Sacral nerve stimulation for faecal incontinence

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Assessment report

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The Medical Services Advisory Committee (MSAC) is an independent committee which has been established to provide advice to the Minister for Health and Ageing on the strength of evidence available on new and existing medical technologies and procedures in terms of their safety, effectiveness and cost-effectiveness. This advice will help to inform government decisions about which medical services should attract funding under Medicare.

MSAC recommendations do not necessarily reflect the views of all individuals who participated in the MSAC evaluation.

This report was prepared by the Medical Services Advisory Committee with the assistance of Dr Silva Zavarsek, Mr Andrew Dalton, Dr Omar Abdulwadud, Ms Anne Parkhill and Ms Sharon King from the Monash Institute of Health Services Research, Monash University and Ms Alex Lloyd from the Department of Health and Ageing. The report was edited by Dr Alana Mitchell, ScienceLink Pty Ltd. The recommendation was endorsed by the Minister for Health and Ageing on 4 July 2005.

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Sacral nerve stimulation (SNS) is comprised of two diagnostic stages followed by a third therapeutic implantation stage. The diagnostic stages of the procedure are the acute and subchronic stages of peripheral nerve evaluation (PNE) and the therapeutic stage involves the permanent implantation of the SNS device and is referred to as chronic therapeutic stimulation (CTS).

The acute phase of PNE establishes the functional integrity of the sacral roots and confirmation of pelvic floor motor responses. It serves to locate the optimal sacral spinal nerves from which to elicit contractions of the muscles of the pelvic floor. Acute PNE can be conducted under local or general anaesthesia. The subchronic phase of PNE evaluates the therapeutic effects of SNS. The electrode is connected by a lead to an external pulse generator. The sacral nerve is stimulated over a period of seven days to assess the therapeutic effects of SNS. Individuals who show a positive response (>50 per cent reduction in symptom episodes) to PNE will proceed to CTS. This stage is performed under local anaesthesia and involves small skin incisions.

CTS requires permanent implantation of the neurostimulator in the upper buttock. An electrode that stimulates the sacral nerves is connected by a subcutaneous lead to the neurostimulator. Chronic stimulation begins the day following surgery and the patient uses a hand-held patient programmer to turn the stimulation on or off. Each stimulator is programmed to suit individual patients. The surgeon uses an external programmer for the non-invasive adjustment of the parameters of electric stimulation by the neurostimulator. When necessary, the stimulation parameters are reprogrammed according to the patient's perception. Continuity of care may require that the device be reprogrammed, which may be performed by nurses trained in optimising stimulation parameters.

SNS is used for the treatment of faecal incontinence (FI), urinary incontinence and intractable chronic pelvic pain. This report assesses the safety, effectiveness and cost-effectiveness of SNS for the treatment of faecal incontinence in adults who have been assessed as refractory to other conservative, non-surgical treatments and who have an anatomically intact, but functionally deficient, anal sphincter (ie, an intrinsically intact or surgically repaired anal sphincter).

SNS for the treatment of FI is expected to be performed by colorectal surgeons specifically trained in the procedure, however neurosurgeons may also be involved in service provision.

Medical Services Advisory Committee – role and approach

The Medical Services Advisory Committee (MSAC) is a key element of a measure taken by the Australian Government to strengthen the role of evidence in health financing decisions in Australia. MSAC advises the Australian Minister for Health and Ageing on the evidence relating to the safety, effectiveness and cost-effectiveness of new and

existing medical technologies and procedures, and under what circumstances public funding should be supported.

A rigorous assessment of the available evidence is thus the basis of decision making when funding is sought under Medicare. A team from the Monash Institute of Health Services Research, Monash University was engaged to conduct a systematic review of literature on SNS for the treatment of faecal incontinence. An Advisory Panel with expertise in this area then evaluated the evidence and provided advice to MSAC.

MSAC's assessment of sacral nerve stimulation for faecal incontinence

This assessment was undertaken to provide the broadest possible advice regarding the safety, effectiveness and cost-effectiveness of SNS for the treatment of faecal incontinence. Evidence was sought for the effectiveness of SNS in adults with faecal incontinence who are assessed as refractory to conservative, non-surgical treatments and who have an anatomically intact but functionally deficient anal sphincter (ie, an intrinsically intact or surgically repaired anal sphincter).

Clinical need

There is significant uncertainty regarding the number of individuals with faecal incontinence in Australia and hence the number who would be eligible for SNS. A systematic review of the literature that included three Australia-based studies and one US-based study estimated that the prevalence of faecal incontinence in the population is 5.5 per cent for males and 5.3 per cent for females. When these prevalence estimates are applied to the Australian population, it is estimated that 442,351 males and 401,138 females (a total of 843,489) have faecal incontinence compared with a range from 395,750 to 1,817,890 individuals derived from the three Australia-based studies. The data available on the burden of disease is insufficient to determine the size of the patient group that has sufficiently severe disease to require surgical intervention. Expert opinion suggests that 15 to 20 per cent of these individuals may be considered for surgical intervention should they seek improvements in symptoms. The nature of the surgical intervention is dependent on the underlying cause and could include overlapping repair, injection augmentation, SNS, graciloplasty, antegrade continence enemas and colostomy. The expectation is that few individuals would proceed to surgery. The proportion that would be eligible for SNS is unknown.

Safety

The safety of sacral nerve stimulation was assessed when used in the treatment of faecal incontinence.

During PNE, the most common adverse event reported was electrode and/or lead problems (including electrode migration and lead displacement) in study participants, with a complication rate of 10.43 per cent (95% confidence interval [CI]: 7.36, 14.58). The number of participants who needed to be treated in order for one individual to experience this adverse event, or the number needed to treat to harm [NNT(H)] was 10 (95% CI: 7, 14). Infections occurred at a complication rate of 6.12 per cent (95% CI:

3.85, 9.57) and the NNT(H) was 16 (95% CI: 10, 26). Adverse events occurring at a complication rate of less than five per cent included electrode and/or lead replacement and/or repositioning and permanent explantation of the SNS device.

During CTS, re-operations were the most common adverse event reported for study participants, with a complication rate of 15.50 per cent (95% CI: 11.67, 20.29) and NNT(H) of 6 (95% CI: 5, 9). Re-operations were mainly due to implant/lead/electrode problems that required repositioning or replacement, or permanent explantation of the device due to pain, infection or fading out of the clinical response. Other adverse events occurring at a complication rate greater than five per cent included pain (6.27%, 95% CI: 3.95, 9.82) and permanent explantation of the device (5.90%, 95% CI: 3.67, 9.37).

From the available evidence, SNS for the treatment of faecal incontinence appears to be a safe procedure as adverse events were not severe. This conclusion is similar to that of the published systematic reviews and health technology assessment reports, however, the conclusion is based on a small number of study participants and a lack of long term safety data.

Effectiveness

The effectiveness of SNS for the treatment of faecal incontinence was assessed from nine case series and one double blind crossover study. In addition, two systematic reviews of non-randomised studies and two health technology assessment reports were identified.

The results from the nine case series and the double blind cross-over study are as follows. The majority of the studies were conducted in Europe, with a maximum follow-up of 72 months. The participants enrolled in each of the studies were similar in age and the majority of participants in all studies were female. The study populations varied in size from 20 to 116 participants. The mean or median duration of faecal incontinence was similar between participants in each of the studies. Most studies, with the exception of two in which some participants had had faecal incontinence for only 0.5 or 0.8 years, included participants who had experienced at least 12 months of faecal incontinence. Where reported, the inclusion and exclusion criteria for each of the studies were also similar. The aetiology of faecal incontinence varied for the majority of participants enrolled in each study. The majority of participants in four studies had idiopathic faecal incontinence, in two studies the majority of participants had faecal incontinence due to neurogenic causes, and obstetric injury was the most common cause of faecal incontinence in one study. Two studies did not report the aetiology of faecal incontinence in their series of participants. The eligibility criteria for participants to continue to CTS varied between studies.

The proportion of participants in the included studies who underwent PNE and were eligible to continue to CTS ranged from 19.0 to 91.9 per cent, and this was largely dependent on the eligibility criteria for continuation to CTS in each of the studies. The proportion of participants who were continent at last follow-up ranged from 35.3 to 100 per cent and the proportion of participants with improved incontinence ranged from 95.7 to 100 per cent. Each of the studies reported the mean or median faecal incontinence episodes experienced by the participants prior to, and following, SNS. These differences in reporting made it difficult to compare the studies and derive an overall estimation of the effectiveness of SNS for the treatment of faecal incontinence.

Many of the studies showed statistically significantly reduced faecal incontinence episodes at follow-up compared with baseline values.

Four studies used incontinence score tools to measure participants' perception of their improvement in their incontinence status. The incontinence score tools used included the American Medical Systems (AMS) Score, Continence Grading System (CGS), the Cleveland Clinic Incontinence Score/Wexner's Incontinence Score and William's Incontinence Score. Three of the four studies showed a statistically significantly improved incontinence score at follow-up compared with baseline values.

Quality of life was also measured in five studies, using the Short Form 36 (SF-36), American Society of Colon and Rectal Surgeons (ASCRS) Fecal Incontinence Quality of Life and Faecal Incontinence Quality of Life (FIQL) questionnaires. Statistically significant differences were reported at follow-up compared with baseline values for a number of categories in each of the questionnaires. Three of the four studies that used the SF-36 questionnaire showed a statistically significant improvement in quality of life for the social function category – a quality of life category deemed as one of the prime objectives of treatment for faecal incontinence in patients with neuropathic faecal incontinence. Other categories that reached statistically significant differences in at least one study included role-emotional, mental health, vitality and physical functioning. All studies that used the ASCRS Fecal Incontinence Quality of Life and FIQL questionnaires showed a statistically significant improvement in quality of life in all four categories of the questionnaire – lifestyle, coping behaviour, depression and self-perception, and embarrassment.

Most of the studies showed an improvement in incontinence episodes per week and in quality of life using various quality of life measures. The magnitude of this treatment effect was strong, with up to 100 per cent of participants achieving continence or an improvement in incontinence in the included studies. In addition, the changes in quality of life as measured by various tools also showed that SNS had a strong effect on improving quality of life for individuals with faecal incontinence. However, the following issues highlight the limitations of the data presented.

- The data is derived from nine case series and one crossover study. In the absence of a comparator arm in the case series, it cannot be ruled out that the improvements observed in study participants following SNS occurred spontaneously.
- The results presented may be biased due to the following reasons:
  - None of the studies included in this review stated that participants were enrolled consecutively, hence there may have been selection bias.
  - There may have been selective reporting of positive outcomes.
  - Participants withdrew and were lost to follow-up.
  - The participants enrolled in each of the series may not represent a spectrum of severity of faecal incontinence.

- Participants enrolled in each of the series had faecal incontinence due to different aetiologies. Data were not reported in a way to allow for subgroup analyses to assess if one patient group would be more likely to benefit than another.

- Differences in the reporting of faecal incontinence episodes over a given time frame between the included studies does not allow for easy comparison of results between studies or for an overall estimate of the effectiveness of SNS.

- The length of follow-up in these studies was limited to 72 months. Therefore the long-term effectiveness of SNS has not been established.

Similarly, the identified systematic reviews and health technology assessment reports concluded that SNS was effective in reducing the number of faecal incontinence episodes per week, decreasing urgency to defecate and improving quality of life. However, various limitations to the data have been identified:

- All data is from case series so benefits beyond that of a placebo effect cannot be determined.

- There may be bias affecting the results due to selective reporting of results, selection of participants and withdrawals and losses to follow-up.

- There were too few participants studied to observe rare adverse events.

- Heterogeneity in the units of measure of faecal incontinence episodes make the data difficult to compare across studies.

- The maximum length of follow-up was 99 months.

Cost-effectiveness

A review of the literature failed to identify any studies of the relative cost-effectiveness of SNS compared to either conservative, non-surgical treatment or stoma formation for the treatment of faecal incontinence.

The Application (Section 11) provides a cost-analysis of the procedure based upon an expert statement. However, costs considered by the Applicant appear to represent a financial analysis of costs to the Commonwealth Government and are thus incomplete as an economic analysis. The economic evaluation of SNS versus conservative, non-surgical treatment developed for this review addresses these issues from a societal perspective as far as possible, given the available data. It has not been possible to prepare an economic evaluation of SNS versus stoma formation.

The outcome measure applied in the evaluation is 'continence' or 'improved continence'. Ideally, a suitable measure of quality of life would have been used. As noted in the main body of the review, quality of life results have been reported in the literature for study participants at baseline and after implantation with the SNS device using a variety of instruments including the SF-36 questionnaire. While the reported results tend to favour SNS, the SF-36 questionnaire is not suitable for direct estimation of the magnitude of quality of life gains in an economic evaluation and neither are the disease-specific instruments.

The model presented is based on data from a published health technology assessment report of outcomes and adverse events that provides brief commentary on the treatment of adverse events. The incremental cost-effectiveness ratio was found to be $3,200 per patient-year of continence and/or improved continence.

This result from the economic evaluation is subject to many limitations, including the necessary use of data from case series and considerable uncertainty in relation to costs. However, sensitivity analysis shows some strength in the result, most likely due to the dominance in the cost estimates of the cost of the device itself.

Recommendation

MSAC recommended that there is evidence of safety for sacral nerve stimulation in adults with faecal incontinence refractory to conservative, non-surgical treatment and who have an anatomically intact but functionally deficient anal sphincter. The total number of patients is small; there is some evidence of effectiveness and cost-effectiveness. MSAC supports public funding in these circumstances.

The Minister for Health and Ageing endorsed this recommendation on 4 July 2005.

Introduction

The Medical Services Advisory Committee (MSAC) has reviewed the use of sacral nerve stimulation (SNS), a therapeutic device for faecal incontinence in adults with an anatomically intact, but functionally deficient, anal sphincter. MSAC evaluates new and existing health technologies and procedures for which funding is sought under the Medicare Benefits Scheme in terms of their safety, effectiveness and cost-effectiveness, while taking into account other issues such as access and equity. MSAC adopts an evidence-based approach to its assessments, based on reviews of the scientific literature and other information sources, including clinical expertise.

MSAC's terms of reference and membership are at Appendix A. MSAC is a multidisciplinary expert body, comprising members drawn from such disciplines as diagnostic imaging, pathology, surgery, internal medicine and general practice, clinical epidemiology, health economics, consumer health and health administration.

This report summarises the assessment of the current evidence for SNS for faecal incontinence in adults with an anatomically intact, but functionally deficient, anal sphincter.

Background

Sacral nerve stimulation for faecal incontinence

Faecal incontinence

Faecal incontinence occurs when there is a disruption in the structure and function of the normal anatomy or physiology of the anorectum (Rao 2004a) that results in the involuntary loss of faecal matter through the anal canal (Madoff et al 2004). Faecal incontinence may manifest as passive or urge incontinence or as faecal seepage (Rao 2004b).

