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NATIONAL INSTITUTE FOR CLINICAL EXCELLENCE

REVIEW BODY REPORT

Title	Systematic review of the efficacy and safety of sacral nerve stimulation for faecal incontinence
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The Health Services Research Unit (HSRU), University of Aberdeen is core-funded by the Chief Scientist Office of the Scottish Executive Health Department, and has responsibility for the following general remit:

1. To study or evaluate clinical activities with a view to improving effectiveness and efficiency in health care;
2. To work for the implementation of proven changes in clinical activities;
3. To encourage and support similar work throughout Scotland;
4. To train NHS staff in Scotland, and others, in the principles and practice of health services research in general, and health care evaluation in particular.

In pursuit of this remit, the Unit has established a portfolio of health services research focusing on two main programmes – health care assessment and delivery of care.

Contributions of review team and clinical advisors

Graham Mowatt screened the search results, assessed full text studies for inclusion, undertook data abstraction and quality assessment, and drafted parts of the review. Cathryn Glazener screened the search results, provided advice on analysis and interpretation of data and commented on drafts of the review. Cynthia Fraser developed and ran the search strategies, obtained papers and formatted the references. Adrian Grant and Michael Kamm took overall responsibility for the systematic reviewing and clinical aspects, respectively. They were involved in scoping the review, commenting on the protocol, and contributed to the writing of the report. Michael Jarrett provided clinical advice, helped assess the full text studies for inclusion, and also contributed to the writing of the report.

Moderation

Liz Cross and Yolanda Bravo repeated the data extraction to validate the results. Jon Nicholl moderated a small number of disagreements and re-drafted the results, discussion and conclusions to reflect his interpretation of the data which has been reviewed.

Conflict of interest

The first version of this review was undertaken under the auspices of the section of the Review Body for Interventional Procedures Programme based within the University of Aberdeen. During the course of their work, that group sought expert clinical advice from Professor Michael Kamm and Mr Michael Jarrett, both at St Marks Hospital London. Professor Kamm acted to assist Professor Adrian Grant (review team leader in Aberdeen) on the clinical aspects of the procedure. Mr Jarrett's involvement however was more substantial in that he helped assessed the full text studies for inclusion, duplicated some of the data extraction that was being undertaken in Aberdeen and also went on to assist with drafting sections of the report.

When the completed report was first presented to the Interventional Procedures Advisory Committee in December 2003 concerns were expressed by committee members that there was a potential conflict of interest because both Professor Michael Kamm and Mr Michael Jarrett are authors of a study included in the review describing the UK experience of sacral nerve stimulation for faecal incontinence. This study received financial support from Medtronic Inc, the company that make the equipment for sacral nerve stimulation used by St Mark's and other hospitals, and provide training in its use. The funding is in the form of an unrestricted research financial grant to St Mark's Hospital Physiology Unit although study designs, performance, analysis and reporting have been conducted without the influence of Medtronic. The committee therefore sought reassurance that there was no bias in the reporting because of the concerns they had about the involvement of Professor Michael Kamm and Mr Michael Jarrett.

For this reason, the Sheffield partner of the Review Body independently performed a 'blind' extraction of data from the papers originally included using two reviewers working separately and then subjected these two new sets of data to a comparison with the data extraction from Aberdeen. This work was led by Professor Jon Nicholl of Sheffield University, Acting Project Director for the Review Body. In the light of this, Professor Nicholl then moderated reporting of the findings, and revised the text of the report.

At the conclusion of this process no substantial differences were found between the data as utilised by Aberdeen in their draft of the report and the data as independently

extracted by reviewers in Sheffield. A number of changes were made to the text to reflect the differences in data that were noted and to remove any ambiguous or unclear phrasing.

The review reported here is the revised version of the report. It was presented to the Interventional Procedures Advisory Committee in May 2004, and it was this version that was considered by the Committee when it made recommendations about this procedure to NICE.

Acknowledgements

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EXECUTIVE SUMMARY

Background

Faecal incontinence is a socially embarrassing and physically disabling condition. It may result from damage to the anal sphincter mechanism, idiopathic degeneration of the sphincter, spinal injury or other neurological causes. In the UK major faecal incontinence affects an estimated 1.4% of the population over 40 years of age.

Treatment is initially conservative, consisting of dietary advice, anti-diarrhoeal medication and physical and behavioural therapy. While such measures are effective in the majority of patients, those with persistent, severe incontinence may be offered more invasive treatment. Surgical intervention has been the next step in the management of these patients. Overlapping sphincter repair may be undertaken for external anal sphincter defects; early results have shown good symptomatic relief but tend to deteriorate over time. Dynamic graciloplasty and artificial bowel sphincter implants may improve continence, but require major surgery and have high morbidity and failure rates. Permanent stoma placement is another surgical option.

Sacral nerve stimulation (SNS) is a relatively new, minimally invasive approach to the management of faecal incontinence. It involves applying a low voltage electrical current to a sacral nerve via an electrode, placed through the corresponding sacral foramen. Commonly, the procedure is tested in each patient, over a two to three week period, with a temporary percutaneous peripheral nerve electrode attached to an external stimulator. If significant benefit is achieved, then the definitive implantable pulse generator (IPG) can be implanted

Number and quality of included studies

Thirty-one reports were identified (including 13 abstracts) that met our inclusion criteria. Many of these papers were updates on essentially the same patients reported in other papers but with a longer follow-up and with some additional cases. We included only the most recent report (published or unpublished) from each country, resulting in the inclusion of six prospective case series. In addition, a small UK-based double-blind

crossover study and a European multicentre study (MDT-301) were considered separately in the review as at least some of these patients would also have been included in the individual country studies.

The six case series were set in: Austria, France, Germany, Italy, Netherlands and the UK. In all, 266 patients were enrolled and received peripheral nerve evaluation (PNE), with 149 (56%) going on to receive permanent implants following positive test stimulation. The period of follow-up in the studies ranged from six months to a maximum of 99 months.

Two patients took part in a UK double-blind crossover trial. This consisted of two two-week periods, with each patient's stimulator being turned on for two weeks and off for two weeks or vice-versa. The MDT-301 European multicentre study, a prospective non-randomised trial, included 37 patients, of whom 34 (92%) went on to receive permanent implants. The study covered the period from January 1999 to June 2001, with a mean follow-up of 21.3 months.

In the six case series, all of the patients had previously received maximal conservative therapy. Follow-up was long enough to assess whether effects were sustained over some months. In five out of six studies the participants were considered to be a representative sample of the range of patient groups who might benefit from SNS; in the sixth study 75% of participants had faecal incontinence of neurological origin. In five studies the inclusion and/or exclusion criteria were clearly specified, important prognostic indicators were identified, and objective outcome measures were used. In four studies the recruitment period was clearly stated, all outcomes considered to be important for the review were reported, and the main findings were clearly described. Patient selection was consecutive in two studies.

The small UK crossover study was assessed as a randomised or quasi-randomised study. The main investigator and the patients were blinded as to the status of the stimulators. As with the case series, the MDT-301 study met most of the criteria in the checklist for case series, except that it was unclear whether patient selection was consecutive and outcomes assessors were blinded.

Summary of evidence of efficacy

Following permanent implantation, 41-75% of patients achieved complete faecal continence and 75-100% experienced an improvement of 50% or more in the number of faecal incontinence episodes. All studies reported a decrease in the number of episodes of incontinence per week, with statistical significance achieved in four studies (including the MDT-301 study). Five studies reported an improvement in the ability to defer defaecation, with two, including MDT-301, achieving statistical significance. All three studies using the Cleveland Clinic Incontinence Score demonstrated statistically significant improvements.

Five studies employing the American Society of Colon and Rectal Surgery (ASCRS) faecal incontinence quality of life instrument reported improvements in all categories (reaching statistical significance in three studies, including MDT-301). Short Form (SF) 36 Health Survey quality of life data were reported for three studies, including MDT-301. In two studies all categories of the SF-36 either stayed the same or improved, with one study reporting statistically significant improvements in the categories of general health, vitality, social functioning, role-emotional and mental health. The MDT-301 study noted statistically significant improvements in social function and mental health.

Of studies reporting anal manometry data, there was a statistically significant increase in maximal resting pressure in one study and in maximal squeeze pressure in three. Following permanent implantation, three studies reported the rectum becoming more sensitive to balloon distention with air at threshold, urge and maximal tolerated volumes, with one study reporting statistical significance at all three points. One study indicated no change in anal manometry data and such measurements went largely unreported in the MDT-301 study.

Summary of evidence of safety

Of 266 patients receiving PNE, ten (4%) experienced an adverse event. Lead dislodgement occurred in nine patients and a superficial skin infection occurred in one patient at the site the PNE lead exited the skin. All PNE adverse events were resolved on removal of the test stimulation apparatus. The MDT-301 study reported nine of 37

patients tested (24%) developing an infection. All were treated with antibiotics, and eight proceeded to permanent IPG implantation.

Amongst 149 patients receiving permanent implants, 19 adverse events were reported. Three patients from the same centre developed infections of their implants, requiring device removal in each case. Eight leads dislodged in seven patients; five were relocated, one of which dislodged a second time and was removed. One IPG was removed as the patient was unwilling to have the electrode relocated and one case had yet to be addressed. An interruption of the electrode lead occurred in one patient, necessitating replacement. A superficial wound dehiscence experienced by one patient healed uneventfully.

Six patients complained of pain. Three patients experienced pain from the leads running subcutaneously over the iliac crest to the IPG, which was placed in the abdominal wall; injection of local anaesthetic and steroid resolved the problem in all cases. One patient experienced pain from the IPG when it had been set as the anode; this settled on reprogramming of the IPG with the external telemetry device. The pain characteristics and management of two patients remained unspecified.

Of the 34 permanently implanted patients in the MDT-301 study, one developed an infection of the IPG, requiring removal. There were ten episodes of pain in nine patients. In four patients, pain settled with reprogramming, in three by repositioning the IPG and in one by medication, while two episodes were unspecified. A broken lead in one patient was replaced. Of three patients who experienced deterioration in bowel symptoms, one improved, one had the IPG removed and the outcome for the third patient was unspecified.

Conclusions

Six case series from different European countries were included. In addition, a European multicentre study and a UK-based double-blind crossover trial containing at least some patients also included in the six studies by country were also included but considered separately. The direction of evidence from each of these studies was consistent with permanent SNS resulting in significant improvements in patients with severe faecal

incontinence resistant to medical or conservative treatment. This was reflected in improvement in the outcome measures of cure, improvement, faecal incontinence episodes per week, and ability to defer defaecation. Both disease-specific and general quality of life scores also showed improvements. Follow-up of patients to date suggests that the improvement in continence is maintained over at least several months. Some types of adverse events occurring early in the series were later circumvented by modifications to the procedure. All adverse events appeared to be resolvable and to date no longstanding complications have been reported.

Need for further audit or research

The centres currently undertaking this procedure in the UK submit data to a UK registry database established by Medtronic, Inc. This continuing description and follow-up of patients would be valuable for audit purposes and ongoing safety and efficacy surveillance.

LIST OF ABBREVIATIONS

ASCRS	American Society of Colon and Rectal Surgery	NS	Not significant
BP	Bodily pain	PF	Physical function
CI	Confidence interval	PNE	Peripheral nerve evaluation
FDA	Food and Drug Administration	RCT	Randomised controlled trial
FI	Faecal incontinence	RE	Role-emotional
GH	General health	RP	Role-physical
IBD	Inflammatory bowel disease	SD	Standard deviation
IPG	Implantable pulse generator	SF	Social function
MH	Mental health	SF-36	Short Form-36 Health Survey Quality of Life Questionnaire
MS	Multiple sclerosis	SNS	Sacral nerve stimulation
NICE	National Institute for Clinical Excellence	Vit	Vitality

1 OBJECTIVE OF THE REVIEW

To systematically review the evidence for efficacy and safety of sacral nerve stimulation for the management of faecal incontinence in adults.

2 BACKGROUND

2.1 The interventional procedure under review

2.1.1 Description of the interventional procedure

Sacral nerve stimulation (SNS) involves applying a low voltage electrical current to a sacral nerve via an electrode, placed through the corresponding sacral foramen. SNS has the advantage of being able to test each patient, over a two to three week period, with a percutaneous peripheral nerve electrode attached to an external stimulator. If a significant benefit is achieved, implantation of the definitive Implantable Pulse Generator (IPG) can then be carried out.

2.1.2 Proposed clinical indications/contraindications and putative impact of the procedure (this section also covers Section 2.3)

The first stimulators for SNS were implanted by Tanagho and Schmidt in 1981[1] and were performed for urinary urge incontinence and non-obstructive urinary retention. Since that time observations have noted benefits beyond voiding disorders. These include re-establishment of pelvic floor muscle awareness, resolution of pelvic floor muscle tension and pain, decrease in bladder pain (e.g. in interstitial cystitis) and normalisation of bowel function.[2]

In the field of coloproctology SNS has been used in the context of clinical trials since 1995 in patients who have an intact external anal sphincter and faecal incontinence resistant to conservative treatments (anti-diarrhoeal drugs, pelvic floor muscle training, biofeedback).[3] Over time, the indication spectrum has evolved and patients with faecal incontinence caused by idiopathic sphincter degeneration, iatrogenic sphincter damage, partial spinal cord injury,[4] scleroderma,[5] following rectal prolapse repair or low anterior resection of the rectum have all received SNS implantation. The spectrum of indications continues to widen

with benefit being reported most recently in patients with both slow and normal transit constipation.[6]

As a general rule, patients considered for SNS, have had life altering incontinence (such as at least one episode of faecal incontinence per week to either solid or liquid stool), and have also failed maximal medical therapy, including use of anti-diarrhoeal medication and a course of pelvic floor muscle training including biofeedback therapy. Specific inclusion and exclusion criteria that have been followed are outlined in Appendix 1.

Major surgical intervention would be the next stage in the treatment offered to this group of patients. The option of a minimally invasive treatment, with the added potential advantage of preliminary testing prior to definitive implantation, might therefore have a major impact on this group of people.

2.1.3 Personnel involved (e.g. surgeons, anaesthetists, nurses), skill/experience required and setting

Hitherto, the procedure has been undertaken in only a small number of centres. These have been able to provide prior intensive conservative treatments and more specialised investigations (e.g. endoanal ultrasound, anorectal physiology). This is in line with current National Institute for Clinical Excellence (NICE) provisional guidance on SNS for faecal incontinence (August 2003), which recommends that the procedure be performed only in centres where full anorectal investigation is available.[8]

A standard theatre team is required for implantation of both the temporary and permanent implants and image intensification equipment for permanent 'tined' lead insertion.

2.1.4 Current use in the UK (including existing guidance)

The use of SNS in patients with faecal incontinence in the UK was pioneered at St. Mark's Hospital, Harrow.[7] Two other centres (Castle Hill Hospital, Hull and The Royal Victoria

Infirmary, Newcastle) are also now performing the technique, but in smaller numbers. All submit data to a UK registry of SNS for faecal incontinence, originally established by Medtronics, Inc. A recent paper (M.E.D. Jarrett, St Mark's Hospital, London, 2003) currently undergoing editorial review at the British Journal of Surgery, gives an overview of the UK experience of SNS for faecal incontinence to date. It includes prospective data on 59 patients who had undergone test peripheral nerve evaluation (PNE), of whom 46 went on to permanent SNS implantation between October 1996 and May 2003. Recently more UK centres have begun to show interest in the technique.

2.1.5 Equipment or devices required

The technique for implantation of both temporary and permanent SNS devices has been previously described in the literature.[9] Modifications have occurred over time, however, and there have been minor variations in approach between centres. In the past, test stimulation used a percutaneous wire electrode (Medtronic model 041830; Medtronic InterStim, Minneapolis, Minnesota, USA) that attached to a portable stimulator (Medtronic model 3625). This wire was easily dislodged and led to some patients having a fixed electrode (Medtronic model 3080) implanted at open operation, which was connected to the external stimulator using an extension cable. The extension cable was removed prior to the IPG (Medtronic model 3023) being connected to the fixed electrode to minimise the risk of infection. Subsequently a helical wire electrode (Medtronic model 3057) was developed which, due to its ability to stretch, was less easily dislodged.

