical, intravesical or psychological therapies.[4] For patients refractory to initial treatment, there is emerging evidence that sacral neuromodulation may play a role in pelvic pain management.[5]

Sacral neuromodulation (SNM) involves the electrical stimulation of afferent sacral nerve roots S3 or S4 by a percutaneous implanted electrode. The electrode lead has four contact points which form a voltage-driven electrical field that depolarizes sacral nerve axons. Patients usually undergo a temporary evaluation period, and if successful, insertion of an implantable pulse generator (IPG). The mechanism of neuromodulation in relieving pelvic pain is not well understood; however, there are several theories. Sacral nerve roots S1–S4 innervate urogenital organs and the pelvic floor via somatic and parasympathetic nerves. According to the gate theory of pain, nonnociceptive stimuli from SNM transmitted via Aβ-fibers inhibit nociceptive stimuli of CPP in C-fibers via the gating mechanisms of spinal cord dorsal horn interneurons.[6]

SNM for CPP remains off-licence although it is included in EAU and AUA guidelines as an option for patients who have failed initial treatments.[7] Current literature reporting the use of SNM for CPP predominantly comprises pilot studies and other IDEAL 1–2a stage studies with short-term follow-up. Demonstrating the reliability of results in the medium to long term is particularly important for implant surgery like SNM. The aim of this systematic review is to evaluate the available literature on the effectiveness of SNM in managing CPP in the medium to long term.

2 | MATERIALS AND METHODS

This systematic review was conducted following preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines.[8] The protocol is registered on the Open Science Framework (osf.io/75hxz).[9]

2.1 | Data information sources and search

MEDLINE, EMBASE and Cochrane CENTRAL databases were searched systematically from inception to January 14, 2022. The search strategy was piloted before use and consisted of keywords and MeSH terms. Ongoing relevant clinical trials were identified by searching ClinicalTrials.gov, ISRCTN and EU Clinical Trials Register with authors contacted for preliminary data. Finally, a reference review of included studies and identified systematic reviews was conducted. The detailed search strategy is appended.

2.2 | Eligibility criteria

2.2.1 | Types of studies

Study types eligible for inclusion were randomized controlled trials, observational studies of prospective or retrospective design including cohort studies, case control studies or case series regardless of language. All literature not reporting original data, conference abstracts and case reports (≤4 patients) were excluded. In cases of duplicate datasets, the most recent and comprehensive study was included.

2.2.2 | Types of participants

We included studies that enrolled adults over the age of 18 with any etiology of CPP. The Royal College of Obstetrics and Gynecology definition of CPP was used; "intermittent or constant pain in the lower abdomen or pelvis... of at least 6 months in duration not occurring exclusively with menstruation or intercourse and not associated with pregnancy." Animal, pediatric and non-CPP studies were excluded. Where a study contained a mixed population of conditions treated with SNM, studies were excluded if data specific to CPP patients could not be extracted.

2.2.3 | Types of intervention

CPP treated by percutaneous electrical sacral nerve stimulation for any period of time. Studies investigating other nerve stimulation technique including pudendal nerve, dorsal root ganglion, spinal cord or tibial nerve stimulation were excluded.

2.3 | Study selection

Two independent reviewers (Julian Greig and Quentin Mak) independently searched all databases. The two review authors independently extracted relevant data. Discrepancies were resolved via discussion. No additional information was required beyond published data.

2.4 | Data collection and data items

All data were extracted to a predefined extraction datasheet. Primary outcome measure was change in numerical pain score on a 10-point scale including average and standard deviations where reported. Secondary outcome measures were QoL assessment, change in analgesia use and complications

2.5 | Data analysis

Pooled analysis of the change in pain score was performed using mean and standard deviation (SD). Effect size was reported with weighted mean difference (WMD), with 95% confidence intervals and two-sided *p*-values. A random-effect model was used given study heterogeneity. Pain scores were standardized to the 10-point scale. For example, a 3-point scale was multiplied by 4/3. If not reported, mean and SD were calculated from reported data. Studies which met inclusion criteria for which standard deviations could not be calculated were not included in the meta-analysis, however, the relevant data was recorded and presented (Supporting Information: Appendix). Analyses were conducted using Review Manager (RevMan version 5.4).

2.6 | Risk of bias (quality) assessment

Risk of bias was assessed using the Newcastle-Ottawa Quality Assessment Scale for cohort studies and case series.[10] Risk of Bias domains were judged as "very high risk" (0–2 stars), "high risk" (3–4 stars), "moderate risk" (5–6 stars) or "low risk" (7–9 stars) (Figure 5).

3 | RESULTS

3.1 | Study selection

One thousand and twenty-six articles were identified. After removal of duplicates, 36 studies were selected for full-text eligibility assessment. Ten studies were excluded on full text review leaving 26 studies included. Twenty studies were appropriate for pooled analysis (see PRISMA flowchart, Figure 1).

