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ORIGINAL ARTICLE

Meta-analysis: sacral nerve stimulation versus conservative therapy in the treatment of faecal incontinence

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Abstract
Aim Sacral nerve stimulation (SNS) has recently been used in the management of faecal incontinence (FI). This study compared SNS to conservative management with regards to functional and quality of life outcomes.
Methods Meta-analysis of studies published between 1995 and 2008 on SNS for FI was performed. Outcomes evaluated were functional, physiological and quality of life. A random-effects model was used and sensitivity analyses performed. Subgroup analyses were performed on age and sphincter status.
Results Thirty-four studies were included, reporting on 944 patients undergoing peripheral nerve evaluation; 665 underwent permanent SNS. Weekly incontinence episodes (weighted mean difference [WMD] −6.83; 95% confidence intervals [CI] −8.05, −5.60; $p<0.001$) and incontinence scores (WMD −10.57; 95% CI −11.89, −9.24; $p<0.001$) were significantly reduced with SNS; ability to defer defecation (WMD 7.99 min; 95% CI 5.93, 10.05; $p<0.001$) was increased. Most SF-36 and FIQL domains improved following SNS, and mean anal pressures increased significantly ($p<0.001$). Results remained consistent on sensitivity analysis. The under-56 years age group showed smaller functional but greater physiological and quality of life improvements. Results were similar between sphincter intact and impaired subgroups. The complication rate was 15% for permanent SNS, with 3% resulting in permanent explantation.
Conclusion SNS results in significant improvements in objective and subjective measures for faecally incontinent patients.

Keywords Faecal incontinence · Sacral neuromodulation · Sacral nerve stimulation · Minimally invasive therapy

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Introduction

Faecal incontinence (FI) is the inability to control the passage of faecal matter through the anus [1, 2]. It can be a debilitating problem with medical and social implications [3], including shame, embarrassment and even depression. Patients often have to plan their lives around it [1], impairing their quality of life [4].

The true prevalence of FI is difficult to determine due to inadequate standardisation of definitions [1] and reticence of patients in reporting the disorder due to the social stigma attached [5]. Studies have estimated varying rates between 0.004% and 20.7% [6–12], with predominance in females and the elderly [10]. Rates in the institutionalised population can reach up to 50%, with prominent risk factors including immobility, the use of physical restraints and concurrent urinary incontinence [13]. In the younger patient, the most common aetiology is obstetric perineal trauma, with 13% of primigravidas and 23% of multigravidas developing FI [14]. Other common causes include neurological disorders, rectal or pelvic organ prolapse, sphincter degeneration and previous pelvic floor or rectal surgery [15].

Management of FI is primarily by conservative means including dietary and lifestyle changes, antidiarrhoeal medication [16], biofeedback therapy [17], absorbent pads and anal plugs [18]. Surgical options include sphincteroplasty, postanal repair and more recently, sacral nerve stimulation (SNS) [1, 2, 5]. SNS is a minimally invasive technique that allows modulation of the nerves, and therefore muscles, of the pelvic floor via the application of an electrical current to a sacral nerve by insertion of an electrode through the corresponding sacral foramen [19]. Sacral nerve stimulators were first implanted in 1981 for the treatment of urinary urge incontinence [20], with SNS first used for the treatment of FI in 1995 [21].

In its current form, SNS involves extradural stimulation within the sacral canal, which has reduced complications compared with previous transcutaneous, transvaginal and transrectal techniques [22]. SNS involves a testing phase known as peripheral nerve evaluation (PNE). PNE determines the feasibility of electrode implantation into the sacral foramina, followed by a 2–3-week period of stimulation with a temporary electrode to assess the potential benefits of SNS [22]. This allows identification of patients who are likely to have a positive response to SNS, into whom a permanent electrode can be inserted [22].

Although SNS has been in use for the treatment of FI for close to a decade and a half and its benefits are well established, there remains very little evidence regarding which patients and pathological conditions may benefit most. Studies are usually small in scale and non-randomised. The aim of the present study was to evaluate the functional, physiological and quality of life outcomes of SNS versus conservative management in the treatment of FI. Meta-analytical techniques and sensitivity analyses were used to assess the potential advantages of SNS.

Methods

Study selection

A PubMed search was performed between 1995 and 2008 for all studies on the use of SNS for FI. The following MeSH search headings were used: “faecal incontinence”, “comparative study” and “treatment outcome”. The above terms and their combinations were also searched as text-words, as were “sacral nerve stimulation”, “sacral neuromodulation” and “minimally invasive surgery”. The “related articles” function was used to broaden the search, and all abstracts, studies and citations scanned were reviewed. References of the articles acquired were also searched by hand. No language restrictions were made. The latest date for this search was 31 December 2008.

Data extraction

Two reviewers (MS and ET) independently extracted the following from each study: first author, year of publication, study population characteristics, study design, inclusion and exclusion criteria, number of subjects who underwent temporary and permanent stimulation and duration of follow-up. There was 100% agreement between the two reviewers.

Inclusion criteria

In order to be included in the analysis, studies had to: (a) Compare SNS with maximal conservative therapy (MCT) in patients with FI; (b) Report on at least one of the outcome measures; and (c) Clearly document whether PNE or permanent SNS was being tested and how many patients underwent each procedure.

Exclusion criteria

Studies were excluded from the analysis if: (a) Outcomes of interest were not clearly reported as either baseline (having failed conservative therapy) or treatment (SNS). (b) It was impossible to extract or calculate the appropriate data from the published results.

Outcomes of interest and definitions

The following outcomes were used to compare MCT with SNS.

1. *Functional outcomes*: weekly incontinence episodes, Wexner (Cleveland) incontinence scores [23] and ability to defer defecation. Where other incontinence scores were used (e.g. American Medical Systems score), these were standardised as a score out of 20 to match Wexner [24].
2. *Quality of Life outcomes*: the eight categories of the SF-36 questionnaire [25] and the four categories of the faecal incontinence quality of life (FIQL) questionnaire (the American Society of Colon and Rectal Surgery [ASCRS] quality of life questionnaire) [26].
3. *Anal manometry*: the resting and squeeze pressures, measured in millimetres of mercury. Where reported in centimetres of H_2O, conversion was performed using the formula 1 cmH_2O=0.735541 mmHg. Squeeze pressure was taken as the total squeeze pressure, converted accordingly where reported as incremental squeeze.
4. *Rectal sensitivity*: the threshold, urge and maximum tolerable volumes in millilitres.

Other outcomes of interest where meta-analysis was not possible including the pudendal nerve terminal motor

latency (PNTML), anal canal length and complications were reviewed systematically. MCT values were taken as baseline values where conservative therapy had failed. All SNS values were taken at the last follow-up for each patient where possible, and where not possible, taken at the median follow-up.

Statistical analysis

Meta-analysis was performed in line with recommendations from the Cochrane Collaboration and the Quality of Reporting Meta-analyses (QUORUM) guidelines [27, 28]. Statistical analysis of variables, which were all continuous, was carried out using the weighted mean difference (WMD) [29], reported with 95% CI. WMDs summarise the differences between the conservative and SNS groups, accounting for sample size. The DerSimonian–Laird [29] method was used to combine the means for the outcomes of interest using a "random-effects" meta-analytical model. In such a meta-analysis, where differences between studies are likely, this model is more appropriate than a "fixed-effects" model as it incorporates statistical heterogeneity, which is reflected in the effect estimate [30].

For studies that presented the data as means and range values, the standard deviations were calculated using statistical algorithms and checked using "bootstrap" re-sampling techniques—thus all continuous data were standardised for analysis. In the graphical representation of results, squares indicate the point estimates of the treatment effect (WMD) with 95% confidence intervals indicated by horizontal bars. The diamond represents the summary estimate from the pooled studies with 95% confidence intervals.

The quality of the studies was assessed using the Newcastle-Ottawa Scale (NOS) [31], which evaluates the quality of a study using a star system to rate studies by design, content and ease of incorporation into a meta-analysis [30]. Studies achieving seven or more stars were considered to be high quality.

Heterogeneity was assessed by two methods. Firstly, graphical exploration with funnel plots was used to evaluate publication bias [32, 33]. Secondly, sensitivity analysis was undertaken using subgroups of studies of a higher quality and those with a large patient sample size, taken as 20 or more patients undergoing permanent SNS. Analysis was conducted by using the statistical Review Manager™ Version 4.2 (The Cochrane Collaboration, Software Update, Oxford).

Subgroup analyses were performed on studies with a mean age below and above 56 years and those with or without sphincter impairment. Mean age was taken as the mean age of patients undergoing permanent SNS where available. The sphincter-impaired subgroup included studies either with the inclusion criteria of a sphincter defect or with more than 75% of patients defined as having internal or external sphincter impairment. The sphincter intact subgroup included studies either with the inclusion criteria of an intact sphincter or with all the patients otherwise defined as being sphincter intact. An attempt was made to subgroup analyse studies according to the aetiology of FI was considered. However, due to the manner of reporting of results in the studies, this was not possible.