Further innovation has led to permanent electrodes being placed using a percutaneous technique,[10] necessitating only a very small skin incision to place a 'tined' lead (Medtronic model 3093). This lead incorporates tines to prevent electrode displacement. An incision is still required to make a subcutaneous pocket for the IPG. The IPG is now placed in a pocket below the superficial fascia in the buttock, positioned away from the midline to prevent it being felt whilst the patient is seated. In the past the IPG was placed in the anterior

abdominal wall. However, this occasionally led to pain where wires connecting the device to the spinal electrode ran subcutaneously over the iliac crest.

These changes - the percutaneous technique of permanent electrode placement and the placing of the IPG in the buttock, which eliminates the need to turn the patient during the operation – have reduced the operation time.

It is usual practice to administer prophylactic intravenous antibiotics at the onset of surgery. Gentamicin solution (Gentamicin 80mg in 500ml normal saline) may be used to soak all implanted equipment. Post-operative antibiotics are also sometimes given.

2.2 Description of the underlying health problem

2.2.1 Epidemiology

Faecal incontinence is a socially embarrassing and physically disabling condition. It may be defined as the uncontrolled loss of faeces (liquid or solid) from the bowel. It may occur passively (without the person affected being aware of passing faeces) or be preceded by a sense of 'urgency'. In the UK major faecal incontinence (soiling of underwear, outer clothing, furnishing, or bedding, several times a month or more) affects an estimated 1.4% of the population over 40 years of age.[11] In a small proportion of these people, conservative measures alone do not relieve symptoms or provide adequate containment.

2.2.2 Underlying causes

Faecal incontinence may result from damage to the anal sphincter mechanism (either from direct trauma or damage to its nerve supply), idiopathic degeneration of the sphincter, spinal injury or other neurological causes. Obstetric trauma is the most important aetiological factor.

2.2.3 Burden of disease

Faecal incontinence has emotional, psychological and social effects for the person affected. With the number of patients affected and the potentially progressive nature of the problem the cost to society and to the health service is substantial.

2.3 Population

(See Section 2.1.2.)

2.4 Current management and alternative procedures

Standard treatment of faecal incontinence is conservative in the first instance. Dietary advice, anti-diarrhoeal medication and physical and behavioural therapy[12,13] (e.g. pelvic floor muscle training and biofeedback) may be undertaken, and those affected may resort to containment using absorbent pads or anal plugs. While these measures will prove effective in the majority of patients, a proportion remains with persistent severe incontinence that warrants consideration of more intensive treatment.

Injectable biomaterials have been tried in patients with passive faecal incontinence due to internal anal sphincter dysfunction. Some benefit has been noted but studies remain small and follow-up is short.[14]

Surgical intervention has been the next option in the management of these patients. For external anal sphincter defects, overlapping sphincter repair may be undertaken. Early results show good symptomatic relief in 70-80% of patients,[15,16] but results have been shown to deteriorate with time with no patient maintaining full continence and only 50% having improved continence after a median of five years.[17]

Dynamic graciloplasty and artificial bowel sphincter implants may be attempted to improve continence, but require major surgery and are associated with significant perioperative and

longer-term rbidity and failure rates.[18,19] Permanent stoma placement is another surgical option.

3 EFFICACY AND SAFETY

3.1 Methods for reviewing evidence on efficacy and safety

3.1.1 Search strategy

Electronic searches were conducted to identify both published and unpublished studies evaluating the efficacy and safety of SNS for faecal incontinence. The following databases were searched and full details of the searches are documented in Appendix 2:

MEDLINE (1966 to Week 2 May 2003)

MEDLINE Extra (29th May 2003)

EMBASE (1980 to Week 21 2003)

CINAHL (1985 to May 2003)

BIOSIS (1985 to May 2003)

Science Citation Index (1981 to June 2003)

Web of Science Proceedings (1990 to June 2003)

Cochrane Controlled Trials Register (Cochrane Library Issue 2 2003)

Cochrane Database of Systematic Reviews (Cochrane Library Issue 2 2003)

Database of Abstracts of Reviews of Effectiveness (May 2003)

HTA Database (May 2003)

Journals@Ovid Full Text (June 10th 2003)

National Research Register (Issue 2 2003)

Clinical Trials (May 2003)

Current Controlled Trials (May 2003)

Research Findings Register (May 2003)

In addition, the reference lists of all included studies were scanned and authors were contacted for other potentially eligible reports. Selected websites (for listing see Appendix 2) were also searched for eligible evidence-based reports.

A total of 1021 reports were identified from searching. From screening the titles and where possible, the abstracts, 106 were identified as being potentially relevant. Thirty-two of these

were published only as abstracts; a further seven were non-English language and were noted but copies were not obtained; while for the remaining 67 reports, the full papers were obtained and assessed. Twenty-nine papers (16 full text and 13 abstracts) met the criteria for inclusion in the review. A further two unpublished papers that were included in the review were obtained from their authors.

3.1.2 Inclusion and exclusion criteria

Types of studies

Systematic reviews, randomised controlled trials, controlled clinical trials, comparative observational studies, population-based registry studies, case series, case reports and narrative reviews.

Types of participants

Adults with faecal incontinence.

If the evidence allowed, we planned to assess the efficacy and safety of SNS in specific subgroups of patients for whom SNS might be particularly efficacious (or non-efficacious). These subgroups were patients with faecal urgency, with structural versus functional defects of the anal sphincter, those with spinal injury, and those with central neurological disease. However, in the event, there were insufficient data regarding subgroups to allow this.

Types of intervention

Sacral nerve stimulation.

The use of SNS for constipation and for pelvic pain, was included in the scope of the search strategy but subsequently not included in the review. Magnetic SNS was not considered. A systematic review of SNS for urinary urge incontinence is being undertaken separately for the Interventional Procedures Programme.

Types of outcome

The primary measures of efficacy for the review were (a) episodes of faecal incontinence per week, (b) ability to defer defaecation and (c) quality of life. Outcomes were considered in the following categories:

(1) Faecal incontinence (number cured or improved, episodes of faecal incontinence per week, ability to defer defaecation, urgency, use of pads, use of anal plugs, incontinence score, and need for further treatment such as medication or surgery).

(2) Quality of life (generic and condition-specific).

(3) Surrogate measures, such as anorectal manometry (resting pressure, maximal squeeze pressure, rectal sensory threshold to balloon distention, sensation of urgency to balloon distention and maximal tolerated rectal volume to balloon distention).

(4) Adverse effects (infection and/or pain at the implantation site, displacement of the electrodes, technical failure requiring removal and/or detrimental change in urinary function).

3.1.3 Quality assessment strategy

Two reviewers independently assessed the quality of all included studies. Two separate quality assessment checklists were used in the review. The 17-question checklist used to assess the quality of the case series (Appendix 3) was adapted from the NHS Centre for Reviews and Dissemination's guidance for those carrying out or commissioning reviews, 2001 and from Downs and Black, 1998.[20] The 11-question checklist used for assessing the study by Vaizey and colleagues[21] (Appendix 4) is a modified version of the Delphi List (a criteria list for quality assessment of RCTs developed by Delphi consensus methods by Verhagen and colleagues[22]) to assess the quality of RCTs.

3.1.4 Data extraction strategy

The titles and abstracts (where available and written in English) of all papers identified by the search strategy were screened. We obtained full text copies of all studies deemed to be potentially relevant and two reviewers independently assessed them for inclusion. Reviewers were not blinded to the names of studies' authors, institutions or publications. Any disagreements were resolved by consensus or arbitration by a third party.

We developed and piloted a data extraction form (Appendix 5). Two reviewers independently extracted details of study design, methods, participants, interventions and outcomes.

3.1.5 Data analysis

We planned to consider evidence in order of design quality if possible, the hierarchy of designs depending on the parameter being considered. We planned to summarise results using standard statistical methods where possible.

3.2 Results

3.2.1 Type and quantity of available evidence

Thirty-one reports (including 13 abstracts) were identified that met our inclusion criteria. Twenty-nine of these reports were set in a number of different countries and presented data on increasingly large series with patients being followed up over longer periods of time. To overcome the potential problem of double counting, we decided to include only the most recent report (published or unpublished) from each country. We therefore included six case series,[4,23-26] one of which was unpublished (M.E.D. Jarrett, St Mark's Hospital, London, 2003).

A small UK double-blind crossover study[21] was also included. This study is presented separately from the other included studies as its participants have been included in the most recent report of the UK experience (M.E.D. Jarrett, St Mark's Hospital, London, 2003).

We also included an unpublished European prospective multicentre (eight institutions) non-randomised trial, (MDT-301 study) reported by Matzel and colleagues (K.E. Matzel, University Hospital Erlangen, 2003). Data from this study are also presented separately as most, if not all, of the participants would have been included in the case series. A list of the included studies, with related references, is given in Appendix 6. The characteristics and results of the six case series, the double-blind study by Vaizey and colleagues, and the multicentre MDT-301 study are given in Appendix 7.

3.2.2 Number and type of included studies

The six case series were prospective and set in different European countries (Austria, France, Germany, Italy, Netherlands and the UK). In all, 266 patients were enrolled and received PNE, with 149 (56%) going on to receive permanent implants following successful test stimulation (Table 1). The study by Matzel and colleagues,[26] however, only included patients who went on to permanent implantation. Of the other studies, Uludag and colleagues,[25] Jarrett and colleagues (M.E.D. Jarrett, St Mark's Hospital, London, 2003) and Rosen and colleagues[4] had similar successful stimulation rates of 77%, 78% and 80%. Leroi and colleagues[24] and Ganio and colleagues[23] (who had five patients with a successful PNE refuse a permanent implant) had success rates of 55% and 30% respectively. The MDT-301 study (K.E. Matzel, University Hospital Erlangen, 2003) had a success rate at test stimulation of 92%.

The mean or median age of the patients in the studies was between 50 and 56 years (range 11-79 years). The percentage of women in the studies ranged from 70%[4] to 88%.[26] The recruitment period ranged from one year[24] to six years and eight months (M.E.D. Jarrett, St Mark's Hospital, London, 2003), with follow-up ranging from an average of six months[24] to 32.5 months[26] and a range up to 99 months[26] (Table 1). The aetiology of faecal incontinence

reported by the studies included idiopathic (31 patients), obstetric trauma (30 patients), surgery (28 patients), scleroderma (five patients), spinal cord trauma/pathology (19 patients) and low anterior resection (three patients) (Table 2).

Table 1 Patient numbers and follow-up

Study id	Enrolled	Received PNE	Received permanent implant (%)	Months of follow-up (range)	Lost to follow-up
Ganio 2002	116	116	31 (27%)	25.6* (1-56)	0
Jarrett 2003	59	59	46 (78%)	12# (1-72)	0
Leroi 2001	11	11	6 (55%)	6	1
Matzel 2003	16	16	16 (100%)	32.5# (3-99)	0
Rosen 2001	20	20	16 (80%)	15# (3-26)	0
Uludag 2002	44	44	34 (77%)	11*	0
Total	266	266	149 (56%)	-	1
MDT-301	37	37	34 (92%)	21.3* (1-36)	1

Note:
1. * mean, # median

The UK double-blind crossover trial by Vaizey and colleagues[21] involved two patients. It consisted of two two-week periods per patient with each patient's stimulator turned on for two weeks and off for two weeks, or vice-versa. The main investigator and the patients were blinded as to whether the stimulator was turned on or off (the stimulators were set at sub-threshold amplitude levels so that the patients were unaware as to their status). The two women patients enrolled were aged 65 and 61 and had received permanent implants nine months previously. The cause of their faecal incontinence was degeneration of the internal anal sphincter (scleroderma induced and idiopathic respectively).

The report of the MDT-301 European multicentre study, a prospective non-randomised trial, covered the period January 1999 to June 2001, with a mean follow-up of 21.3 months.

Thirty-seven patients were enrolled (33 women), with a mean age of 54.3 years, of whom 34 went on to receive permanent implants. The aetiology of faecal incontinence was idiopathic (19 patients), scleroderma (two patients), obstetric trauma (ten patients) and perineal surgery (six patients) (K.E. Matzel, University Hospital Erlangen, 2003) (Table 2).

3.2.3 Number and type of excluded studies; reasons for exclusion

Studies identified by the search strategy that did not meet our stated inclusion criteria given in Section 3.1.2 in terms of the study design, participants, intervention or outcomes were excluded. Studies reporting on only the PNE phase but not the implanted phase were excluded. Potentially relevant non-English language papers were noted but excluded from the review unless they contained an English language abstract providing sufficient information to meet the inclusion criteria, in which case an attempt was made to obtain further information about the study. A list of (a) studies reporting on only the PNE phase and (b) potentially relevant non-English language studies is given in Appendix 8.

3.2.4 Quality of available evidence

The results of the quality assessment of the six included case series are summarised in Table 3. In these studies, all participants were entering the studies after they had failed maximal conservative therapy. Data collection was prospective in two studies and probably prospective in the others but this was not certain from the reports.

None of the studies explicitly stated that the surgeons performing the operation were experienced in the procedure or the facilities where the patients were treated provided an appropriate environment for performing the procedure. Follow-up in the six studies was for 6 – 30 months and is probably long enough to detect important effects on the outcomes of interest.

Judging the representativeness of the samples was not straight-forward. While two included all patients receiving SNS for faecal incontinence in a particular country, the ways

in which these patients came to be selected for SNS was not clear. In two studies patient selection was consecutive[24,26] while in the remainder it was unclear from the information provided whether this was the case. For five, the aetiological types and the distribution of patients between the types appeared to be in line with what might be expected from the epidemiology of severe faecal incontinence. However, in one study[4] this was not the case as the cause of the participants' faecal incontinence in 15/20 (75%) of the patients considered for permanent implant was of neurological origin. In five studies the inclusion and/or exclusion criteria were specified, important prognostic indicators were considered to have been identified, and objective outcome measures were used, while in one[25] these criteria were either not met or insufficient information was provided for this to be determined. Studies provided information on dropouts where this occurred.

In four studies the recruitment period was clearly stated (M.E.D. Jarrett, St Mark's Hospital, London, 2003).[4,23,24] Four studies reported all primary outcome measures (episodes of faecal incontinence per week, ability to defer defaecation, quality of life), while one[24] did not report quality of life and another[25] provided insufficient information to determine whether this criterion had been met. The main findings were clearly described in four studies (M.E.D. Jarrett, St Mark's Hospital, London, 2003).[4,24,26] In one study[24] the participants lost to follow-up were considered likely to introduce bias (for four of the six implanted patients, either no baseline or six month manometry data were provided). No study attempted to blind outcomes assessors.

Table 2 Aetiology of faecal incontinence in the case series and multicentre study

Aetiology	Ganio 2002	Jarrett 2003	Leroi 2001	Matzel 2003	Rosen[1] 2001	Uludag 2002	MDT-301
Idiopathic	15	7	2	2	4	-	19
Obstetric	-	25	3	2	-	-	10
Surgery:	10	8	1	9	-	-	6
Fistula	(2)	(1)	-	(2)	-	-	-
Haemorrhoidectomy	(1)	(1)	-	(2)	-	-	-
Haemorrhoid banding	-	(1)	-	-	-	-	-
Lateral sphincterotomy	-	(1)	-	-	-	-	-
Rectocoele repair	(2)	-	-	-	-	-	-
Abdominal rectopexy	(1)	-	(1)	(2)	-	-	-
Prolapse surgery	-	(4)	-	(2)	-	-	-
Duhamel for Hirschsprung's	(1)	-	-	-	-	-	-
Vaginal hysterectomy	-	-	-	(1)	-	-	-
Post partum sphincteroplasty	(3)	-	-	-	-	-	-
Perineal	-	-	-	-	-	-	(6)
Scleroderma	1	4	-	-	-	-	2
Spinal cord trauma/pathology (MS, whiplash, Friedrich's Ataxia)	4	2	-	2	-	3	-
Low anterior resection	-	-	-	1	-	2	-
Missing	1	-	-	-	12	29	-
Total	31	46	6	16	16	34	37

1. Aetiology is reported for the 20 patients tested for permanent implant but not the 16 who received permanent implants for whom results are reported.