3.2 | Study characteristics

Seventeen studies were prospective observational studies and nine were retrospective reviews of records. None included a control or comparator group. Nineteen studies reported SNM for only CPP and seven studies investigated SNM for treating a number of conditions; CPP, urge incontinence, overactive bladder and chronic nonobstructive urinary retention (CNOUR). Only data for CPP are reported in this review. Seven hundred and ten patients with CPP in 26 studies underwent stage I SNM evaluation. Testing ranged from 5 to 28 days. Four studies reported only stage I SNM.[11–14] Five hundred and fifteen patients underwent permanent implantation. Reported implantation rates from 17 studies was 64.3% (range 44.4%–100.0%) (Appendix). Sex was inconsistently reported: 17.2% of patients were male. Nine studies reported CPP associated with interstitial cystitis (IC)/bladder pain syndrome (BPS),[11–13,15–17] and three reported on functional anorectal pain.[14,18,19] Other indications were endometriosis, pudendal neuralgia, postsurgical or obstetric, and idiopathic CPP.[20–27] Mean follow-up was 42.5 months (range 0–59 months). Details of the included trials are presented in Table 1. Four methods were reported for tined lead

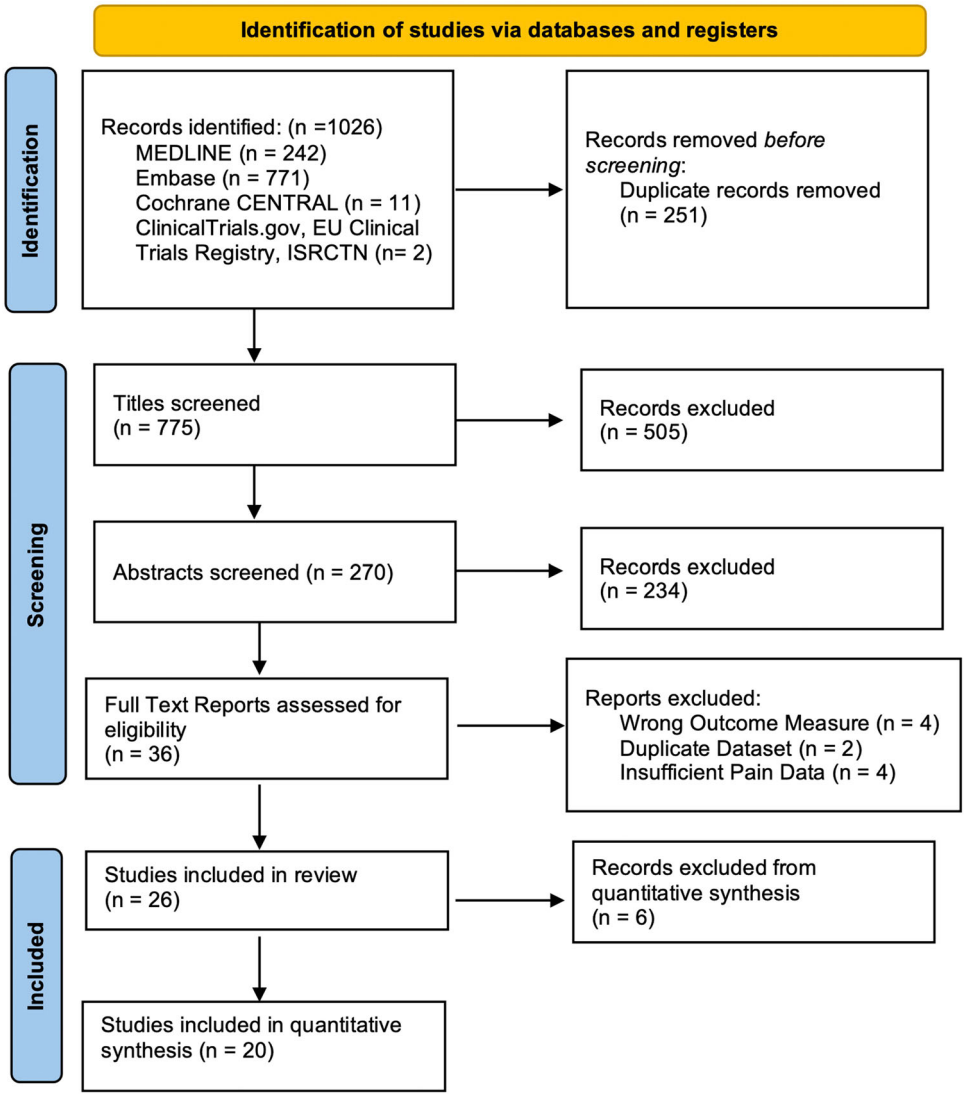


FIGURE 1 Preferred reporting items for systematic reviews and meta-analyses flow chart of study selection.

placement. The percutaneous S3 transforaminal approach was utilized in 20 studies. The retrograde approach in which leads are advanced from lumbar epidural puncture in the cephalocaudal direction was employed by one study.[15] The anterograde approach involving lead advancement via the sacral hiatus was used in three studies.[24–26] One study utilized an experimental laparoscopic lead placement.[28]

3.3 | Synthesis of results

3.3.1 | Primary outcome

Quantitative analysis of the effect of SNM on CPP

Four hundred and sixty patients across 20 studies were included in pooled analysis. The WMD in pain score on a 10-point scale after SNM was −4.64 (95% CI = −5.32 to −3.95, $p < 0.00001$) (Figure 2). Six studies were excluded from quantitative analysis as they did not report mean ± SD VAS.[14,21,26,28–30] Three of these studies reported a significant decrease in pain score after SNM ($p < 0.05$). The remaining three reported a decrease in pain score but did not perform statistical analysis (Supporting Information: Appendix).