Results

Eligible studies

The literature search identified 34 studies on the use of SNS in the treatment of FI which matched the selection criteria and were included in the analysis [34–67]. The flow diagram for the literature search and list of included and excluded studies is shown in Fig. 1. The studies were published between 2000 and 2008, reporting on 944 patients in whom PNE was performed. Six hundred sixty-

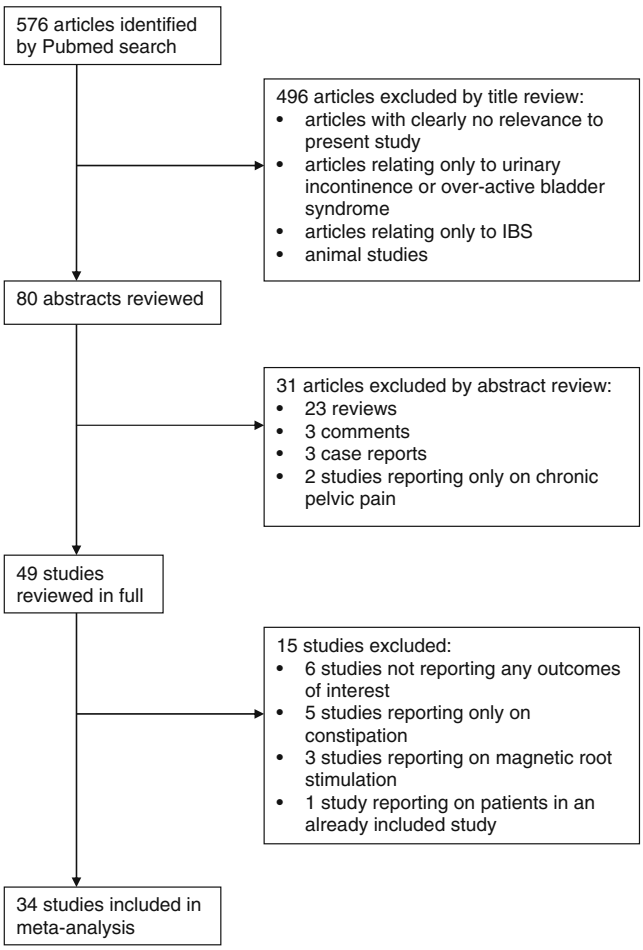


Fig. 1 Flow diagram for included and excluded studies

Table 1 Characteristics of included studies

Author	Year	Design	Number of patients[a]		Inclusion criteria	Exclusion criteria	Mean/ median age	Sphincter impaired (%)	Quality (Max nine stars)
			MCT	SNS					
Altomare[34]	2004	PNR	14	14	NM	NM	53.21	42.9	*******
Conaghan[35]	2005	PNR	5	3	1, 2, 4	NM	46.8	100	*******
Ganio[37]	2001a	PNR	16	16	1–3	3, 8	59.56	0.0	*******
Ganio[36]	2001b	PNR	25	25[b]	1–3	3, 8	50.2	0.0	******
Gstaltner[38]	2008	RCO	11	5	1, 2	NM	46.6	0.0	*****
Hetzer[39]	2007	PNR	37	30	2	NM	65	45.9	*******
Holzer[40]	2007	PNR	36	29	1–3	NM	49	0.0	******
Holzer[41]	2008	RCO	5	5	2, 3	NM	57	0.0	******
Jarrett[46]	2004	PNR	46	46	1, 2, 5	1–9	56	78.3	*******
Jarrett[43]	2005a	PNR	13	12	1–3, 5	1–9	58.5	0.0	******
Jarrett[45]	2005b	PNR	2	2	1–3, 5	1–7, 9	61.5	0.0	******
Jarrett[44]	2005c	PNR	4	4	1–3, 5	1–9	57.25	25.0	******
Jarrett[42]	2008	PNR	8	8	1, 2, 4, 5	1–9	46	100	*******
Kenefick[49]	2002a	PNR	4	4	1, 2	NM	61	0.0	******
Kenefick[48]	2002b	PNR	15	15	1, 2	NM	60	26.7	*******
Kenefick[47]	2006	PNR	19	19	1, 2	NM	58	–	*******
Koch[50]	2005	PNR	8	8	1, 3	1, 2	58.5	0.0	******
Leroi[51]	2001	PNR	6	6	1, 2	3, 4, 8	51.6	66.7	******
Leroi[52]	2005	DBXO	28	28	1, 2	NM	57	51.9	******
Malouf[53]	2000	PNR	5	5	1, 2	NM	59	20.0	******
Matzel[55]	2001	PNR	6	6	1, 2	NM	49.83	0.0	******
Matzel[54]	2004	PNR	37	30	1–3, 5	1–9	54.3	0.0	*******
Melenhorst[56]	2006	PNR	134	100	2, 3, 5	1–9	55	0.0	*******
Melenhorst[57]	2008A[c]	PNR	20	16	1, 3	1–9	55.8	0.0	*******
Melenhorst[57]	2008B[c]	PNR	20	14	1, 4	1–9	52.1	100	*******
Michelsen[58]	2006	PNR	29	29	2	NM	58	20.7	*****
Navarro[59]	2005	PNR	26	26	1, 2, 3	5, 6, 8	56.52	0.0	*******
Rasmussen[60]	2004	PNR	37	37	NM	NM	59	–	******
Ratto[61]	2005	PNR	4	4	NM	2, 4, 6	61.7	0.0	******
Ripetti[62]	2002	PNR	21	21[b]	1, 2, 3	NM	55.7	19.0	******
Rosen[63]	2001	PNR	20	16	1, 2, 3	NM	50.1	0.0	*******
Tjandra[64]	2008	RCT	60	53	1	1, 3–8	63.2	46.9	********
Uludag[65]	2004	PNR	62	46	1–3, 5	1–6	52	0.0	*******
Vaizey[66]	2000	DBXO	2	2	NM	NM	63	0.0	*****
Vitton[67]	2008	PNR	5	5	2	2	52	100	******

[a]Number of patients=maximum number of patients in each study on which data is reported—for some outcomes, data is reported only on a proportion of patients

[b]For Ganio 2001b and Ripetti, PNE data reported as SNS

[c]Melenhorst 2008 – two subgroups within study analysed separately

Design: *PNR* prospective non-randomised, *RCO* retrospective cohort study, *RCT* randomised controlled trial, *DBXO* double-blind cross-over

Inclusion criteria: *LNM* none mentioned, *1* defined faecal incontinence, *2* failed conservative therapy, *3* intact/repaired external anal sphincter, *4* impaired external anal sphincter, *5* age 18–75 years

Exclusion criteria: *NM* none mentioned, *1* congenital anorectal malformation, *2* rectal surgery in previous 12 months, *3* present external rectal prolapse, *4* chronic bowel disease or diarrhoea, *5* stoma in situ, *6* neurological diseases, *7* bleeding complications, *8* pregnancy, *9* anatomical limitations

five subsequently underwent permanent SNS implantation. A total of 279 patients did not proceed to permanent implantation, 154 of which were lost to follow-up. The total number of patients from the relevant studies which were included in this study was therefore 790, of which 665 received a permanent implant.

The study characteristics and patient demographic details are shown in Table 1. One study [57] reported on sphincter intact and sphincter impaired patients as two separate groups. These groups were analysed as separate studies in the pooled analysis, labelled Melenhorst 2008A and Melenhorst 2008B.

Twenty-eight studies were prospective non-randomised trials. The remaining six included two retrospective trials [38, 41], one prospective cross-sectional study [59] and two double-blind cross-over trials [52, 66]. The last study was a randomised controlled trial (RCT) [64], the only RCT that reported on the outcomes of interest. The outcomes of interest reported by each study are summarised in Table 2.

Sensitivity analyses were performed on 15 high quality studies which scored seven or more stars on the Newcastle-Ottawa Scale [34, 35, 37, 39, 42, 46–48, 54, 56, 57, 59, 63–65] and on the 12 studies with 20 or more patients undergoing permanent SNS [39, 40, 46, 52, 54, 56–60, 64,

Table 2 Studies reporting outcomes of interest

Author	Year	1	2	3	4	5	6	7	8	9	10
Altomare	2004	√	√				√	√	√	√	√
Conaghan	2005	√					√	√			
Ganio	2001a	√	√				√	√	√	√	
Ganio	2001b	√					√	√	√	√	
Gstaltner	2008		√								
Hetzer	2007	√	√		√						
Holzer	2007	√		√		√	√	√	√	√	√
Holzer	2008					√	√	√	√	√	√
Jarrett	2004	√	√	√			√	√	√	√	√
Jarrett	2005a	√				√					
Jarrett	2005b	√			√						
Jarrett	2005c	√				√					
Jarrett	2008	√	√			√	√	√	√	√	√
Kenefick	2002a	√		√			√	√	√	√	√
Kenefick	2002b	√		√	√		√	√	√	√	√
Kenefick	2006	√		√				√	√		√
Koch	2005	√					√	√	√	√	√
Leroi	2001	√		√			√	√		√	√
Leroi	2005	√	√			√	√	√	√	√	√
Malouf	2000	√	√		√		√	√	√	√	√
Matzel	2001		√				√	√			
Matzel	2004	√			√	√	√	√			
Melenhorst	2006	√					√	√	√	√	√
Melenhorst	2008A	√		√			√	√	√	√	√
Melenhorst	2008B	√		√			√	√	√	√	√
Michelsen	2006	√	√				√	√	√	√	√
Navarro	2005		√				√	√			
Rasmussen	2004		√				√	√	√		√
Ratto	2005	√	√		√		√	√	√	√	√
Ripetti	2002						√	√	√	√	
Rosen	2001	√		√		√	√	√	√	√	√
Tjandra	2008	√	√			√	√	√			
Uludag	2004	√									
Vaizey	2000	√			√		√	√	√	√	√
Vitton	2008						√	√			

1 incontinence episodes, *2* incontinence score, *3* deferring defecation times, *4* SF-36 outcome, *5* FIQL outcome, *6* resting pressure, *7* squeeze pressure, *8* threshold volume, *9* urge volume, *10* maximum tolerable volume

65]. Further subgroup analyses were performed on 15 studies where patients' mean/median age was less than 56 years [34–36, 38, 40, 42, 51, 54–57, 62, 63, 65, 67], 19 studies with a mean/median age greater or equal to 56 years [37, 39, 41, 43–50, 52, 53, 58–61, 64, 66], five studies where patients had more than 75% sphincter injury [35, 42, 46, 57, 67] and 18 studies where no sphincter injury was present [36–38, 40, 41, 43, 45, 49, 50, 54–57, 59, 61, 63, 65, 66].

Results from the overall meta-analysis of the studies are summarised in Table 3. Follow-up ranged from 2 weeks (Conaghan et al.) to 35 weeks (Holzer et al.). The table displays the number of studies reporting on each outcome, the total number of patients reported on for both MCT and SNS in each outcome, the WMD, the 95% confidence intervals for each WMD and the p value. The Chi-squared test for heterogeneity between the studies and its relevant p value are also indicated.

Functional outcomes

Twenty-eight studies reported on incontinence episodes per week (Fig. 2). All studies reported a decrease following SNS, the overall WMD of −6.83 (95% CI −8.05, −5.60; $p<0.001$) showing a significant decrease for SNS compared with MCT. Fourteen studies reported on pre- and post-operative incontinence scores. All the incontinence scores used were represented symptoms in a linear fashion, so these were converted to a score out of 20 to match for the Wexner score: 0=perfect continence, 20=complete incontinence [24]. There was a decrease in each of the studies with SNS, with an overall WMD of −10.57 (95% CI −11.89, −9.24) reaching statistical significance ($p<0.001$). Sixteen studies reported at the time patients were able to defer defecation. Seven of these had to be excluded as data were reported in groups. In the nine included studies, there was a significant increase in ability to defer defecation following SNS (WMD 7.99 min, 95% CI 5.93, 10.05; $p<0.001$).