Table 3 Summary of the quality assessment of the case series

Criteria	Yes	No	Unclear
1. Were participants a representative sample selected from a relevant patient population?	0	11	1
2. Are the inclusion/exclusion criteria of patients in the study clearly described?	5	1	0
3. Were participants entering the study at a similar point in their disease progression?	6	0	0
4. Was selection of patients consecutive?	2	0	4
5. Were all important prognostic factors identified?	5	0	1
6. Was data collection undertaken prospectively?	2	0	04
7. Was the recruitment period clearly stated?	4	2	0
8. Was the intervention that which is being considered in the review?	6	0	0
9. Was an attempt made to blind outcomes assessors?	0	6	0
10. Was the operation undertaken by someone experienced in performing the procedure?	0	0	6
11. Did the staff, place, and facilities where the patients were treated provide an appropriate environment for performing the procedure?	0	0	6
12. Were objective (valid and reliable) outcome measures used?	5	0	1
13. Were all the important outcomes considered?	4	1	1
14. Was follow-up long enough to detect important effects on outcomes of interest?	6	0	0
15. Was information provided on non-respondents, dropouts?	5	1	0
16. Were participants lost to follow-up likely to introduce bias?	1	5	0
17. Were the main findings clearly described?	4	1	1

The small UK crossover study by Vaizey and colleagues[21] was assessed using the checklist for RCTs. This study was considered to be a randomised or quasi-randomised study although the method of assigning stimulator settings for the two two-week periods was not explicitly stated. The assignment allocation was deemed to be adequately concealed in that only the investigator responsible for turning the stimulator on or off at the beginning of the two-week period knew whose stimulator was to be switched on and whose stimulator was to be switched off. The eligibility criteria for the study were specified. The two patients were similar at baseline in terms of prognostic factors and both were treated in the same way. The main investigator and the patients were blinded as to the status of the stimulators. No measures of variability were presented for the primary outcome data. As both patients received the intervention in the allocated order and were available for follow-up, there was no need to consider intention to treat analysis.

The MDT-301 European multicentre study (K.E. Matzel, University Hospital Erlangen, 2003) was assessed using the checklist for case series. As with the individual countries' case series reports, most criteria were regarded as being met. It was unclear, however, whether patient selection was consecutive and no attempt was made to blind outcomes assessors.

3.2.5 Summary of efficacy findings

The six case series were considered together (M.E.D. Jarrett, St Mark's Hospital, London, 2003).[4,23-26] The MDT-301 study (K.E. Matzel, University Hospital Erlangen, 2003) is presented separately (as some of the patients in this study are also presented in the case series) and the single double-blind crossover trial[21] is also examined and reported separately.

In patients who had permanent implants, complete continence to solid and liquid motion was reported in 41-75% of patients (Table 4), while there was a ≥ 50% improvement in the number of incontinent episodes in 75-100%(Table 4). There appeared to be a good level of reproducibility of clinical effect between temporary and permanent stimulation.

Table 4 Patients cured and improved at latest follow-up

Study id	Cured	%	Improved	%
Jarrett 2003	19/46	41	44/46	96
Leroi 2001	2/4	50	3/4	75
Matzel 2003	12/16	75	16/16	100
Rosen 2001	-	-	16/16	100
Total	32/66	48	79/82	96
MDT-301	15/33	45	29/33	88

Notes:
1. Cured = complete continence to solid and liquid motion; improved = >50% improvement in the number of incontinent episodes.
2. Patients improved include those cured.
3. Rosen and colleagues did not provide separate data on number of patients cured.

The number of faecal incontinent episodes per week decreased in each of the studies with statistical significance being reported by Jarrett and colleagues (M.E.D. Jarrett, St Mark's Hospital, London, 2003), Matzel and colleagues[26] and Uludag and colleagues[25] ($p<0.0001$, $p<0.001$, $p<0.01$ respectively) (Table 5). The MDT-301 study (K.E. Matzel, University Hospital Erlangen, 2003) also reported a significant decrease in faecal incontinent episodes ($p<0.0001$).

Table 5 Episodes of faecal incontinence per week

Study id	Measure	Patients	Baseline	Follow-up	alue	Change (%)
Ganio 2002	Mean (range)	31	7.5 (1 to 11)	0.15 (0 to 2)	NR	-7.35 (-98%)
Jarrett 2003	Median (range)	46	7.5 (1 to 78)	1.00 (0 to 39)	< 0.0001	-6.50 (-87%)
Leroi 2001	Mean (± SD)	4	3.0 (± 2.7)	0.50 (± 0.6)	NR	-2.50 (-83%)
Matzel 2003	Median	16	40%[1]	0%	< 0.001	
Rosen 2001	Median (range)	16	2.0 (1 to 5)	0.67 (0 to 1.67)	NR	-1.33 (-67%)
Uludag 2002	Mean	34	8.66	0.67	< 0.01	-7.99 (-92%)
MDT-301	Mean (± SD)	37; 33[2]	16.4 (± 19.3)	2.7 (± 4.8)	< 0.001	-13.70 (-84%)

Notes:
1. Matzel and colleagues reported the percentage of bowel movements that were faecally incontinent.
2. MDT-301. Number of patients: baseline 37; follow-up 33.
3. NR = Not recorded

An improvement in the ability to defer defaecation is a further important outcome measure for patients with an urge component to their incontinence. A significant improvement was noted in the two unpublished studies by Jarrett and colleagues (M.E.D. Jarrett, St Mark's Hospital, London, 2003) and the MDT-301 study (K.E. Matzel, University Hospital Erlangen, 2003) ($p<0.0001$). Leroi and colleagues,[24] Rosen and colleagues[4] and Uludag and colleagues[25] also reported an improvement in patients' ability to defer defaecation following permanent SNS but this did not achieve statistical significance (Table 6).

Table 6 Ability to defer defaecation (minutes)

Study id	Measures	Patients	Baseline	Follow-up	p-value	Change
Jarrett 2003	Median (range)	39	< 1 (0 to 5)	5 to 15 (1 to > 15)	< 0.0001	+9
Leroi 2001	Mean (SD)	4	0.25 (0.5)	19 (13.9)	NS[1]	+18.75
Rosen 2001	Median (range)	16	2 (0 to 5)	7.5 (2 to 15)	NS	+ 5.5
Uludag 2002	Mean	34	Not reported	10 to 15	NS	
MDT-301	Median (range)	33; 32[2]	< 1 (0 to 5)	5 to 15 (0 to > 15)	< 0.0001	+9

Notes:
1. NS = not significant.
2. MDT-301. Number of patients: baseline 33; follow-up 32.

Only Leroi and colleagues[24] reported the number of urgency episodes per week. The four patients studied at six months reported an overall improvement of 52% in urgency episodes (Table 7).

Table 7 Episodes of urgency per week

Study id	Measure	Patients	Baseline	Follow-up	Change (%)
Leroi 2001	Mean (SD)	4	4.75 (3.86)	2.3 (3.1)	-2.45 (-52%)

Pad use per day was reported only in the study by Ganio and colleagues[23] and in contrast to all other outcome measures showed an increase in usage. The reasons for this are unclear and no explanation is given in the paper (Table 8).

Table 8 Pad use per day

Study id	Measure	Patients	Baseline	Follow-up	Change (%)
Ganio 2002	Mean	31	1.25	1.9	+0.65 (+52%)

The Cleveland Clinic scoring system[27] was used in three studies. As well as measuring incontinent episodes, the score takes account of pad use and lifestyle impairment. Jarrett and colleagues (M.E.D. Jarrett, St Mark's Hospital, London, 2003), Matzel and colleagues[26] and Ganio and colleagues[23] used this scoring system and showed a significant improvement ($p<0.0001$, $p=0.003$, $p<0.01$ respectively, Table 9).

Table 9 Faecal incontinence score (Cleveland Clinic[1])

Study id	Measure	Patients	Baseline	Follow-up	p-value	Change (%)
Ganio 2002	Mean (range)	31	14.6 (6 to 20)	4.2 (3 to 9)	< 0.01	-10.4 (-71%)
Jarrett 2003	Median (range)	27	14 (5 to 20)	6 (1 to 12)	< 0.0001	-8.0 (-57%)
Matzel 2003	Median (range)	11	17 (11 to 20)	5 (0 to 15)	0.003	-12.0 (-71%)

Note:
1. The Cleveland Clinic Incontinence Score ranges from a best score of 0 to a maximum (worst) score of 20.

No adverse changes in urinary function were reported. The study by Leroi and colleagues,[24] however, reported that of three faecally incontinent patients with concomitant urinary stress incontinence, no patient showed any improvement with respect to urinary stress incontinence; of two faecally incontinent patients with detrusor overactivity, urinary urgency improved in one patient (Table 10).

Table 10 Change in urinary symptoms

Study id	Stress urinary incontinence			Urgency symptoms		
Leroi 2001	**Baseline**	**Follow-up**	**Change (%)**	**Baseline**	**Follow-up**	**Change (%)**
Patients with stress urinary incontinence	3/3	3/3	0 (0%)	Not reported	0/3	
Patients with detrusor overactivity				2/2	1/2	-1 (-50%)

Quality of Life

The scores from the faecal-incontinence-specific American Society of Colon and Rectal Surgery (ASCRS) quality of life evaluation improved significantly, at latest follow-up, in the studies by Jarrett and colleagues (M.E.D. Jarrett, St Mark's Hospital, London, 2003) and Rosen and colleagues[4] ($p<0.001$ and $p<0.01$ in all categories respectively) (Table 11). Uludag and colleagues[25] and Matzel and colleagues[26] also reported improvement in all categories, but without reaching statistical significance. The MDT-301 study (K.E. Matzel, University Hospital Erlangen, 2003) also reported significant improvement in all categories of the ASCRS quality of life evaluation ($p<0.0001$).

Only two of the six included studies reported Short Form (SF) 36 Health Survey quality of life questionnaire results (Table 11). In the study by Jarrett and colleagues (M.E.D. Jarrett, St Mark's Hospital, London, 2003) all categories of the SF-36 improved and in the study by Ganio and colleagues[23] all categories improved with the exception of mental health, which stayed the same. In the study by Jarrett and colleagues (M.E.D. Jarrett, St Mark's Hospital, London, 2003) there were significant improvements ($p<0.05$) in the categories of social function, mental health, vitality, emotional role and general health. In the MDT-301 study (K.E. Matzel, University Hospital Erlangen, 2003) there were significant improvements ($p<0.05$) in social function and mental health only.

Table 11 Quality of life results

Study		ASCRS[1]				SF-36[2,3]							
		Lifestyle	Coping/ behaviour	Depression/ self-perception	Embarrassment	PF	RP	BP	GH	Vit	SF	RE	MH
Ganio 2002 (n=31)	**Baseline**	-	-	-	-	58	49	49	46	43	49	40	50
	Follow-up	-	-	-	-	64	70	57	57	51	58	51	50
Jarrett 2003 (n=46)	**Baseline**	2.0	1.52	2.16	1.85	62	50	53	49	37	53	49	54
	Follow-up	3.6#	2.66#	3.10#	2.81#	65	60	55	55*	46*	67*	64*	64*
Leroi 2001 (n=4)	**Baseline**	-	-	-	-	-	-	-	-	-	-	-	-
	Follow-up	-	-	-	-	-	-	-	-	-	-	-	-
Matzel 2003 (n=16)	**Baseline**	1.10	1.07	1.84	1.17	-	-	-	-	-	-	-	-
	Follow-up	3.74^	3.18^	4.02^	3.50^	-	-	-	-	-	-	-	-
Rosen 2001 (n=16)	**Baseline**	2.1	2.0	2.6	1.7	-	-	-	-	-	-	-	-
	Follow-up	3.9~	3.7~	3.7~	3.8~	-	-	-	-	-	-	-	-
Uludag 2002 (n=34)		States 'improvement in all categories' at 11 months				States 'improvement in all categories' at 11 months							
MDT-301 (n=34)	**Baseline**	2.7	1.7	2.8	1.8	65	46	65	55	49	61	57	63
	Follow-up	3.5#	2.8#	3.9#	3.0#	69	56	57	59	56	85~	72	73*

Notes:

1. The ASCRS ranges from a best score of 5 to a worst score of 1.
2. The SF-36 ranges from a best score of 100 to a worst score of 0.
3. SF-36. PF = physical functioning, RP = role-physical, BP = bodily pain, GH = general health, Vit = vitality, SF = social functioning, RE = role-emotional, MH = mental health.
4. * $p < 0.05$; # $p < 0.0001$; ^ $p = 0.07$; ~ $p < 0.01$.

Anorectal manometry

The role of anorectal physiology measurements in patient selection or outcome evaluation remains unclear. Most trials, however, have performed such measurements. The anorectal manometry results for the included studies are presented in Table 12.

Only the study by Rosen and colleagues[4] showed a significant improvement in maximal resting pressure. Jarrett and colleagues (M.E.D. Jarrett, St Mark's Hospital, London, 2003), Matzel and colleagues[26] and Rosen and colleagues[4] all reported a significant increase in maximal squeeze pressure ($p<0.01$, $p=0.009$, $p=0.005$ respectively).

A trend toward the rectum becoming more sensitive to balloon distention with air at threshold, urge and maximal tolerated volumes was seen in the studies by Ganio and colleagues[23] and Rosen and colleagues;[4] only Jarrett and colleagues (M.E.D. Jarrett, St Mark's Hospital, London, 2003), however, reported the change to be significant at all three measurement points ($p<0.0001$, $p<0.001$, $p<0.01$ respectively).

Manometry results were said to show no change in the study by Uludag and colleagues[25] and went largely unreported in the MDT-301 study (K.E. Matzel, University Hospital Erlangen, 2003).

Table 12 Anorectal manometry results

Study	Maximal resting pressure		Maximal squeeze pressure		Rectal volume sensation					
					Threshold		Urge		Maximal tolerated	
	Baseline	Follow-up	Baseline	Follow-up	Baseline	Follow-up	Baseline	Follow-up	Baseline	Follow-up
Ganio 2002 (n=31)[1,4]	37 (SD 19)	46 (SD 20) (NS)	73 (SD 37)	79 (SD37) (NS)	-	-	117 (SD 88)	57 (SD35) (NS)	-	-
Jarrett 2003 (n=46)[1,3]	46 (SD23)	49 (SD24) (p=0.3)	62 (SD 53)	93 (SD 47) (p<0.01)	41 (SD 22)	27 (SD 18) (p<0.0001)	92 (SD40)	71 (SD 38) (p<0.001)	129 (SD 39)	107 (SD 42) (p<0.01)
Leroi 2001 (n=4)[1,3]	61 (SD 18)	61 (SD 14)	49 (SD 46)	40 (SD 35)	10ml	10ml	200 (SD226)	130 (SD 113)	200 (SD226)	255 (SD 149)
Matzel 2003 (n=16)[2,4]	63 (47-101)	59 (10-102) (p=0.906)	69 (14-101)	97 (59-136) (p=0.009)	40 (20-70)	25 (20-100) (p=0.263)	60 (40-140)	70 (40-270) (p=0.386)	150 (70-290)	200 (80-290) (p=0.161)
Rosen 2001 (n=16)[2,4]	27 (16-39)	50 (29-76) (p=0.005)	59 (28-87)	120 (57-193) (p=0.005)	90 (15-300)	60 (10-300)	100 (20-300)	100 (50-300)	180 (35-300)	160 (70-300)
Uludag 2002 (n=34)	States 'Anal manometry during stimulation showed no increase of sphincter pressures.'									
MDT-301 (n=34)	Largely unreported									

Notes:

1. Ganio 2002, Jarrett 2003 and Leroi 2001: values are mean (SD).
2. Matzel 2003 and Rosen 2001: values are median (range).
3. Jarrett 2003 and Leroi 2001: pressure in cmH_2O, volume in ml.
4. Ganio 2002, Matzel 2003 and Rosen 2001: pressure in mmHg, volume in ml.
5. NS = not significant.

Double-blind crossover trial

The results of the double-blind crossover trial by Vaizey and colleagues[21] are presented in Table 13.