Five studies reported pain scores at 6 months, six at 12 months and four at 24 months. Significant benefit of SNM was maintained at 6, 12, and 24 months (Figure 3A–C). Seven studies described their follow-up as long-term but did not report data specifically at 12 or 24 months.[16,22,31–35] Sensitivity analysis comparing these studies with those that reported VAS measurements at 12 and 24 months demonstrated no significant difference in VAS (−4.87 [6.12 to −3.63] vs. −4.58 [−5.92 to −3.24] respectively). Three studies did not provide mean and standard deviation for pooled analysis, but described a

TABLE 1 Study characteristics.

Study	Study type	Age	Number stage I	Number stage II	Diagnoses	Method	Outcomes	Follow-up average (months)
Whitworth 1999	Prospective case series	NR	10	10	IC	Retrograde S2, S3, S4	VAS, narcotic use, urgency, and frequency	(4–10)
Chai 2000	Prospective case series	NR	6	0 (PNE only)	IC	Transforaminal S3	VAS, urgency, frequency	NR
Maher 2001	Prospective case series	NR	15	0 (PNE only)	IC	Transforaminal S3, S4	VAS, frequency, nocturia, urgency, SF-36, and SUDI	NR
Siegel 2001	Prospective case series	48	10	10	IC	Transforaminal S3, S4	VAS, RAND SF-36, BDI	19ψ (6–74)
Aboseif 2002	Prospective case series	47	160	64 (41 with CPP)	CPP, voiding dysfunction	Transforaminal S3	VAS, frequency	24 (6–36)
Whitmore 2003	Prospective case series	44[a]	30	17	IC	Transforaminal S3	Frequency, VAS, ICSI, ICPI, O'Leary-Sant	NR
Comiter 2003	Prospective case series	46	25	17	IC	Transforaminal S3	Frequency, nocturia, pain 0–10, ICSI, ICPI	14 (2–28)
Lavano 2006	Prospective case series	NR	7	5	CPP	Transforaminal S3	VAS, SF-36	8 (6–14)
Kessler 2007	Prospective case series	58[a]	209 (17 with CPP)	91 (7 with CPP)	CPP, voiding dysfunction	Transforaminal S3	Pain 0–10, frequency	10ψ (IQR 4–11)
Falletto 2008	Prospective case series	61.0	27	12	Anal Pain	Transforaminal S3	Pain 0–10, SF-36	15 (3–80)
Peters 2008	Prospective case series	47.9[a]	93	85 (38 with CPP)	Urgency frequency, CPP	Transforaminal S3	Frequency, urgency, pain 0–10	(3–6)
Govaert 2010	Retrospective case series	58.3	9	4	FAP	Transforaminal S3	VAS, global perceived effect	(4–24)
Ghazwani 2011	Retrospective case series	44.3[b]	21	11	IC/BPS	NR S3	Urgency, frequency, nocturia, medication use, pain 0–10	71.5 ± 9.3

(Continues)

TABLE 1 (Continued)

Study	Study type	Age	Number stage I	Number stage II	Diagnoses	Method	Outcomes	Follow-up average (months)
Martellucci 2012	Prospective case series	53 51.7[b]	27	16	CPP (Anal, vaginal, perineal, diffuse CPP, pelvic surgery)	Transforaminal S3	VAS, SF-36	37 (12–71)
Dudding 2013	Prospective case series	50	6	3	FAP	Transforaminal S3	VAS, SF-36, BDI	(1–5)
Sokal 2015	Prospective case series	57	9	9	FBSS, CPP	Caudal via sacral hiatus, S2,3,4	VAS	(1–48)
Guardo 2016	Prospective case series	60	12	8	CPP, IC	Caudal via sacral hiatus, S3, S4	VAS, subjective improvement % (VAS can be calculated)	24
Vancaillie 2018	Retrospective case series	50.5	64	52 (40 with CPP)	CPP, pudendal neuralgia	Caudal via sacral hiatus, S3, S4	Pain 0–10, quality of life	(3–72)
Cerruto 2018	Prospective case series	43	22	19	CPP	Transforaminal S3 Cyclical 30 min on 3 h off.	McGill pain questionnaire, VAS, SF-36,	21.3
Marinkovic 2019	Retrospective case series	49.9	170	148	IC, BPS	Transforaminal S3	Frequency, urgency, nocturia, ICSI, ICPI, O'Leary Sant, PUF, VAS,	120.1 ± 33.3
Rongqing 2019	Prospective case series	46.5	120	0 (PNE only)	FAP	Transforaminal S3 20 min stimulation, once daily for 10 days	VAS, SF-36	12
Kashif 2019	Retrospective case series	54.3	24	12	CPP (rectal, postsurgical), IC	Transforaminal S3, S4	NRS, HADS, ODI, EQ-5D, BPI	12
Zhang 2019	Retrospective case series	55.7	434 (81 with CPP)	247 (59 with CPP)	IC, voiding dysfunction	Transforaminal S3	Urgency, frequency, nocturia, QoL, VAS, O'Leary Sant, PUF	20.1 ± 12.8
Zegrea 2020	Retrospective case series	43[a]	51	28	CPP (obstetric, idiopathic, endometriosis, postsurgical)	Transforaminal S3, S4	VAS	3.2ψ (0.3–98.9)

TABLE 1 (Continued)

Study	Study type	Age	Number stage I	Number stage II	Diagnoses	Method	Outcomes	Follow-up average (months)
Kolodziej 2020	Retrospective case series	37.7	N/D	6	Endometriosis	Laparoscopic implantation. S1, S2, S3 in four patients, S3 in two patients.	NRS, EQ-5D-5L, BDI	6
Hernandez-Hernandez 2021	Retrospective case series	52.9	106 (19 with CPP)	64 (12 with CPP)	IC, voiding dysfunction	Transforaminal S3	GRA, ICIQ-SF, QoL, NRS	75.35 ± 55.10 (14–220)

Note: NR represents no reported data. Standard deviation is represented by ±. All averages are mean values aside from those followed by ψ which are median.