Passive incontinence is the involuntary discharge of faecal matter or flatus without awareness and is suggestive of a loss of perception and/or impaired anorectal reflexes, either with or without sphincter dysfunction (Rao 2004b).

Urge incontinence is the discharge of faecal matter or flatus in spite of attempts to retain these contents and is suggestive of the disruption of sphincter function or rectal capacity to retain stool and/or flatus (Rao 2004b).

Faecal seepage refers to the undesired leakage of stool. Faecal seepage most likely occurs as a result of incomplete evacuation of stool and/or impaired rectal sensation. Sphincter function and pudendal nerve function are mostly intact (Rao 2004b).

The causes of faecal incontinence are diverse. They include sphincter damage (secondary to obstetric injury or surgical trauma), constipation, diarrhoea and neurological compromise (Boyd-Carson 2003).

The anal sphincter

The anal sphincter consists of the internal and the external anal sphincter (IAS and EAS, respectively) and the puborectalis muscle. The resting tone of the anal canal is maintained by the internal and external sphincters and the expansion of anal vascular cushions. The EAS and the puborectalis muscle function as a single unit and provide voluntary contraction during defecation. The EAS is innervated by the pudendal nerve and the puborectalis muscle is directly innervated by the sacral nerves, S3 and S4 (Madoff et al 2004).

Congenital malformations can cause faecal incontinence, the severity of which depends on the development of the pelvic floor muscles and the degree of impairment of the sensory mechanisms. However, most cases of faecal incontinence are acquired. The most common cause of sphincter dysfunction is vaginal delivery in women and anorectal surgery or trauma in men (Madoff et al 2004).

Constipation

In the elderly, constipation resulting from physical disability or impaired mobility is the single most common underlying cause of faecal incontinence. In individuals with spinal cord injuries, 52 per cent experience faecal impaction. Constipation leads to faecal

incontinence as hard stool promotes the production of excessive amounts of mucous, which results in watery seepage around the impacted faecal matter, otherwise referred to as spurious diarrhoea. In addition, the impacted faecal matter results in rectal distension that leads to relaxation of the internal and external sphincters and eventual incontinence. Excessive straining also weakens the anal sphincters (Boyd-Carson 2003).

Diarrhoea

The likelihood of incontinence is increased with loose stool or diarrhoea caused by any gastrointestinal disorder. This may be temporary, as in the case of gastroenteritis, or chronic, as experienced by individuals with inflammatory bowel disease (Boyd-Carson 2003).

Neurological compromise

Maintenance of continence requires an intact central nervous system. The reflex activity of the anorectum is impaired in individuals with spinal cord injuries, where the ability to contract the external anal sphincter diminishes or is even absent following injury increasing the risk of incontinence. Faecal incontinence has been reported in up to 61 per cent of individuals with spinal cord injuries and 11 per cent of these individuals report incontinence episodes occurring at least weekly. Normal rectal sensations can distinguish between solid, liquid or gas, so any neurological disorder that impairs the ability to sense a full rectum may result in some degree of faecal incontinence. Defective anorectal sensation may result from numerous central or peripheral neuropathies that include: degenerative disorders (multiple sclerosis or motor neuron disease), spinal cord injury, cerebrovascular disease, diabetic neuropathy or dementia (Boyd-Caron 2003).

The severity of faecal incontinence varies between individuals. Some individuals may be able to manage their symptoms with the use of pads, anal plugs, medication or toileting strategies, whilst other individuals may require surgery.

Table 1 summarises the type, cause and mechanistic effects of the pathophysiological mechanisms leading to faecal incontinence.

Table 1 Pathophysiological mechanisms leading to faecal incontinence (Rao 2004a)

Type	Cause	Mechanistic effect
Structural		
Anal sphincter muscle	Obstetric injury	Sphincter weakness
	Haemorroidectomy, anal dilatation secondary to neuropathy	Loss of sampling reflex
Rectum	Inflammation, IBS, radiation, prolapse, ageing, IBD	Loss of accommodation
		Loss of sensation, hypersensitivity
Puborectalis muscle	Excessive perineal descent, ageing, trauma	Obtuse anorectal angle
		Sphincter weakness
Pudendal nerve	Obstetric/surgical injury	Sphincter weakness
	Excessive straining/perineal descent	Sensory loss, impaired reflexes
CNS, spinal cord, ANS	Spinal cord injury, head injury, back surgery, multiple sclerosis, diabetes, stroke, avulsion injury	Loss of sensation, impaired reflexes, secondary myopathy, loss of accommodation
Function		
Anorectal sensation	Obstetric, CNS, ANS injury	Loss of stool awareness
		Rectoanal agnosia
Faecal impaction	Dyssynergic defecation	Faecal retention with overflow
		Impaired sensation
Stool characteristics		
Volume and consistency	Infection, IBD, IBS, drugs, metabolic	Diarrhoea and urgency
		Rapid stool transport
		Impaired accommodation
Irritants	Bile salt malabsorption, laxatives	Diarrhoea
Hard stools/retention	Dyssynergia, drugs	Faecal retention with overflow
Miscellaneous		
Physical mobility/cognitive function	Ageing, dementia, disability	Multifactorial changes
Psychosis	Wilful soiling	Multifactorial changes
Drugs	Anticholinergics	Constipation
	Laxatives	Diarrhoea
	Antidepressants	Altered sensation/constipation
	Caffeine/muscle relaxants	Relaxes sphincter tone
Food intolerance	Lactose/fructose/sorbitol	Diarrhoea/flatus
		Malabsorption

Abbreviations: ANS, autonomic nervous system; CNS, central nervous system; IBD, inflammatory bowel disease; IBS, irritable bowel syndrome

The procedure

SNS may be used as a second-line therapy when the anal sphincter is intrinsically intact or a third-line therapy when the anal sphincter has been repaired surgically. The intervention is comprised of two diagnostic stages followed by a third therapeutic implantation stage (Tjandra et al 2004). The diagnostic stages of the procedure are the acute and subchronic stages of peripheral nerve evaluation (PNE) and the therapeutic stage comprises the permanent implantation of the sacral nerve stimulation device and is referred to as chronic therapeutic stimulation (CTS).

- Diagnostic – PNE acute and sub-chronic testing. PNE facilitates the selection of individuals with adequate innervation of their anal sphincter and other pelvic floor musculature who thus have the greatest potential of benefiting from SNS. The device is temporarily implanted to measure the therapeutic effects in the patients over a period of seven days; and

- Treatment – CTS, permanent placement of the device.

Diagnostic phase: Peripheral nerve evaluation

Acute

The acute phase of PNE establishes the functional integrity of the sacral roots and confirmation of pelvic floor motor responses (Ganio et al 1999) and serves to locate the optimal sacral spinal nerves to elicit contractions of the muscles of the pelvic floor (Tjandra et al 2004). Acute PNE can be conducted under local or general anaesthesia (Tjandra et al 2004). An electrode is inserted through a small skin puncture in the lower back into the S2, S3 and S4 foramina to locate and test sacral spinal nerves. The most frequently used level is S3. Response is based on observation of muscle response twitching, contraction etc, confirming the integrity of nerves supplying the pelvic floor.

Subchronic

The subchronic phase evaluates the therapeutic effects of SNS on incontinence (Ganio et al 1999). The electrode is connected by an electrode lead to an external pulse generator. The sacral nerve is stimulated over a period of seven days to assess the therapeutic effects of SNS. Individuals who show a positive response (>50 per cent reduction in faecal incontinence episodes) to PNE will continue to CTS. This stage is performed under local anaesthesia using small skin incisions.

The acute and subchronic phases of PNE can be performed using either a temporary electrode or a tined lead. The temporary electrode is secured by an adhesive dressing and the position of the electrode is confirmed by radiography. Following the cessation of subchronic PNE, the electrode is removed (Tjandra et al 2004). The alternative is use of a tined lead (quadripolar foramen electrode) that, in the event of a successful subchronic phase, is retained and connected to the permanent implant (Tjandra et al 2004).

Treatment phase: Chronic therapeutic stimulation

Permanent implantation

The electrode is connected by a subcutaneous electrode lead to a neurostimulator that is implanted subcutaneously in the upper buttock. Chronic stimulation begins the day following surgery. To turn the stimulation on or off, the patient uses a hand-held patient programmer. The patient interrupts the pulse for defecation and urinary voiding.

Programming of the device

Each stimulator is programmed to suit individual patients. The surgeon uses an external programmer to non-invasively adjust the parameters of electric stimulation produced by the neurostimulator. When necessary, the stimulation parameters are reprogrammed

according to the patient's perception of muscular contraction of the perineum and anal sphincter (Ganio et al 2001b). Continuity of care may require that the device be reprogrammed, which may be performed by nurses trained in optimising stimulation parameters according to expert advice.

The procedure is expected to be performed by colorectal surgeons (members of the Colorectal Association of Australia), specifically trained in the procedure, however neurosurgeons may also be involved in service provision. In addition, nurses may also be involved in re-programming of the stimulation parameters during CTS. Specific training of colorectal surgeons and nurses would be required for device implantation and optimising stimulation parameters, respectively. Expert advice has also suggested that there may be a learning curve for surgeons, such that highly experienced professionals produce better outcomes for patients.

An algorithm for SNS proposed by Tjandra et al (2004) is depicted in Figure 1.

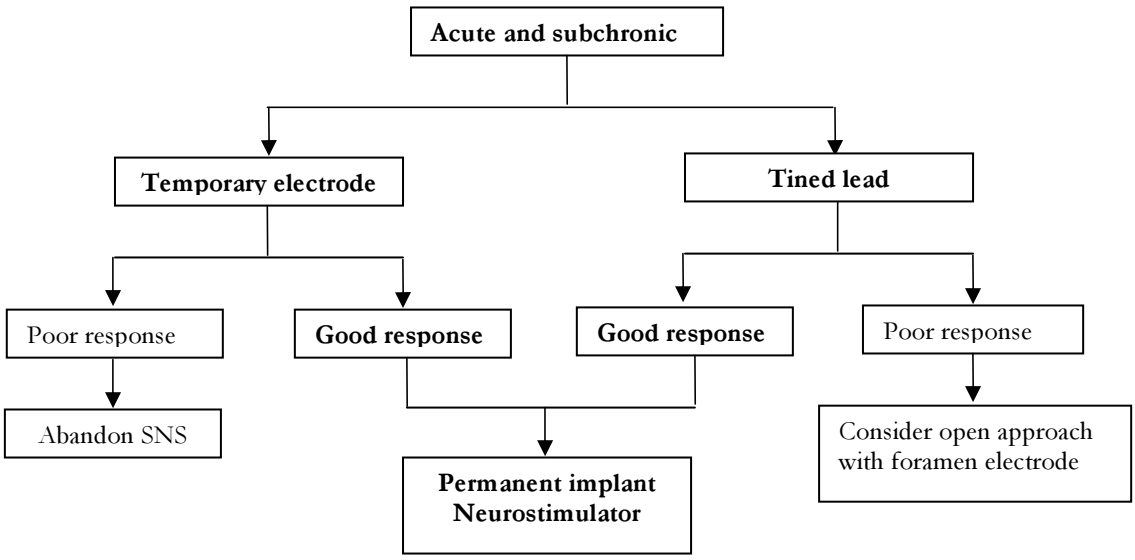

Figure 1 Algorithm for SNS (from Tjandra et al 2004)

Intended purpose

SNS is indicated for the treatment of faecal incontinence in adults with an anatomically intact but functionally deficient anal sphincter. These individuals will also have had severe, neuropathic faecal incontinence for at least 12 months and have failed other more conservative treatments.

According to expert opinion, individuals (adults and children) with the following conditions would be ineligible for PNE:

- medically unfit for surgery
- irritable bowel syndrome
- congenital anorectal malformations

- active anal abscesses or fistulas
- anorectal organic bowel disease, including cancer
- functional effects of previous pelvic irradiation
- rectal or anal surgery within 12 months
- pregnant or planning pregnancy
- congenital or acquired malformations of the sacrum.

SNS is also used for the treatment of urinary incontinence and intractable chronic pelvic pain. The evaluation of the evidence presented in the previous application (MSAC 2000) for urinary incontinence raised concerns about the safety as well as uncertainty about long-term effectiveness and unfavourable cost-effectiveness of the SNS device as a result of which it was recommended that listing should not be granted. These indications were not included in the current Application to MSAC and have not been assessed.

Clinical need/burden of disease

The prevalence of faecal incontinence has been estimated, from a systematic review of the literature including three Australian-based studies and one US-based study, to be 5.3 per cent in women (ranging from 1.3 to 25 per cent) and 5.5 per cent in men (ranging from 0.5 to 56.3 per cent) (Chiarelli et al 2003). The source of the heterogeneity in the prevalence estimates between studies was not apparent (Chiarelli et al 2003). When prevalence rates of 5.5 per cent for men and 5.3 per cent for women are applied to the population estimates of persons aged 18 years or over (Australian Bureau of Statistics 2002), it is estimated that 442,351 males and 401,138 females have faecal incontinence in Australia.

Expert opinion estimates that 80 to 85 per cent of these individuals could manage their symptoms by conservative, non-surgical treatments. Conservative, non-surgical treatments for faecal incontinence include dietary modifications, medications to change stool consistency, pelvic floor physiotherapy, biofeedback and 'toileting' strategies. The remaining 15 to 20 per cent of these individuals (an estimated 126,523 to 168,698 individuals) may be considered for surgical intervention should they seek improvements in symptoms. Appropriate surgical interventions, dependent on the underlying cause and pathology, include overlapping repair, injection augmentation, SNS, graciloplasty, antegrade colonic enemas and colostomy.

It is expected that a small percentage of individuals would proceed to surgical intervention of any type (expert opinion). It is also important to clarify that individuals who may be considered appropriate for SNS are a subset of the 15 to 20 per cent of individuals who may be considered for any surgical intervention. Therefore, the number of individuals who may be considered for SNS for the treatment of faecal incontinence is unknown, but is likely to be considerably less than 15 to 20 per cent.

A summary of the three studies assessing the prevalence of faecal incontinence in the Australian population is provided in Table 2. Two studies (Kalantar et al 2002, Lam et al 1999) used mail-out questionnaires and the study by MacLennan et al (2000) reported

results from a face to face interview. Kalantar et al (2002) and Lam et al (1999) presented similar prevalence estimates, and subsequently similar numbers. The prevalence estimated by MacLennan et al (2000) was significantly lower than those reported in the Kalantar et al (2002) and Lam et al (1999) studies. Whilst an overall prevalence rate was reported in Kalantar et al (2002) and Lam et al (1999) (and calculated for MacLennan et al [2000]), estimated numbers were calculated for the review from the reported prevalence of faecal incontinence according to age group and sex (see Table 3). Kalantar et al (2002) also reported that 9/33 (27.3%, 95% CI: 12.1%, 42.5%) participants had sought medical advice for their symptoms. It is unclear if only 33 participants were questioned about this.