Table 13 Results of the double-blind crossover study by Vaizey and colleagues

	Age	Stimulation	Faecal incontinent episodes per week	Maximal resting pressure	Maximal squeeze pressure	Rectal volume sensation (ml)		
						Threshold	Urge	Max tolerated
Patient 1	61 years	Off	10	35	70	25	70	120
		On	1	45	100	45	85	130
Patient 2	65 years	Off	2	50	60	50	100	150
		On	0	70	90	90	120	150

Note:
1. Maximal resting pressure and maximal squeeze pressure: values are in cmH_2O.

3.2.6 Summary of safety findings

The adverse events documented in the six case series[4,23-26] (M.E.D. Jarrett, St Mark's Hospital, London, 2003) are summarised in Table 14; those from the MDT-301 study (K.E. Matzel, University Hospital Erlangen, 2003) are summarised in Table 15. The events can be broadly divided between those occurring in the test PNE phase and those following definitive IPG implantation. It should be borne in mind that implantation techniques have been modified over the period of the studies in order to address and combat potential adverse events.

From 266 patients receiving test PNE evaluation, ten patients were reported as having an adverse event. Nine patients had lead dislodgement inside the minimum trial period with the consequence that the effect of PNE could not be accurately assessed. One patient had a superficial skin infection outside the minimum trial period but this settled after removal of the test wire. All the complications that arose were resolved when the test stimulation apparatus was removed.

In the MDT-301 study (K.E. Matzel, University Hospital Erlangen, 2003) nine patients (of 37 tested) were reported to have developed an infection. All were treated with antibiotics. Four patients required lead removal prior to the proposed removal date, although past the minimum follow-up time. All nine patients had at least 50% improvement in episodes of faecal incontinence and eight went on to permanent IPG implantation. One patient had lead dislodgement and one was unable to comply with the use of the equipment and did not go on to permanent implantation.

Table 14 Adverse events (PNE and implanted phase) in the six case series

Patients receiving PNE	**266**
No improvement	58
Insufficient improvement	44
Lead dislodgement	9
Successful PNE but refused permanent implantation	5
Successful PNE and awaiting implantation at time of study	1
Superficial skin infection	(1)

Patients receiving permanent implants	**149**
Lead migration (1 removed; 5 replaced, of which 1 dislodged again and was removed; 1 awaiting reassessment)	8
Pain from leads (Local anaesthetic and steroid injection settled all 3)	3
Pain at IPG site (Device reprogrammed to stop IPG acting as anode)	1
Pain (unspecified)	2
Infection (3 removed, of which 1 replaced and 2 awaiting replacement)	3
Interruption of electrode (Replaced)	1
Superficial wound dehiscence	1
In total four devices were completely removed. One was replaced and two are awaiting replacement.	

Table 15 Adverse events (PNE and implanted phase) in the MDT-301 study

Patients receiving PNE	**37**
Infection (All showed improvement. Leads from 4 patients removed early. All but 1 patient went on to permanent implantation)	9
Non-compliance	1
Lead dislodgement	1

Patients receiving permanent implants	**34**
Pain from implanted electrode or IPG (9 patients, 10 episodes. 4 devices reprogrammed, 3 repositioned and 1 settled with analgesia. 2 unknown outcomes)	10
Lead breakage (Replaced)	1
Infection (Removed)	1
Deterioration of bowel symptoms (1 improved on its own, 1 removed at 20 months, 1 outcome unknown)	3

From the six case series reviewed, 149 permanent implants were inserted and 19 adverse events were reported. Most important were the three patients (2%) from the same centre[4] who developed infections of their implants within three months of their operations. Each patient required implant removal. Rosen and colleagues reported that one patient had subsequently undergone uncomplicated re-implantation and the other two patients were suitable candidates for re-implantation.

Leads became dislodged on eight occasions in seven patients (at three days, one month, three months (two), one year and two years; two were unreported). Five of the eight leads were relocated, one of which dislodged for a second time and was removed. One IPG was removed as the patient did not wish to have the electrode relocated and one was awaiting reassessment at the time of reporting. There was also interruption of the electrode lead in one patient, necessitating replacement. Six patients complained of pain relating to their

implant. Three patients had pain from the leads running subcutaneously over the iliac crest to the IPG placed in the abdominal wall, prior to a change in technique to buttock placement. Injection of local anaesthetic and steroid resolved the problem in all cases. One patient had pain over the IPG when it had been set as the anode and this settled on reprogramming with the external telemetry device. Two patients' pain characteristics and management were unspecified. One superficial wound dehiscence was also reported which healed uneventfully.

Of the 34 patients in the MDT-301 study (K.E. Matzel, University Hospital Erlangen, 2003) who received permanent implants, one patient (3%) acquired an infection of the permanent implant, requiring removal. There were ten episodes of pain in nine patients. In four cases pain settled with reprogramming, in three the IPG was repositioned and in one case pain settled with medication. Two cases remain unaccounted for.

In one patient a broken lead needed replacing and in three patients bowel symptoms deteriorated. One of these three patients improved, one had the implant removed at 20 months and one remained unaccounted for. No effect was reported on any patient's urinary or sexual function.

4. DISCUSSION

4.1 Discussion of main results

The results of the review are consistent with SNS being efficacious on average in patients with faecal incontinence due to a range of underlying causes. The studies included in the review have largely presented data for their case series as a whole and it proved impossible to examine effects in patient subgroups. However, the study by Rosen and colleagues[4] contained a preponderance of patients with faecal incontinence from a neurological cause, and Kenefick and colleagues[5] have reported the use of SNS in a series of patients with faecal incontinence secondary to scleroderma. None of the studies that met our inclusion criteria compared SNS for faecal incontinence with any alternative treatments.

Data describing the main measures of outcome were generally available from all studies, although pad use per day[23] and episodes of urgency per week and changes in urinary symptoms.[24] were each reported for only a single study.

4.1.1 Discussion of efficacy results

The efficacy of SNS for a wide range of aetiologies (Table 2) is supported in the studies reviewed, for the major outcome measures of reduced faecal incontinent episodes, decreased urgency and improved quality of life (Tables 4 to 11). SNS for faecal incontinence does not work for all patients potentially eligible for the procedure and only about half of those screened go on to have a permanent implant. However, the test stimulation phase enables the selection of those patients for whom SNS is usually effective.

Anorectal manometry measurements, although commonly reported in studies, do not as yet aid patient selection for SNS (Table 12).

4.1.2 Discussion of safety results

Three types of electrode have been used during the test stimulation phase, either a temporary lead, or the definitive 'tined' percutaneous lead, or a lead placed at open operation with a percutaneous extension. The temporary lead is the one most commonly employed and is presently used in all cases in the UK. The wire has been modified and is now of helical design, and this may result in a reduction in the number of premature lead dislodgements. The lead can be removed without anaesthetic or sedation, for example if any significant infection occurs that does not settle with antibiotics. If the lead is removed before a decision can be made on whether to proceed to permanent implant, the option remains to place a fresh lead and retest the patient.

The main potential complication with permanent lead and IPG placement appears to be infection. In the reviewed series three patients, and in the MDT-301 study one patient, had infections requiring device removal. Infection appears to occur in 2-3% of implants although this estimate may be inflated by the fact that all three infected devices in the case series were from the same centre.[4]

Pain occurred in 6/149 (4%) of patients in the case series and in 10/34 (29%) of patients in the MDT-301 study. Lead pain occurred in three patients when the IPGs were placed abdominally. This occurred at the point where the leads were tunnelled subcutaneously over the iliac crest. Local anaesthetic and steroid injections resolved the problem in all cases. Modifying the procedure by implanting the IPG in the buttock rather than the abdominal wall may have eliminated this particular complication.

Lead migration or breakage requires relocation or replacement respectively and occurred in 8/149 (5%) of the permanently implanted patients in the case-series. The use of the more recently developed percutaneous 'tined' lead may reduce this but this requires further auditing.

In one patient setting the battery casement as the anode caused pain at the IPG site and, again, avoiding this practice should prevent this happening in the future.

The pattern of adverse events in the six case series and the MDT-301 study were broadly similar although the numbers of events were too few to judge this reliably. There were no reports of any longstanding problems. In cases of implant infection it was possible to remove and then re-implant the device once the infection had resolved. The fully implanted system is made up of three constituent parts (electrode, extension lead, IPG) and a single section can be replaced if it becomes dislodged or malfunctions.

4.1.3 Discussion of double-blind crossover study[21]

Episodes of faecal incontinence to liquid and solid stool were taken as the main outcome measure in the double-blind crossover study by Vaizey and colleagues. A worsening was noted when the IPG was switched off in the two patients involved in the study, despite their being unaware of whether or not the IPG was active. The study showed an almost immediate return to baseline levels on switching off the stimulator. This is suggestive of a neurological mechanism rather than any chronic changes in the continence mechanism.

4.2 Assumptions, limitations, and uncertainties

The principal limitation is that most of the data reviewed come from case series. None of the studies compared SNS directly with other treatments for faecal incontinence. Each patient acted as his or her own control with follow-up measures being compared with baseline measures. Consequently, the results may reflect spontaneous improvement (on the basis that the electrode had been inserted when symptoms were at their worst) or a placebo effect. However, the size of the improvement, its persistence, and the findings of the small crossover study make this explanation unlikely. Equally, even if the observed improvement results directly from SNS we do not know whether similar or better results might have been achieved in these patients with other procedures.

Another concern, common to all case series, is the possibility of bias caused by selective reporting, either through selection of patients to include in a series or from subsequent withdrawals or loss to follow-up. Two of the six series were reported to be consecutive, but the process was unclear for the others. Judged on the reports, few patients were lost to follow-up, and the numbers described were too few to cause significant bias. In two of the series data collection was reported to be prospective, but this was uncertain for the other four.

One of the case-series has been assessed only on the basis of a published abstract[25], another is currently unpublished (MED, Jarrett, et al), and the international eight centre case series (MDT-301) which has also been reviewed is also unpublished. The number of patients studied in the six case series is only 266. This is insufficient to rule out currently unrecognised rare complications. The length of follow-up, while over a year in most cases, is also still limited and the possibility of complications due to long-term stimulation cannot be addressed.

The maximum length of follow-up is currently 99 months. However, the median in the UK is 12 months (maximum 72), and hence longer-term efficacy and safety cannot be addressed in this report.

Although the outcome measures used in each study were largely the same, the presentation of the results varied. The use of mean or median, standard deviation or range and the way faecal incontinent episodes were reported were not standard across the series reviewed. As the data in each study was generally aggregated and not given for each patient, recalculating the data to present it in a standard format to allow combination was not always possible.

Subgroups of patients tended not to be reported separately despite the range of underlying causes. Hence it was not possible to address the relative efficacy and safety of SNS for faecal incontinence in different subgroups of patients.

4.3 Aspects of the procedure that might be improved

The equipment and techniques used for both temporary and permanent SNS insertions have evolved over time, both to limit any potential complications and also to make the procedure less invasive and easier to perform. At present no particular aspect of the procedure stands out as having the potential for further improvement.

5 CONCLUSIONS

The evidence from the included studies is consistent with permanent SNS leading on average to clinically significant improvement in continence in selected patients with severe faecal incontinence that had not responded to non-surgical management. Appproximately half the patients screened for this technique go on to have a permanent implant, about half of these are cured and nearly all improve by >50% in terms of reduced episodes of faecal incontinence. There is also an improvement in the ability to defer defaecation (urgency). A corresponding improvement in both disease-specific and general quality of life scores was also seen. Long-term follow-up of these patients to date (maximum 99 months) suggests that the improvement in continence is maintained over this time.

SNS appears to be efficacious in patients with a range of causes of incontinence. Use of a temporary PNE wire aims to allow patients to be tested for a two to three week period and hence enhance selection of patients for a permanent implant. There is a good correlation between temporary and permanent stimulation outcomes, reflected in the high proportions of patients improving after permanent implantation.

There is no evidence that anorectal manometry measurements aid patient selection but they may be useful in trying to elucidate the mechanism by which SNS works.

There are reports of temporary PNE electrodes becoming infected, but the experience reported in the case series is that these can be managed successfully with antibiotics or lead removal. In the UK series there was a single superficial skin infection during temporary screening that settled on removal of the electrode. Lead dislodgement may also occur. Once patients have been tested for a sufficient period (usually 7-10 days) then a decision can be taken on whether to recommend permanent implants. If, for whatever reason, patients do not complete the test period, then most later undergo successful re-testing.

Permanent implants may also become infected (2-3%), dislodged (5%) or cause pain (4%). Infection necessitates removal of the device but does not preclude re-implantation once the

infection has settled. Lead dislodgement or breakage is commonly followed by relocation or replacement of the lead. Pain has been caused in the past from placing the IPG abdominally, but it is reported that this has been resolved by placing it in the buttock. Pain has also resulted from setting the battery casement as the anode. This practice has now been discontinued for this reason.

There are no reports of longstanding complications from either temporary or permanent SNS implantation.

6 NEED FOR FURTHER AUDIT OR RESEARCH

6.1 Collection of further data

In the United Kingdom data are contributed to a UK registry database established by Medtronic, Inc. Continuation of the Registry, particularly if involving all UK centres, would provide more robust data than are reviewed here. The possibility of unanticipated long-term complications could be addressed most reliably by continued follow-up of currently registered patients.

6.2 **Further investigation** (new data collection/trials)

The procedure is not licensed in the USA as Food and Drug Administration (FDA) approval has not yet been granted. Patients are currently being recruited in the USA for a trial of SNS for faecal incontinence, with FDA approval in mind.

The use of bilateral sacral spinal nerve stimulation[28] has been suggested as a solution for patients who do not respond satisfactorily to unilateral stimulation; only one such patient, however, has been reported in the literature and this warrants further research.

In the case series to date patients have acted as their own controls. It is possible that future trials may randomly allocate patients to receive either SNS or an alternative treatment, either operative or conservative. No alternative treatment, apart from sphincter bulking injections, falls into the minimally invasive category between conservative treatment and major interventional surgery. As the benefits of SNS appear to be large, judged on the case series to date, the choice of comparator is not obvious.

7 REFERENCES

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Appendix 1 Patient selection criteria

Inclusion criteria:

Signed informed consent

Age 18- 75 years

≥1 episode of faecal incontinence/week (assessed by means of a baseline bowel habit diary)

Intact external sphincter +/- previous repair

Failed conservative therapy (anti-diarrhoeals/biofeedback)

Competent to fill in questionnaires and attend clinics

Exclusion criteria:

Congenital anorectal malformations

Rectal surgery done <12 months ago (<24 months for cancer)

Present external rectal prolapse

Chronic bowel diseases (e.g. IBD)

Chronic diarrhoea, unmanageable by diet or drugs

Altered bowel habit associated with abdominal pain.