Abbreviations: CPP, chronic pelvic pain; IPG, implantable pulse generator.

[a]All study participants, including those without CPP.

[b]Data for those participants implanted with IPG.

continued significant reduction in pain score at a 5-year follow-up.[17,23,29] Martellucci et al. reported outcomes for three patients to 60 months with a maintained VAS of 2; Dudding et al. reported one patient to 5 years with a post-SNM VAS of 0 and Ghazwani reported a reduction of VAS from 8.09 to 4.5 at 5 years. In contrast, Sokal et al. and Aboseif et al. reported loss of efficacy at 12 and 24 months, respectively.[22,24]

Interstitial cystitis/BPS versus noninterstitial cystitis/BPS CPP etiology

Three hundred IC/BPS patients across nine studies and 46 non-IC/BPS patients across five studies were included in this subgroup analysis. Studies that included IC/BPS and non-IC/BPS patients, or did not explicitly specify cause of CPP were excluded. Non-IC/BPS patients showed a significantly higher decrease in pain score after SNM compared to IC/BPS patients WMD = −5.77, (95% CI = −6.15 to −5.39) versus WMD −4.55 (95% CI = −5.26 to −3.83) ($p = 0.003$) (Figure 4).

Qualitative analysis of the effect of SNM on CPP

Six studies were not included in quantitative analysis.[14,21,26,28–30] Two hundred and sixty patients with CPP across the studies underwent a test phase, 96 were implanted with IPGs. One study did not report IPG implantation, resulting of an implantation rate of 66.7% across remaining studies. Three studies included a statistical analysis and all reported statistically significant improvement of VAS at last follow-up.[21,26,28] Improvement in pain score on a 10-point scale ranged between 1.9 and 6.5. Kessler et al. reported a prospective case series of seven CPP patients implanted with an IPG. Although median VAS decreased from 8 to 2 ($p = 0.03$), two patients had loss of efficacy at last follow-up.[21] Dudding et al. reported loss of efficacy in 2/3 patients.[29]

3.3.2 | Secondary outcomes

Change of analgesic medication use with SNM

Medication use was reported in four studies. Ghazwani et al. noted a mean decrease of 3.01 medications ($p = 0.001$).[17] Whitmore, Sokal and Kolodziej found that 100%, 90%, and 66% of participants, respectively either reduced or completely withdrew analgesic medication at last follow-up.[13,24,28]

QoL

Eleven studies assessed patients' QoL all of which reported improvements in various QoL domains. Eight studies employed the RAND SF-36 health survey questionnaire and six reported individual domains.[12,14,18,20,29,31,34] All six

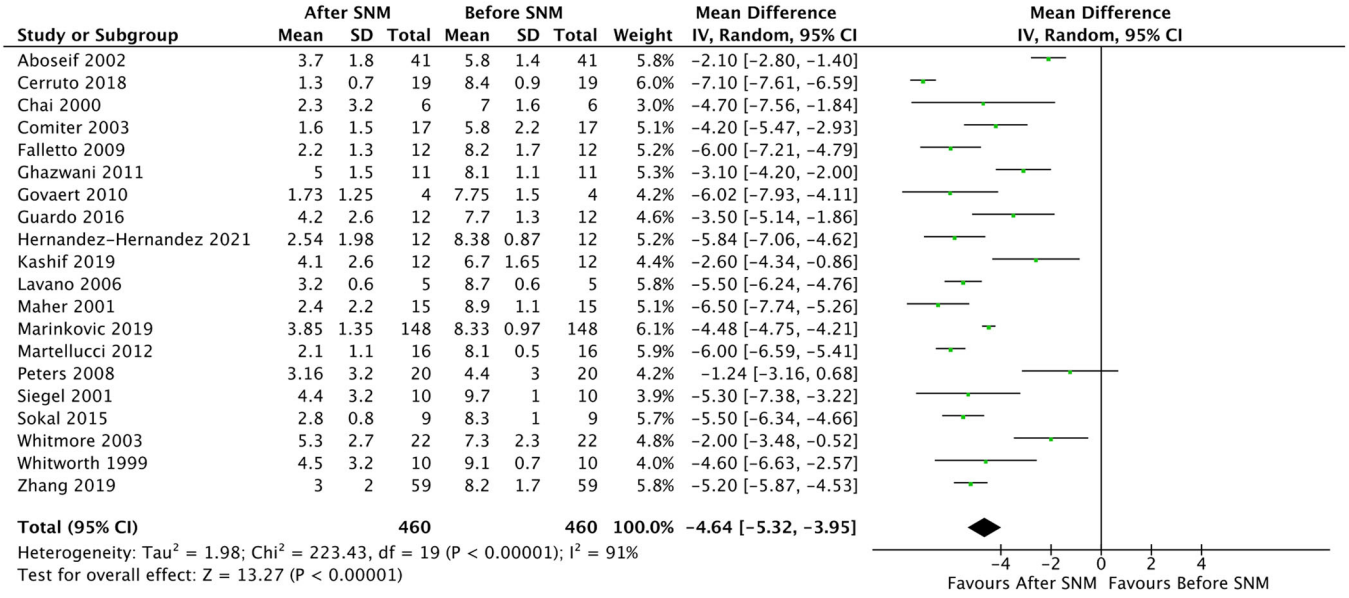
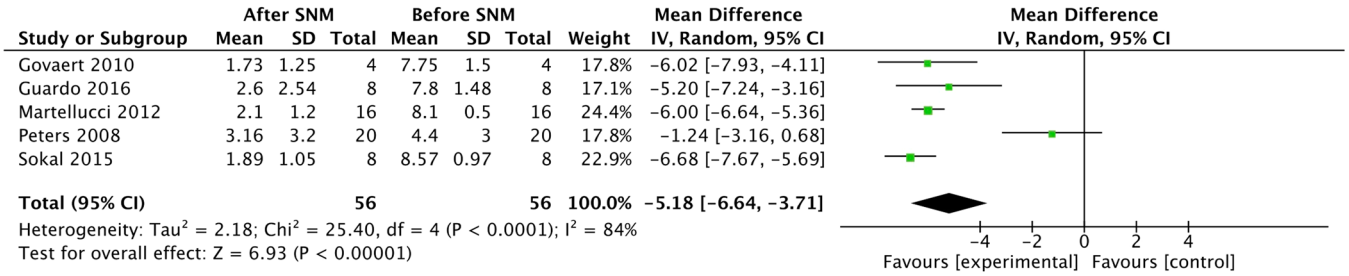