Quality of life outcomes

Seven studies reported on SF-36 outcomes (Fig. 3a, b). There was an increase in the WMD of all SF-36 outcomes in favour of SNS, with all but one (bodily pain, $p=0.13$) reaching significance. The FIQL questionnaire is reported as four subcategories, each graded between 1 and 4, with 1 being quality of life alteration present most of the time, and 4 being none of the time [68]. Nine studies reported pre- and post-operative FIQL scores, with each study reporting an

Table 3 Results of meta-analysis comparing SNS with MCT

Outcome of interest	No of studies	No of patients		WMD	95% CI	p Value	HG chi-square	HG p value
		MCT	SNS					
Functional outcome								
Incontinence episodes/week	28	622	574	−6.83	−8.05, −5.60	<0.001	536.25	<0.001
Incontinence scores	14	289	272	−10.57	−11.89, −9.24	<0.001	101.95	<0.001
Deferring defecation (mins)	9	165	158	7.99	5.93, 10.05	<0.001	54.93	<0.001
SF-36 outcomes								
Physical functioning	7	102	87	11.99	7.37, 16.61	<0.001	16.53	0.01
Social functioning	7	102	87	20.91	12.52, 29.29	<0.001	15.10	0.02
Role physical	7	102	87	33.82	20.95, 46.70	<0.001	34.13	<0.001
Role emotional	7	98	87	18.48	8.28, 28.68	<0.001	9.33	0.05
Mental health	7	102	87	13.43	9.85, 17.01	<0.001	5.72	0.46
Vitality	7	102	87	10.77	4.66, 16.87	<0.001	9.76	0.14
Bodily pain	7	102	87	7.99	−2.32, 18.30	0.13	27.38	<0.001
General health	7	102	87	14.92	4.10, 25.74	0.007	69.47	<0.001
FIQL outcome								
Lifestyle	9	199	169	1.23	0.68, 1.78	<0.001	245.49	<0.001
Coping/behaviour	9	199	169	1.28	0.96, 1.59	<0.001	102.02	<0.001
Depression/self-perception	9	199	169	1.16	0.81, 1.50	<0.001	105.50	<0.001
Embarrassment	9	199	168	1.41	0.86, 1.96	<0.001	285.00	<0.001
Anal manometry								
Resting pressure (mmHg)	28	613	440	6.40	2.57, 10.22	<0.001	101.61	<0.001
Squeeze pressure (mmHg)	29	632	455	16.19	9.40, 22.98	<0.001	88.64	<0.001
Rectal sensitivity								
Threshold volume (ml)	22	462	391	−6.53	−12.46, −0.60	0.03	53.60	<0.001
Urge volume (ml)	21	441	370	−7.22	−19.50, 5.07	0.25	85.98	<0.001
Max tolerable volume (ml)	20	406	334	−5.33	−20.07, 9.42	0.48	75.02	<0.001

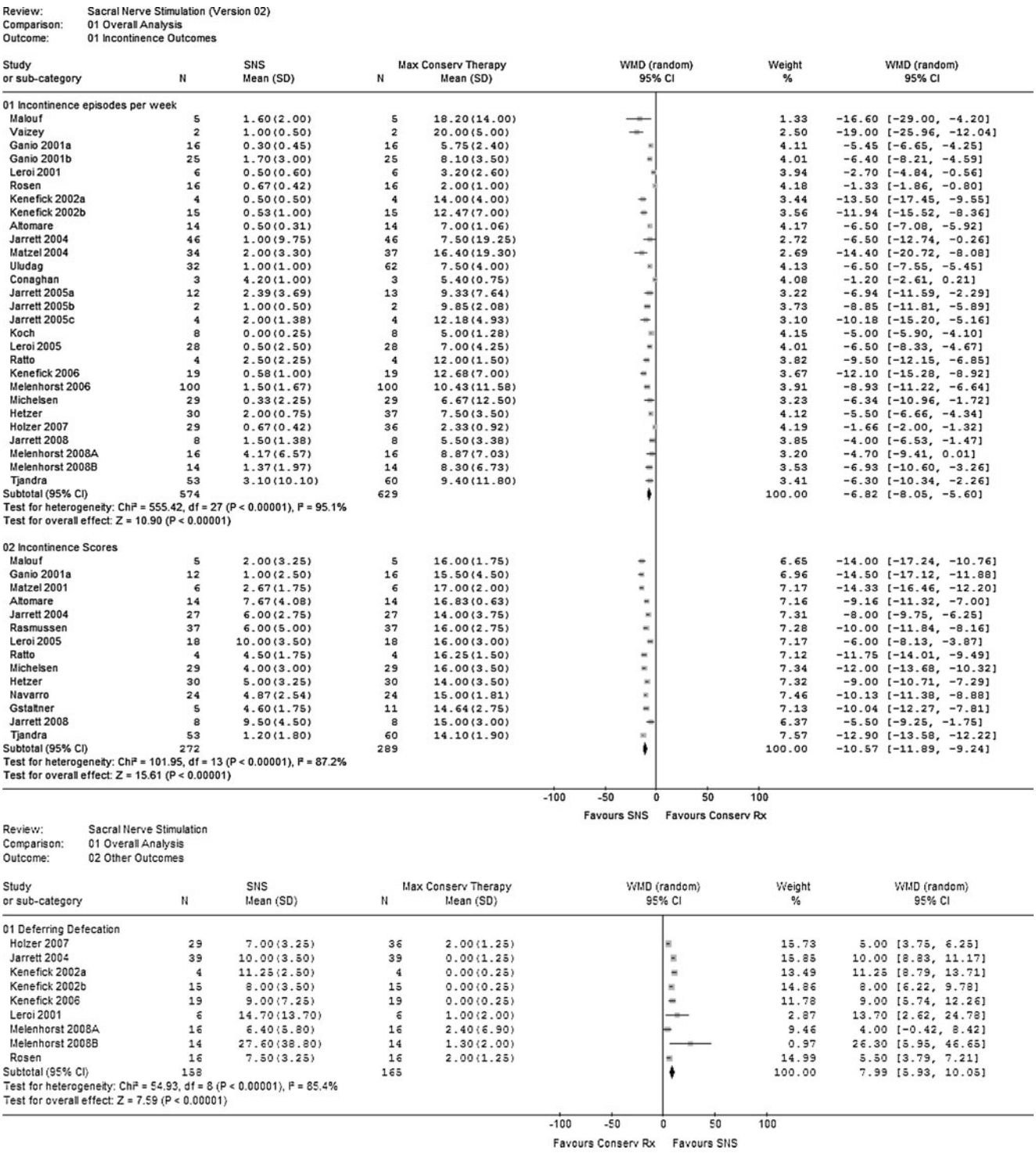
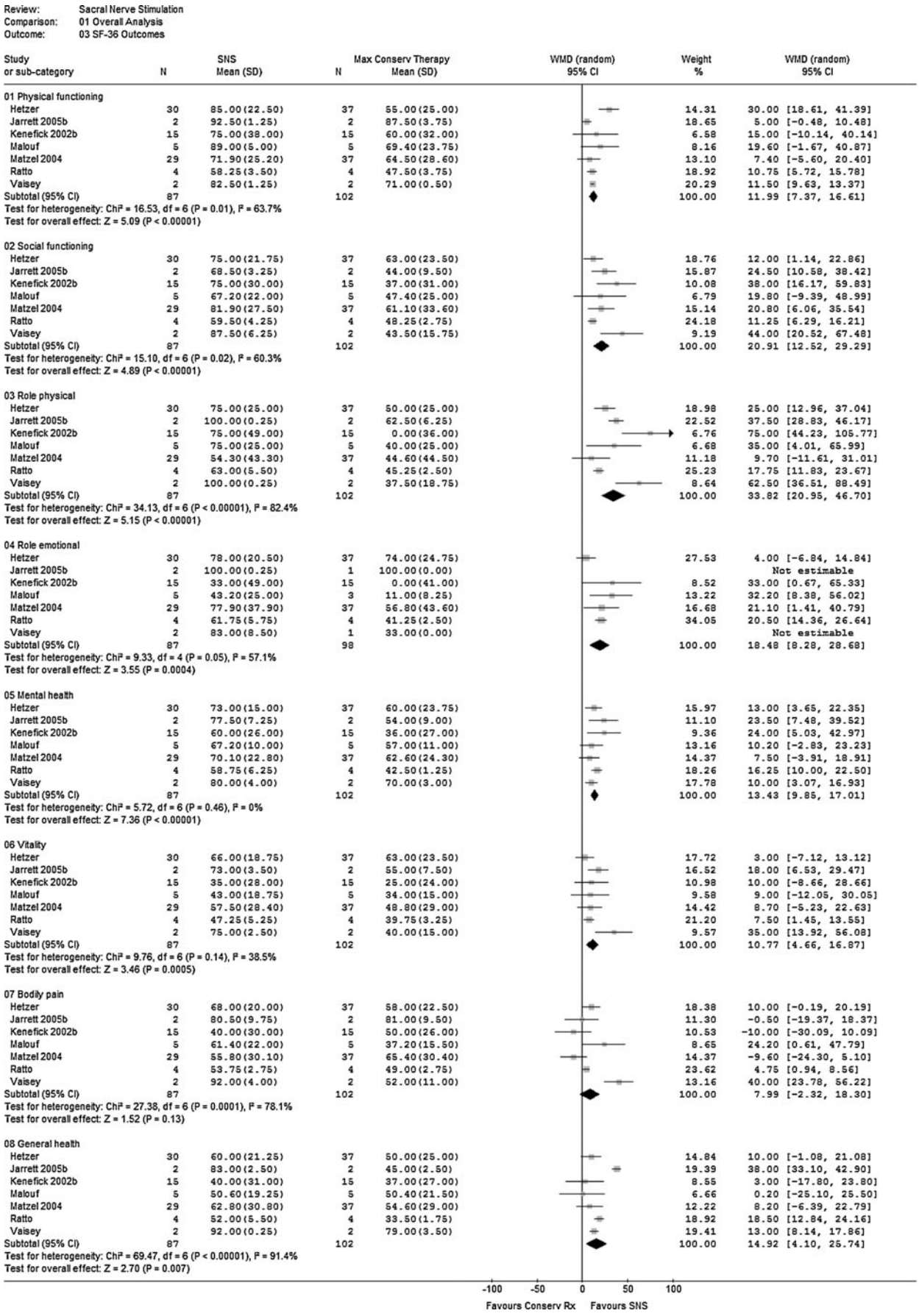


Fig. 2 Forest plot for overall analysis of functional outcomes

improvement in each of the subcategories with SNS. Overall, there was a significant increase in the SNS group in all subcategories: lifestyle 1.23 (95% CI 0.68, 1.78; $p<0.001$), coping/behaviour 1.28 (95% CI 0.96, 1.59; $p<0.001$), depression/self-perception 1.16 (95% CI 0.81, 1.50; $p<0.001$), embarrassment 1.41 (95% CI 0.86, 1.96; $p<0.001$).