Stoma in situ

Neurological diseases (e.g. diabetic neuropathy, multiple sclerosis or Parkinson's disease)

Bleeding complications

Pregnancy

Anatomical limitations preventing placement of an electrode

Skin disease risking infection (e.g. pyoderma, pilonidal sinus)

Psychiatric or physical inability to comply with the study protocol

Patients for whom patient materials are not available in a language understood by the patient

Source: lead author's clinical project file (MDT–301 study - sacral nerve stimulation for faecal incontinence)

Appendix 2 Literature search strategies

1 MEDLINE (1966- May Week 2 2003) EMBASE (1980 – Week 21 2003) Ovid Multifile Search URL: http://gateway.ovid.com/athens

1 ((sacral or s3) adj3 (stimulat$ or modulat$)).tw.
2 ((sacral or s3) adj3 (neurostimulat$ or (neural adj1 stimulat$) or (nerve adj1 stimulat$))).tw.
3 ((sacral or s3) adj3 (neuromodulat$ or (neural adj1 stimulat$) or (nerve adj1 stimulat$))).tw.
4 ((sacral or s3) adj3 (electrostimulat$ or electrical stimulat$)).tw.
5 sacral nerve stimulation/ use emez
6 or/1-5
7 electric stimulation therapy/
8 transcutaneous electric nerve stimulation/
9 electrodes,implanted/
10 neuromodulation/ use emez
11 nerve stimulation/ use emez
12 (stimulat$ or modulat$).tw.
13 (neurostimulat$ or (neural adj1 stimulat$) or (nerve adj1 stimulat$)).tw.
14 (neuromodulat$ or (neural adj1 modulat$) or (nerve adj1 modulat$)).tw.
15 (electrostimulat$ or electrical stimulat$).tw.
16 ((implant$ or insert$) adj3 (neuroprosthes$ or neural prosthes$)).tw.
17 ((implant$ or insert$) adj3 (neurostimulat$ or neural stimulat$)).tw.
18 ((implant$ or insert$) adj3 (electrostimulat$ or electrical stimulat$)).tw.
19 ((implant$ or insert$) adj3 pulse generator?).tw.
20 or/7-19
21 (sacral$ or sacrum or sacro$).tw.
22 sacrum/
23 lumbosacral plexus/
24 Sacrococcygeal region/ use mesz
25 sacral spinal cord/ use emez
26 spinal root/ use emez
27 lumbosacral spine/ use emez
28 or/21-27
29 6 or (20 and 28)
30 animal/ or nonhuman/
31 human/
32 30 not 31
33 29 not 32
34 ae.fs. use mesz
35 co.fs
36 i.fs. use emez
37 equipment failure/
38 equipment safety/
39 (lead adj (migrat$ or avulsion)).tw.
40 ((surgical or surgery) adj3 (revision or interven$ or reinterven$)).tw.
41 (implant adj3 (remov$ or replac$)).tw.
42 re operat$.tw.
43 or/34-42
44 33 and 43
45 fecal incontinence/
46 constipation/

47 anus sphincter/ use emez
48 anus/ use mesz
49 ((faecal or fecal or feces or anal) adj3 incontinence).tw.
50 constipation.tw
51 anorectal.tw.
52 anal sphincter?.tw.
53 (faecal or fecal) adj3 urgency).tw.
54 or/47-53
55 33 and 54
56 44 or 55
57 Remove duplicates from 56

2. CINAHL 1985 – May 2003
Ovid URL: http://gateway.ovid.com/athens

1 ((sacral or s3) adj3 (stimulat$ or modulat$)).tw.
2 ((sacral or s3) adj3 (neurostimulat$ or (neural adj1 stimulat$) or (nerve adj1 stimulat$))).tw.
3 ((sacral or s3) adj3 (neuromodulat$ or (neural adj1 stimulat$) or (nerve adj1 stimulat$))).tw.
4 ((sacral or s3) adj3 (electrostimulat$ or electrical stimulat$)).tw.
5 or/1-4
6 electric stimulation/
7 electric stimulation,neuromuscular/
8 transcutaneous electric nerve stimulation/
9 electrodes,implanted/
10 (stimulat$ or modulat$).tw.
11 (neurostimulat$ or (neural adj1 stimulat$) or (nerve adj1 stimulat$)).tw.
12 (neuromodulat$ or (neural adj1 modulat$) or (nerve adj1 modulat$)).tw.
13 (electrostimulat$ or electrical stimulat$).tw.
14 ((implant$ or insert$) adj3 (neuroprosthes$ or neural prosthes$)).tw.
15 ((implant$ or insert$) adj3 (neurostimulat$ or neural stimulat$)).tw.
16 ((implant$ or insert$) adj3 (electrostimulat$ or electrical stimulat$)).tw.
17 ((implant$ or insert$) adj3 pulse generator?).tw.
18 or/6-17
19 (sacral$ or sacrum or sacro$).tw.
20 sacrum/
21 lumbosacral plexus/
22 spinal nerve roots/
23 spinal nerves/
24 or/19-23
25 5 or (18 and 24)
26 animal/
27 human/
28 26 not 27
29 25 not 28
30 ae.fs.
31 co.fs.
32 equipment failure/
33 equipment safety/
34 (lead adj (migrat$ or avulsion)).tw.
35 ((surgical or surgery) adj3 (revision or interven$ or reinterven$)).tw.

36 (implant adj3 (remov$ or replac$)).tw.
37 re operat$.tw.
38 or/30-37
39 fecal incontinence/
40 constipation/
41 ((faecal or fecal or anal) adj3 incontinence).tw.
42 constipation.tw.
43 anorectal.tw.
44 anal sphincter?.tw.
45 ((faecal or fecal) adj3 urgency).tw.
46 or/39-45
47 29 and 38
48 29 and 46
49 47 or 48

3 BIOSIS 1985 – 28th May 2003
Edina URL:http://edina.ac.uk/biosis/

(((((al: (anal n1 sphincter)) or al:(faecal n1 urgency)) or al: (fecal n1 urgency)) or (((al: (anal n1 incontinence)) or al: (constipation)) or al: (anorectal))) or (((al: (fecal n1 incontinence)) or al: (faecal n1 incontinence)) or al: (feces n1 incontinence))) or
(((((((al: (surg* n3 revision)) or al: (surg* n3 interven*)) or al: (surg* n3 reinterven*)) or (((al: (implant n3 remov*)) or al: (implant n3 replac*)) or al: (re n operat*))) or ((al: (lead n1 migration)) or al: (lead n1 avulsion))) or ((al: (equipment n1 failure)) or al: (equipment n1 safety))) or (((al: (adverse n1 effect*)) or al: (adverse n1 event*)) or al: (complication*)))
and
(((((((((al: (pulse n1 generator)) or al: (electrostimulat*)) or al: (electrical n1 stimulat*)) or (((al: (neuromodulat*)) or al: (neural n1 modulat*)) or al: (nerve n1 modulat*))) or (((al: (implant)) or al: (neuroprosthes*)) or al: (neural prosthes*))) or (((al: (neurostimulat*)) or al: (neural n1 stimulat*)) or al: (nerve n1 stimulat*))) and ((al: (lumbosacral)) or (((al: (sacral)) or al: (sacro*)) or al: (sacrum)))) or
((((((al: (sacral n3 stimulat*)) or al: (s3 n3 stimulat*)) or ((al: (sacral n3 modulat*)) or al: (s3 n3 modulat*))) or (((al: (s3 n3 neurostimulat*)) or al: (s3 n3 neuromodulat*)) or al: (s3 n3 electrostimulat*))) or (((al: (sacral n3 neurostimulat*)) or al: (sacral n3 neuromodulat*)) or al: (sacral n3 electrostimulat*))) or ((mq: (sacral)) or ((mq: (interstim)) or (((mq: (sacral nerve stimulat*)) or mq: (neurostimulat*)) or mq: (neuromodulat*)))))) and (su: (humans)))

4 **Science Citation Index 1981 – 8th June 2003**
Web of Science Proceedings 1990 – 8th June 2003
Web of Knowledge URL: http://wok.mimas.ac.uk/

((((sacral or s3) SAME (stimulat* or modulat*)) or neurostimulat* or neuromodulat* or electrostimulat* or neuroprosthes*)) and (((faecal or fecal or anal) same incontinence) or constipation or anorectal or anal or anus)

5 Cochrane Library Issue 2,2003
URL: http://www.update-software.com/clibng/cliblogon.htm

1. SR-Incont
2. Sacral
3. S3
4. #1 and (#2 or #3)
5. SACRUM single term (MeSH)
6. LUMBOSACRAL PLEXUS single term (MeSH)
7. SACROCOCCYGEAL REGION single term (MeSH)
8. (neurostimulat* or neuromodulat* or stimulat* or electrostimulat*)
9. ELECTRIC STIMULATION THERAPY single term (MeSH)
10. TRANSCUTANEOUS ELECTRIC NERVE STIMULATION single term (MeSH)
11. ELECTRODES IMPLANTED single term (MeSH)
12. (#2 or #3 or #5 or #6 or #7)
13. (#8 or #9 or #10 or #11)
14. (#12 and #13)
15. (#4 or #14)

6. Journals@Ovid Full Text (June 10th 2003)
Ovid URL: http://gateway.ovid.com/athens

1 gut.jn.
2 (colorectal disease or colorectal disease supplement).jn.
3 diseases of the colon & rectum.jn.
4 1 or 2 or 3
5 (sacral or s3).tw.
6 (stimulat$ or modulat$).tw.
7 (neurostimulat$ or (neural adj1 stimulat$) or (nerve adj1 stimulat$)).tw.
8 (neuromodulat$ or (neural adj1 modulat$) or (nerve adj1 modulat$)).tw.
9 (electrostimulat$ or electrical stimulat$).tw.
10 ((implant$ or insert$) adj3 (neuroprosthes$ or neural prosthes$ or neurostimulat$ or neural stimulat$ or electrostimulat$ or electrical stimulat$)).tw.
11 ((implant$ or insert$) adj3 pulse generator?).tw.
12 5 and (6 or 7 or 8 or 9 or 10 or 11)
13 4 and 12
14 ((fecal or faecal or anal) adj3 incontinence).tw.
15 constipation.tw.
16 anorectal.tw.
17 anal sphincter?.tw.
18 12 and (14 or 15 or 16 or 17)
19 american journal of surgery.jn.
20 annals of surgery.jn.
21 (anz journal of surgery or australian & new zealand journal of surgery).jn.
22 (british journal of surgery or british journal of surgery supplement).jn.
23 canadian journal of surgery.jn.
24 clinics in colon & rectal surgery.jn.
25 journal of pelvic surgery.jn.
26 surgery.jn.
27 or/19-26
28 18 and 27
29 13 or 28

7 DARE and HTA Database (May 2003)
NHS Centre for Reviews & Dissemination
URL:http://nhscrd.york.ac.uk/welcome.htm

(Sacral and stimulat*)
or electrostimulat*
or neurostimulat*
or neuromodulat*
or faecal incontinence
or fecal incontinence

8 National Research Register (May 2003)
URL: http://www.update-software.com/National/

Sacral nerve stimulation
Or
Sacral or stimulat* or electrostimulat* or neurostimulat* or neuromodulat* or incontinent*

9. Clinical Trials (May 2003)URL: http://clinicaltrials.gov/ct/gui/c/r
Current Controlled Trials (May 2003) URL: http://www.controlled-trials.com/
Research Findings Register (May 2003) URL:
http://tap.ukwebhost.eds.com/doh/refr_web.nsf/Home?OpenForm

Sacral or stimulat* or electrostimulat* or neurostimulat* or neuromodulat* or incontinence

In addition the following Websites were searched for evidence-based reports (accessed May 2003):

Alberta Heritage Foundation for Medical Research URL: http://www.ahfmr.ca/
American Gastroenterological Association URL: http://www.gastro.org/
ASERNIP-S URL: http://www.surgeons.org/asernip-s/
Association of Coloproctology of Great Britain & Ireland URL: http://www.acpgbi.org.uk/
Blue Cross Blue Shield Technology Evaluation Center URL:
http://www.bcbs.com/tec/tecassessments.html
CCOHTA URL: http://www.ccohta.ca/
Centers for Medicare & Medicaid Services URL:
http://cms.hhs.gov/mcd/index_list.asp?list_type=tech
Colorectal Eporediensis Centre URL: http://www.colorep.it/
ECRI URL: http://www.ecri.org/
FDA Center for Devices & Radiological Health URL: http://www.fda.gov/cdrh/
International Continence Society URL: http://www.continet.org/
Medicines & Healthcare Products Regulatory Agency URL: http://www.medical-devices.gov.uk/
Medtronic URL: http://www.medtronic.com/
SUMSEARCH URL: http://sumsearch.uthscsa.edu
TRIP database URL: http://www.update-software.com/scripts/clibng/usauth.exe?Server=TRIPUSER&Product=TRIP&Guest=YES

Appendix 3 Sacral nerve stimulation for adults with faecal incontinence

Checklist for quality assessment - case series

(adapted from CRD's Guidance for those Carrying out or Commissioning Reviews, 2001 and from Downs and Black, 1998)

Paper number: _____ **Study identifier:** _____
Assessor initials: _____ **Date form completed:** _____

Criteria	Yes	No	Unclear	Comments
1. Were participants a representative sample selected from a relevant patient population?				
2. Are the inclusion/exclusion criteria of patients in the study clearly described?				
3. Were participants entering the study at a similar point in their disease progression?				
4. Was selection of patients consecutive?				
5. Were all important prognostic factors identified?				
6. Was data collection undertaken prospectively?				
7. Was the recruitment period clearly stated?				
8. Was the intervention that which is being considered in the review? (or was it a significant modification?)				
9. Was an attempt made to blind outcomes assessors?				
10. Was the operation undertaken by someone experienced in performing the procedure?				
11. Did the staff, place, and facilities where the patients were treated provide an appropriate environment for performing the procedure? (e.g. was the intervention undertaken in a centre with necessary back-up facilities?)				
12. Were objective (valid and reliable) outcome measures used?				
13. Were all the important outcomes considered?				
14. Was follow-up long enough to detect important effects on outcomes of interest?				
15. Was information provided on non-respondents, dropouts?				
16. Were participants lost to follow-up likely to introduce bias? (e.g. high drop-out rate; no description of those lost)				
17. Were the main findings clearly described?				

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Appendix 4 Sacral nerve stimulation for adults with faecal incontinence

Checklist for quality assessment - RCTs

(adapted from Verhagen et al., 1998)

Paper number: _____ **Study identifier:** _____

Assessor initials: _____ **Date form completed:** _____

Criteria	Yes	No	Unclear	Comments
1. Was the assignment to the treatment groups really random? **Adequate approaches to sequence generation** • computer-generated random tables • random number tables **Inadequate approaches to sequence generation** • use of alternation, case record numbers, birth dates or week days				
2. Was the treatment allocation concealed? **Adequate approaches to concealment of randomisation** • centralised or pharmacy-controlled randomisation • serially-numbered identical containers • on-site computer based system with a randomisation sequence that is not readable until allocation • other approaches with robust methods to prevent foreknowledge of the allocation sequence to clinicians and patients **Inadequate approaches to concealment of randomisation** • use of alternation, case record numbers, birth dates or week days • open random numbers lists • serially numbered envelopes (even sealed opaque envelopes can be subject to manipulation)				
3. Were the groups similar at baseline in terms of prognostic factors?				
4. Were the eligibility criteria specified?				
5. Were the groups treated in the same way apart from the intervention received?				
6. Was the outcome assessor blinded to the treatment allocation?				
7. Was the care provider blinded?				
8. Were the patients blinded?				
9. Were the point estimates and measures of variability presented for the primary outcome measures?				
10. Was the withdrawal/drop-out rate likely to cause bias?				
11. Did the analyses include an intention-to-treat analysis?				