Table 2 Study design of the Australian community-based studies examining the prevalence of faecal incontinence

Study	Sampling method	Sample demographic characteristics	Data collection method	Definition of faecal incontinence, duration, type	Who completed the questionnaire?	Overall prevalence (%) (95% CI)
Kalantar et al (2002) (Western Sydney)	Random sample from electoral roll 990 questionnaires sent out	The population sampling frame is demograph-ically similar to the Australian population, but younger and with higher socio-economic status	Self Administered questionnaire (validated: O'Keefe et al 1992; Talley et al 1989; Talley et al 1995) NOT IN REFS . long quest (32 questions) . short quest 7 questions)	Involuntary loss of anal sphincteric control that led to unwanted release of liquid or solid faeces (not flatus) at an inappropriate time or in an inappropriate place Symptom measured over the past 12 months	Not clearly stated (possible that any member of the household responded for all members in the household)	11.2 (8.8, 13.7)
Lam et al (1999) (Southern Sydney)	Random sample from electoral roll 995 questionnaires sent out	Not clearly reported	Self administered questionnaire (validated: O'Keefe et al 1992)	Answering in the affirmative at least two of three questions which incorporated stool leakage, wearing a pad for faecal soiling, or frequent incontinence of flatus (>25% of the time) Duration of symptoms not reported	Not clearly stated (possible that any member of the household responded for all members in the household)	Stool >1/week 1.8 (0.8, 2.9) Stool <1/week 7.8 (5.7, 9.9) Pad use 1.0 (0.2, 1.8) Flatus often 7.8 (5.7, 9.9)
MacLennan et al (2000) (South Australia)	Random sample from metropolitan Adelaide and country towns (clustered, self weighting, multi-stage, systematic area sample) 4,400 households chosen	25% of those sampled were born overseas	Face to face interview in the respondents homes (South Australian Health Omnibus Survey)	Flatus incontinence (poor control of wind) or faecal incontinence (lost control of motions) Symptom measured within the last year	Interview was conducted with the person who last had a birthday	Overall: . Stool:2.9 (2.4, 3.6) Men: . Stool: 2.3 (1.6, 3.2) Women: . Stool: 3.5 (2.7, 4.5)

The prevalence rates reported in the studies according to age group and sex are summarised in Table 3. Applying these prevalence estimates to the Australian population, (by age group and sex), the number of individuals with faecal incontinence ranges from 395,750 (MacLennan et al 2000) to 1,817,890 Lam et al (1999), which includes participants with frequent flatus, but is similar to the estimate from Kalantar et al (2002) of 1,694,389 that does not include participants with frequent flatus.

Assuming that 15 to 20 per cent of individuals with faecal incontinence may benefit from surgical treatment for their condition, the following total numbers of patients have been estimated:

- Kalantar et al (2002): 254,158–338,878. Estimates for faecal incontinence only and based on a self-administered questionnaire.

- Lam et al (1999): 272,684–363,578. Based on a self-administered questionnaire. Includes participants with flatulence, but excludes individuals >85 years as the ABS (2002) data did not break down population numbers for 85–89, 90–94 and 95–99 year-olds where the prevalence of faecal incontinence is as high as 50 per cent.

- MacLennan et al (2000): 59,362–79,150. May be an underestimate as this was interview based rather than an anonymous questionnaire as used in Kalantar et al (2002) and Lam et al (1999). This study also included participants aged from 15 years.

However, the proportion of the individuals included in these estimates who would be eligible for SNS is unknown. Overall, there is a significant level of uncertainty in the estimates of the prevalence of faecal incontinence in Australia, as demonstrated by the differences in estimates from the three Australian-based studies.

An alternative method for estimating the potential number of individuals who may be eligible for SNS would be to examine the number of patients who have undergone stoma formation for the treatment of faecal incontinence, however no publications reporting such numbers were identified in Australia. The number of osteomates currently registered with the Australian Council of Stoma Associations is approximately 28,500 (personal communication) and it is anticipated that very few of these individuals would have had a stoma formed for the treatment of faecal incontinence (expert opinion). A study by Catena et al (2002) retrospectively reviewed 44 patients who had undergone elective sigmoid colostomy for faecal incontinence at St Mark's Hospital in the United Kingdom between January 1991 and December 1998. It is unclear from the publication whether this review included all patients undergoing the procedure over this eight-year period, however it is anticipated that the number of patients considering stoma formation for the treatment of faecal incontinence would be small (expert opinion). Whilst this method may underestimate the potential number of individuals eligible for PNE and subsequently permanent implantation with the SNS device (as SNS may be considered more favourable than stoma formation), it is acknowledged that the prevalence estimates reported above are likely to be an overestimation.

As the procedure will be performed by appropriately trained professionals in a tertiary care setting after an individual's eligibility for the procedure has been assessed by appropriate initial investigations, it is anticipated that approximately 1–2 tertiary centres per capital city in Australia will perform the procedure (expert opinion). Expert opinion also suggests that approximately 100 individuals nationally may be considered for PNE annually.

Table 3 Australian prevalence of faecal incontinence study results applied to Australian population by age and sex (ABS 2002)

Study	Sex	Age	Prevalence (%)[a]	Persons with faecal incontinence[b]	Conservative	Surgical
					80-85%	15-20%
Kalantar et al (2002)	Overall	18–39 40–59 >60	6 12 18	375,332 632,358 600,568 Total = 1,608,257	1,286,606– 1,367,019	241,239–321,651
	Male	18–39 40–59 >60	8 11 16	250,321 289,526 245,113 Total = 784,960	627,968–667,216	117,744–156,992
	Female	18–39 40–59 >60	6 13 21	187,591 342,887 378,952 Total = 909,429	727,543–773,015	136,414–181,886
	Male + Female			Total = 1,694,389	1,355,511– 1,440,231	254,158–338,878
Lam et al (1999)	Male	20–24 25–29 30–34 35–39 40–44 45–49 50–54 55–59 60–64 65–69 70–74 75–79 80–84 85–89 90–94 94–99	0 14 5 28 13 20 34 22 31 26 16 18 19 25 50 0	0 96,376 37,101 205,019 97,462 136,512 220,995 120,956 132,360 89,319 48,476 41,969 26,130 ND[c] ND[c] ND[c] Total = 1,252,676	1,002,141– 1,064,775	187,901–250,535
	Female	20–24 25–29 30–34 35–39 40–44 45–49 50–54 55–59 60–64 65–69 70–74 75–79 80–84 85–89 90–94 94–99	0 7 0 11 7 10 22 10 19 16 13 14 5 12 50 0	0 48,339 0 81,597 53,171 69,258 27,942 53,545 79,709 56,730 43,151 41,185 10,587 ND[c] ND[c] ND[c] Total = 565,214	452,171–480,432	84,782–113,043
	Male + Female			Total = 1,817,890	1,454,312– 1,545,207	272,684–363,578

Table 3 **Australian prevalence of faecal incontinence study results applied to Australian population by age and sex (ABS 2002) [cont]**

Study	Sex	Age	Prevalence (%)[a]	Persons with faecal incontinence[b]	Conservative	Surgical
					80-85%	15-20%
MacLennan et al (2000)	Male	15–24 25–34 35–44 45–54 55–64 65–74 >75	1 1 3 1 3 4 5	13,853 14,304 44,458 13,325 29,303 25,861 22,924 Total = 164,028	131,222–139,424	24,606–32,806
	Female	15–24 25–34 35–44 45–54 55–64 65–74 >75	1 1 3 3 3 7 6	13,369 14,479 45,041 40,277 28,649 48,055 41,851 Total = 231,722	185,377–196,963	34,758–46,344
	Male + Female			Total = 395,750	316,599–336,387	59,362–79,150

[a] Approximate prevalence (estimated from graphs)
[b] According to 2002 ABS data
[c] Not determined as ABS data did not provide numbers of persons in the specified age groups

Existing procedures

The current clinical management of faecal incontinence includes conservative treatments. Most individuals will benefit from conservative, non-surgical treatments and those who do not may be considered for stoma formation.

Comparator

The appropriate comparators for SNS for faecal incontinence are:

- Conservative, non-surgical treatments including dietary modifications, medications to change stool consistency, pelvic floor physiotherapy, biofeedback and 'toileting' strategies.

- Stoma, ie a surgical opening into the abdomen that permits faecal waste to drain from the body, bypassing the natural/normal route. For example, a colostomy opens into the colon or large intestine and an ileostomy opens into the ileum or small intestine. Both procedures are usually performed under general anaesthesia and can be temporary or permanent.

Marketing status of the device

Table 4 summarises the components of the SNS device that are listed on the Australian Register of Therapeutic Goods (ARTG). Also included are the ARTG numbers and the date of commencement of listing for each of the components.

Table 4 Details of Australian Register of Therapeutic Goods (ARTG) listing for all SNS components

ARTG Name	ARTG Number	Commencement date of registration/ listing
Medtronic stimulators and accessories, non-sterile {Medtronic, MN USA}	AUST L 33200	4 November 1991
Medtronic medical electrodes, medical and associated equipment, sterile {Medtronic Inc Minneapolis USA}	AUST L 33210	4 November 1991
Medtronic stimulators and accessories, sterile {Columbia HTS USA}	AUST L 33287	4 November 1991
Medtronic stimulators and accessories, sterile {Medtronic BV, The Netherlands}	AUST L 46778	14 October 1993
Lead introducer kit (various models)	92057	26 November 2002
Implantable muscle/neurostimulators – Stimulator, electrical, neuromuscular, incontinence, implantable	98338	26 November 2003

Current reimbursement arrangement

SNS is not covered for use in any indication under existing Medicare Benefits Schedule (MBS) arrangements.

Approach to assessment

Review of literature

The medical literature was searched to identify relevant studies and reviews for the period between 1966 and 2004. All searches with the exception of the safety search for conservative, non-surgical treatments were conducted between December 14 and 22 2004 via the following electronic databases (Table 5). The safety search for conservative, non-surgical treatments was conducted on March 8 2005 via the same databases.

Table 5 Electronic databases searched in this review

Database	Period covered
Medline (OVID)	1966 to Present with daily update (December 2004)
Medline in process and other non-indexed citations (OVID)	to 10/12/04
EMBASE (OVID)	1980–December 2004
Cochrane Library	1991 - December 2004
CINAHL (OVID)	1982 – December 2004
Biological Abstracts (OVID)	1980 – December 2004
Australasian Medical Index	1968 - December 2004

Several search strategies were required for coverage of all aspects needed for this topic. The main areas were safety, effectiveness and cost-effectiveness.

To identify all of the relevant information published in journal articles, the search was performed as a number of separate strategies (Appendix C).

All terms that can be used to describe SNS for the treatment of faecal incontinence were identified. This set of words (the core terms) formed the core of our searching (see Appendix C).

For safety, the terms for safety, complications and adverse events were combined with the intervention terms.

Internet sites from health technology assessment, clinical trials registers and other relevant professional bodies were also searched (Appendix D).

Selection criteria

Criteria developed *a priori* to determine eligibility of relevant studies (Table 6) were based on those agreed upon by MSAC and the members of the Advisory Panel.

Table 6 ***A priori*** **selection criteria for included studies**

In adults with faecal incontinence who are assessed as refractory to other conservative, non-surgical treatments and who have an anatomically intact but functionally deficient anal sphincter (where the anal sphincter is intrinsically intact or surgically repaired), is SNS as safe, effective and cost-effective as continued use of conservative, non-surgical treatments or stoma formation?		
Characteristics	**Inclusion**	**Exclusion**
Participants	Adults with faecal incontinence who are assessed as refractory to other conservative, non-surgical treatments and who have: . an anatomically intact but functionally deficient anal sphincter (where the anal sphincter is intrinsically intact or has been repaired surgically), and . had faecal incontinence for at least 12 months	Children with faecal incontinence, refractory to other conservative treatments Adults or children with faecal incontinence for less than 12 months Adults or children without an anatomically intact anal sphincter Adults or children with urinary incontinence in isolation Adults or children with chronic pain in isolation Adults or children ineligible for PNE: . Medically unfit for surgery . Irritable bowel syndrome . Congenital anorectal malformations . Active anal abscesses or fistulas . Anorectal organic bowel disease including cancer . Functional effects of previous pelvic irradiation . Rectal or anal surgery within 12 months . Pregnant or planning pregnancy . Congenital or acquired malformations of the sacrum
Intervention	**SNS** Service is provided in two phases: Diagnostic: PNE . Acute testing . Sub-chronic testing Treatment: CTS For participants achieving greater than 50 per cent improvement in faecal incontinence episodes during PNE on a validated continence score Programming According to the patient's perception of muscular contraction of the perineum and anal sphincter	None defined
Comparators	Conservative, non-surgical treatments including: dietary modifications, medications to change stool consistency, pelvic floor physiotherapy, biofeedback and 'toileting' strategies OR Stoma formation, including: colostomy, ileostomy, cecostomy, appendicostomy and antegrade colonic enema (ACE)	None defined

Table 6 (cont'd) *A priori* selection criteria for included studies

Characteristics	Inclusion	Exclusion
Outcomes	. Faecal incontinence: number continent or improved, episodes per week, ability to defer defecation, urgency, use of pads, use of anal plugs, incontinence score, need for further treatment eg surgery or medication. . Quality of life. . Adverse events: infection and/or pain at implantation site, displacement of electrodes, technical failure requiring removal and/or detrimental change in urinary function.	Mechanisms of action: anorectal manometry (resting pressure, maximal squeeze pressure, rectal sensory threshold to balloon distension, sensation of urgency to balloon distension and maximal tolerated rectal volume to balloon distension)
Study design	Health technology assessments, systematic reviews, meta-analyses and RCTs sought initially If these are unavailable, other controlled trials, comparative studies and cohort studies may be assessed In the event that these too are unavailable, case series of consecutively selected participants may be considered for inclusion	Narrative reviews, editorials and other opinion pieces, articles identified as preliminary reports when results are published in later versions, articles in abstract form only, case reports Studies only evaluating the effectiveness of SNS during PNE Case series enrolling fewer that 20 participants
Publication	English-language articles or well-designed RCTs published in any language	None defined

Assessment of validity

Critical appraisal refers to the process of evaluating the study design of included articles. The most rigorous study design for assessing the validity of therapeutic interventions is considered to be an randomised controlled trial (Guyatt et al 1993, Sackett et al 2000).