FIGURE 2 Forest plot of improvement of pain after sacral neuromodulation.

(A)



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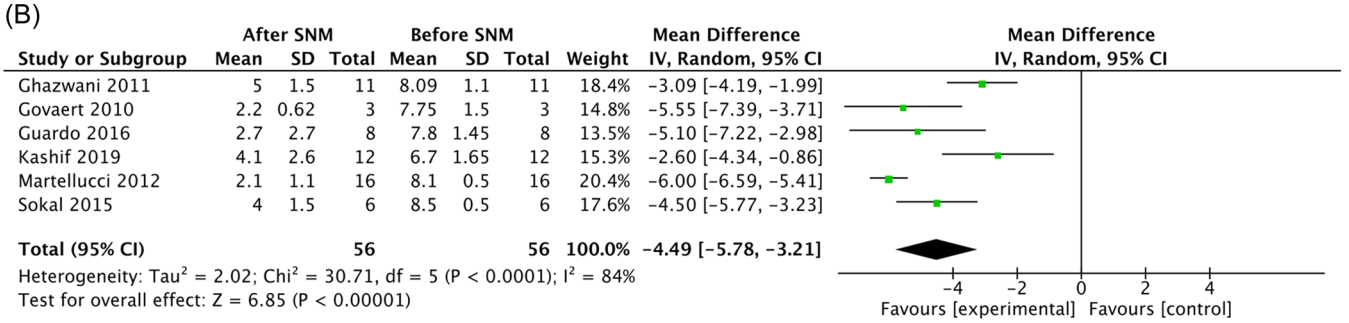

(C)

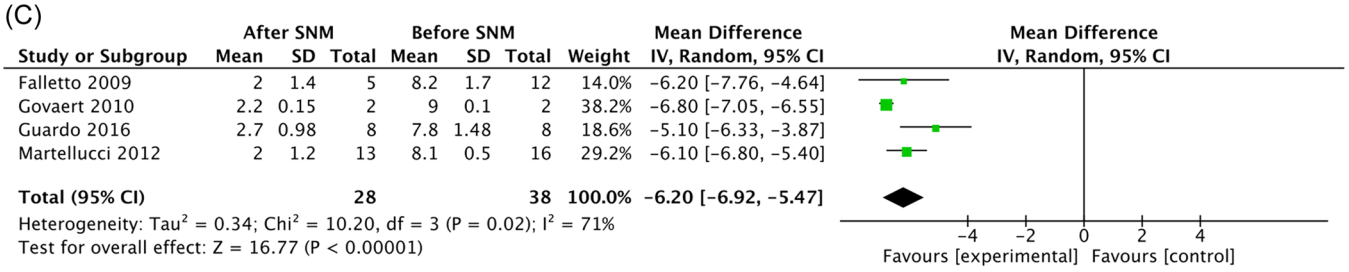

FIGURE 3 (A) Forest plot of effect of SNM at 6-month follow-up. (B) Forest plot of effect of SNM at 12-month follow-up. (C) Forest plot of effect of SNM at 24-month follow-up.