Anal manometry and rectal sensitivity

Twenty-eight studies reported on resting pressure and 29 on squeeze pressure (Fig. 4a, b). Both were found to be significantly higher in the SNS group—resting pressure by 6.40 mmHg (95% CI 2.57, 10.22; $p<0.001$) and incremental


Review: Sacral Nerve Stimulation
Comparison: 01 Overall Analysis
Outcome: 03 SF-36 Outcomes
Study or sub-category | N | SNS Mean (SD) | N | Max Conserv Therapy Mean (SD) | WMD (random) 95% CI | Weight % | WMD (random) 95% CI
01 Physical functioning
Hetzer 30 85.00(22.50) 37 55.00(25.00) 14.31 30.00 [18.61, 41.39]
Jarrett 2005b 2 92.50(1.25) 2 87.50(3.75) 18.65 5.00 [-0.48, 10.48]
Kenefick 2002b 15 75.00(38.00) 15 60.00(32.00) 6.58 15.00 [-10.14, 40.14]
Malouf 5 89.00(5.00) 5 69.40(23.75) 8.16 19.60 [-1.67, 40.87]
Matzel 2004 29 71.90(25.20) 37 64.50(28.60) 13.10 7.40 [-5.60, 20.40]
Ratto 4 58.25(3.50) 4 47.50(3.75) 18.92 10.75 [5.72, 15.78]
Vaisey 2 82.50(1.25) 2 71.00(0.50) 20.29 11.50 [9.63, 13.37]
Subtotal (95% CI) 87 102 100.00 11.99 [7.37, 16.61]
Test for heterogeneity: Chi² = 16.53, df = 6 (P = 0.01), I² = 63.7%
Test for overall effect: Z = 5.09 (P < 0.00001)
02 Social functioning
Hetzer 30 75.00(21.75) 37 63.00(23.50) 18.76 12.00 [1.14, 22.86]
Jarrett 2005b 2 68.50(3.25) 2 44.00(9.50) 15.87 24.50 [10.58, 38.42]
Kenefick 2002b 15 75.00(30.00) 15 37.00(31.00) 10.08 38.00 [16.17, 59.83]
Malouf 5 67.20(22.00) 5 47.40(25.00) 6.79 19.80 [-9.39, 48.99]
Matzel 2004 29 81.90(27.50) 37 61.10(33.60) 15.14 20.80 [6.06, 35.54]
Ratto 4 59.50(4.25) 4 48.25(2.75) 24.18 11.25 [6.29, 16.21]
Vaisey 2 87.50(6.25) 2 43.50(15.75) 9.19 44.00 [20.52, 67.48]
Subtotal (95% CI) 87 102 100.00 20.91 [12.52, 29.29]
Test for heterogeneity: Chi² = 15.10, df = 6 (P = 0.02), I² = 60.3%
Test for overall effect: Z = 4.89 (P < 0.00001)
03 Role physical
Hetzer 30 75.00(25.00) 37 50.00(25.00) 18.98 25.00 [12.96, 37.04]
Jarrett 2005b 2 100.00(0.25) 2 62.50(6.25) 22.52 37.50 [28.83, 46.17]
Kenefick 2002b 15 75.00(49.00) 15 0.00(36.00) 6.76 75.00 [44.23, 105.77]
Malouf 5 75.00(25.00) 5 40.00(25.00) 6.68 35.00 [4.01, 65.99]
Matzel 2004 29 54.30(43.30) 37 44.60(44.50) 11.18 9.70 [-11.61, 31.01]
Ratto 4 63.00(5.50) 4 45.25(2.50) 25.23 17.75 [11.83, 23.67]
Vaisey 2 100.00(0.25) 2 37.50(18.75) 8.64 62.50 [36.51, 88.49]
Subtotal (95% CI) 87 102 100.00 33.82 [20.95, 46.70]
Test for heterogeneity: Chi² = 34.13, df = 6 (P < 0.00001), I² = 82.4%
Test for overall effect: Z = 5.15 (P < 0.00001)
04 Role emotional
Hetzer 30 78.00(20.50) 37 74.00(24.75) 27.53 4.00 [-6.84, 14.84]
Jarrett 2005b 2 100.00(0.25) 1 100.00(0.00) Not estimable
Kenefick 2002b 15 33.00(49.00) 15 0.00(41.00) 8.52 33.00 [0.67, 65.33]
Malouf 5 43.20(25.00) 3 11.00(8.25) 13.22 32.20 [8.38, 56.02]
Matzel 2004 29 77.90(37.90) 37 56.80(43.60) 16.68 21.10 [1.41, 40.79]
Ratto 4 61.75(5.75) 4 41.25(2.50) 34.05 20.50 [14.36, 26.64]
Vaisey 2 83.00(8.50) 1 33.00(0.00) Not estimable
Subtotal (95% CI) 87 98 100.00 18.48 [8.28, 28.68]
Test for heterogeneity: Chi² = 9.33, df = 4 (P = 0.05), I² = 57.1%
Test for overall effect: Z = 3.55 (P = 0.0004)
05 Mental health
Hetzer 30 73.00(15.00) 37 60.00(23.75) 15.97 13.00 [3.65, 22.35]
Jarrett 2005b 2 77.50(7.25) 2 54.00(9.00) 11.10 23.50 [7.48, 39.52]
Kenefick 2002b 15 60.00(26.00) 15 36.00(27.00) 9.36 24.00 [5.03, 42.97]
Malouf 5 67.20(10.00) 5 57.00(11.00) 13.16 10.20 [-2.83, 23.23]
Matzel 2004 29 70.10(22.80) 37 62.60(24.30) 14.37 7.50 [-3.91, 18.91]
Ratto 4 58.75(6.25) 4 42.50(1.25) 18.26 16.25 [10.00, 22.50]
Vaisey 2 80.00(4.00) 2 70.00(3.00) 17.78 10.00 [3.07, 16.93]
Subtotal (95% CI) 87 102 100.00 13.43 [9.85, 17.01]
Test for heterogeneity: Chi² = 5.72, df = 6 (P = 0.46), I² = 0%
Test for overall effect: Z = 7.36 (P < 0.00001)
06 Vitality
Hetzer 30 66.00(18.75) 37 63.00(23.50) 17.72 3.00 [-7.12, 13.12]
Jarrett 2005b 2 73.00(3.50) 2 55.00(7.50) 16.52 18.00 [6.53, 29.47]
Kenefick 2002b 15 35.00(28.00) 15 25.00(24.00) 10.98 10.00 [-8.66, 28.66]
Malouf 5 43.00(18.75) 5 34.00(15.00) 9.58 9.00 [-12.05, 30.05]
Matzel 2004 29 57.50(28.40) 37 48.80(29.00) 14.42 8.70 [-5.23, 22.63]
Ratto 4 47.25(5.25) 4 39.75(3.25) 21.20 7.50 [1.45, 13.55]
Vaisey 2 75.00(2.50) 2 40.00(15.00) 9.57 35.00 [13.92, 56.08]
Subtotal (95% CI) 87 102 100.00 10.77 [4.66, 16.87]
Test for heterogeneity: Chi² = 9.76, df = 6 (P = 0.14), I² = 38.5%
Test for overall effect: Z = 3.46 (P = 0.0005)
07 Bodily pain
Hetzer 30 68.00(20.00) 37 58.00(22.50) 18.38 10.00 [-0.19, 20.19]
Jarrett 2005b 2 80.50(9.75) 2 81.00(9.50) 11.30 -0.50 [-19.37, 18.37]
Kenefick 2002b 15 40.00(30.00) 15 50.00(26.00) 10.53 -10.00 [-30.09, 10.09]
Malouf 5 61.40(22.00) 5 37.20(15.50) 8.65 24.20 [0.61, 47.79]
Matzel 2004 29 55.80(30.10) 37 65.40(30.40) 14.37 -9.60 [-24.30, 5.10]
Ratto 4 53.75(2.75) 4 49.00(2.75) 23.62 4.75 [0.94, 8.56]
Vaisey 2 92.00(4.00) 2 52.00(11.00) 13.16 40.00 [23.78, 56.22]
Subtotal (95% CI) 87 102 100.00 7.99 [-2.32, 18.30]
Test for heterogeneity: Chi² = 27.38, df = 6 (P = 0.0001), I² = 78.1%
Test for overall effect: Z = 1.52 (P = 0.13)
08 General health
Hetzer 30 60.00(21.25) 37 50.00(25.00) 14.84 10.00 [-1.08, 21.08]
Jarrett 2005b 2 83.00(2.50) 2 45.00(2.50) 19.39 38.00 [33.10, 42.90]
Kenefick 2002b 15 40.00(31.00) 15 37.00(27.00) 8.55 3.00 [-17.80, 23.80]
Malouf 5 50.60(19.25) 5 50.40(21.50) 6.66 0.20 [-25.10, 25.50]
Matzel 2004 29 62.80(30.80) 37 54.60(29.00) 12.22 8.20 [-6.39, 22.79]
Ratto 4 52.00(5.50) 4 33.50(1.75) 18.92 18.50 [12.84, 24.16]
Vaisey 2 92.00(0.25) 2 79.00(3.50) 19.41 13.00 [8.14, 17.86]
Subtotal (95% CI) 87 102 100.00 14.92 [4.10, 25.74]
Test for heterogeneity: Chi² = 69.47, df = 6 (P < 0.00001), I² = 91.4%
Test for overall effect: Z = 2.70 (P = 0.007)
-100 -50 0 50 100
Favours Conserv Rx
Favours SNS

◀ **Fig. 3** **a** Forest plot for overall analysis of quality of life: SF-36 outcomes. **b** Forest plot for overall analysis of quality of life: FIQL outcomes

squeeze pressure by 16.19 mmHg (95% CI 9.40, 22.98; $p<0.001$). Figure 4b shows the forest plot for the meta-analysis of rectal sensitivity outcomes. Twenty-two studies reported on threshold, 21 on urge and 20 on maximum tolerable volumes. All showed a decrease with SNS, although this was only significant for threshold volume (WMD −6.53; 95% CI −12.46, −0.60; $p=0.03$). Decreases in urge volume −7.22 (95% CI −19.50, 5.07) and maximum tolerable volume −5.33 (95% CI −20.07, 9.42) did not reach statistical significance ($p=0.25$ and $p=0.48$, respectively).