Assessment of primary studies

The evidence presented in the selected studies was assessed and classified using the dimensions of evidence defined by the National Health and Medical Research Council (NHMRC 2000). These dimensions (Table 7) consider important aspects of the evidence supporting a particular intervention and include three main domains: strength of the evidence, size of the effect and relevance of the evidence. The first domain is derived directly from the literature identified as informing a particular intervention. The last two require expert clinical input as part of their determination.

Table 7 Evidence dimensions

Type of evidence	Definition
Strength of the evidence	
Level	The study design used, as an indicator of the degree to which bias has been eliminated by design[a]
Quality	The methods used by investigators to minimise bias within a study design.
Statistical precision	The *p*-value or, alternatively, the precision of the estimate of the effect. It reflects the degree of certainty about the existence of a true effect.
Size of effect	The distance of the study estimate from the "null" value and the inclusion of only clinically important effects in the confidence interval.
Relevance of evidence	The usefulness of the evidence in clinical practice, particularly the appropriateness of the outcome measures used.

[a]See Table 8

The three sub-domains (level, quality and statistical precision) are collectively a measure of the strength of the evidence. The designations of the levels of evidence are shown in Table 8.

Table 8 Designations of levels of evidence

Level of evidence	Study design
I	Evidence obtained from a systematic review of all relevant randomised controlled trials
II	Evidence obtained from at least one properly-designed randomised controlled trial
III-1	Evidence obtained from well-designed pseudorandomised controlled trials (alternate allocation or some other method)
III-2	Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case-control studies, or interrupted time series with a control group
III-3	Evidence obtained from comparative studies with historical control, two or more single arm studies, or interrupted time series without a parallel control group
IV	Evidence obtained from case series, either post-test or pre-test/post-test

[Modified from NHMRC (1999)]

The NHS Centre for Reviews and Dissemination (2001) assembled a list of criteria used to evaluate the validity of evidence from various study designs. The relevant validity criteria used in this review for assessing the quality of evidence are listed in Table 9.

Table 9 Validity criteria according to study design

Study design	Validity criteria
Randomised controlled trial	Randomised method; allocation concealment; blinding of patients, investigators and outcome assessors; proportion lost to follow-up; intention to treat analysis
Cohort	Prospective/retrospective; comparable groups at inception; identification and adjustment for confounding factors; blind outcome assessment; sufficient duration of follow-up; proportion lost to follow-up
Case-control	Explicit definition of cases; adequate details of selection of controls; comparable groups with respect to confounding factors; interventions and other exposures assessed in same way for cases and controls; appropriate statistical analysis
Case series	Indication was comparable across patients; disease severity was comparable across patients; explicit entry criteria; outcome assessed in all patients; follow-up time uniform; outcomes assessed objectively; outcomes assessed in a blinded manner; outcome measures quantified

[Modified from NHS Centre for Reviews and Dissemination (2001)]

Data extraction

Data were extracted using standardised instruments created for the assessment. Two reviewers examined each article and any discrepancies in evaluation were discussed and resolved through consensus. Contact with corresponding authors was attempted to clarify specific issues relating to validity or results.

Data analysis

The number needed to treat to harm NNT(H) was calculated as follows:

$$NNT(H) = \frac{1}{Complication\ rate}$$

Expert advice

An Advisory Panel with expertise in health technology assessment, neurology, colorectal surgery, clinical nursing and consumer health was established to evaluate the evidence and provide advice to MSAC from a clinical perspective. In selecting members for Advisory Panels, MSAC's practice is to approach the appropriate medical colleges, specialist societies and associations and consumer bodies for nominees. Membership of the Advisory Panel is provided at Appendix B.

Results of assessment

Search results

Sacral nerve stimulation

The articles identified, excluded and included from the systematic search strategy are shown in Figure 2. The search strategy identified 342 articles. Following the review of the abstracts, 60 articles were ordered for full text assessment. Of these, 15 articles met the inclusion criteria – nine case series, one crossover study, two systematic reviews of non-randomised studies, two health technology assessment reports and one protocol for a systematic review.

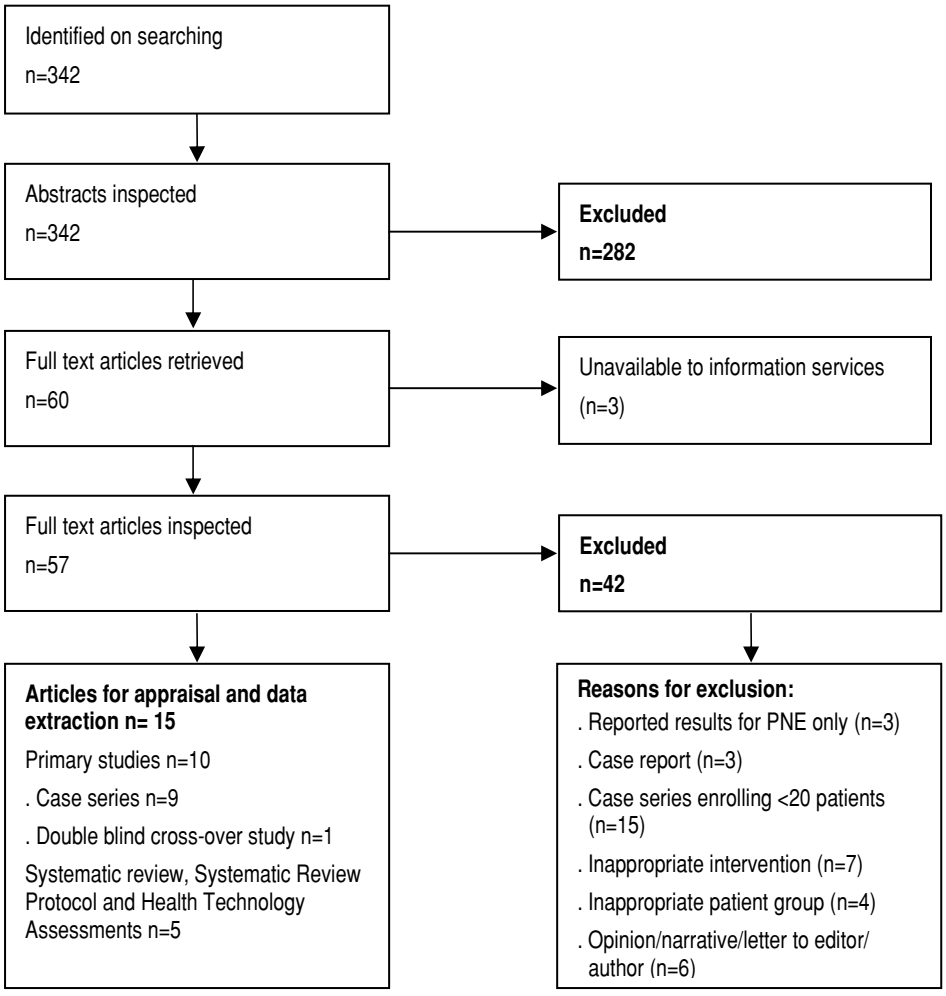

Figure 2 Flowchart demonstrating the selection of articles assessing the effectiveness of SNS for faecal incontinence

Forty-two articles were excluded for reasons including the reporting of effectiveness results during PNE only, case reports and case series enrolling fewer than 20 participants.

An ongoing study is being performed at the Cleveland Clinic by the Department of Colorectal Surgery.

In addition, an RCT comparing SNS with standard medical care for severe refractory faecal incontinence is currently under way at the Royal Melbourne, Royal Women's and Epworth Hospitals in Melbourne, Australia (Tjandra et al 2004).

Conservative, non-surgical treatment

The search strategy for the safety of conservative, non-surgical treatments identified 1,188 articles. Following the review of the abstracts, 98 articles were ordered for full text assessment. Five articles were subsequently included in the assessment of the safety of conservative, non-surgical treatments.

Stoma

The search strategy identified 1,208 articles. Following the review of the abstracts, 34 articles were ordered for full text assessment. Of these, no articles met the inclusion criteria. A summary of the available evidence for the effectiveness of stoma formation for the treatment of faecal incontinence is presented at Appendix F.

Is it safe?

Sacral nerve stimulation

A systematic search of the literature was undertaken to assess the safety of SNS for the treatment of faecal incontinence (Table C2, Appendix C).

Safety results from case series

Table 10 summarises the adverse events reported during PNE of SNS when used in the treatment of faecal incontinence. (Table E1, Appendix E summarises adverse events reported in the individual primary studies).

During PNE, the most common adverse event reported was electrode and lead problems in study participants being treated for faecal incontinence with a complication rate of 10.43 per cent, (95% CI: 7.36, 14.58) and NNT(H) of 10 (95 % CI: 7, 14). The rate of infections for participants undergoing PNE for the treatment of faecal incontinence was 6.12 per cent (95% CI: 3.85, 9.57) and NNT(H) was 16 (95% CI: 10, 26). There were no reports of generator problems or pain.

Table 10 Complication rates for SNS for the treatment of faecal incontinence during peripheral nerve evaluation

Complication[a]	Number of events per number of participants	Complication rate (%) (95% CI)	NNT(H) (95% CI)
Electrode/lead replaced/repositioned	3/278	1.08 (0.37, 3.12)	93 (32, 270)
Permanent explants	7/278	2.52 (1.22, 5.11)	40 (20, 82)
Generator problems	0/278	NA	NA
Electrode and lead problems	29/278	10.43 (7.36, 14.58)	10 (7, 14)
Pain	0/278	NA	NA
Infection	17/278	6.12 (3.85, 9.57)	16 (10, 26)

Abbreviations: CI, confidence interval; NNT(H), number needed to treat to harm, NA, not applicable
[a] Refer to Table E1 of Appendix E for results from individual studies

Of the infections reported during PNE:

- one was resolved by removal of the temporary electrode wire (Jarrett et al 2004b)
- all nine participants experiencing an infection were treated with antibiotics, however four participants required lead removal (Matzel et al 2004a)
- three of 15 participants who underwent trial screening with a permanent electrode required removal of the percutaneous extension electrode and treatment with antibiotics (Rasmussen et al 2004)
- infections developed in four of six participants undergoing trial screening with a permanent electrode and an external stimulation cable. Three required removal of the permanent electrode and the pacemaker was also removed from one participant because the stimulation device had been implanted.

The type, severity and locations of the infections experienced by study participants during PNE were not reported.

Table 11 summarises the adverse events reported during CTS for SNS when used in the treatment of faecal incontinence. Table E2, Appendix E, presents the adverse events reported in the individual primary studies.

During CTS, the most common adverse event reported was re-operation with a rate of 15.50 per cent (95% CI: 11.67, 20.29) and NNT(H) of 6 (95% CI: 5, 9). Re-operations were mainly due to implant/lead/electrode problems requiring repositioning or replacement, or permanent explantation due to infection, pain or fading out of clinical response. Pain was reported at a rate of 6.27 per cent (95% CI: 3.95, 9.82) in participants being treated for faecal incontinence. The infection rate for participants was 3.32 per cent (95% CI: 1.76, 6.19) with NNT(H) of 30 (95% CI: 16, 57). Seroma was reported at a rate of 4.06 per cent (95% CI: 2.28, 7.12). Wound problems were uncommon in participants, with a rate of 0.37 per cent (95% CI: 0.07, 2.06).

Kenefick et al (2002), whose adverse event data were included in Jarrett et al (2004b), reported that some study participants experienced a minor localised electric shock when passing through ambient electrical or magnetic fields.

Table 11 Complication rates for SNS for the treatment of faecal incontinence during CTS

Complication[a]	Number of events per number of participants	Complication rate (%) (95% CI)	NNT(H) (95% CI)
Re-operations	42/271	15.50 (11.67, 20.29)	6 (5, 9)
IPG/electrode/lead replaced/repositioned	12/271	4.43 (2.55, 7.58)	23 (13, 40)
Permanent explants	16/271	5.90 (3.67, 9.37)	17 (11, 27)
Generator problems	8/271	2.95 (1.50, 5.72)	34 (17, 67)
Electrode and lead problems	12/271	4.43 (2.55, 7.58)	23 (13, 40)
Pain	17/271	6.27 (3.95, 9.82)	16 (10, 25)
Infection	9/271	3.32 (1.76, 6.19)	30 (16, 57)
Seroma	11/271	4.06 (2.28, 7.12)	25 (14, 44)
Wound problems	1/271	0.37 (0.07, 2.06)	270 (49, 1,429)
Other	6/271	2.21 (1.02, 4.75)	45 (21, 98)

Abbreviations: CI, confidence interval; IPG, implantable pulse generator; NNT(H), number needed to treat to harm
[a] Refer to Table E2, Appendix E, for results from individual studies

Of the infections reported during chronic stimulation therapy:

- one participant had a mild infection at the site of the electrode implant which resolved with antibiotic therapy (Altomare et al 2004a)
- a total of eight participants required removal of the system (Matzel et al 2004a, Rasmussen et al 2004, Rosen et al 2001, Uludag et al 2004). The type, severity and locations of the infections experienced by participants during chronic stimulation were not reported in three studies (Matzel et al 2004a, Rasmussen et al 2004, Uludag et al 2004). Rosen et al (2001) described all three cases as severe.

Safety results from the systematic reviews and health technology assessment reports

The safety results for SNS when used for the treatment of faecal incontinence reported in the identified systematic reviews (Jarrett et al 2004a, Matzel et al 2004b) and health technology assessment reports (National Institute for Clinical Excellence [NICE] 2004, Australian Safety and Efficacy Register of New Interventional Procedures - Surgical [ASERNIP-S] 2003) are summarised below.

Of the 266 study participants undergoing PNE, 10 reported an adverse event. Nine of these had lead dislodgement that prevented an adequate testing period and one had a superficial skin infection that cleared upon removal of the lead (Jarrett et al 2004a, NICE 2004).

Nineteen adverse events were reported for the 149 study participants who underwent permanent implantation of the device (Jarrett et al 2004a, NICE 2004):

- Three participants developed an infection of the implant and subsequently had the device removed. One of them underwent reimplantation.
- Eight lead dislodgements occurred in seven participants – five were reimplanted (one dislodged again and was removed); one requested removal of the device and another was awaiting reassessment.

- One participant experienced interruption of the electrode lead and required device replacement.
- Six participants experienced implant-related pain that was resolved by the injection of steroids and local anaesthetic.
- One participant reported a superficial wound dehiscence that healed uneventfully.
- No adverse effects on urinary or sexual function were reported.

Of the 34 study participants receiving permanent implants in the MDT-301 study (Matzel et al 2004a):

- One developed an infection and required device removal.
- Nine participants reported 10 episodes of pain that was resolved in four by reprogramming the device, in three by repositioning the device and in one with medication. Resolution of pain was not specified for two episodes.
- Three participants experienced deterioration in bowel symptoms – one improved, one had the device removed and the outcome for the remaining participant was not reported (NICE 2004).
- No adverse events were reported in the crossover study (Jarrett et al 2004a, NICE 2004, Vaizey et al 2000).