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Appendix 5 Efficacy and safety of SNS for faecal incontinence - data extraction form

Reviewer ID: _____ **Date information extracted:** _____

Study Details
Study ID: **Refman ID number:**
Published ☐ **Unpublished** ☐
Other papers this study may link with: _____ _____ _____ (Refman id/study id nos.) _____ _____ _____
Study Design
RCT ☐ **Case report** ☐
Comparative observational study ☐ **Systematic review** ☐
Population-based registry ☐ **Other** ☐
Case series ☐
Additional comments on study design:
Details of interventions
(List all included in study)
A: SNS
B:
Setting/Timing
Study setting:
Source of participants:
Recruitment period:
Length of follow-up:
Source(s) of funding for study:

Characteristics of the participants
Inclusion criteria (please tick all that apply): ☐ **Signed informed consent** ☐ **Aged 18-75 years** ☐ **Faecal incontinence defined as incontinence to solid or liquid stool > 1/week (assessed by means of a bowel habit diary)** ☐ **Intact external anal sphincter** ☐ **Circumferentially intact, no previous surgery** ☐ **Circumferentially intact, previous repair (for > 50% of the length of the anal canal)** ☐ **Failed medical therapy** ☐ **Failed biofeedback therapy** ☐ **Willing and competent to fill out study questionnaire** ☐ **Willing to travel for all required visits** ☐ **Other (please state):**
Exclusion criteria (please tick all that apply): ☐ **Congenital anorectal malformations** ☐ **Previous rectal surgery** ☐ **Present external rectal prolapse** ☐ **Chronic bowel diseases** ☐ **Chronic diarrhoea, unmanageable by diet or drugs** ☐ **Alternating bowel habit, associated with abdominal pain** ☐ **Stoma in situ** ☐ **Bleeding complications** ☐ **Pregnancy** ☐ **Anatomical limitations that would prevent implantation** ☐ **Pilonidal sinus** ☐ **Psychiatric or physical inability to comply with the study protocol** ☐ **Patients for whom study materials are not available in the patient's language** ☐ **Other (please state):**
☐ ☐

	Group A	Group B	All
Number enrolled in trial			
Number receiving: **(a) Acute testing** **(b) PNE**			
Reasons if difference between (a) and (b)			
Reasons if number receiving PNE differ from number enrolled			
Number receiving permanent implant			
Reasons if number receiving permanent implant differ from number receiving PNE			
Number lost to follow-up			
Number analysed			
Number for whom baseline data given			
Mean age (range)			
Gender	**M:** **F:**	**M:** **F:**	**M:** **F:**
Duration of symptoms			
With co-existing urinary incontinence: **Stress** **Urge** **Mixed**			
With co-existing urinary retention			
Causes of FI			
Other comorbidities:			

Characteristics of the intervention(s)		
Make and model of SNS equipment used:		
Temporary wire electrode Medtronic 004 ☐		
Temporary wire electrode Medtronic 3057 ☐		
Permanent electrode Medtronic 3080 ☐		
Percutaneous tined electrode Medtronic 3090 ☐		
Portable external stimulator Medtronic 3625 ☐		
Implantable pulse generator Medtronic 3023 ☐		
Other (please state): ☐		
Stimulation parameters	**PNE phase**	**Implanted phase**
Amplitude (volts):		
Frequency (Hz):		
Pulse width:	210 microseconds	210 microseconds
Continuous:	☐	☐
Cyclical:	☐	☐
Criteria for PNE being considered positive/patients being offererd implantable pulse generator:		
≥ 50% improvement in continence, in terms of: ☐		
(a) Number of days affected ☐		
(b) Number of incontinent episodes ☐		
Other (please state) ☐		
Duration of PNE phase: _____ days		
Sacral nerves used:	**PNE phase**	**Implanted phase**
S2	☐	☐
S3	☐	☐
S4	☐	☐
Unilateral	☐	☐
Bilateral	☐	☐
Implant placed in:		
Abdominal wall		☐
Buttock		☐
Patient clinical diary used: Yes ☐ **No** ☐ **If yes, period covered:** _____		
Type of information recorded:		

Outcomes			
	Group A	**Group B**	**All**
Number cured: (continent) **Pre-PNE** **Implanted,** **latest follow-up** **____ months**			
Number improved: **Pre-PNE** **Implanted,** **latest follow-up** **____ months**			
Episodes of FI: **Pre-PNE** **Implanted,** **latest follow-up** **____ months**			
Urgency: **Pre-PNE** **Implanted,** **latest follow-up** **____ months**			
Number of patients using absorbent pads: **Pre-PNE** **Implanted,** **latest follow-up** **____ months**			
Number of patients using anal plugs: **Pre-PNE** **Implanted,** **latest follow-up** **____ months**			
Improvement/alteration in urinary incontinence: **Pre-PNE** **Implanted,** **latest follow-up** **____ months**			

	Group A	Group B	All
Adverse events (PNE PHASE) requiring: **(a) No intervention** **(b) Non-surgical intervention:** ***(i) Antibiotics*** ***(ii) Local anaesthetic/ steroid injection*** ***(iii) Alteration of stimulator settings*** **(c) Surgical intervention:** ***(i) Relocation of electrode*** ***(ii) Explantation of electrode*** **ADVERSE EVENTS:** **Pain at implant site** **Pain at implanted pulse generator site** **Pain from leads** **Lead migration** **Infection/skin irritation** **Increased electrical sensation** **Adverse change in bowel functions** **Adverse change in urinary function** **Numbness** **Technical problems** **Other (please state):**			

	Group A	Group B	All
Adverse events (IMPLANTED PHASE) requiring: **(a) No intervention** **(b) Non-surgical intervention:** ***(i) Antibiotics*** ***(ii) Local anaesthetic/ steroid injection*** ***(iii) Alteration of stimulator settings*** **(c) Surgical intervention:** **(*i) Relocation of electrode*** ***(ii) Explantation of stimulator and electrode*** ***(iii) IPG replacement*** **ADVERSE EVENTS:** **Pain at implant site** **Pain at implanted pulse generator site** **Pain from leads** **Lead migration** **Infection/skin irritation** **Increased electrical sensation** **Adverse change in bowel functions** **Adverse change in urinary function** **Numbness** **Technical problems** **Other (please state):**			

	Group A	Group B	All
Incontinence score: Wexner Score ☐ Cleveland Clinic Score ☐ Other (please state): ☐			
Pre-PNE **Implanted, latest follow-up: ____ months**			
Quality of life: condition-specific: ASCRS ☐ Other (please state): ☐			
Pre-PNE **Implanted, latest follow-up: ____ months**			
Quality of life: generic: SF-36 ☐ Other (please state): ☐			
Pre-PNE **Implanted, latest follow-up: ____ months**			
Anorectal manometry			
Resting pressure (mmHg): **Pre-PNE** **Implanted, latest follow-up ____ months**			
Maximal squeeze pressure (mmHg): **Pre-PNE** **Implanted, latest follow-up ____ months**			
Rectal sensory threshold to balloon distention: **Pre-PNE** **Implanted, latest follow-up ____ months**			

Anorectal manometry (cont)	Group A	Group B	All
Sensation of urgency to balloon distention: **Pre-PNE** **Implanted, latest follow-up ____ months**			
Maximal tolerated rectal volume to balloon distention: **Pre-PNE** **Implanted, latest follow-up ____ months**			

Additional comments

This form was last amended on 10 July 2003.

Appendix 6 List of included studies with related references

Ganio 2002

Primary reference:

Ganio E, Realis Luc A, Ratto C, Doglietto GB, Masin A, Dodi G et al. Sacral nerve modulation for fecal incontinence: functional results and assessment of quality of life. URL: www colorep it. (accessed May 2003)

Related references:

Ganio E, Ratto C, Masin A, Luc AR, Doglietto GB, Dodi G et al. Neuromodulation for fecal incontinence: outcome in 16 patients with definitive implant. The initial Italian Sacral Neurostimulation Group (GINS) experience. Diseases of the Colon & Rectum 2001;44(7):965-70.

Ganio E, Luc AR, Clerico G, Trompetto M. Sacral nerve stimulation for treatment of fecal incontinence: a novel approach for intractable fecal incontinence. Diseases of the Colon & Rectum 2001;44(5):619-29.

Ganio E. Sacral nerve modulation for fecal incontinence. Diseases of the Colon & Rectum 2001;44(4):A9-A10.

Ratto C, Morelli U, Paparo S, Parello A, Doglietto GB. Minimally invasive sacral neuromodulation implant technique: modifications to the conventional procedure. Diseases of the Colon & Rectum 2003;46(3):414-7.

Ripetti V, Caputo D, Ausania F, Esposito E, Bruni R, Arullani A. Sacral nerve neuromodulation improves physical, psychological and social quality of life in patients with fecal incontinence. Techniques in Coloproctology 2002;6(3):147-52.

Jarrett 2003

Primary reference:

Jarrett ME, Varma JS, Duthie GS, Nicholls RJ, Kamm MA. Sacral nerve stimulation for faecal incontinence: the United Kingdom experience. (unpublished)

Related references:

Kenefick NJ, Vaizey CJ, Cohen RC, Nicholls RJ, Kamm MA. Medium-term results of permanent sacral nerve stimulation for faecal incontinence. British Journal of Surgery 2002;89(7):896-901.

Kenefick NJ, Vaizey CJ, Nicholls RJ, Cohen R, Kamm MA. Sacral nerve stimulation for faecal incontinence due to systemic sclerosis. Gut 2002;51(6):881-3.

Kenefick NJ, Vaizey CJ, Malouf AJ, Cohen I, Nicholls RJ, Kamm MA. Sacral nerve neuromodulation for the treatment of resistant faecal incontinence. British Journal of Surgery 2002;89(Suppl 1):14.

Kenefick NJ, Malouf AJ, Vaizey CJ, Cohen R, Nicholls RJ, Kamm MA. Sacral nerve stimulation for faecal incontinence: a five-year experience. Gastroenterology 2002;122(4 Suppl 1):A446.

Kenefick NJ, Vaizey CJ, Nicholls RJ, Cohen R, Kamm MA. Treatment of faecal incontinence due to systemic sclerosis with sacral nerve stimulation. Gut 2002;50(Suppl 2):A58.

Kenefick NJ, Vaizey CJ, Nicholls RJ, Cohen R, Kamm MA. Sacral nerve stimulation for faecal incontinence in systemic sclerosis. Gastroenetrology 2002;122(4 Suppl 1):A-447.

Kenefick NJ, Vaizey CJ, Nicholls RJ, Cohen R, Kamm MA. Neuromodulation as a new surgical treatment for faecal incontinence due to scleroderma. British Journal of Surgery 2002;89(Suppl 1):80.

Kenefick NJ, Vaizey CJ, Malouf AJ, Cohen R, Nicholls RJ, Kamm MA. Cumulative long-term experience of sacral nerve stimulation for faecal incontinence. Colorectal Disease 2002;4(Suppl 1):34-5.

Kenefick NJ. A single-center experience of permanent sacral nerve neuromodulation for faecal incontinence. Diseases of the Colon & Rectum 2002;45(12):A34-A36.

Malouf AJ, Kamm MA, Nicholls RJ. Effect of acute changes in sacral nerve stimulation amplitude on anorectal function in faecal incontinence. Colorectal Disease 2000;2(6):336-9.

Malouf AJ, Vaizey CJ, Nicholls RJ, Kamm MA. Permanent sacral nerve stimulation for fecal incontinence. Annals of Surgery 2000;232(1):143-8.

Malouf AJ, Vaizey CJ, Nicholls RJ, Kamm MA. Results of permanent sacral nerve stimulation for fecal incontinence. Diseases of the Colon & Rectum 1999;42(4):A12.

Vaizey CJ, Kamm MA, Roy AJ, Nicholls RJ. Double-blind crossover study of sacral nerve stimulation for fecal incontinence. Diseases of the Colon & Rectum 2000;43(3):298-302.

Leroi 2001

Primary reference:

Leroi AM, Michot F, Grise P, Denis P. Effect of sacral nerve stimulation in patients with fecal and urinary incontinence. Diseases of the Colon & Rectum 2001;44(6):779-89.

Matzel 2003

Primary reference:

Matzel KE, Bittorf B, Stadelmaier U, Hohenberger W. [Sacral nerve stimulation in the treatment of faecal incontinence]. Chirurg 74(1):26-32, 2003.

Related references:

Matzel KE, Stadelmaier U, Hohenfellner M, Gall FP. Electrical stimulation of sacral spinal nerves for treatment of faecal incontinence. Lancet 1995;346(8983):1124-7.

Matzel K. Treatment of fecal incontinence by sacral spinal nerve stimulation using implantable foramen and cuff electrodes. Diseases of the Colon & Rectum 1998;41(4):A31.

Matzel KE, Stadelmaier U, Hohenfellner M, Hohenberger W. Chronic sacral spinal nerve stimulation for fecal incontinence: long-term results with foramen and cuff electrodes. Diseases of the Colon & Rectum 2001;44(1):59-66.

Matzel KE, Stadelmaier U, Bittorf B, Hohenfellner M, Hohenberger W. Bilateral sacral spinal nerve stimulation for fecal incontinence after low anterior rectum resection. International Journal of Colorectal Disease 2002;17(6):430-4.

Rosen 2001

Primary reference:

Rosen HR, Urbarz C, Holzer B, Novi G, Schiessel R. Sacral nerve stimulation as a treatment for fecal incontinence. Gastroenterology 2001;121(3):536-41.

Related references:

Rosen HR, Urbarz C, Novi G, Holzer B, Schiessel R. Sacral nerve stimulation for faecal incontinence - the Austrian experience. Colorectal Disease 2001;3(Suppl 2):68.

Uludag 2002

Primary reference:

Uludag O, Dejong HC, Baeten CG. Sacral neuromodulation for faecal incontinence. Diseases of the Colon & Rectum 2002;45(12):A34-A36.

Related references:

Baeten CG, Uludag O. Second-line treatment for faecal incontinence. Scandinavian Journal of Gastroenterology - Supplement 2002;(236):72-5.

MDT-301 2003

Primary reference:

Matzel KE, Kamm MA, Stosser M, Baeten CG, Christiansen J, Madoff R et al. Sacral spinal nerve stimulation for fecal incontinence: a multicenter study. (unpublished)

Appendix 7 Characteristics of the included studies

(a) Case series

Study details	Participants	Outcomes				Notes
		Faecal incontinence	Health status	Anorectal manometry	Adverse events	
Study id: Ganio 2002[23] **Related references:**[29-33] **Type:** case series **Inclusion criteria:** at least 1 faecal incontinent episode per week to either solid or liquid stool during the preceding 2 months; intact external anal sphincter; failed medical therapy; failed biofeedback therapy **Exclusion criteria:** inflammatory bowel disease; pregnancy; cardiac disease; aged over 75 years; pathologic conditions of the sacrum such as spina bifida; skin disease in the sacral area **Country/setting:** Italy (GINS: the Italian SNS Research Group) **Recruitment period:** Jan 1996 – Dec 2001 **Length of follow-up:** **Mean (range)** 25.6 (1-56) months	**Enrolled:** 116 **Received PNE:** 116 **Received permanent implant:** 31 **Lost to follow-up:** 0 **Age** **Mean (range) (for the 36 patients selected for definitive implant):** 55.2 (26-77) **Gender:** M7, F29 **Site of implant:** abdominal wall or buttock **Not reported:** duration of symptoms; co-existing urinary incontinence; co-existing urinary retention	**Episodes of FI per week (31 patients).** **Mean (range)** **Baseline:** 7.5 (1-11) **12 month follow-up:** 0.15 (0-2) **Pad use (per day)** **Mean** **Baseline:** 1.25 **12 month follow-up (7 patients):** 1.9 **Not reported:** cured; improved; ability to defer defaecation; episodes of urgency; use of pads; use of anal plugs; improvement in urinary incontinence	**Incontinence score** Cleveland Clinic **Mean (range)** **Baseline:** 14.6 (6-20) **Follow-up:** 4.2 (3-9) **QOL: generic** SF-36 **Mean** **Baseline (18 patients); 12 month follow-up (7 patients)** Physical functioning: 58; 64 Role-physical: 49; 70 Bodily pain: 49; 57 General health: 46; 57 Vitality: 43; 51 Social functioning: 49; 58 Role-emotional: 40; 51 Mental health: 50; 50 **Not reported:** QOL: condition specific	**Number of patients: not reported** **Mean (±SD)** **Resting pressure (maximal) (mmHg)** **Baseline:** 37.3 (± 19.2) **3 month follow-up:** 46.1 (± 20.0) p=NS **Max squeeze pressure (mmHg)** **Baseline:** 73.6 (± 37.1) **3 month follow-up:** 79.0 (± 37.1) p=NS **Rectal volume for first urge sensation (cc)*** **Baseline:** 117 (**±** 88) **12 month follow-up:** 57 (± 35) **Not reported:** rectal sensory threshold to balloon distention; sensation of urgency to balloon distention; max tolerated rectal volume to balloon distention	**Pain at implant site (when IPG case was used as anode - unipolar impulse):** 1/31. Action taken: alteration of stimulator settings. **Lead migration (after 3 months):** 1/31. Action taken: relocation of electrode. **Infection:** 0 (no local sepsis). **Other: interruption of the electrode causing decreased effectiveness (at 11 months):** 1/31. Action taken: lead was changed and the patient recovered continence. **Not reported:** pain at IPG site; pain from leads; increased electrical sensation; adverse change in bowel function; adverse change in urinary function; numbness; technical problems.	NS = Not significant The Cleveland Clinic Incontinence Score ranges from a best score of 0 to a max (worst) score of 20. SF-36: best score is 100, worst is 0. Values for the subscales were estimated from Figure 2 of study paper. * Authors' interpretation of poorly reported data. Not reported: adverse events at PNE