Sensitivity analyses

Analysis of high-quality studies (≥7 stars, Table 4) mimicked the overall results in all outcomes except for SF-36 bodily pain, which showed no significant change. In all outcome measures, statistical heterogeneity was reduced. Interestingly, statistical significance was reached for the decrease in urge volume (WMD −14.68, 95% CI −25.22, −4.14; $p=0.006$) and maximum tolerable volume (WMD −20.48, 95% CI −29.96, −10.99; $p<0.001$) in the SNS group, with a reduction in statistical heterogeneity. Analysis of the large studies (≥20 patients undergoing permanent SNS, Table 5) also mimicked the overall results with a decrease in statistical heterogeneity.

Review: Sacral Nerve Stimulation
Comparison: 01 Overall Analysis
Outcome: 04 FIQL Outcomes

Study or sub-category	N	SNS Mean (SD)	N	Max Conserv Therapy Mean (SD)	WMD (random) 95% CI	Weight %	WMD (random) 95% CI
01 Lifestyle							
Holzer 2007	28	3.70(0.35)	36	2.20(0.45)		12.14	1.50 [1.30, 1.70]
Holzer 2008	5	4.00(0.45)	4	2.00(0.38)		10.39	2.00 [1.46, 2.54]
Jarrett 2005a	12	3.00(0.13)	12	2.90(0.18)		12.32	0.10 [-0.03, 0.23]
Jarrett 2005c	4	3.23(0.40)	4	2.30(0.68)		8.88	0.93 [0.16, 1.70]
Jarrett 2008	7	3.50(0.58)	7	2.00(0.53)		10.14	1.50 [0.92, 2.08]
Leroi 2005	19	3.20(0.53)	19	1.70(0.70)		11.27	1.50 [1.11, 1.89]
Matzel 2004	29	3.50(0.60)	37	2.70(0.90)		11.44	0.80 [0.44, 1.16]
Rosen	12	3.90(0.43)	20	2.10(0.45)		11.68	1.80 [1.49, 2.11]
Tjandra	53	3.31(0.72)	60	2.31(0.89)		11.75	1.00 [0.70, 1.30]
Subtotal (95% CI)	169		199			100.00	1.23 [0.68, 1.78]
Test for heterogeneity: Chi² = 245.49, df = 8 (P < 0.00001), I² = 96.7%							
Test for overall effect: Z = 4.41 (P < 0.0001)							
02 Coping/behaviour							
Holzer 2007	28	3.80(0.33)	36	2.00(0.30)		11.80	1.80 [1.64, 1.96]
Holzer 2008	5	3.60(0.30)	4	2.00(0.30)		10.86	1.60 [1.21, 1.99]
Jarrett 2005a	12	2.50(0.13)	12	1.60(0.20)		11.85	0.90 [0.77, 1.03]
Jarrett 2005c	4	2.68(0.43)	4	1.28(0.18)		10.52	1.40 [0.94, 1.86]
Jarrett 2008	7	2.00(0.65)	7	1.10(0.13)		10.32	0.90 [0.41, 1.39]
Leroi 2005	19	2.70(0.75)	19	1.50(0.45)		10.86	1.20 [0.81, 1.59]
Matzel 2004	29	2.80(0.90)	37	1.70(0.60)		10.93	1.10 [0.72, 1.48]
Rosen	12	3.70(0.28)	20	2.00(0.30)		11.66	1.70 [1.49, 1.91]
Tjandra	53	2.68(0.87)	60	1.86(0.88)		11.21	0.82 [0.50, 1.14]
Subtotal (95% CI)	169		199			100.00	1.28 [0.96, 1.59]
Test for heterogeneity: Chi² = 102.02, df = 8 (P < 0.00001), I² = 92.2%							
Test for overall effect: Z = 8.00 (P < 0.00001)							
03 Depression/self-perception							
Holzer 2007	28	3.70(0.25)	36	2.40(0.40)		12.25	1.30 [1.14, 1.46]
Holzer 2008	5	3.70(0.28)	4	2.20(0.40)		10.89	1.50 [1.04, 1.96]
Jarrett 2005a	12	3.20(0.13)	12	2.80(0.20)		12.31	0.40 [0.27, 0.53]
Jarrett 2005c	4	2.90(0.68)	4	1.20(0.10)		9.55	1.70 [1.03, 2.37]
Jarrett 2008	7	3.70(0.75)	7	2.10(0.60)		9.29	1.60 [0.89, 2.31]
Leroi 2005	19	3.60(0.60)	19	2.20(0.78)		11.01	1.40 [0.96, 1.84]
Matzel 2004	29	4.00(0.90)	37	2.80(1.00)		10.91	1.20 [0.74, 1.66]
Rosen	12	3.70(0.28)	20	2.60(0.35)		12.06	1.10 [0.88, 1.32]
Tjandra	53	3.25(0.80)	60	2.64(0.84)		11.74	0.61 [0.31, 0.91]
Subtotal (95% CI)	169		199			100.00	1.16 [0.81, 1.50]
Test for heterogeneity: Chi² = 105.50, df = 8 (P < 0.00001), I² = 92.4%							
Test for overall effect: Z = 6.57 (P < 0.00001)							
04 Embarrassment							
Holzer 2007	28	3.80(0.30)	36	1.80(0.35)		12.20	2.00 [1.84, 2.16]
Holzer 2008	5	3.80(0.35)	4	1.50(0.35)		10.86	2.30 [1.84, 2.76]
Jarrett 2005a	12	2.50(0.10)	12	2.00(0.20)		12.28	0.50 [0.37, 0.63]
Jarrett 2005c	4	3.85(0.40)	4	2.68(0.70)		8.74	1.17 [0.38, 1.96]
Jarrett 2008	7	2.70(0.75)	7	1.30(0.18)		10.17	1.40 [0.83, 1.97]
Leroi 2005	19	2.30(0.75)	19	1.30(0.50)		11.17	1.00 [0.59, 1.41]
Matzel 2004	29	3.00(0.90)	37	1.80(0.90)		10.99	1.20 [0.76, 1.64]
Rosen	12	3.80(0.40)	20	1.70(0.30)		11.86	2.10 [1.84, 2.36]
Tjandra	53	2.76(0.94)	60	1.78(0.61)		11.72	0.98 [0.68, 1.28]
Subtotal (95% CI)	169		199			100.00	1.41 [0.86, 1.96]
Test for heterogeneity: Chi² = 285.00, df = 8 (P < 0.00001), I² = 97.2%							
Test for overall effect: Z = 5.01 (P < 0.00001)							

-4 -2 0 2 4
Favours Conserv Rx Favours SNS

Fig. 3 (continued)

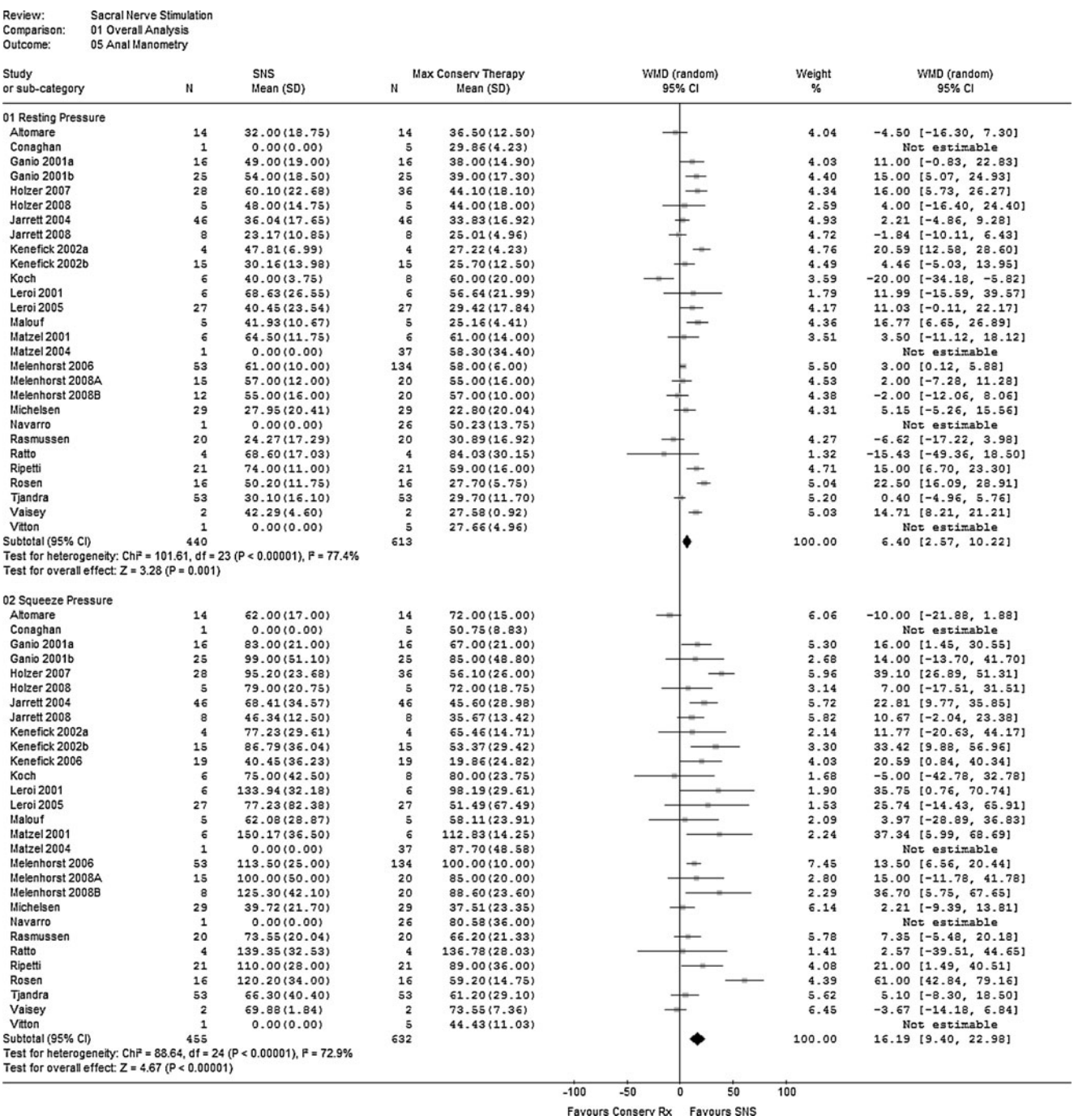


Fig. 4 **a** Forest plot for overall analysis of anal physiology: manometry. **b** Forest plot for overall analysis of anal physiology: rectal sensitivity

Subgroup-age

Fifteen studies reported a mean age <56 years and 19 reported a mean age≥56 (Tables 6 and 7). The improvements in weekly incontinence episodes, incontinence scores and ability to defer defecation were greater in the over-56 years group ($p<0.01$). The improvement in FIQL outcomes was greater in the under-56 years group ($p<0.02$). As only one study in the under-56 years group reported SF-36 outcomes, this was not considered. The increases in anal pressures were significantly higher in the under-56 years group ($p<0.01$).