A further systematic review assessing the safety and effectiveness of SNS in the treatment of faecal incontinence by Matzel et al (2004b) reported that complications varied between zero and 50 per cent in the studies included in their review. The complications reported included pain at the site of the electrode or pulse generator, electrode dislodgement or breakage, infection, loss of therapeutic effect and deterioration in bowel symptoms. Discontinuation of therapy in a limited number of study participants was due to loss of therapeutic effect, deterioration of symptoms, pain, lead dislocation and infection. No incidences of central nervous system infectious complications or permanent injury as a result of any complications were reported.

Two studies included in Matzel et al (2004b) and the ASERNIP-S (2003) health technology assessment reports (Kenefick et al 2002a, Matzel et al 2001) were not included in the Jarrett et al (2004a) or the NICE (2004) reviews due to updated information being available for the latter two reviews. In summary, the ASERNIP-S (2003) review found that a small proportion of individuals experienced complications such as infection, dislodgement of the permanent electrode, explantation of the leads and generator and pain at the position of the electrode and the implantation site.

Summary of the safety of sacral nerve stimulation for the treatment of faecal incontinence

The safety of SNS for the treatment of faecal incontinence was similar for the current review and those reported in the identified systematic reviews and health technology assessment reports. To date, the adverse events reported are not severe; hence SNS for

the treatment of faecal incontinence appears to be safe as assessed from the available evidence, however:

- only a small number of individuals have been analysed
- too few participants have been analysed to observe rare adverse events
- there has been limited follow-up (up to 99 months) of the participants included in each of the studies.

Conservative, non-surgical treatments

In a systematic review of the literature, Cheetham et al (2002) assessed the safety and effectiveness of drug treatment for faecal incontinence in adults:

- The review included two trials that assessed the safety and effectiveness of loperamide versus placebo, one trial assessed this in patients with an ileoanal pouch and the other in patients with constipation. More patients receiving loperamide experienced adverse events such as constipation, abdominal pain, diarrhoea, headache and nausea as compared to those receiving placebo.

- Further assessment of the safety and effectiveness of drugs enhancing anal sphincter tone versus placebo were reported. Four trials were identified of which three tested phenylephrine gel – two in people with passive faecal incontinence and structurally intact anal sphincters and one in people with ileoanal pouches following colectomy for ulcerative colitis. The final trial assessed sodium valproate in patients with ileoanal pouches due to either colectomy for ulcerative colitis or familial polyposis. More participants experienced adverse events such as localised dermatitis and stinging or burning sensation following application of phenylephrine than with placebo. Adverse events such as abdominal pain and nausea were reported more often in participants receiving sodium valproate compared with placebo.

- Comparison of one drug versus another drug or combination of drugs was also included in the review. One trial comparing loperamide versus codeine versus diphenoxylate plus atropine in patients with idiopathic diarrhoea reported that more adverse events were experienced by participants receiving diphenoxylate than those receiving either loperamide or codeine. The nature and severity of the adverse events were not reported.

Cundall et al (2003) reported on the use of hyperbaric oxygen therapy in the treatment of faecal incontinence secondary to pudendal neuropathy in 13 participants. All but one participant completed the treatment without complications (with the exception of reversible myopia which is expected with prolonged hyperbaric oxygen therapy). The patient reporting complications experienced severe sinus pain following two treatments. Another participant experienced an upper respiratory tract infection which resulted in the treatment being delayed.

Adverse events experienced in 190 patients with defecation disturbances undergoing retrograde colonic irrigation were reported in Gosselink et al (2005). Five per cent of patients in the group with faecal incontinence and 67 per cent of patients experiencing

soiling discontinued retrograde colonic irrigation due to irrigation-related problems and loss of irrigation fluid during the day. Of the 76 patients who continued with retrograde colonic irrigation, 74 per cent experienced irrigation-related problems. Adverse events included technical problems, abdominal cramping, loss of irrigation fluid during the day and anal pain.

Osterberg et al (2004) reported adverse events experienced by patients in an RCT comparing conservative and surgical treatment of neurogenic faecal incontinence. One patient of 28 undergoing anal plug electrostimulation reported a burning sensation in the vagina two weeks after treatment.

Sander et al (1999) reported the adverse events experienced by three patients with faecal incontinence undergoing pelvic floor exercises alone or pelvic floor exercises with concomitant transanal electrical stimulation. All three participants undergoing pelvic floor exercises with concomitant transanal electrical stimulation dropped out of the study due to unacceptable anal pain during stimulation, as a result of which this method of treatment was subsequently abandoned. One year following treatment with pelvic floor exercises, one of 34 participants complained of anal pain during defecation, two presented with symptoms of urinary incontinence and four complained of dyspareunia.

Stoma

The systematic search for the assessment of the safety of stoma formation was restricted to stoma formation for the treatment of faecal incontinence (Table C4, Appendix C). Many of the studies identified reported combined results for the children and adults reported in the series – studies in which the adult and child data could not be separated were not included. As a result, the safety results of stoma formation for the treatment of faecal incontinence in adults were extracted from five studies.

Branagan et al (2003) reported on complications experienced by 35 individuals with spinal cord injury who had a stoma formed. It is unclear if combined adverse event data for adults and children were reported. Complications occurred in 14 (40.0%) patients and included leakage of mucus and occasionally blood and pus from the rectum in eight (22.9%), three (8.6%) developed parastomal hernias, two (5.7%) developed bowel obstruction (one participant required a laparotomy), and one participant undergoing a laparoscopically-assisted Trephine colostomy had the distal end of the bowel brought out to the abdominal surface and the proximal end closed inadvertently, requiring a laparotomy to repair the situation.

Bruce et al (1999) reported on the use of the antegrade continence enema in seven individuals (four women and three men) with refractory neurogenic faecal incontinence. Complications experienced by these seven participants included an obese participant requiring early operative revision five weeks following the operation due to stomal stenosis, which was associated with catheter dissection at the level of the skin between the skin and gastric stoma. Bruce et al (1999) also reported the requirement for the application of an antacid tablet directly to the stoma site and the use of a skin barrier due to gastric acidity.

Catena et al (2002) reported the retrospective results of 44 individuals (35 women) who underwent an end sigmoid colostomy for untreatable faecal incontinence. Problems with

the rectal stump were reported by 25 patients (56.8%) following prior colostomy. Twelve patients (27.3%) underwent secondary proctectomy.

Complications experienced by nine individuals undergoing ileal neoappendicostomy for antegrade colonic irrigation were reported by Christensen et al (2001). Six participants (66.7%) had minor liquid reflux, two (22.2%) experienced low level leakage of gas and two (22.2%) reported a periodic bad smell from the ileal conduit. One (11.1%) participant had a stenosis of the ileal conduit that required dilation under general anaesthesia. Four (44.4%) participants reported transient adverse events during irrigation that included chills, mild abdominal cramps and nausea.

Stone et al (1990) reported on complications experienced in 20 individuals with spinal cord injury treated with stoma for chronic gastrointestinal problems, perineal ulcers and low rectal cancer. One death (5.0%) from pneumonia was reported. One study participant (5.0%) developed a wound dehiscence and another developed stomal ischemia, both of which required re-operation. The individual receiving stoma for cancer of the rectum (5.0%) developed a peristomal hernia and two participants (10.0%) experienced peristomal skin infections, both cleared with local therapy.

Is it effective?

This report assessed the effectiveness of SNS for the treatment of faecal incontinence. No RCTs or comparative studies were identified that compared SNS with continued conservative, non-surgical treatment or stoma formation. However, the baseline or pre-SNS results of the participants enrolled in the identified case series could be considered to be equivalent to the continued use of conservative, non-surgical treatment for the management of faecal incontinence.

Sacral nerve stimulation

The assessment of the effectiveness of SNS was completed by the critical appraisal of nine case series and one crossover study, two systematic reviews of non-randomised studies and two health technology assessment reports which included a subset of the case series and the crossover study.

Critical appraisal of case series and a double blind crossover study

The descriptive characteristics of the nine case series identified from a systematic search of the literature and meeting the *a priori* inclusion criteria are listed in Table 12. Four of the studies were conducted in Italy, one in Denmark, one in the UK, one in Austria, one in The Netherlands and a multicentre study that included centres in Europe and the USA. The minimum and maximum length of follow-up was 24 (Ripetti et al 2002) and 72 (Jarrett et al 2004b) months, respectively. Three studies did not report the length of follow-up. The study population varied in size from 20 (Rosen et al 2001) to 116 (Ganio et al 2002). The majority of participants in all of the studies were female. The mean or median age of the participants included in the studies was similar between studies. The mean or median duration of faecal incontinence was also similar between studies (where reported) and fulfilled the inclusion requirement for this review of having faecal incontinence for at least 12 months, with the exception of participants in Matzel et al (2004a) and Rosen et al (2001) where some participants had faecal incontinence for 0.8

and 0.5 years, respectively. Three studies did not report the mean or median duration of faecal incontinence in participants included in each study (Ganio et al 2001a, Ganio et al 2002, Rasmussen et al 2004), however all participants included in the study by Rasmussen et al (2004) had faecal incontinence for greater than one year (personal communication). It is uncertain whether participants enrolled in Ganio et al (2001a) are also reported in Ganio et al (2002).

Table 12 Descriptive characteristics of case series for SNS

Study	Location	Enrolment period	Maximum length of follow-up (months)	Study population			
				N	№ Male (%)	Age (years)	Duration of faecal incontinence (years)
Altomare et al (2004a)	Italy	1998–2002	48	41[a]	3/14[a] (21.4)	Median: 54 Range: 21–74	Median: 6.2 Range: 2–42
Ganio et al (2001a)	Italy	December 1995–December 1999	37	23	5 (22.0)	Median: 54.9 Range: 28–71	Not reported
Ganio et al (2002)	Italy	January 1996–December 2001	56	116	18 (16.0)	Mean: 55.2 Range: 26–77[b]	Not reported
Jarrett et al (2004b)	UK	October 1996–May 2003	72	59	6/46[c] (13.0)	Median: 56 Range: 35–68[d]	Median: 5 Range: 1–21[d]
Matzel et al (2004a)	Multicentre – US and Europe	January 1999–June 2001	36	37	4 (10.8)	Mean: 54.3 SD: 11.3	Median: 5.1 Range: 0.8–26.9
Rasmussen et al (2004)	Denmark	Not reported	Not reported	45	11 (24.4)	Median: 59 Range: 27–82	Not reported All participants had FI for >1 year[e]
Ripetti et al (2002)	Italy	1998–2000	24	21	1 (4.8)	Mean: 55.7	Mean: 5 Range: 2–21
Rosen et al (2001)	Austria	November 1998–December 2000	26	20	6 (30.0)	Median: 50.1 Range: 11–79	Median (range) Idiopathic 3 (0.5–5.0) Neurologic 5 (1–15) All 5 (0.5–15.0)
Uludag et al (2004)	The Netherlands	Not reported	48	75	9 (12.0)	Mean: 53 Range: 26–75	Median: 5 Range: 1–66

Abbreviations: FI, faecal incontinence; IQR, interquartile range
[a] 41 participants were eligible for PNE. Results of 14/16 participants that went on to CTS are reported
[b] Study population demographics of the 36 participants that were eligible for chronic stimulation therapy
[c] Proportion of men in the group that went on to CTS (n=46)
[d] Study population demographics of the 46 participants that went on to CTS
[e] Personal communication

Table 13 summarises the inclusion and exclusion criteria used to recruit participants in the nine studies, two of which (Altomare et al 2004a, Rasmussen et al 2004) did not report their inclusion criteria.

One study specified that individuals with faecal incontinence for at least one year were eligible for inclusion (Rosen et al 2001). Two studies specified that participants were required to have had faecal incontinence episodes at least twice every two weeks (Ganio et al 2001a) or once per week (Ganio et al 2002) for the preceding two months. Three

studies (Jarrett et al 2004b, Matzel et al 2004a, Uludag et al 2004) included individuals aged 18 or over and five studies (Ganio et al 2001a, Ganio et al 2002, Jarrett et al 2004b, Matzel et al 2004a, Uludag et al 2004) excluded individuals aged over 75 years old. Where inclusion criteria were reported, four studies specified that individuals with a structurally intact EAS were to be included in each of the studies (Ganio et al 2002, Matzel et al 2004a, Rosen et al 2001, Uludag et al 2004). Ganio et al (2001a) included individuals with structurally intact external and internal anal sphincters and Ripetti et al (2002) stated that individuals with an anatomically intact anal sphincter were to be included. Jarrett et al (2004b) did not explicitly state that an intact anal sphincter was required for inclusion in their study. Six studies also specified that to be eligible for inclusion, participants had to have failed more conservative therapy (Ganio et al 2001a, Ganio et al 2002, Jarrett et al 2004b, Matzel et al 2004a, Rosen et al 2001, Uludag et al 2004).