Study details	Participants	Outcomes				Notes
		Faecal incontinence	Health status	Anorectal manometry	Adverse events	
Study id: Jarrett 2003 (M.E.D. Jarrett, St Mark's Hospital, London, 2003) **Related references:**[5,21,34-44] **Type:** population-based registry (UK only) **Inclusion criteria:** at least 1 faecal incontinent episode per week to either solid or liquid stool; failed medical therapy; failed biofeedback therapy **Exclusion criteria:** not reported **Country/setting:** UK/3 centres (St Mark's Hospital, London; Castle Hill Hospital, Hull; Royal Victoria Infirmary, Newcastle-upon-Tyne) **Recruitment period:** Oct 1996 – May 2003 **Length of follow-up:** **Median (range)** 12 (1-72) months	**Enrolled:** 59 **Received PNE:** 59 **Received permanent implant:** 46 **Lost to follow-up:** 0 **Age** **Median (range):** 56 (35-68) years **Gender:** M6, F40 **Duration of symptoms:** **Median (range)** 5 (1-21) years **Site of implant:** early part of series: abdominal wall; later part of series: buttock **Not reported:** with co-existing urinary incontinence; with co-existing urinary retention	**Cured** **Median 12 month follow-up:** 19/46 **Improved (includes cured)** **Median 12 month follow-up:** 44/46 **Episodes of FI per week (46 patients)** **Median (range)** **Baseline:** 7.5 (1-78) **Median 12 month follow-up:** 1 (0-39) P<0.0001 **Ability to defer defaecation (minutes) (39 patients)** **Median (range)** **Baseline:** <1 (0-5) **Median 12 month follow-up:** 5-15 (1->15) p<0.0001 **Not reported:** episodes of urgency; use of pads; use of anal plugs; improvement in urinary incontinence	**Incontinence score** Cleveland Clinic (27 patients) **Median (range)** **Baseline:** 14 (5-20) **Follow-up:** 6 (1-12) p<0.0001 **QOL: condition specific** ASCRS (36 patients) **Median scores** **Baseline; median 12 month follow-up** Lifestyle: 2.0; 3.6# Coping/behaviour: 1.52; 2.66# Depression: 2.16; 3.10# Embarrassment: 1.85; 2.81# **QOL: generic** SF-36 (46 patients) **Mean scores** **Baseline; median 12 month follow-up:** Role-emotional: 49; 64* Role-physical: 50; 60 Physical functioning: 62; 65 Social functioning: 53; 67* General health: 49; 55* Mental health: 54; 64* Bodily pain: 53; 55 Vitality: 37; 46*	**n=46** **Mean (± SD)** **Resting pressure (maximal) (cmH2O)** **Baseline:** 46 (± 23) **Median 12 month follow-up:** 49 (± 24) p=0.3 **Max squeeze pressure (cmH2O)** **Baseline:** 62 (± 53) **Median 12 month follow-up:** 93 (± 47) p<0.01 **Rectal sensory threshold to balloon distention (ml air)** **Baseline:** 41 (± 22) **Median 12 month follow-up:** 27 (± 18) p<0.0001 **Sensation of urgency to balloon distention (ml air)** **Baseline:** 92 (± 40) **Median 12 month follow-up:** 71 (± 38) p<0.001 **Max tolerated rectal volume to balloon distention (ml air)** **Baseline:** 129 (± 39) **Median 12 month follow-up:** 107 (± 42) p<0.01	**Pain from leads:** 3/46 (early in series when IPG implanted in anterior abdominal wall). Action taken: in all patients problem resolved after local injection of local anaesthesia and steroid injections. Subsequent implants were placed in buttock. **Lead migration:** 4/46. Early in series (1 at 3 days, 1 at 1 month, 1 at 1 year and 1 at 2 years). Action taken: the first 3 patients had their leads repositioned successfully; the fourth was offered replacement but wanted the implant removed. **Not reported:** pain at implant site; pain at IPG site; infection/skin irritation; increased electrical sensation; adverse change in bowel function; adverse change in urinary function; numbness; technical problems.	Ability to defer defaecation: 34/39 patients improved. The Cleveland Clinic Incontinence Score ranges from a best score of 0 to a max (worst) score of 20. SF-36: best score is 100, worst is 0. * = p<0.05 versus baseline. ASCRS: best score is 5, worst is 1. # = p<0.0001 versus baseline. Adverse events at PNE: 1 patient had a superficial skin infection that settled on removal of the screening electrode wire; 7 temporary leads became displaced. Adverse events at permanent implant: there were no major complications.

Study details	Participants	Outcomes				Notes
		Faecal incontinence	Health status	Anorectal manometry	Adverse events	
Study id: Leroi 2001[24] **Related references:** none identified **Type:** case series **Inclusion criteria:** passive or urge incontinence for solid and/or liquid stools at least once per week for at least 3 months; failed medical therapy; patients with external anal sphincter damage on ultrasound were included in the study if the defect was not considered to be the main cause of faecal incontinence **Exclusion criteria:** rectal prolapse; inflammatory bowel disease; pregnancy; psychiatric or physical inability to comply with the study protocol; procidentia; cauda equina lesions, sacral agenesia; diabetes mellitus; patients who had previously undergone pelvic floor irradiation or proctectomy; patients with abnormal rectoscopy and barium enema or colonoscopy **Country/setting:** France/Physiology Unit, Rouen Hospital Centre **Recruitment period:** May 1998 – April 1999	**Enrolled:** 11 **Received PNE:** 11 **Received permanent implant:** 6 Lost to follow-up: 1 **Age** **Mean (range):** 51.6 (33-71) **Gender:** M3, F8 **Duration of symptoms** **Median (range):** 2.7 (1-5) years **With co-existing urinary incontinence:** 10 (urge 3, mixed 7) **With co-existing urinary retention:** 1 **Not reported:** site of implant	**Cured** **6 month follow-up:** 2/4 **Improved (includes cured)** **6 month follow-up:** 3/4 **Episodes of FI per week (4 patients)** **Mean (±SD)** **Baseline:** 3.0 (± 2.7) **6 month follow-up:** 0.5 (± 0.6) **Ability to defer defaecation (minutes) (4 patients)** **Mean (±SD)** **Baseline:** 0.25 (± 0.5) **6 month follow-up:** 19.0 (± 13.9) **Episodes of urgency per week (4 patients)** **Mean (±SD)** **Baseline:** 4.75 (± 3.86) **6 month follow-up:** 2.3 (± 3.1) **Improvement in urinary incontinence** (a) Patients with stress urinary incontinence **Baseline:** 0/3 **3 month follow-up:** 0/3 (b) Urgency **Baseline:** 0/3	**Not reported:** Incontinence score; QOL: condition specific; QOL: generic	**Mean (± SD)** **Resting pressure (maximal) (cmH2O) (4 patients)** **Baseline:** 61.25 (± 17.5) **6 month follow-up:** 61.0 (± 14.3) **Max squeeze pressure (cmH2O) (4 patients)** **Baseline:** 49.25 (± 45.78) **6 month follow-up:** 39.5 (± 34.6) **Rectal sensory threshold to balloon distention (10 ml) (number of patients not reported)** **Baseline:** Normal **6 month follow-up:** Normal **Sensation of urgency to balloon distention (ml) (2 patients)** **Baseline:** 200 (± 226.27) **6 month follow-up:** 130 (± 113.14) **Max tolerated rectal volume to balloon distention (ml) (2 patients)** **Baseline:** 200 (± 226.27) **6 month follow-up:** 255 (± 148.5)	**Lead migration**: 1/4 **Infection/skin irritation:** 0/4 **Other: superficial wound dehiscence:** 1/4 **Not reported:** pain at implant site; pain at IPG site; pain from leads; increased electrical sensation; adverse change in bowel function; adverse change in urinary function; numbness; technical problems	Adverse events at PNE: the most important and frequent complication was electrode migration before the end of the 7 days of testing, occurring in 2 of 11 patients. Adverse events at implantation: no timescales were given indicating when adverse events occurred.

Study details	Participants	Outcomes				Notes
		Faecal incontinence	Health status	Anorectal manometry	Adverse events	
Length of follow-up: 6 months		**3 month follow-up:** 3/3 (c) Patients with detrusor overactivity **Baseline:** 0/2 **6 month follow-up**: 1/2 **Not reported:** use of pads; anal plugs				

Study details	Participants	Outcomes				Notes
		Faecal incontinence	Health status	Anorectal manometry	Adverse events	
Study id: Matzel 2003[26] **Related references:**[28,45-47] **Type: c**ase series **Inclusion criteria:** intact anal sphincter; failed medical therapy; failed biofeedback therapy **Exclusion criteria:** sacral pathology that would make placement difficult, including skin changes, infection; pilonidal sinus; high infection risk; urinary difficulties that might be made worse by SNS; pregnancy; intellectual, emotional or psychological problems; general comorbidity; pacemaker; sphincter defect that could be treated surgically **Country/setting:** Germany/Surgical Clinic, University of Erlangen-Nürnberg **Recruitment period:** not reported **Length of follow-up:** **Median (range)** 32.5 (3-99) months	**Enrolled:** 16 **Received PNE:** 16 **Received permanent implant:** 16 **Lost to follow-up**: 0 **Age** **Mean (range):** 54 (35-68) **Gender:** M2, F14 **Duration of symptoms** **Median (range):** 8.5 (2-30) years **Not reported:** with co-existing urinary incontinence; with co-existing urinary retention; site of implant	**n=16** **Percentage cured** **Latest follow-up:** 12/16 (75%) **Percentage improved (includes cured)** **Latest follow-up:** 16/16 (100%) **Percentage of bowel movements that were incontinent** **Median (range)** **Baseline:** 40% (5-100%) **Latest follow-up:** 0% (0-20%) p=0.001 **Not reported:** ability to defer defaecation; episodes of urgency; use of pads; use of anal plugs; improvement in urinary incontinence	**Incontinence score** Cleveland Clinic (11 patients) **Median (range)** **Baseline:** 17 (11-20) **12 month follow-up**: 5 (0-15) p=0.003 **QOL:** **condition specific** ASCRS (4 patients) **Median (range)** **Baseline; median 18 month follow-up** Lifestyle: 1.10 (1.00-2.10); 3.74 (3.40-4.00) p=0.068 Coping/behaviour: 1.07 (1.00-1.33); 3.18 (2.89-3.25) p=0.066 Depression: 1.84 (1.00-2.20); 4.02 (3.71-4.25) p=0.068 Embarrassment: 1.17 (1.00-2.50); 3.50 (3.22-4.00) p=0.068 **Not reported:** QOL: generic	**n=16** **Median (range)** **Resting pressure (mmHg)** **Baseline:** 63 (47-101) **Latest follow-up:** 59 (10-102) p=0.906 **Max squeeze pressure (mmHg)** **Baseline:** 69 (14-101) **Latest follow-up:** 97 (59-136) p=0.009 **Rectal sensory threshold to balloon distention (ml)** **Baseline:** 40 (20-70) **Latest follow-up:** 25.2 (20-100) p=0.263 **Sensation of urgency to balloon distention (ml)** **Baseline:** 60 (40-140) **Latest follow-up:** 70 (40-270) p=0.386 **Max tolerated rectal volume to balloon distention (ml)** **Baseline:** 150 (70-290) **Latest follow-up:** 200 (80-290) p=0.161	**Pain at implant site:** 1/16. Action taken: repositioning of device at 27 months. Pain continued and device removed at 45 months. [Same patient whose device became mobile after weight loss – see below]. **Pain from leads:** 1/16 experienced pain from electrode. Action taken: device removed after 5 months. **Adverse change in urinary function:** 1/16 developed urinary retention. Action taken: IPG switched off. **Other:** (a) Worsening efficacy: 1/16. Action taken: alteration of stimulator settings, but to no effect. Patient was found to have progressive neurological disease. (b) Device became mobile after weight loss: 1/16. Action taken: repositioning of device at 14 months **Not reported:** lead	The Cleveland Clinic Incontinence Score ranges from a best score of 0 to a max (worst) score of 20. ASCRS: best score is 5, worst is 1.

Study details	Participants	Outcomes				Notes
		Faecal incontinence	Health status	Anorectal manometry	Adverse events	
					migration; infection/skin irritation; increased electrical sensation; adverse change in bowel function; numbness; technical problems	

Study details	Participants	Outcomes				Notes
		Faecal incontinence	Health status	Anorectal manometry	Adverse events	
Study id: Rosen 2001[4] **Related references:**[48] **Type:** case series **Inclusion criteria:** informed consent; at least 1 faecal incontinent episode per week to solid stool; intact external anal sphincter documented by endoanal ultrasonography and/or MRI; failed biofeedback therapy; minimum history of FI of 1 year after a neurologic event (surgery, trauma, stroke). **Exclusion criteria:** evidence of diabetes or connective tissue disorders. **Country/setting:** Austria/Dept of Surgery, Danube Hospital, Vienna **Recruitment period:** Nov 1998 – Dec 2000 **Length of follow-up:** Median 15 (range 3-26) months	**Enrolled:** 20 **Received PNE**: 20 **Received permanent implant**: 16 **Lost to follow-up:** 0 **Age** **Median (range):** 50.1 (11-79) **Gender:** M6, F14 **Duration of symptoms:** Minimum 1 year **Not reported:** with co-existing urinary incontinence; with co-existing urinary retention; site of implant.	**Improved (includes cured)** **Median 15 month follow-up:** 16/16 **Episodes of FI per week** **Median (range)** **Baseline:** 2 (1-5) **Median 15 month follow-up:** 0.67 (0-1.67) **Ability to defer defaecation (minutes)** **Median (range)** **Baseline:** 2 (0-5) **Median 15 month follow-up:** 7.5 (2-15) **Not reported:** cured; episodes of urgency; use of pads; use of anal plugs; improvement in urinary incontinence	**QOL:** **condition specific** ASCRS **Median (range)** **Baseline** **(20 patients);** **6 month follow-up** **(16 patients):** Lifestyle: 2.1 (1.0-2.8); 3.9 (2.7-4.4)* Coping/behaviour: 2.0 (1.3-2.5); 3.7 (3.0-4.1)* Depression/self-perception: 2.6 (1.7-3.1); 3.7 (3.2-4.3)* Embarassment: 1.7 (1.0-2.2); 3.8 (3.0-4.6)* **Not reported:** incontinence score; QOL: generic	**n=16** **Median (range)** **Resting pressure (mmHg)** **Baseline:** 27.7 (16-39) **3 month follow-up:** 50.2 (29-76) p=0.005 **Max squeeze pressure (mmHg)** **Baseline:** 59.2 (28-87) **3 month follow-up:** 120.2 (57-193) p=0.005 **Rectal sensory threshold to balloon distention (ml air)** **Baseline:** 90 (15-300) **3 month follow-up:** 60 (10-300) **Sensation of urgency to balloon distention (ml air)** **Baseline:** 100 (20-300) **3 month follow-up:** 100 (50-300) **Max tolerated rectal volume to balloon distention (ml air)** **Baseline:** 180 (35-300) **3 month follow-up:** 160 (70-300)	**Infection:** 3/16. Action taken: explantation of the leads and the generator and drainage of the wounds 0-3 months after implantation **Other: dislocation of permanent electrode:** 1/16. Action taken: reintervention and new placement. When a second dislocation occurred 3 months later, the permanent electrode was explanted. **Not reported:** pain at implant site; pain at IPG site; pain from leads; lead migration; increased electrical sensation; adverse change in bowel function; adverse change in urinary function; numbness; technical problems	ASCRS: best score is 5, worst is 1. * = p<0.01 versus baseline. Not reported: adverse events at PNE

Study details	Participants	Outcomes				Notes
		Faecal incontinence	Health status	Anorectal manometry	Adverse events	
Study id: Uludag 2002[25] **Related references:**[49] **Type:** case series **Country/setting:** Netherlands/ Dept of Surgery, Academic Hospital, Maastricht **Length of follow-up:** **Mean** 11 months **Not reported:** inclusion criteria; exclusion criteria; recruitment period	**Enrolled:** 44 **Received PNE:** 44 **Received permanent implant:** 34 **Lost to follow-up**: 0 **Age** **Mean (range):** 53 (26-73) years **Gender:** M8, F36 **Not reported:** duration of symptoms; with co-existing urinary incontinence; with co-existing urinary retention; site of implant	**n=34** **Episodes of FI per week** **Baseline:** 8.66 **Mean 11 month follow-up:** 0.67 p<0.01 **Number of incontinent days per week** **Baseline:** 4.0 **Mean 11 month follow-up:** 0.5 p<0.01 **Ability to defer defaecation (minutes)** **Baseline:** not reported **11 month follow-up:** Mean 10-15 **Outcomes not reported:** cured; improved; episodes of urgency; use of pads; use of anal plugs; improvement in urinary incontinence	**Number of patients:** not reported **Data:** not reported **QOL: condition specific** ASCRS Paper states 'Improvement in all categories' **QOL: generic SF-36** Paper states 'Improvement in all categories' **Not reported:** incontinence score	**Number of patients:** not reported **Data**: not reported Paper states 'Anal manometry during stimulation showed no increase of sphincter pressures' **Not reported:** rectal sensory threshold to balloon distention; sensation of urgency to balloon distention; max tolerated rectal volume to balloon distention	**Not reported:** pain at implant site; pain at IPG site; pain from leads; lead migration; infection/skin irritation; increased electrical sensation; adverse change in bowel function; adverse change in urinary function; numbness; technical problems	Not reported: adverse events at PNE ASCRS: best score is 5, worst is 1. SF-36: best score is 100, worst is 0. * = p<0.05 versus baseline.