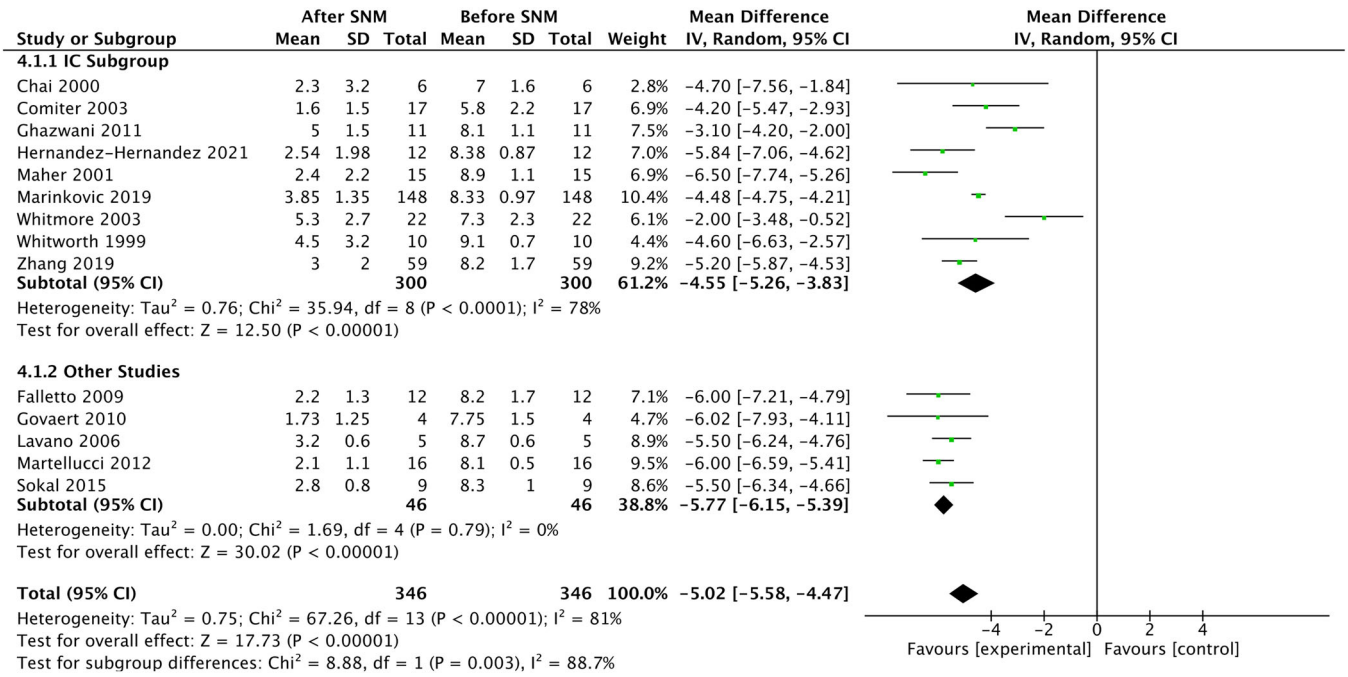

FIGURE 4 Forest plot and subgroup analysis of pain response to sacral neuromodulation (SNM) in interstitial cystitis/bladder pain syndrome (BPS) and noninterstitial cystitis (IC)/BPS etiology.

studies reported improvements in bodily pain domain. Physical function, social function, physical role, general health improved in four studies; mental health and vitality improved in three studies and change in emotional role reached significant improvement in one study. One study utilized the EQ-5D questionnaire; mobility, self-care, discomfort and depression improved significantly after 6 months.[28] A study of short-term SNM demonstrated only a temporary improvement in QoL which was not maintained at follow-up regardless of pain symptoms.[14]

Complications

There were 189 reported complications in 24 studies comprising 1555 patients (Table 2). The most common complications were pain at the implant site (35 cases, 2.2%) (Clavien-Dindo grade I) followed by infection (23 cases, 1.48%) (grade II-IIIb). Five infections were superficial, 18 required device or test lead removal. Clavien-Dindo Grade IIIb complications included lead complications like displacement or fracture requiring surgical revision. Forty-four IPGs were explanted (4.7% of IPGs); 15 due to infection, 14 due to loss of efficacy, 2 due to device failure, 2 due to pain at implant site. Other recorded reasons included excessive granulation tissue, and removal for MRI. Device removal rate ranged from 0% to 66%. Surgical revision rates were between 0% and 20%. No Clavien-Dindo Grade IIIa or ≥4 were recorded. Less common complications included seroma at implantation site, urinary tract infection and unpleasant sensations during pulses.

3.4 | Risk of bias assessment

Risk of bias for individual studies was performed using the Newcastle-Ottawa Scale for cohort studies. Most domains across all trials were assessed to be of moderate to high-risk for bias (Figure 5). One study was found to have a high risk of bias, 11 a moderate risk of bias and 14 a low risk of bias. All studies were case series without a control or comparator. A main source of bias for such study designs stems from selection bias.[36] Principle limitations of the studies were poorly reported inclusion and exclusion criteria, incomplete outcome data, lack of inclusion of all participants in analysis, or not reporting all outcomes stated in methods. One study had a high risk of recall bias as patient's were asked to remember their pre-SNM pain.[26] Six studies declared conflicts of interest relating to funding and support from Medtronic Inc.

4 | DISCUSSION

The results of this systematic review and meta-analysis demonstrate that SNM has significant benefits in reducing pain and improving QoL in selected patients

TABLE 2 Adverse events during sacral neuromodulation (SNM) and follow-up.