Table 13 Participant selection criteria for case series for SNS

Study	Inclusion	Exclusion
Altomare et al (2004a)	Not reported	Not reported
Ganio et al 2001a	Faecal incontinence (passive or urge) for solid or liquid stool at least twice every two weeks during the previous two months Failure of conventional drugs or biofeedback therapy Structurally intact external and internal anal sphincters as confirmed by anal ultrasound Sphincter dysfunction revealed by low resting and/or squeeze pressure combined with symptoms of incontinence	Inflammatory bowel diseases Cardiac disease Aged over 75 years Pregnant
Ganio et al (2002)	Faecal incontinence to solid or liquid stool at least once per week during the preceding two months No response to conventional behavioural and/or medical treatments Structurally intact EAS on anal endosonography	Pathologic conditions of the sacrum (eg spina bifida or skin disease in sacral area) Inflammatory bowel disease Cardiac disease Aged over 75 years Pregnant
Jarrett et al (2004b)	Signed informed consent Aged 18–75 years One or more episodes of faecal incontinence per week Failed conservative therapy (antidiarrhoeals and biofeedback) Competent to fill in questionnaire and attend clinics	Congenital anorectal malformations Rectal surgery less than 12 months ago (<24 months for cancer) Present external rectal prolapse Chronic bowel disease Chronic diarrhoea, unmanageable by diet or drugs Altered bowel habit associated with abdominal pain Stoma *in situ* Neurological diseases (eg diabetic neuropathy, multiple sclerosis, Parkinson's disease) Bleeding complications Pregnancy Anatomical limitations preventing placement of the electrode Skin disease risking infection (eg pyoderma, pilonidal sinus) Psychiatric or physical inability to comply with study protocol

Table 13 (cont'd) Participant selection criteria for case series for SNS

Study	Inclusion	Exclusion
Matzel et al (2004a)	Involuntary passage of solid or liquid faeces at least once a week Intact EAS (If previous repair, at least 50% of its length) Refractory to medical treatment and biofeedback therapy Aged 18–75 years	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 and spinal cord injury Bleeding complications Pregnancy Anatomic limitations obviating surgical access Pyoderm or pilonidal sinus Mental or physical inability to adhere to study protocol
Rasmussen et al (2004)	Not reported Participants selected from a larger group of patients referred for the treatment of faecal incontinence Severe faecal incontinence which constituted a social problem for the patient[a]	Not reported
Ripetti et al (2002)	Anatomically intact anal sphincter, or surgically repaired anal sphincter without recovery from faecal incontinence Selected on the basis of the severity of incontinence and the consequent alteration to quality of life	Not reported
Rosen et al (2001)	At least one incontinence episode per week for solid stool (from incontinence diary) An intact EAS documented by endoanal ultrasonography and/or magnetic resonance imaging History of faecal incontinence for at least one year after neurologic event (surgery, trauma, stroke) Informed consent Failure of a 6-week course of a standardised biofeedback protocol Participants with idiopathic incontinence had to be advised about alternative conventional therapeutic options	Not reported

Table 13 (cont'd) Participant selection criteria for case series for SNS

Study	Inclusion	Exclusion
Uludag et al (2004)	Aged 18–75 years Persistent faecal incontinence despite conventional treatment Structurally intact EAS (confirmed by endoluminal ultrasound) In patients who underwent previous anal repair, the EAS had to be circumferentially intact over more than one half of the length of the anal canal (confirmed by endoluminal ultrasound)	History of congenital anorectal malformations Previous rectal surgery in the last 12 months Presence of a rectal prolapse or stoma Neurologic diseases such as diabetic neuropathy and multiple sclerosis Inflammatory bowel disease Chronic diarrhoea Skin and tissue diseases resulting in an increased risk of infection

Abbreviations: EAS, external anal sphincter
[a] Personal communication with author

Validity of case series

The validity characteristics of the nine case series are summarised in Table 14. Two of the eight studies reported prospective data collection (Jarrett et al 2004b, Matzel et al 2004a), one reported retrospective data collection (Altomare et al 2004a) and the remaining six studies did not report the study design (Ganio et al 2001a, Ganio et al 2002, Rasmussen et al 2004, Ripetti et al 2002, Rosen et al 2001, Uludag et al 2004). None of the included studies reported that the participants were consecutively enrolled and two studies reported that participants were selected from a larger group of patients (Rasmussen et al 2004) or on the basis of the severity of incontinence and the consequent alteration to quality of life (Ripetti et al 2002). Five studies reported explicit inclusion and exclusion criteria (Ganio et al 2001a, Ganio et al 2002, Jarrett et al 2004b, Matzel et al 2004a, Uludag et al 2004), two studies reported explicit inclusion criteria but no exclusion criteria (Ripetti et al 2002, Rosen et al 2001) and two studies reported no inclusion or exclusion criteria (Altomare et al 2004a, Rasmussen et al 2004). Where reported, none of the included studies had uniform follow-up of participants.

The majority of participants (48.4% to 73.3%) included in four of the nine studies had idiopathic faecal incontinence (Ganio et al 2002, Matzel et al 2004a, Rasmussen et al 2004, Uludag et al 2004), whereas the majority of participants enrolled in Altomare et al (2004a) and Rosen et al (2001) had faecal incontinence due to neurogenic causes. The majority of participants enrolled in Jarrett et al (2004b) had faecal incontinence due to obstetric injury. Ganio et al (2001a) and Ripetti et al (2002) did not report the aetiology of faecal incontinence in the participants enrolled in their studies. Common concomitant diseases reported in the enrolled participants included urinary incontinence, pudendopathy and insulin-dependent diabetes.

Table 14 Validity characteristics of case series for SNS

Study	Design	Participants consecutively enrolled	Explicit inclusion/ exclusion criteria	Outcomes assessed in all participants	Uniform follow-up (months)	Indication/disease uniform across participants n/N (%)
Altomare et al (2004a)	Not reported	Not reported Centre treated 196 patients with faecal incontinence, 41 of whom were eligible for PNE	No	No	No Median: 14 Range: 6–48	Aetiology of faecal incontinence: . Neurogenic 8/14 (57.1) . Neurological following sacral trauma/surgery 2/14 (14.3) Previous surgery: . None 4/14 (28.6) . Dynamic graciloplasty 3/14 (21.4)[a] . Hysterectomy 5/14 (35.7)[b] . Anal fistula repair 1/14 (7.1) . Neurinoma 1/14 (7.1) . Sacral trauma 1/14 (7.1) Concomitant urinary incontinence 6/14 (42.9) Insulin-dependent diabetes 2/14 (14.3)
Ganio et al (2001a)	Not reported	Not reported	Yes	No	No Median: 19.2 Range: 5–37	Urge incontinence 18/23 (78.0) Passive incontinence 5/23 (22.0) Previous surgery in pelvic area 8/23 (35.0) Concomitant urinary incontinence 11/23 (48.0)
Ganio et al (2002)	Not reported	Not reported	Yes	No	No Mean: 25.6 Range: 1–56	Aetiology of faecal incontinence[c]: . Idiopathic 15/31 (48.4) . Previous pelviperineal surgery 11/31 (35.5) . Spinal cord injury 2/31 (6.5) . Incomplete D8 lesion 1/31 (3.2) . Scleroderma 1/31 (3.2) . Spastic paraparesis 1/31 (3.2)
Jarrett et al (2004b)	Prospective	Not reported	Yes	No	No Median: 12 Range: 1–72	Aetiology of faecal incontinence[d]: . Obstetric injury 25/46 (54.3) . Idiopathic 7/46 (15.2) . Scleroderma 4/46 (8.7) . Incontinence persisting after repair of complete external rectal prolapse 4/46 (8.7) . Spinal trauma 2/46 (4.3) . Fistula surgery 1/46 (2.2) . Lateral sphincterectomy 1/46 (2.2) . Haemorrhoidectomy 1/46 (2.2) . Haemorrhoidal banding 1/46 (2.2)

Table 14 (cont'd) Validity characteristics of case series for SNS

Study	Design	Participants consecutively enrolled	Explicit inclusion/ exclusion criteria	Outcomes assessed in all participants	Uniform follow-up (months)	Indication/disease uniform across participants n/N (%)
Matzel et al (2004a)	Prospective	Not reported	Yes	No	No Median: 23.9 Interquartile range: 12.1–24.1	Aetiology of faecal incontinence: . Idiopathic 19/37 (51.4) . Scleroderma 2/37 (5.4) . Obstetric trauma 10/37 (27.0) . Perineal surgery 6/37 (16.2) No previous sphincter surgery 29/37 (78.4) Previous sphincter surgery 8/37 (21.6)
Rasmussen et al (2004)	Not reported	Participants selected from a larger group of patients referred for the treatment of faecal incontinence	No	No	Not reported	Aetiology of faecal incontinence: . Idiopathic 24/45 (53.3) . Spinal injury 13/45 (28.9) . Obstetric trauma 5/45 (11.1) . Muscle dystrophia 1/45 (2.2) . Rectal resection 2/45 (4.4)
Ripetti et al (2002)	Not reported	Participants were selected on the basis of the severity of incontinence and the consequent alteration to the quality of life	Explicit inclusion criteria, but no explicit exclusion criteria	No	No Median: 15 Range: 6–24	. Isolated faecal incontinence 3/21 (14.3) . Faecal incontinence and: Anal pain 3/21 (14.3) Pelvic floor dyssynergia 5/21 (23.8) . Urge incontinence for gas and liquid stool 11/21 (52.4) . Passive incontinence for liquid stool 8/21 (38.1) . Incontinence for solid stool 2/21 (9.5) Concomitant urinary incontinence 9/21 (42.9)
Rosen et al (2001)	Not reported	Not reported	Explicit inclusion criteria, but no explicit exclusion criteria	No	No Median: 15 Range: 3–26	Aetiology of faecal incontinence: . Idiopathic 5/20 (25.0) . Neurologic 15/20 (75.0) Spinal cord injury 6/20 (30.0) Spinal cord surgery 4/20 (20.0) Meningomyeocele 2/20 (10.0) Multiple sclerosis 1/20 (5.0) Friedreich syndrome 1/20 (5.0) Spinal stroke 1/20 (5.0)
Uludag et al (2004)	Not reported	Not reported	Yes	No	No Range: 1–48	Aetiology of faecal incontinence: . Idiopathic 55/75 (73.3) . Anal repair 9/75 (12.0) . Spinal operation 6/75 (8.0) . Partial spinal cord injury 3/75 (4.0) . Low-anterior resection 2/75 (2.7) Pudendopathy 36/75 (48.0)

Abbreviations: EAS, external anal sphincter; IAS, internal anal sphincter

[a] In addition to dynamic graciloplasty, one participant had a hysterectomy, and another had rectocele repair and a hysterectomy

[b] One participant also had a Burch operation

[c] Aetiology of faecal incontinence reported for the 31 participants that went on to CTS

[d] Aetiology of faecal incontinence reported for the 46 participants that went on to CTS

Table 15 summarises the eligibility criteria for participants undergoing PNE to be considered for CTS. Five of the nine studies stated that participants needed to show at least a 50 per cent improvement in incontinence (incontinence episodes per week or number of days affected by incontinence per week) (Ganio et al 2002, Jarrett et al 2004b, Matzel et al 2004a, Rasmussen et al 2004, Uludag et al 2004). Altomare et al (2004a) reported that participants required at least a 60 per cent reduction, and Ripetti et al (2002) stated that participants required at least a 75 per cent reduction. Rosen et al (2001) stated that participants whose incontinence status improved would continue to CTS and Ganio et al (2001a) required that participants have complete cessation of incontinence for solid or liquid stool during PNE and display a rapid return to pre-PNE conditions when the stimulation was discontinued.

Table 15 Eligibility criteria for participants undergoing PNE to continue to CTS in the individual case series

Study	Participants were eligible for CTS if they achieved the following during PNE:
Altomare et al (2004a)	At least a 60% reduction in the severity of faecal incontinence, with a significant reduction in the number of episodes of faecal leakage and improvement in rectal sensitivity and time length during which defecation could be postponed
Ganio et al (2001a)	Complete cessation of incontinence for liquid or solid stool during the test period and a rapid return to pre-PNE conditions when stimulation was discontinued
Ganio et al (2002)	Complete cessation or a greater than 50% reduction in leakage episodes for liquid or solid stool during the test period and a rapid return to pre-PNE condition when stimulation was discontinued
Jarrett et al (2004b)	A 50% or greater improvement in either the total number of faecal incontinence episodes or the number of days affected by an incontinence episode
Matzel et al (2004a)	At least a 50% reduction in the number of incontinence episodes per week or a 50% reduction in the number of days with incontinence per week
Rasmussen et al (2004)	At least a 50% reduction in the number of incontinence episodes
Ripetti et al (2002)	At least 75% improvement in incontinence
Rosen et al (2001)	Participants whose continence status improved (no further details provided)
Uludag et al (2004)	At least a 50% reduction in the number of incontinence episodes per week or a 50% reduction in the number of days with incontinence per week

Table 16 summarises the number of participants undergoing PNE in each of the studies, the mean duration of PNE, the location of the permanent electrode and the number of participants who were subsequently eligible for permanent SNS based on the eligibility criteria outlined in Table 15. Table 16 also summarises the location that the permanent electrode was placed. The majority of participants (74.0–95.7% of participants) had the electrode placed at S3 (where reported). The number of participants undergoing PNE who were subsequently eligible for permanent SNS ranged from 19.0 per cent (Ripetti et al 2002) to 91.9 per cent (Matzel et al 2004a). The studies did not define particular subgroups or the characteristics of participants—such as the aetiology or severity of faecal incontinence—who would be likely to benefit from SNS during PNE and continue as a result to CTS. The majority of participants who were eligible for CTS continued to permanent SNS. For those who did not, the main reasons were refusal (Altomare et al 2004a, Ganio et al 2002) or waiting (Altomare et al 2004a, Uludag et al 2004) due to financial reasons or the requirement for re-evaluation. Only Jarrett et al (2004b) reported the mean time between PNE and permanent placement of the electrode for SNS – a median of two months (range 0–10 months).

Table 16 Number of participants undergoing PNE and the proportion of these participants eligible to continue to CTS

Study	PNE			Electrode placement n/N (%)	CTS	
	N	Duration	Eligible for CTS[a] n/N (%)		Yes n/N (%)	No n/N (%)
Altomare et al (2004a)	41	At least 14 days Range: 14–19 days	19/41 (46.3)	Not reported	16/19 (84.2)	Refused: 2/19 (10.5) Waiting: 1/19 (5.3)
Ganio et al (2001a)	23	Median: 10.7 Range: 7–30 days	5/23 (21.7)	S2: 2/23 (8.7) S3: 20/23 (87.0)	5/5 (100)	NA
Ganio et al (2002)	116	Mean 13 Range: 7–20 days	36/116 (31.0)	Not reported	31/36 (86.1)	Refused: 5/36 (13.9)
Jarrett et al (2004b)	59	Median: 14 Range: 7–42 days	46/59 (78.0)	S2: 1/46 (2.2) S3: 44/46 (95.7) S4: 1/46 (2.2)	46/46 (100)	NA
Matzel et al (2004a)	37	Mean: 19.4 SD: 3.2 days	34/37 (91.9)	S3: 22/34 (64.7) S4: 12/34 (35.3)	34/34 (100)	NA
Rasmussen et al (2004)	45	3 weeks	37/45 (82.2)	S2, S3 and S4 used with same frequency	37/37 (100)	NA
Ripetti et al (2002)	21	Mean: 15 Range: 14–16 days	4/21 (19.0)	S3: 16/21 (76.2) S4: 5/21 (23.8)	4/4 (100)	NA
Rosen et al (2001)	20	10 days	16/20 (80.0)	Not reported	16/16 (100)	NA
Uludag et al (2004)	75	3 weeks	Acute: 73/75 (97.3) Subchronic: 62/75 (82.7)	S3: 54/73 (74.0) S4: 19/73 (26.0)	50/62 (80.6)	Waiting: 12/62 (19.4)

Abbreviations: NA, not applicable; SD, standard deviation

[a] As specified in the studies, refer to Table 19

Table 17 summarises the faecal incontinence episodes experienced by participants before and after SNS. The proportion of participants in these included series who were continent at last follow-up ranged from 35.3 per cent (Matzel et al 2004a) to 100 per cent (Ganio et al 2001a). The participants enrolled in Ganio et al (2001a) who proceeded to CTS were required to have a complete cessation of incontinence to liquid or solid stool during PNE. The other studies required at least a 50 per cent improvement in incontinence during PNE, therefore 100 per cent effectiveness may be an overestimation as those participants most likely to succeed continued to CTS. The proportion of participants experiencing an improvement in incontinence ranged from 95.7 per cent (Jarrett et al 2004b) to 100 per cent (Rosen et al 2001).