(b) Double-blind study

Study details	Participants	Outcomes				Notes
		Faecal incontinence	Health status	Anorectal manometry	Adverse events	
Study id: Vaizey 2000[21] **Related references:**[5,34-44] (M.E.D. Jarrett, St Mark's Hospital, London, 2003) **Type:** double-blind crossover study. Main investigator and patients were blinded to status of stimulator. Trial period consisted of two 2-week periods, with the stimulator turned on for 2 weeks and off for 2 weeks. One investigator, not involved in assessment of clinical outcome, turned the stimulator on or off at the beginning of the first 2 week period, without the patients and other investigators' knowledge. **Inclusion criteria:** signed informed consent; intact external anal sphincter; passive faecal incontinence **Country/setting:** UK/St Mark's Hospital, London **Length of follow-up:** 4 weeks **Not reported:** exclusion criteria; recruitment period	**Enrolled:** 2 **Received PNE:** 2 (around 9 months previously) **Received permanent implant:** 2 (around 9 months previously) **Lost to follow-up:** 0 **Age:** Patient 1: 65 years; Patient 2: 61 years **Gender:** M0, F2 **Duration of symptoms before implantation:** passive faecal leakage occurring more than once per day: 3 years (patient 1); passive faecal leakage occurring more than 3 times per week: 2.5 years (patient 2) **Site of implant:** Abdominal wall **Not reported:** with co-existing urinary incontinence; with co-existing urinary retention	**Cured** **4 week follow-up**: 1/2 **Improved (includes cured)** **4 week follow-up:** 2/2 **Episodes of FI** **Pre-stimulation:** Patient 1: 30; Patient 2: 10. **Stimulator off (2 wks):** Patient 1: 20; Patient 2: 4 **Stimulator on (2 wks):** Patient 1: 2; Patient 2: 0. **Not reported:** ability to defer defaecation; episodes of urgency; use of pads; use of anal plugs; improvement in urinary incontinence	**QOL: generic** SF-36 **Scores** Role-emotional Patient 1: pre: not reported; post: 100 Patient 2: pre: 33; post: 66 General health Patient 1: pre: 86; post: 92 Patient 2: pre: 72 ; post: 92 Mental health Patient 1: pre: 76; post: 88 Patient 2 : pre: 64; post: 72 Bodily pain Patient 1: pre: 30; post: 100 Patient 2: pre: 74; post: 84 Physical functioning Patient 1: pre: 70 ; post: 80 Patient 2: pre: 72 ; post: 85 Role-physical Patient 1: pre: 0 ; post: 100 Patient 2: pre: 75 ; post: 100 Social function Patient 1: pre: 12 ; post: 100 Patient 2: pre: 75 ; post: 75 Vitality Patient 1: pre: 10; post: 80 Patient 2: pre: 70; post: 70 **Not reported:** incontinence score; QOL: condition specific	**Resting pressure (maximal) (cmH2O)** **Stimulator off:** Patient 1: 35; patient 2: 50 **Stimulator on:** Patient 1: 45; patient 2: 70 **Max squeeze pressure (cmH2O)** **Stimulator off:** Patient 1: 70; patient 2: 60 **Stimulator on:** Patient 1: 100; patient 2: 90 **Rectal sensory threshold to balloon distention (ml)** **Stimulator off:** Patient 1: 25; patient 2: 50 **Stimulator on:** Patient 1: 45; patient 2: 90 **Sensation of urgency to balloon distention (ml)** **Stimulator off:** Patient 1: 70; patient 2: 100 **Stimulator on:** Patient 1: 85; patient 2: 120 **Max tolerated rectal volume to balloon distention (ml)** **Stimulator off:** Patient 1: 120; patient 2: 150 **Stimulator on:** Patient 1: 130; patient 2: 150	**Not reported:** pain from leads; lead migration; pain at implant site; pain at IPG site; infection/skin irritation; increased electrical sensation; adverse change in bowel function; adverse change in urinary function; numbness; technical problems.	SF-36: best score is 100, worst is 0. Pre = pre-implantation Post = 9 months post implantation

(c) European multicentre trial

Study details	Participants	Outcomes				Notes
		Faecal incontinence	Health status	Anorectal manometry	Adverse events	
Study id: MDT-301 (K.E. Matzel, University Hospital Erlangen, 2003) **Related references:** none identified. **Type:** multicentre (8 institutions) prospective non-randomised trial **Inclusion criteria:** involuntary passage of solid or liquid faeces at least once per week; intact external anal sphincter (if previous repair, intact at least 50% of its length); refractoriness to medical treatment and biofeedback therapy; aged 18 – 75 years. **Exclusion criteria:** congenital anorectal malformation; previous rectal surgery; previous or present rectal prolapse; chronic bowel disease; chronic diarrhoea; altered bowel habits associated with pain; stoma in situ; neurologic diseases such as diabetic neuropathy; multiple sclerosis; Parkinson's disease; spinal cord injury; bleeding complications; pregnancy; anatomic limitations obviating surgical access; pyoderm or pilonidal sinus; mental or physical inability to comply with	**Enrolled:** 37 **Received PNE:** 37 **Received permanent implant:** 34 **Lost to follow-up:** 1 **Age** **Mean (range):** 54.3 (26-73) years **Gender:** M4, F 33 **Duration of symptoms** **Mean (range):** 5.9 (0.5-28) years **Not reported:** with co-existing urinary incontinence; with co-existing urinary retention; site of implant	**Cured** **Latest follow-up:** 15/33 **Improved (includes cured)** **Latest follow-up:** 33/33 **Episodes of FI per week (urgency or passive)** **Mean (± SD)** **Baseline (n=37):** 16.4 (± 19.3) (95% CI 9.9-22.8) **Latest follow-up (n=33):** 2.7 (± 4.8) (95% CI 1.0-4.4) p < 0.0001 **Episodes of FI per week (urgency)** **Mean (± SD)** **Baseline (n=37):** 6.7 (± 8.9) **Latest follow-up (n=33):** 0.8 (± 1.5) p < 0.0001 **Episodes of FI per week (passive)** **Mean (± SD)** **Baseline (n=37):** 9.7 (± 15.2) **Latest follow-up (n=33):** 1.8 (± 3.7) p < 0.0001 **Ability to defer defaecation (minutes)** **Baseline; latest follow-up:** Not at all: 16; 2 <1 min: 10; 3 1-5 mins: 7; 9	**Baseline: n=37** **Latest follow-up: n=32** **Mean (± SD) scores** **QOL: condition specific** ASCRS **Baseline; latest follow-up:** Lifestyle: 2.7 (± 0.9); 3.5 (± 0.6)# Coping/behaviour: 1.7 (± 0.6); 2.8 (± 0.8)# Depression: 2.8 (± 1.0); 3.9 (± 0.9)# Embarrassment: 1.8 (± 0.9); 3.0 (± 0.9)# **QOL: generic** SF-36 **Baseline; latest follow-up:** Physical functioning: 64.5 (± 28.6); 69.0 (± 32.1) p = 0.2949 Social functioning: 61.1 (± 33.6); 85.2 (± 21.9) p = 0.0002 Role-physical: 44.6 (± 44.5); 55.5 (± 41.5) p = 0.2719 Role-emotional: 56.8 (± 43.6); 71.9 (± 40.7) p = 0.1724 Mental health: 62.6 (± 24.3); 73.0 (± 22.5) p = 0.0202	**Mean (± SD) (range) (mmHG)** **Resting pressure** **Baseline:** 58.3 (± 34.4) (10.0-158.0) **Latest follow-up:** not reported **Squeeze pressure** **Baseline:** 29.4 (± 18.9) (3.0-82.0) **Latest follow-up:** not reported **Not reported:** rectal sensory threshold to balloon distention; sensation of urgency to balloon distention; max tolerated rectal volume to balloon distention	**Pain:** 9/33 (10 episodes). Action taken: resolved with reprogramming (n=4), medication (n=1), or repositioning of the IPG (n=3) **Lead breakage:** 1/33. Action taken: lead replacement **Infection:** 1/33 recurrent infection that had responded to medical treatment during the screening phase worsened. Action taken: device removal **Adverse change in bowel function:** 3/33 bowel symptoms deteriorated. Action taken: resolved fully (1), device removal after 20 months (1) **Adverse change in urinary function:** SNS was not reported to interfere with urinary function **Other:** **Device-related:** 12/33	# = p < 0.0001 Adverse events: severity was defined as mild (easily tolerated, interfering minimally or not at all with daily functioning, and not requiring treatment); moderate (interfering with daily functioning or requiring treatment); or severe (incapacitating, or requiring urgent treatment, hospitalisation, surgical intervention, and/or prolonged hospitalisation). Events related to the implantation procedure, to the presence of the device, or to its performance were classified as device-related. Adverse events at PNE: lead dislodgement 1/37; infection 9/37 (all were treated with antibiotics, but 4/37 required lead removal; all 9 had

Study details	Participants	Outcomes				Notes
		Faecal incontinence	Health status	Anorectal manometry	Adverse events	
the study protocol. **Country/setting:** Europe (Dept General Surgery, Danube Hospital, Vienna, Austria; Dept Surgery, Herlev Hospital, Herlev, Denmark; Dept General Surgery, University Hospital Erlangen, Erlangen, Germany; Dept General Surgery, Maastricht University Hospital, Maastricht, The Netherlands; Dept General Surgery, Hospital Mutua de Terrassa, Terrassa, Spain; Dept Surgery, Danderyd Hospital, Stockholm, Sweden; St Mark's Hospital, London, UK; Dept Surgery, University of Minnesota, Minneapolis, USA) **Recruitment period:** Jan 1999 – June 2001 **Length of follow-up** **Mean ±SD (range):** 21.3 ± 9.9 (1-36) months		5-15 mins: 0; 12 > 15 mins: 0; 6 **Days with FI** **Mean (± SD)** **Baseline (n=37):** 4.5 (± 1.8) **Latest follow-up (n=33):** 1.3 (± 1.8) p < 0.0001 **Days with pads** **Mean (± SD)** **Baseline (n=37):** 5.9 (± 2.3) **Latest follow-up (n=33):** 3.3 (± 3.3) p < 0.0001 **Days with stain** **Mean (± SD)** **Baseline (n=37):** 5.6 (± 1.6) **Latest follow-up (n=33):** 2.7 (± 2.7) p < 0.0001 **Outcomes not reported:** episodes of urgency; use of pads; use of anal plugs; improvement in urinary incontinence	Vitality: 48.8 (± 29.0); 56.4 (± 28.4) p = 0.0630 Bodily pain: 65.4 (± 30.4); 57.4 (± 30.7) p = 0.1273 General health: 54.6 (± 29.0); 58.5 (± 30.8) p = 0.2436 **Not reported:** incontinence score		(7 mild, 4 moderate, 8 severe) For all complications, the resolution rate was 63.2%; for the severe events (pain at the IPG, lead breakage, infection, worsening of bowel symptoms), 100% **Not reported**: increased electrical sensation; numbness.	demonstrated a > 50% improvement, and 8 of them underwent subsequent permanent electrode placement).

Appendix 8 List of excluded studies

(a) Studies reporting PNE phase only:

Ganio E, Realis Luc A, Clerico G, Trompetto M. Selection criteria for sacral nerve stimulation in patients with fecal incontinence. Diseases of the Colon & Rectum 2001;44(4):A57.

Ganio E, Masin A, Ratto C, Altomare DF, Ripetti V, Clerico G et al. Short-term sacral nerve stimulation for functional anorectal and urinary disturbances: results in 40 patients: evaluation of a new option for anorectal functional disorders. Diseases of the Colon & Rectum 2001;44(9):1261-7.

Rosenblum N, Eilber KS, Raz S. Herpes zoster following sacral nerve stimulation for overactive bladder. Journal of Urology 2003;169(2):619-20.

Vaizey CJ, Kamm MA, Turner IC, Nicholls RJ, Woloszko J. Sacral nerve stimulation for faecal incontinence: evaluation of short term efficacy and effect on anorectal function. Gut 1997;40(Suppl 1):A53.

Vaizey CJ, Kamm MA, Turner IC, Nicholls RJ, Woloszko J. Effects of short term sacral nerve stimulation on anal and rectal function in patients with anal incontinence. Gut 1999;44(3):407-12.

(b) Non-English language studies:

Ferulano GP, La Manna S, Dilillo S. [Sacral neuromodulation in fecal continence disorders]. Recenti Progressi in Medicina 2002;93(7-8):403-9.

Leroi A-M. [Neuromodulation of the sacral roots and fecal incontinence]. Hepato-Gastro 2000;7(6):453-8.

Linares Quevedo AI, Jimenez Cidre MA, Fernandez FE, Perales CL, Briones MG, Pozo MB et al. [Posterior sacral root neuromodulation in the treatment of chronic urinary dysfunction]. Actas Urologicas Espanolas 2002;26(4):250-60.

Matzel KE, Stadelmaier U, Gall FP. [Direct electrostimulation of sacral spinal nerves within the scope of the diagnosis of anorectal function]. Langenbecks Archiv fur Chirurgie 1995;380(3):184-8.

Matzel KE, Stadelmaier U, Hohenfellner M, Gall FP. [Permanent electrostimulation of sacral spinal nerves with an implantable neurostimulator in treatment of fecal incontinence]. Chirurg 1995;66(8):813-7.

Matzel KE, Stadelmaier U, Hohenfellner M, Hohenberger W. [Treatment of insufficiency of the anal sphincter by sacral spinal nerve stimulation with implantable neurostimulators]. Langenbecks Archiv fur Chirurgie - Supplement - Kongressband 1998;115:494-7.

Matzel KE. [Sacral spinal nerve stimulation]. Chirurgische Gastroenterologie 2001;17(3):230-6.

Michot F, Leroi AM. [Sacral nerve stimulation: promising treatment for anal incontinence?]. Annales de Chirurgie 2002;127(4):247-9.

Rasmussen OO, Christiansen J. [Sacral nerve stimulation in fecal incontinence]. Ugeskrift for Laeger 2002;164(33):3866-8.

Sielezneff I, Pirro N, Ouaissi M, Cesari J, Consentino B, Sastre B. [Surgical treatment of anal incontinence]. Annales de Chirurgie 2002;127(9):670-9.

Uludag O, Darby M, Dejong CH, Schouten WR, Baeten CG. [Sacral neuromodulation is effective in the treatment of fecal incontinence with intact sphincter muscles; a prospective study]. Nederlands Tijdschrift voor Geneeskunde 2002;146(21):989-93.