Study	Total	Reported %	Pain at implant site	Infection	Lead fracture	Lead displacement	Implantable pulse generator migration	Other	Explantation	Reoperation/ revision rate
Whitworth 1999	2	11.7	1	1	-	-	-	2 intrathecal implant	1 (5.8%)	2 (11.7%)
Chai 2000	0	-	-	-	-	-	-	-	-	-
Maher 2001	ND	-	-	-	-	-	-	-	-	-
Siegel 2001	27	-	4	1	-	-	-	Local wound complications in 6, 4 pain location change, 2 UTI, 3 recurred symptoms, 1 electric shock sensation	4 (40%)	2 (20%)
Aboseif 2002	12	18.7	-	3	-	2	-	2 device malfunction. 6 Seroma at IPG site	1 (1.5%)	4 (6.3%)
Whitmore 2003	2	-	-	-	-	-	-	1 pain during PNE, 1 unpleasant sensation at skin	-	-
Comiter 2003	0	-	-	-	-	-	-	-	0	0
Lavano 2006	3	-	1	-	1	1	-	-	0	1 (14.2%)
Kessler 2007	10	11	3	2	1	2	1	1 malfunction after MRI	-	6 (7%)
Falletto 2008	1	-	1	1				1 device failure	1 (8.3%)	1 (8.3%)
Peters 2008	ND	-	-	-	-	-	-	ND	-	-
Govaert 2010	3	75	2	1	-	-	-	-	1 (25%)	2
Ghazwani 2011	3	27.3	3	-	-	-	-	2 batteries changed	0	2 (18.2%)
Martellucci 2012	0	-	-	-	-	-	-	3 battery changed	0	0
Dudding 2013	2	-	1	-	-	-	-	-	2 (66%)	-
Sokal 2015	5	-	-	3	-	2	-	-	3 (33%)	2
Guardo 2016	3	-	2	-	-	1	-	-	-	1 (12.5%)
Vancaillie 2018	25	-	6	1	-	-	-	5 discomfort, 3 bladder dysfunction, 4 bowel dysfunction, 1 sexual dysfunction 2 allergy/ device expelled, 1 leg pain, 1 stress from device usage	10 (19.2%)	-

TABLE 2 (Continued)

Study	Total	Reported %	Pain at implant site	Infection	Lead fracture	Lead displacement	Implantable pulse generator migration	Other	Explantation	Reoperation/ revision rate
Cerruto 2018	0	-	-	-	-	-	-	-	0	0
Marinkovic 2019	13	7.6	-	-	-	-	-	ND	-	3 (1.8%)
Rongqing 2019	ND	-	-	-	-	-	-	ND	-	-
Kashif 2019	1	8.3	-	1	-	-	-	-	2 (16.7%)	-
Zhang 2019	40 (14 IC)	16.1	5	6	-	4	-	Recurrent symptoms	7 (2.8%)	8 (3.2%)
Zegrea 2020	11	22	6	2	1	1	-	Battery malfunction	6 (12%)	6 (12%)
Kolodziej 2020	1	-		1	-	-	-	-	-	-
Hernandez-Hernandez 2021	26	40.6	√	√	-	√	√	Recurrent symptoms	6 (9.4%)	8 (12.5%)

with CPP refractory to conventional treatments. Improvements in pain and reductions in medication use continue up to 2 years. SNM resulted in a mean difference in VAS of −4.64. Pain scores improved by 40%–53% across studies in those who had a full implant. This review is the first to analyse long-term benefit of SNM in CPP. Notably, patients with interstitial cystitis had less improvement in pain scores compared to other CPP aetiologies although overall treatment benefit was still demonstrated. These results need to be considered in the context of the relatively low quality of the included trials. IPG implantation rate was 64.3%. This is slightly lower than testing phase success in neurogenic lower urinary tract dysfunction (66.2%)[37] and OAB (72%).[38]

Results from this review broadly correspond with previous analyses investigating SNM in CPP management.[5,39–42] Overall consistent improvements in pain scores have been uniformly reported. Long-term outcomes following SNM have been inconsistently reported previously. Heterogeneity in included studies has limited analysis. This review reports strong evidence shown that SNM is effective for CPP for up to 2 years with some studies reporting improvement up to 5 years.

The effects of SNM for IC/BPS associated chronic pain are less clear. This review and that of Mahran et al. found that IC/BPS patients had significantly lower improvement in pain scores than non-IC/BPS patients.[5] Nevertheless, pain improvement with SNM in IC/BPS is significant.[40]

Reported complication rates ranged from 0% to 75% and revision rates ranged up to 18.2% which is low in comparison to the reoperation rate of 69.3% stated in the longest retrospective study of SNM.[43] A recent review reported complication and revision rates of 9.6%–41.6% and around 20% respectively for SNM in CNOUR. Explantation rates, mainly due to loss of effect, were higher in pelvic pain compared to CNOUR at 2.6%–66% versus 1.1%–16.6%.[44]

An expanding experience in SNM for CPP has been accompanied by new approaches lead placement and stimulation protocols. Lower voltages (≤3 V) required for motor responses at implantation have been associated with better pain outcomes and improved battery longevity.[33] Cyclical compared to continuous stimulation may also lengthen battery life.[31] Current lead implantation is completed either by a caudal approach via the sacral hiatus, which carries a risk of lead migration, a transforaminal approach via S3 foramen, or the retrograde approach which may have a higher failure rate and inadequate electrode insertion.[45] Kolodziej et al. trialed laparoscopic lead implantation in patients with CPP due to deep-infiltrating endometriosis. This technique is