Subgroup analysis of sphincter status

Five studies reported >75% of patients sphincter impaired and 18 reported 100% sphincter intact (Tables 8 and 9). The improvement in weekly incontinence episodes and incon-

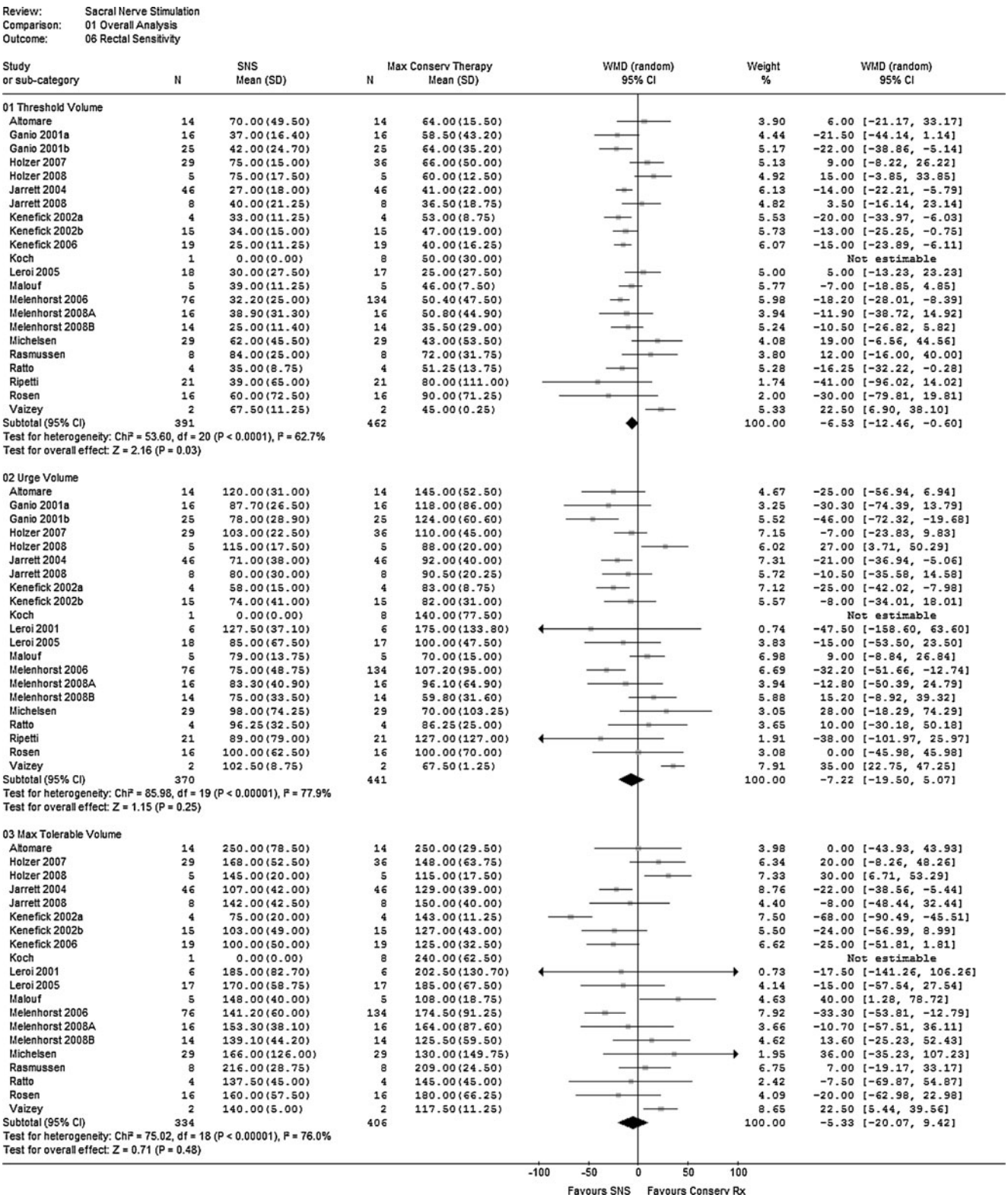


Fig. 4 (continued)

Table 4 Sensitivity analysis of SNS versus MCT—high-quality studies (≥7*)

Outcome of interest	No of studies	No of patients		WMD	95% CI	p value	HG Chi ^{2}	HG p value
		MCT	SNS					
Functional outcome								
Incontinence episodes/week	15	463	416	−6.42	−8.13, −4.71	<0.001	287.55	<0.001
Incontinence scores	7	179	168	−10.05	−12.02, −8.08	<0.001	63.56	<0.001
Deferring defecation (mins)	6	119	119	7.78	5.53, 10.03	<0.001	25.42	<0.001
SF-36 outcomes								
Physical functioning	3	89	74	18.11	1.87, 34.36	0.03	6.71	0.03
Social functioning	3	89	74	20.95	7.74, 34.15	0.002	4.53	0.10
Role physical	3	89	74	33.89	4.92, 62.86	0.02	11.99	0.002
Role emotional	3	89	74	14.90	−1.52, 31.32	0.08	4.34	0.11
Mental health	3	89	74	12.54	5.42, 19.67	<0.001	2.16	0.34
Vitality	3	89	74	5.78	−1.72, 13.28	0.13	0.66	0.72
Bodily pain	3	89	74	−1.76	−16.49, 12.97	0.81	6.12	0.05
General health	3	89	74	8.38	0.25, 16.50	0.04	0.34	0.84
FIQL outcome								
Lifestyle	4	124	101	1.27	0.78, 1.75	<0.001	21.18	<0.001
Coping/behaviour	4	124	101	1.15	0.66, 1.64	<0.001	26.31	<0.001
Depression/self-perception	4	124	101	1.05	0.70, 1.40	<0.001	10.63	0.01
Embarrassment	4	124	101	1.43	0.82, 2.04	<0.001	33.83	<0.001
Anal manometry								
Resting pressure (mmHg)	13	410	251	3.96	−0.87, 8.79	0.11	41.25	<0.001
Squeeze pressure (mmHg)	14	429	266	18.76	8.71, 28.81	<0.001	50.28	<0.001
Rectal sensitivity								
Threshold volume (ml)	10	298	240	−13.68	−17.91, −9.46	<0.001	6.91	0.65
Urge volume (ml)	9	279	221	−14.68	−25.22, −4.14	0.006	11.21	0.19
Max tolerable volume (ml)	9	282	224	−20.48	−29.96, −10.99	<0.001	6.01	0.65

tinence scores were greater in the sphincter intact group ($p<0.01$), but the increase in ability to defer defecation was greater in the sphincter impaired group ($p<0.01$). SF-36 and FIQL outcomes were not considered as there were no studies in the sphincter impaired group that reported on SF-36 and only one on FIQL. The change in resting pressure was significantly greater in the sphincter intact group ($p<0.01$), but there was no significant difference regarding squeeze pressure ($p=0.57$).

Other outcomes of interest

The most common complications among the 665 patients that underwent permanent SNS implantation were pain or local discomfort (37 cases, 6%), lead displacement or breakage (26 cases, 4%), infection (22 cases, 3%) and seroma (17 cases, 3%). Three of the 37 cases of pain were managed by analgesics; 22 were resolved by reprogramming, repositioning or reimplantation of the lead, and eight resulted in permanent removal of the implant. Of the 26 cases of lead displacement or breakage, 22 were resolved by repositioning or replacement, and two resulted in permanent removal. Of the 22 cases of infection, two were resolved by antibiotics; ten required removal and reimplantation of the electrode, and eight resulted in permanent removal. Eight of the 17 cases of seroma were managed by antibiotics, three were drained and one resolved spontaneously.

In the 944 patients who underwent PNE, the most common complications during testing were infection or seroma (20 cases, 2%) and lead displacement or breakage (30 cases, 3%). All cases of infection or seroma were treated with antibiotics, and 15 had the temporary lead removed. Eighteen of the 30 cases of lead displacement or breakage were successfully re-tested with a new extension, and one proceeded to permanent implantation without re-testing.

Sixteen studies reported PNTML results [36, 43, 44, 46, 47, 51–55, 57, 61, 62, 64–66]. However, only five of these studies [54, 55, 57, 61, 65] reported actual times, with the

Table 5 Sensitivity analysis of SNS versus MCT—study size≥20 patients for permanent SNS

Outcome of interest	No of studies	No of patients		WMD	95% CI	*p* Value	HG chi-square	HG *p* value
		MCT	SNS					
Functional outcome								
Incontinence episodes/week	11	458	411	−6.41	−8.58, −4.24	<0.001	173.10	<0.001
Incontinence scores	7	225	218	−9.81	−11.66, −7.96	<0.001	71.21	<0.001
Deferring defecation (mins)	4	105	98	7.30	3.17, 11.43	<0.001	38.64	<0.001
SF-36 outcomes								
Physical functioning	2	74	59	18.93	−3.22, 41.07	0.09	6.57	0.01
Social functioning	2	74	59	15.09	6.35, 23.84	<0.001	0.89	0.35
Role physical	2	74	59	19.98	5.90, 34.06	0.005	1.50	0.22
Role emotional	2	74	59	10.49	−5.77, 26.76	0.21	2.22	0.14
Mental health	2	74	59	10.79	3.56, 18.02	0.003	0.53	0.46
Vitality	2	74	59	4.97	−3.22, 13.15	0.23	0.42	0.52
Bodily pain	2	74	59	0.94	−18.21, 20.10	0.92	4.62	0.03
General health	2	74	59	9.34	0.52, 18.17	0.04	0.04	0.85
FIQL outcome								
Lifestyle	4	152	129	1.21	0.86, 1.56	<0.001	16.15	0.001
Coping/behaviour	4	152	129	1.24	0.72, 1.77	<0.001	37.52	<0.001
Depression/self-perception	4	152	129	1.12	0.75, 1.49	<0.001	16.74	<0.001
Embarrassment	4	152	129	1.31	0.68, 1.93	<0.001	52.08	<0.001
Anal manometry								
Resting pressure (mmHg)	11	448	285	2.97	−0.27, 6.21	0.07	13.39	0.10
Squeeze pressure (mmHg)	11	448	281	16.63	7.76, 25.50	<0.001	26.81	<0.001
Rectal sensitivity								
Threshold volume (ml)	8	300	236	−4.19	−13.42, 5.04	0.37	18.11	0.01
Urge volume (ml)	7	292	228	−9.95	−23.95, 4.05	0.16	13.46	0.04
Max tolerable volume (ml)	8	300	235	−5.75	−22.11, 10.61	0.49	15.92	0.03

rest only reporting the number of patients that had uni- or bi-lateral pudendal neuropathy. None of the studies analysed the results according to pudendal neuropathy, but three studies [54, 64, 65] reported that baseline PNTML had no correlation with clinical outcome of SNS.