The incontinence episodes were reported differently in each of the studies. Some reported the median and interquartile range, others the median and range and others the mean and range or standard deviation. The studies also varied in the number of episodes per time period, that is, some reported episodes of faecal incontinence, as per week, per two weeks or per 21 days.

Altomare et al (2004) reported a statistically significant reduction ($p<0.01$) in the median number of incontinence episodes per two weeks from 14 (interquartile range 11–14) at baseline to a median of zero at three months, one at six months, two at 12 months and one at 24 months.

Ganio et al (2002), while reporting incontinence episodes per two weeks, presented their data as the mean number and range of incontinence episodes. For participants continuing to CTS, they reported reductions in the mean number of faecal incontinence episodes per 14 days from 15 (range 2–22) at baseline to 3.2 (range 0–10) at three months ($p=0.02$), 2.9 (range 0–13) at six months and 0.3 (range 0–4) at 12 months. Ganio et al (2002) also reported a reduction in the mean number of episodes of incontinence to gas and soiling per 14 days from 41.6 (range 2–65) at baseline to 12.6 (range 0–19) at 12 months and a reduction in bowel movements from 28.1 (range 4–52) at baseline to 15.9 (range 11–18) at last follow-up (12 months).

Jarrett et al (2004b) reported a statistically significant decrease in faecal incontinence episodes per week from 7.5 (range 1–78) at baseline to 1.0 (range 0–39) at last follow-up ($p<0.001$). They also reported a statistically significant improvement in the ability of participants to defer defecation from a median of less than 1 minute (range 0–5 minutes) before SNS to 10 minutes (range 1 to more than 5 minutes, $p<0.001$).

Matzel et al (2004a) presented results as the mean number (standard deviation [SD]) of faecal incontinence episodes experienced per week. At baseline, the mean number of faecal incontinence episodes per week was reported to be 16.4 ± 19.3 (95% CI: 9.9, 22.8). A statistically significant decrease in incontinence episodes was reported at 3 months, 3.1 ± 5.5 (95% CI: 1.0, 5.2, $p<0.0001$) and at 24 months, 2.0 ± 3.3 (95% CI: 0.4, 3.5, $p<0.0001$). At the last follow-up at 36 months, the participants evaluated ($n=6$) showed a statistically significant decrease in faecal incontinence episodes per week to 1.8 ± 2.2 (95% CI: –0.5, 4.1, $p = 0.034$).

Rosen et al (2001) reported a reduction in the median number of faecal incontinence episodes of solid or liquid stool per 21 days. The median number of faecal incontinence episodes was reported to be 6 (range 3–15) at baseline and 2 (range 0–5) at last follow-up at a median of 15 months (range 3–26). The four participants continuing to permanent SNS who had idiopathic faecal incontinence had a median of 3.5 (range 3–6) incontinence episodes at baseline that decreased to 0 (range 0–2) at last follow-up. The 12 participants with faecal incontinence due to neurologic events who continued to permanent SNS had a median of 7 (range 4–15) incontinence episodes at baseline, which significantly decreased to 2 (range 0–5) at last follow-up ($p<0.01$).

Rosen et al (2001) also reported the time to defer defecation. At baseline, the time of retention causing an urge until definitive defecation was a median of 2 minutes (range 0–5) and increased to a median of 7.5 minutes (range 2–15) following SNS. The times to defer defecation in the four participants with idiopathic and the 12 participants with neurogenic faecal incontinence were 3.5 minutes (range 2–7) and 2 minutes (range 0–5) at baseline, respectively, and 10 minutes (range 2–15) and 7 minutes (range 2–15) at last follow-up, respectively. A statistically significant increase in the time to defer defecation was reported in participants with neurologic faecal incontinence ($p<0.01$).

Uludag et al (2004) reported that the median number of faecal incontinence episodes experienced per week by participants enrolled in the study, prior to and following PNE

were 7.5 and 0.67, respectively ($p<0.001$). After a median of 12 months of follow-up, Uludag et al (2004) reported that 48 of the 50 participants continuing to CTS sustained the benefits observed after PNE.

Table 17 Incontinence episodes prior to and following SNS

Study	Continent participants at last follow-up n/N (%)	Incontinence episodes			Time to defer defecation (minutes)	
		Baseline	PNE	CTS	Baseline	CTS
Altomare et al (2004a)	Not reported	Median: 14 per 2 weeks IQR: 11–14	Not reported	Median per 2 weeks at: 3 months: 0[a] 6 months: 1[a] 12 months: 2[a] 24 months: 1[a]	Not reported	Not reported
Ganio et al (2001a)	5/5 (100)	Not reported	Not reported	Not reported	Not reported	Not reported
Ganio et al (2002)	Not reported	Incontinence to solid or liquid stool				
		Mean: 11 Range: 4–28 (For all) Mean: 15 per 14 days Range: 2–22 (for the 31 continuing to CTS)	Mean: 3 Range: 2–18 (For all)	Per 14 days at: 3 months: Mean: 3.2[b] Range: 0-10 6 months: Mean: 2.9 Range: 0–13 12 months: Mean: 0.3 Range: 0–4	Not reported	Not reported
		Incontinence to gas and soiling				
		Mean: 41.6 Range: 2–65	Not reported	At 3 months: Mean: 4.2 Range: 0–13 At 6 months: Mean: 16.8 Range: 0–23 At 12 months: Mean: 12.6 Range: 0–19	Not reported	Not reported
		Bowel movements				
		Mean: 28.1 Range: 4–52	Not reported	At 12 months: Mean: 15.9 Range: 11–18	Not reported	Not reported
Jarrett et al (2004b)	19/46 (41.3) Improved: 25/46 (54.3) Total improved: 44/46 (95.7)	Median: 7.5 per week Range: 1–78	Not reported	Median (Range) per week 1 (0-39)[c]	Median: 1 Range:0–5	Median: 10 Range:1–>15[c]

Table 17 (cont'd) Incontinence episodes prior to and following SNS

Study	Continent participants at last follow-up n/N (%)	Incontinence episodes			Time to defer defecation (minutes)	
		Baseline	PNE	CTS	Baseline	CTS
Matzel et al (2004a)	12/34 (35.3)	Mean: 16.4 per week SD: 19.3 95% CI: 9.9, 22.8	Mean: 22 per week SD: 2.9	At 3 months: Mean:3.1 SD: 5.5 95% CI: 1.0, 5.2[d] At 24 months: Mean: 2.0 SD: 3.3 95% CI: 0.4, 3.5[d] At 36 months[e]: Mean: 1.8 SD: 2.2 95% CI: –0.5, 4.1[f]	Not reported	Not reported
Rasmussen et al (2004)	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported
Ripetti et al (2002)	Not reported	Median: 12 Range: 9–17[g]	Not reported	Not reported	Not reported	Not reported
Rosen et al (2001)	Improved 16/16 (100)	Per 21 days: All: Median: 6 Range: 3–15 Idiopathic: Median: 3.5 Range: 3–6 Neurologic: Median: 7 Range: 4–15	Not reported	Per 21 days: All: Median: 2 Range: 0–5 Idiopathic: Median: 0 Range: 0–2 Neurologic: Median: 2 Range: 0-5[a]	All: Median: 2 Range: 0–5 Idiopathic: Median: 3.5 2–7 Neurologic: Median: 2 Range: 0–5	All: Median: 7.5 Range: 2–15 Idiopathic: Median: 10 Range: 2–15 Neurologic: Median: 7 Range: 2–15[a]
Uludag et al (2004)	48/50 (96.0) maintained improved continence at 12 months	Median per week: 7.5	Median per week: 0.67 [c]	Symptomatic response reproduced after implantation of the permanent electrode and IPG	Not reported	Not reported

Abbreviations: CI, confidence interval; IPG, implantable pulse generator; IQR, interquartile range; SD, standard deviation
[a] p<0.01
[b] p=0.02
[c] p<0.001
[d] p<0.0001
[e] In participants evaluated
[f] p=0.0034
[g] In the four participants continuing to CTS

Matzel et al (2004a) also reported on the mean (standard deviation) number of urgency, passive and overall incontinence episodes, number of days with incontinence, days with stain and days with pads per week at baseline, during PNE, and at 3, 6, 12, 24 and 36 months of follow-up during CTS. These results are summarised in Table 18. A statistically significant difference compared with baseline values was observed for all outcome measures during PNE and at each follow-up visit with the exception of the mean number of days with pads at 36 months, for which p was 0.1747. Ganio et al (2002) also reported an increase in the number of pads used per day in the seven participants evaluated at 12 months of follow-up, despite there being a reduction in the number of incontinence episodes.

Table 18 **Mean (SD) number of incontinence episodes (urgency and passive), days of incontinence, days with stain and days with pads per week as reported in Matzel et al (2004a)**

Outcome measures	Baseline n=37	PNE[a] n=36	CTS (months)				
			3 months n=30	6 months n=30	12 months n=30	24 months n=21	36 months n=6
	Mean (Standard deviation)						
Incontinence episodes:	16.4[b] (19.3)	2.2 (1.9)	1.2 (1.9)	1.6 (2.2)	3.1 (5.5)	2.0 (3.3)	1.8 (2.2) p=0.0034
. Urgency	6.7 (8.9)	1.1 (1.9)	0.5 (0.9)	0.8 (1.4)	0.9 (1.8)	1.1 (2.9)	0.3 (0.6) p=0.0077
. Passive	9.7 (15.2)	1.1 (1.6)	0.8 (1.5)	0.8 (1.3)	2.2 (4.6)	0.8 (1.8)	1.5 (2.1) p=0.0017
Days with incontinence	4.5 (1.8)	1.2 (1.5)	0.8 (1.1)	1.1 (1.4)	1.4 (2.0)	1.2 (1.8) p=0.0004	1.3 (1.7) p=0.0016
Days with stain	5.6 (1.6)	1.6 (1.7)	2.0 (2.3)	2.3 (2.7)	2.4 (2.6)	2.5 (2.6) p=0.0004	2.2 (2.8) p=0.0212
Days with pads	5.9 (2.3)	3.7 (3.2)	2.9 (3.2)	3.3 (3.3)	3.7 (3.4)	3.4 (3.5) p=0.0002	4.7 (3.6) p=0.1747

[a] Except where indicated, p<0.0001
[b] All data were taken from Matzel et al (2004a)

Four studies (Altomare et al 2004a, Jarrett et al 2004b, Rasmussen et al 2004, Ripetti et al 2002) reported the results of incontinence tools used in the studies to determine the participants' perception of improvement in their incontinence status. Altomare et al (2004a) used the American Medical Systems (AMS) Score and the Continence Grading System (CGS) and reported that a significant improvement in incontinence status was observed at 3, 6, 12 and 24 months of follow-up compared with baseline values. Jarrett et al (2004b) and Rasmussen et al (2004) reported a significant difference in incontinence status between baseline and last follow-up in participants enrolled in their study using the Cleveland Clinic Incontinence Score and Rasmussen et al (2004) also showed a significant improvement in incontinence status between baseline and last follow-up in their study participants as measured by Wexner's incontinence score. Conversely, Ripetti et al (2002) found no significant differences in incontinence status of participants between baseline and last follow-up using either Wexner's or William's incontinence scores. These results are summarised in Table 19 below.

Table 19 Incontinence scores prior to and following SNS

Study	Incontinence Tool	N	Baseline	PNE	CTS	p-value
Altomare et al (2004a)	American Medical Systems (AMS) Score	14 14 12 5	Median: 101 IQR: 92–107 N=14	NR	Median at: 3 months: 46 6 months: 46 12 months: 65 24 months: 67	 p<0.01 p<0.01 p<0.01 p<0.01
	Continence Grading System (CGS)	14 14 8 5	Median: 15 IQR: 12.5–17.5 N=14	NR	Median at: 3 months: 4.0 6 months: 5.5 12 months: 6.0 24 months: 2.0	 p<0.01 p<0.01 p<0.01 p<0.01
Jarrett et al (2004b)	Cleveland Clinic Incontinence Score	27	Median: 14 Range: 5–20	NR	Median: 6 Range: 1–12	p<0.001
Rasmussen et al (2004)	Wexner's incontinence score	NR	Median: 16	NR	Median: 6	p<0.0001
Ripetti et al (2002)	William's incontinence score	21	Median: 4.1	Median: 3.3	NR	NS
	Wexner's incontinence score		Median: 12.2	Median: 9.8	NR	NS

Abbreviations: IQR, interquartile range; NR, not reported; NS, not significant.

Table 20 summarises the quality of life assessment prior to and following sacral nerve evaluation, using a variety of quality of life measures. Four studies evaluated improvement in quality of life from baseline to last follow-up using the short form 36 (SF-36) questionnaire (Ganio et al 2002, Jarrett et al 2004b, Matzel et al 2004a, Ripetti et al 2002). A significant improvement was reported in five categories of the SF-36 questionnaire for participants enrolled in Jarrett et al (2004b) – social function, role-emotional, mental health, vitality and general health, in three categories for participants enrolled in Matzel et al (2004a) – role-physical, mental health and mental component summary and in three categories for participants enrolled in Ripetti et al (2002) – emotional, social and physical functioning.

Ganio et al (2002) reported the results of the SF-36 questionnaire of 18 participants at baseline. The results showed a decreased mean baseline value compared to the Italian general population for both mental and physical health status. At three months of follow-up, the improvement in incontinence experienced by participants undergoing SNS had a positive impact on the health state, in particular, a reduction in physical limitations or disabilities. At six months of follow-up, the positive effects were more evident. The improvement in quality of life was not sustained at 12 months follow-up, as assessed in seven participants. An overall analysis showed a significant improvement in the physical ($p<0.05$) and mental ($p<0.05$) health of participants after SNS (Ganio et al 2002).

Three studies assessed the improvement in quality of life from baseline to last follow-up using the American Society of Colon and Rectal Surgeons (ASCRS) Fecal Incontinence Quality of Life tool (Jarrett et al 2004b, Matzel et al 2004a, Rosen et al 2001). All three studies reported significant differences in the quality of life of participants in all four categories of lifestyle, coping/behaviour, depression/self perception and embarrassment. Jarrett et al (2004b) also reported the results of the ASCRS questionnaire for participants that were continent at last follow-up and those with improved continence. Again, significant differences in all four categories were reported for both continent and improved participants.

Altomare et al (2004a) assessed the improvement in participants' quality of life using the Faecal Incontinence Quality of Life questionnaire. A significant improvement in all four categories of the questionnaire – lifestyle, coping behaviour, depression and self-perception and embarrassment was observed between baseline and last follow-up.