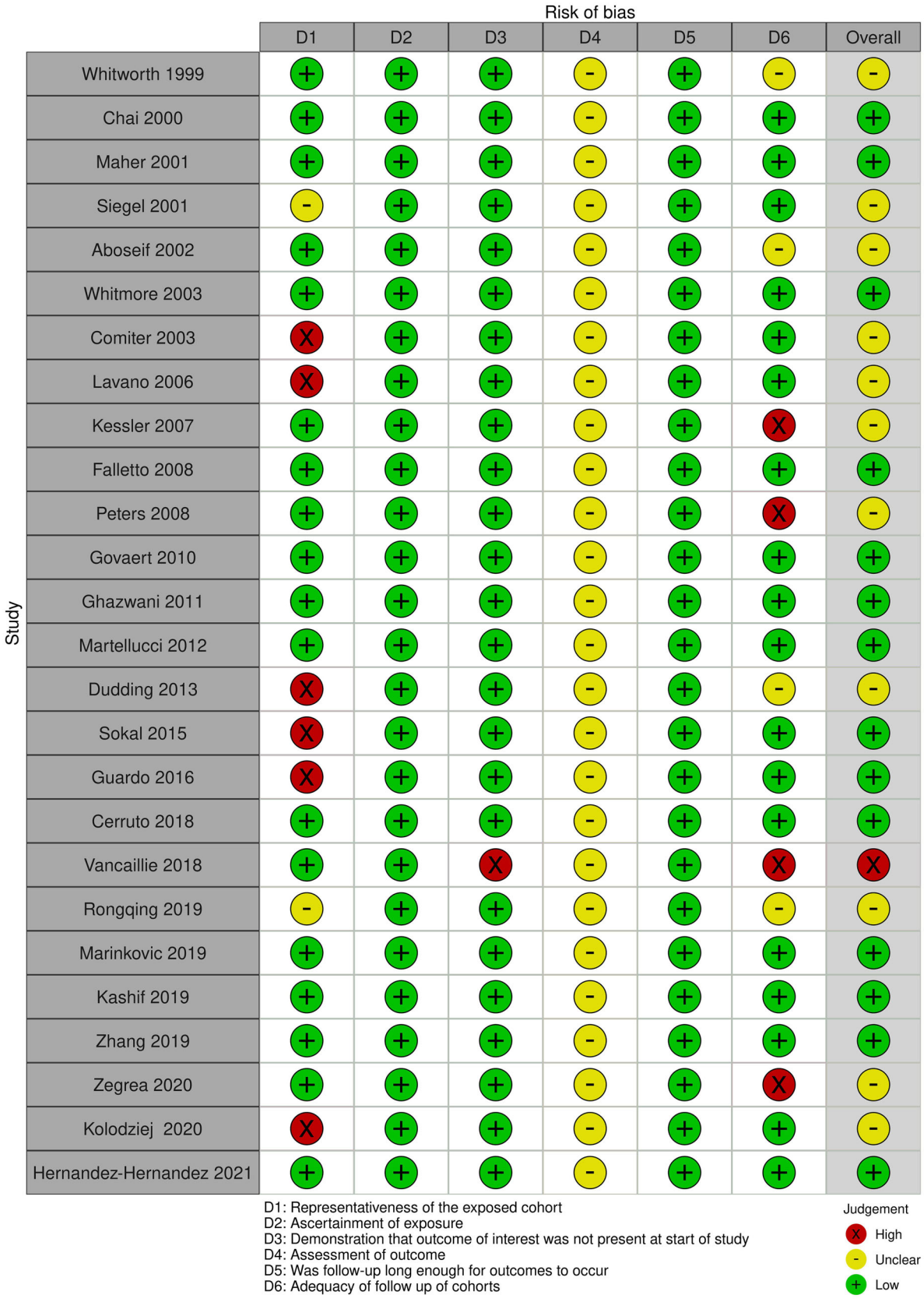

FIGURE 5 Risk of bias diagram illustrating risk of bias elicited via the Newcastle Ottawa Scale for Cohort Studies. Constructed using RoBVis Tool. Domains regarding selection and comparability of controls were not included as studies were all single-arm case series.

more invasive, but allows for precise nerve-specific lead placement with a clear view of the sacral nerves. Pudendal nerve stimulation (PNS) is thought to stimulate more nerve root afferents from its origins in S2–S4 than S3 root stimulation alone. A small-scale randomized controlled trial by Peters et al. demonstrated a greater reduction in VAS score of 49% (7.9–4.0) in PNS compared to 29% (4.5–3.2) in SNM.[46] PNS may be useful in patients who have failed SNM or be combined with SNM for effective long-term pain relief.[47]

4.1 | Limitations

This review has several limitations. All studies included in the review were limited by the lack of a control arm. Sample sizes were small and there were wide ranges in follow-up time with loss to follow-up of patients with unsuccessful SNM which may cause overestimation of the reported effect of SNM. Caution must be used when interpreting follow-up data (Figure 3A–C) due to potential loss to follow-up bias of the studies included. The majority of participants in included studies were female. Whilst CPP does affect more females than males, CPP in males is underrepresented in the literature.

5 | CONCLUSION

This review demonstrates that SNM is an effective and safe treatment for patients with refractory CPP and successful test-phase, improving pain relief and QoL. This success extends into the long term for selected IPG-implanted patients. Studies of higher levels of evidence including randomized controlled prospective trials with a long-term follow-up comparing SNM with other neuromodulation modalities and conventional treatments are needed for conclusive evidence of effectiveness of SNM to make robust clinical recommendations.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The protocol of this review is freely available on the Open Science Framework at https://osf.io/75hxz/. The datasets within the review are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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