One study (Hetzer et al. 2006 [69]), not included in the meta-analysis, investigated the cost of SNS compared with other interventions for FI. The authors reported that the 5-year cumulative cost for SNS was €22,150 per patient, compared with €33,996 for colostomy, €31,590 for dynamic graciloplasty and €3234 for conservative treatment.

Publication bias

A "funnel plot" of the studies reporting on the SF-36 outcomes for conservative therapy versus SNS is shown in Fig. 5a. This is a scatter plot of the treatment effect estimated from individual studies plotted on the horizontal axis (WMD), against the standard error of the estimate shown on the vertical axis (SE[WMD]) [30]. Twelve studies are shown to lie outside the 95% confidence intervals, with an even distribution around the vertical. When only large studies were considered (Fig. 5b), only three studies lie outside the 95% confidence intervals, with an even distribution around the vertical, showing little evidence of publication bias.

Discussion

The results of this meta-analysis demonstrate that SNS can be a highly effective treatment for FI, improving both functional and quality of life outcomes in patients where MCT has failed. Patients with intact sphincters and those with varying degrees of sphincter impairment were assessed. All studies reported an improvement in functional outcome measures following SNS implantation.

These results show an increase in both resting and squeeze pressures following SNS implantation. However, the increase in resting pressure does not reach statistical

Table 6 Subgroup analysis of SNS versus MCT—age <56 years

Outcome of interest	No of studies	No of patients		WMD	95% CI	*p* Value	HG Chi-square	HG *p* value
		MCT	SNS					
Functional outcome								
Incontinence episodes/week	11	230	197	−4.53	−6.24, −2.82	<0.001	309.29	<0.001
Incontinence scores	4	39	33	−9.97	−13.21, −6.74	<0.001	20.87	<0.001
Deferring defecation (mins)	5	88	81	5.44	3.66, 7.22	<0.001	6.89	0.14
SF-36 outcomes								
Physical functioning	1	37	29	7.40	−5.60, 20.40	0.26	–	–
Social functioning	1	37	29	20.80	6.06, 35.54	0.006	–	–
Role physical	1	37	29	9.70	−11.61, 31.01	0.37	–	–
Role emotional	1	37	29	21.10	1.41, 40.79	0.04	–	–
Mental health	1	37	29	7.50	−3.91, 18.91	0.20	–	–
Vitality	1	37	29	8.70	−5.23, 22.63	0.22	–	–
Bodily pain	1	37	29	−9.60	−24.30, 5.10	0.20	–	–
General health	1	37	29	8.20	−6.39, 22.79	0.27	–	–
FIQL outcome								
Lifestyle	4	100	76	1.40	1.00, 1.80	<0.001	17.39	<0.001
Coping/behaviour	4	100	76	1.44	1.09, 1.79	<0.001	20.73	<0.001
Depression/self-perception	4	100	76	1.24	1.11, 1.37	<0.001	3.10	0.38
Embarrassment	4	100	76	1.74	1.38, 2.10	<0.001	16.36	0.001
Anal manometry								
Resting pressure (mmHg)	13	219	154	7.89	1.05, 14.73	0.02	41.03	<0.001
Squeeze pressure (mmHg)	13	219	150	25.25	9.67, 40.84	0.001	58.92	<0.001
Rectal sensitivity								
Threshold volume (ml)	8	150	143	−7.03	−17.33, 3.27	0.18	10.92	0.14
Urge volume (ml)	9	156	149	−13.68	−27.56, 0.19	0.05	13.57	0.09
Max tolerable volume (ml)	7	110	103	3.00	−12.60, 18.60	0.71	3.51	0.74

significance when only high quality and large studies are analysed. The forest plot in Fig. 5 shows that some studies, despite reporting an improved functional outcome, reported minimal or no change in resting pressure. The increased squeeze pressure remains significant across all other subgroup analyses. Whilst the mechanism of action of SNS remains unclear, the present study adds substance to the original hypothesis that direct action on the anal sphincter to increase pressure may be responsible for the improvement in continence [21].

This however is unlikely to be the sole mechanism as some studies showed no significant change in resting or squeeze pressure with stimulation [34, 42, 50, 53, 60, 64], whilst recording clinical improvement. Interestingly, Melenhorst et al [57] showed a significant increase in squeeze pressure only in the sphincter impaired and not the sphincter intact group. However, there was no significant difference in either pressure between the two groups when compared. If enhanced rectal motor function does in fact play a role, it is most likely mediated by a combination of muscle hypertrophy, changes in fibre type (transformation of type II fast-twitch fatigable fibres into type I slow-twitch fatigue-resistant fibres [70]) and recruitment of atrophic motor units [49].

As well as the influence on rectal motor function, it may be that SNS influences rectal sensory function. This meta-analysis has shown an increase in rectal sensitivity as demonstrated by decreased balloon distension for threshold, urge and maximal tolerable volumes. In the present study values reached statistical significance when analysing high-quality studies only. One study not included in this meta-analysis [71] also demonstrated an increase in rectal sensitivity. This improved sensation may contribute to an increased awareness of rectal content, and hence continence. There was however significant heterogeneity among the studies. However, it should be noted that a patient's sensation on testing may be different from the feeling of urgency due to distension. Hence, the value of rectal sensitivity in assessing functional outcome after SNS is still in question.

Table 7 Subgroup analysis of SNS versus MCT—age ≥56 years

Outcome of interest	No of studies	No of patients		WMD	95% CI	*p* Value	HG chi-square	HG *p* value
		MCT	SNS					
Functional outcome								
Incontinence episodes/week	17	392	377	−8.39	−9.75, −7.02	<0.001	77.88	<0.001
Incontinence scores	10	250	239	−10.74	−12.27, −9.20	<0.001	79.89	<0.001
Deferring defecation (mins)	4	77	77	9.55	8.22, 10.87	<0.001	5.43	0.14
SF-36 outcomes								
Physical functioning	6	65	58	12.57	7.51, 17.63	<0.001	16.19	0.006
Social functioning	6	65	58	21.44	11.64, 31.24	<0.001	14.47	0.01
Role physical	6	65	58	37.63	23.59, 51.66	<0.001	31.84	<0.001
Role emotional	6	61	58	18.48	5.93, 31.03	0.004	9.22	0.03
Mental health	6	65	58	14.08	10.31, 17.84	<0.001	4.57	0.47
Vitality	6	65	58	11.44	4.20, 18.67	0.002	9.74	0.08
Bodily pain	6	65	58	11.01	−0.18, 22.20	0.05	22.92	<0.001
General health	6	65	58	15.93	4.18, 27.69	0.008	66.15	<0.001
FIQL outcome								
Lifestyle	5	99	93	1.09	0.34, 1.85	0.005	102.56	<0.001
Coping/behaviour	5	99	93	1.15	0.86, 1.43	<0.001	16.13	0.003
Depression/self-perception	5	99	93	1.07	0.56, 1.58	<0.001	45.79	<0.001
Embarrassment	5	99	93	1.17	0.58, 1.75	<0.001	62.90	<0.001
Anal manometry								
Resting pressure (mmHg)	15	394	286	5.37	0.75, 9.99	0.02	53.68	<0.001
Squeeze pressure (mmHg)	16	413	305	10.28	5.07, 15.50	<0.001	20.66	0.11
Rectal sensitivity								
Threshold volume (ml)	14	312	248	−6.10	−13.43, 1.23	0.10	42.18	<0.001
Urge volume (ml)	12	285	221	−2.11	−19.69, 15.46	0.81	67.14	<0.001
Max tolerable volume (ml)	13	296	231	−7.27	−26.96, 12.43	0.47	69.37	<0.001

The wide range of patients and consistently positive results in functional outcomes suggest that a placebo effect [52] is unlikely. This is reinforced by similarly positive results with the presence of a control group in the only RCT to date [64]. Further RCTs would be useful in confirming this, although the randomisation of potential SNS candidates into a conservative therapy group has ethical implications. Further cross-over trials may be possible, however.

Regardless of its mechanism of action, the objective improvement in continence described above also translates into subjective improvement in most cases. All subcategories of both questionnaires showed a significant improvement, with the exception of bodily pain (p=0.13). This could be explained as nearly 6% of patients in the analysed studies reported pain following permanent implantation, perhaps relating to the formation of a subcutaneous pocket or the subsequent electrical stimulation of sensory and motor nerves. The improvement in quality of life was commensurate with the improved continence.

Subgroup analysis of age showed a smaller objective improvement in the under-56 years group compared with the over-56 years group, despite a greater increase in anal pressures and a greater subjective improvement in the under-56 years group. Reasons for the more modest objective improvement could relate to the baseline levels. Younger patients with a better physical recovery capacity may have slightly improved continence already following treatment with current medical and biofeedback therapy. They would therefore have less to gain functionally from SNS compared with slightly older patients. This is even more likely in patients with previous surgical repair, where younger patients with a more recent repair will already have some degree of improvement. Conversely, they may have an injury so severe that complete recovery may be impossible. Older patients with co-morbidities are likely to have more significant baseline incontinence and thus have more to gain functionally. The greater increase in pressures in the younger patients can be attributed to a greater functional capacity and thus a greater reserve, which may then be recruited by SNS.

Table 8 Subgroup analysis of SNS versus MCT—sphincter impaired

Outcome of interest	No of studies	No of patients		WMD	95% CI	*p* Value	HG chi-square	HG *p* value
		MCT	SNS					
Functional outcome								
Incontinence episodes/week	4	71	71	−4.07	−6.98, −1.16	0.006	11.76	0.008
Incontinence scores	2	35	35	−7.32	−9.50, −5.14	<0.001	1.40	0.24
Deferring defecation (mins)	2	53	53	14.85	0.24, 29.46	0.05	2.46	0.12
SF-36 outcomes								
Physical functioning	0	–	–	–	–	–	–	–
Social functioning	0	–	–	–	–	–	–	–
Role physical	0	–	–	–	–	–	–	–
Role emotional	0	–	–	–	–	–	–	–
Mental health	0	–	–	–	–	–	–	–
Vitality	0	–	–	–	–	–	–	–
Bodily pain	0	–	–	–	–	–	–	–
General health	0	–	–	–	–	–	–	–
FIQL outcome								
Lifestyle	1	7	7	1.50	0.92, 2.08	<0.001	–	–
Coping/behaviour	1	7	7	0.90	0.41, 1.39	<0.001	–	–
Depression/self-perception	1	7	7	1.60	0.89, 2.31	<0.001	–	–
Embarrassment	1	7	7	1.40	0.83, 1.97	<0.001	–	–
Anal manometry								
Resting pressure (mmHg)	5	84	68	−0.05	−4.79, 4.68	0.98	0.72	0.70
Squeeze pressure (mmHg)	5	84	64	19.21	7.28, 31.15	0.002	3.20	0.20
Rectal sensitivity								
Threshold volume (ml)	3	68	68	−10.18	−18.94, −1.41	0.02	2.61	0.27
Urge volume (ml)	3	68	68	−6.72	−28.26, 14.82	0.54	6.02	0.05
Max tolerable volume (ml)	3	68	68	−11.61	−31.93, 8.71	0.26	2.88	0.24

Subgroup analysis of sphincter status showed a significantly greater improvement in incontinence episodes, scores and resting pressures in the intact group, with a greater improvement in ability to defer defecation in the impaired group. This is most likely attributable to poor baseline ability to defer defecation that would be expected in patients with sphincter impairment. Despite the greater improvement in the intact group for the other outcomes, there is still significant improvement overall for the sphincter impaired group. This suggests that SNS also has a role to play in these patients, as demonstrated by three of the studies in this meta-analysis [35, 42, 57]. Indeed, Melenhorst et al. [57] showed no significant differences in outcome measures between the two groups. The effectiveness of SNS for sphincter impaired patients also suggests that rectal motor function is probably not the sole mechanism of action of SNS.

As well as its benefits compared with conservative therapy as demonstrated by this meta-analysis, SNS has advantages over other surgical procedures for the treatment of FI. It has been demonstrated to be cost-effective relative to other surgical interventions [69], with further cost reductions possible through strict patient selection. SNS has a unique advantage with regards to patient selection as PNE offers a quick, safe and minimally invasive technique to predict the outcome of permanent implantation, thus allowing only patients who will potentially benefit to proceed.

The results of this meta-analysis show a complication rate of less than 15% in the 665 patients that received a permanent implant, most of which were resolved. Only 3% resulted in permanent explantation. This is comparable with previous reports on SNS complications [22]. SNS is associated with a lower morbidity compared with more invasive alternatives, such as sphincter repair or dynamic graciloplasty [42, 72], which can be associated with up to 42% rate of peri- and post-operative complications [72].

Other than PNE, there appears to be little value in other predictive tests for SNS outcome. Three studies in this meta-analysis reported no correlation between baseline

Table 9 Subgroup analysis of SNS versus MCT—sphincter intact

Outcome of interest	No of studies	No of patients		WMD	95% CI	*p* Value	HG chi-square	HG *p* value
		MCT	SNS					
Functional outcome								
Incontinence episodes/week	14	334	300	−7.02	−8.67, −5.38	<0.001	303.99	<0.001
Incontinence scores	5	61	51	−12.03	−13.96, −10.11	<0.001	18.15	0.001
Deferring defecation (mins)	4	72	65	6.54	3.76, 9.31	<0.001	21.03	<0.001
SF-36 outcomes								
Physical functioning	4	45	37	9.74	6.63, 12.85	<0.001	5.11	0.16
Social functioning	4	45	37	21.90	9.95, 33.85	<0.001	10.40	0.02
Role physical	4	45	37	30.04	13.23, 46.84	<0.001	23.70	<0.001
Role emotional	4	43	37	20.55	14.69, 26.42	<0.001	0.00	0.95
Mental health	4	45	37	13.30	7.99, 18.60	<0.001	4.28	0.23
Vitality	4	45	37	14.41	4.83, 23.99	0.003	7.80	0.05
Bodily pain	4	45	37	8.40	−8.41, 25.20	0.33	21.97	<0.001
General health	4	45	37	20.06	6.44, 33.68	0.004	58.62	<0.001
FIQL outcome								
Lifestyle	5	109	86	1.23	0.41, 2.05	0.003	221.35	<0.001
Coping/behaviour	5	109	86	1.42	0.98, 1.87	<0.001	88.62	<0.001
Depression/self-perception	5	109	86	1.08	0.61, 1.55	<0.001	87.57	<0.001
Embarrassment	5	109	86	1.61	0.78, 2.45	<0.001	280.57	<0.001
Anal manometry								
Resting pressure (mmHg)	14	339	182	8.69	2.35, 15.02	0.007	68.26	<0.001
Squeeze pressure (mmHg)	14	339	182	18.72	7.06, 30.39	0.002	55.14	<0.001
Rectal sensitivity								
Threshold volume (ml)	11	266	194	−7.92	−19.20, 3.36	0.17	36.83	<0.001
Urge volume (ml)	11	266	194	−7.64	−28.17, 12.88	0.47	70.22	<0.001
Max tolerable volume (ml)	9	225	153	−8.15	−36.52, 20.21	0.57	59.60	<0.001

PNTML and SNS outcome [54, 64, 65], and it appears that there is limited value in PNTML as a predictive test [22, 54, 64]. However, controversy still surrounds this issue, with some studies reporting a poor PNE result in patients with complete pudendal lesions [36].

This meta-analysis is the largest to date of its kind, with nearly 800 analysed patients across 34 studies, including some of the most recently published work in this field [41, 42, 57, 64]. This large number of patients would be almost impossible to gather in a single trial. Despite this, there are limitations to this meta-analysis. Only one of the studies [64] analysed was an RCT. Many of the studies were small in size and non-randomised, thus patients and results may not reflect the true population, while non-randomisation may give rise to selection bias. There was also significant heterogeneity in some results, but this was minimised with the subgroup and sensitivity analyses.

SNS is a relatively new procedure, which in itself leads to potential limitations in a meta-analysis. Positive findings are much more likely to be published than negative results, giving rise to a degree of publication bias. There is also a lack of data on long-term outcomes and complications since SNS has only been performed since 1995.

More research with larger patient groups is needed to determine the precise mode of effect of SNS for different patient demographics and aetiologies. Future research could be directed towards comparing outcomes in different age groups and in incontinence from different aetiologies. Long-term adverse events also need to be monitored, although this is best achieved using a national registry database [19]. Research into alternative predictive factors for SNS success may complement PNE to ensure strict patient selection for permanent implantation, thus reducing cost and improving outcome. Research into the central and local mechanisms of action may lead to an improved understanding and therefore allow a more evidence-based selection of patients.

SNS modulates the extrinsic neural supply to the distal bowel and modulates the contractility of the external anal sphincter and pelvic floor musculature. It is already an

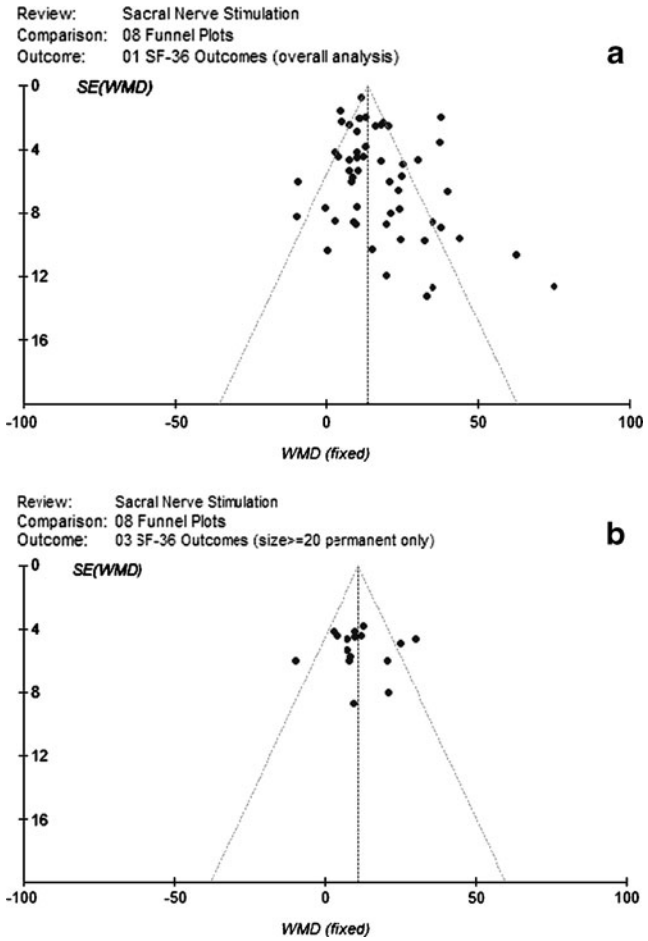


Fig. 5 Funnel plot illustrating **a** overall meta-analysis of SF-36 outcomes, and **b** effect of sensitivity analysis: studies of size≥20 patients for permanent SNS

established therapy for faecal and urinary incontinence. Its effectiveness cannot solely be due to motor stimulation, since patients are not likely to tolerate voltages at which skeletal muscle contracts forcefully. While inserting the SNS electrodes, high voltages (between 6–10 V) are often applied to assess optimal position with visualisation of sphincter and pelvic floor contraction. In practice, patients are likely to tolerate much lower voltages and only maintain stimulation at a baseline sensory threshold. Voltages at which large-scale voluntary muscle contraction take place would not be tolerated. It has been postulated that modulation of afferent and autonomic pathways, and hence cerebral activity, all occur with SNS. The complexity of these pathways requires further evaluation.

Conclusion

Meta-analysis has shown that SNS improves functional outcomes and quality of life in faecally incontinent patients where conventional non-surgical therapies have failed. Benefits are maintained even in patients with anal sphincter disruption. SNS is associated with a reduced complication rate and cost compared with more invasive surgical interventions for these patients. More research is needed into its mechanism of action, factors predictive of success, long-term outcomes and which patient demographics and aetiologies benefit most.

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