Table 20 Quality of life prior to and following SNS

Study	Quality of Life Tool Categories	N	Results			
			Normal	Baseline	CTS	p-value
Altomare et al (2004a)	Faecal Incontinence Quality of Life (FIQL)	9	NR	Median: 1.59 IQR: 1.4–1.9	Median: 3.3 IQR: 2.72–3.58 at 12 months	p<0.01
	. Lifestyle			1.50	3.50	p<0.008
	. Coping behaviour			1.33	3.11	p<0.007
	. Depression and self-perception			2.28	3.42	p<0.008
	. Embarrassment			1.33	2.66	p<0.008
Jarrett et al (2004b)	Short form 36 (SF-36)	46	UK Normal N = 213		Last follow-up[a]	
			Mean score	Mean score	Mean score	
	. Physical function		83	62	65	0.703
	. Social function		83	53	67	0.013
	. Role – physical		78	50	60	0.147
	. Role – emotional		76	49	64	0.034
	. Mental health		72	54	64	0.008
	. Vitality		57	37	46	0.009
	. Bodily pain		76	53	55	0.639
	. General health		72	49	55	0.024
	American Society of Colon and Rectal Surgeons (ASCRS) Fecal Incontinence Quality of Life	36	NR	NR	NR	
	. Lifestyle					<0.001
	. Coping behaviour					<0.001
	. Depression and self perception					<0.001
	. Embarrassment					<0.001
	Continent participants	19	NR	NR	NR	
	ASCRS Fecal Incontinence Quality of Life					
	. Lifestyle					0.004
	. Coping behaviour					0.003
	. Depression and self perception					0.010
	. Embarrassment					0.003
	Improved participants	25	NR	NR	NR	
	ASCRS Fecal Incontinence Quality of Life					
	. Lifestyle					<0.001
	. Coping behaviour					<0.001
	. Depression and self perception					<0.001
	. Embarrassment					<0.001

Table 20 (cont'd) Quality of life prior to and following SNS

Study	Quality of Life Tool Categories	N	Results			
			Normal	Baseline	CTS	P-value
Matzel et al (2004a)	American Society of Colon and Rectal Surgeons (ASCRS) Fecal Incontinence Quality of Life	NR	NR	N = 37 Mean (SD)	At 12 months N = 29 Mean (SD)	
	. Lifestyle			2.7 (0.9)	3.5 (0.6)	<0.0001
	. Coping behaviour			1.7 (0.6)	2.8 (0.8)	<0.0001
	. Depression			2.8 (1.0)	4.0 (0.9)	<0.0001
	. Embarrassment			1.8 (0.9)	3.0 (0.9)	<0.0001
	Short form 36 (SF-36)	NR	NR	N = 37 Mean (SD)	At 12 months N = 29 Mean (SD)	
	. Physical functioning			64.5 (28.6)	71.9 (25.2)	
	. Social functioning			61.1 (33.6)	81.9 (27.5)	0.0002
	. Role physical			44.6 (44.5)	54.3 (43.3)	
	. Role emotional			56.8 (43.6)	77.9 (37.9)	
	. Mental health			62.6 (24.3)	70.1 (22.8)	0.0007
	. Vitality			48.8 (29.0)	57.5 (28.4)	
	. Bodily pain			65.4 (30.4)	55.8 (30.1)	
	. General health			54.6 (29.0)	62.8 (30.8)	
	. Physical component summary			41.8 (12.3)	41.6 (12.0)	
	. Mental component summary			43.3 (14.3)	52.1 (12.8)	0.0006
Ripetti et al (2002)	Short form 36 (SF-36)	4	NR	NR	NR	
	. Emotional functioning					<0.01
	. Social functioning					<0.05
	. Physical functioning					<0.05
Rosen et al (2001)	American Society of Colon and Rectal Surgeons (ASCRS) Fecal Incontinence Quality of Life	NR	NR	N=20 Median (Range)	N=12 at 6 months Median (Range)	
	. Lifestyle			2.1 (1.0–2.8)	3.9 (2.7–4.4)	<0.01
	. Coping behaviour			2.0 (1.3–2.5)	3.7 (3.0–4.1)	<0.01
	. Depression			2.6 (1.7–3.1)	3.7 (3.2–4.3)	<0.01
	. Embarrassment			1.7 (1.0–2.2)	3.8 (3.0–4.6)	<0.01

Abbreviations: NR, not reported.

[a] Median follow-up 12 months, range 1–72 months

Double blind crossover study

The crossover study reported by Vaizey et al (2000) included two women, aged 61 and 65 years, of whom one had faecal incontinence due to scleroderma and the other had idiopathic faecal incontinence. The participant with faecal incontinence due to scleroderma had a three year history of passive faecal leakage and the participant with idiopathic faecal incontinence had experienced passive faecal leakage for 2.5 years prior to implantation of the device. The two participants had received their permanent implants nine months prior to the study and each participant had their implant turned on for two weeks and turned off for two weeks or *vice versa*. The main investigator and both participants were blinded as to whether their stimulators were turned on or off (the implants were set at subthreshold levels in order to keep participants blinded to their status). Faecal incontinence episodes were reported to be improved from 2 and 10

episodes per week with the stimulator turned off to 1 and 0 with the stimulator turned on, for the two women, respectively. In addition to demonstrating the effectiveness of SNS in these participants, the study also demonstrated that the effect is reversible following nine months of stimulation.

Discussion of case series and a double blind crossover study

The results of the effectiveness of SNS for the treatment of faecal incontinence were assessed from nine case series and one double blind crossover study. Whilst most of the studies reported an improvement in incontinence episodes per week and in quality of life using various measures, the following issues highlight the limitations of the data presented:

- Most data are derived from case series. In the absence of a comparator arm, it cannot be ruled out that the improvements observed in the participants enrolled in the studies following SNS occurred spontaneously. However, as most of the studies reported improvements in the number of incontinence episodes over a given time frame and significant differences were measured for various categories of quality of life questionnaires, this appears to be unlikely. The results of the two participants in the double blind crossover study also suggest that the improvements resulted from SNS.

- The results of the studies presented in this assessment may be biased for the following reasons:

  - None of the studies included in this review stated that participants were enrolled consecutively. Two studies in fact stated that participants were selected from a larger group of patients or due to the severity of their faecal incontinence and subsequent improvement in quality of life.

  - There may have been selected reporting. Two of the nine case series explicitly stated prospective data collection, one explicitly stated retrospective data collection and the remaining studies did not specify how the data were collected.

  - Study participants withdrew and were lost to follow-up. The extent and reasons for withdrawal or losses to follow-up were poorly reported.

  - All but two of the nine case series specified the baseline number of incontinence episodes experienced by participants per given time frame. There was no indication, however, of whether the participants enrolled in each of the series represented a spectrum of severity of faecal incontinence.

- Participants enrolled in each of the series had faecal incontinence due to different aetiologies, however the data were not presented in a way as to allow for subgroup analyses to determine if one subgroup was less or more likely to benefit from SNS, or if any differences existed between any groups.

- Differences in the reporting of faecal incontinence episodes per a given time frame between the included studies does not allow for an overall estimate of the effectiveness of SNS.

- The length of follow-up in these studies was limited to 72 months. The long-term effectiveness of SNS has not been established.

It is important however to emphasise the improvements in quality of life reported in each of the series using various quality of life tools. Byrne et al (2002) reported the assessment of quality of life in the treatment of patients with neuropathic faecal incontinence using the Direct Questioning of Objectives quality-of-life questionnaire. The most frequently stated objective of treatment for faecal incontinence was the quality of life category concerned with the ability to leave the home, to socialise outside of the home, to go shopping and not to have to worry about the location of the nearest toilet whilst outside of the home (Byrne et al 2002). Fewer patients nominated their treatment objective as a quality of life category that was concerned with the physical act of soiling (Byrne et al 2002). It is therefore important to emphasise that three of the four studies assessing the effectiveness of SNS and utilising the SF-36 quality of life questionnaire showed statistically significantly increased quality of life scores for 'social functioning' compared with baseline values - a quality of life category that was deemed as one of the prime objectives in treatment of faecal incontinence. Similarly, the use of disease-specific quality of life questionnaires, such as the ASCRS Fecal Incontinence Quality of Life tool, showed a consistent, significant improvement in all four categories of lifestyle, coping/behaviour, depression/self perception and embarrassment, where the category of lifestyle encompasses one of the prime objectives nominated by patients in the treatment of faecal incontinence.

Critical appraisal of published systematic reviews and health technology assessment reports

Two systematic reviews (Jarrett et al 2004a, Matzel 2004b), a protocol for a Cochrane systematic review (Mowatt et al 2003) and two health technology assessment reports (ASERNIP-S 2003, NICE 2004) reviewing the effectiveness of SNS for the treatment of faecal incontinence were identified. These reviews contain a subset of the individual studies described above. The results of the validity assessment of the reviews and the results of the effectiveness of sacral nerve stimulation for the treatment of faecal incontinence as determined by the reviews are summarised below.

Validity of systematic reviews and health technology assessment reports

The validity assessment of the identified systematic reviews and health technology assessment reports assessing the effectiveness of SNS for the treatment of faecal incontinence is summarised in Table 21. The validity of the two systematic reviews (Jarrett et al 2004b, Matzel et al 2004b) and the two health technology assessment reports only (ASERNIP-S 2003, NICE 2004) will be discussed in Tables 21 and 22 and pages 43 to 49 of the Report as the results of the Mowatt et al (2003) Cochrane protocol are yet to be published

All systematic reviews and health technology assessment reports had a focussed question that was generally to assess the safety and effectiveness of SNS for faecal incontinence. The exception to this was the study of Jarrett et al (2004a) that also assessed the safety and effectiveness of the procedure for the treatment of constipation. Inclusion and exclusion criteria for study participants and studies (where reported) were also similar between the systematic reviews and health technology assessment reports and were appropriate to the scope of this review.

Neither of the systematic reviews reported the search strategy used, however Jarrett et al (2004b) explicitly reported that multiple databases were searched, whereas the search used in Matzel et al (2004b) was limited to Medline. ASERNIP-S (2003) did not report the search strategy used and the NICE (2004) review explicitly reported a comprehensive search strategy. Both health technology assessment reports searched multiple databases. The validity of the included studies was assessed in three of the four included reviews (ASERNIP-S 2003, Jarrett et al 2004a, NICE 2004).

Table 21 Validity of systematic reviews and health technology assessment reports

Validity component	Study				
	Jarrett et al (2004a)	**Matzel et al (2004b)**	**ASERNIP-S (2003) Rapid Review**	**NICE (2004)**	**Mowatt et al (2003) [Protocol]**
Focused question	Assess the efficacy and safety of SNS for faecal incontinence and constipation	An overview of SNS in the treatment of faecal incontinence	SNS for treatment of faecal incontinence	Efficacy and safety of SNS for faecal incontinence	Assess the effects of SNS using implanted electrodes for the treatment of faecal incontinence in adults
Inclusion and exclusion criteria for participants	Inclusion[a]: . Signed informed consent . Age 18–75 years . One or more episodes of faecal incontinence per week . Intact EAS with or without previous repair . Failed conservative therapy . Able to fill in questionnaires and attend clinics Exclusion: . Congenital anal malformations . Rectal surgery within previous 12 months (within 24 months for cancer) . Present external rectal prolapse, chronic diarrhoea unmanageable by diet or drugs, chronic bowel diseases, altered bowel habit associated with abdominal pain . Stoma present . Neurological diseases . Bleeding complications . Pregnancy anatomical limitations preventing placement of electrode . Skin disease risking infection . Psychiatric or physical inability to comply with study protocol . Participants for whom information was not available in a language understood by the participant	Inclusion: . Patients with faecal incontinence as a result of reduced striated muscle function from various causes with concomitant urinary incontinence and in a spectrum of neurogenic causes Exclusion[b]: . Pathologic conditions of the sacrum . Skin diseases at area of implantation . Sphincter damage amenable to direct repair requiring a sphincter substitute . Trauma sequelae with micturition disorders or low bladder capacity . Pregnancy . Bleeding complications . Psychological instability . Low mental capacity . Presence of cardiac pacemaker or implantable defibrillator	Not reported	Inclusion: . Adults with faecal incontinence . If the evidence allowed, subgroup analysis was to be undertaken in the following groups: . patients with faecal urgency . patients with structural versus functional defects of the anal sphincter . patients with spinal injury . patients with central neurological disease Exclusion: . Not explicitly stated	Inclusion: Adults with faecal incontinence If the evidence allows, subgroup analysis to be undertaken in the following groups: . patients with faecal urgency . patients with structural defects of the anal sphincter . patients with partial spinal cord injury . patients with central neurological disease Exclusion: . Not explicitly stated

Table 21 (cont'd) Validity of systematic reviews and health technology assessment reports

Validity component	Study				
	Jarrett et al (2004a)	Matzel et al (2004b)	ASERNIP-S (2003) Rapid Review	NICE (2004)	Mowatt et al (2003) [Protocol]
Inclusion and exclusion criteria for studies	Inclusion: . Systematic reviews, RCTs, comparative observational studies, population-based registry studies, case series, case reports and narrative reviews Exclusion: . Non-English language papers (but these were noted). . Studies reporting solely on the PNE phase, except for those on idiopathic constipation	Inclusion: . All articles on SNS for faecal incontinence that were covered on Medline were reviewed. . With multiple articles from an institution, the most recent reports with the longest follow-up and largest cohort of participants were selected, unless information from earlier reports was relevant Exclusion: . Multiple articles from an institution for which longer-term results had been published	Not reported	Inclusion: . Systematic reviews, RCTs, controlled clinical trials, comparative observational studies, population-based registry studies, case series, case reports and narrative reviews Exclusion: . Not reported	Inclusion: . Randomised or quasi randomised trials Exclusion: . Not reported
Explicit comprehensive search strategy	Search strategy not reported Implies that greater more than one database was searched, but databases not reported Reference list of all included studies scanned for other potentially eligible studies	Search strategy not reported Search limited to Medline	Search strategy not reported Multiple databases searched	Comprehensive search strategy and multiple databases searched	Refers to the comprehensive Cochrane Incontinence Group search strategy Multiple databases searched and reported The reference lists of the included studies scanned for other potentially eligible studies
Assessed validity of included studies	Yes	No	Yes	Yes	Yes

[a] Inclusion criteria of participants for most of the included studies
[b] Contraindications

Results from the systematic reviews and health technology assessment reports

The effectiveness results for SNS for the treatment of faecal incontinence reported in the identified systematic reviews (Jarrett et al 2004a, Matzel et al 2004b) and health technology assessment reports (ASERNIP-S 2003, NICE 2004) are slightly different due to differences in the primary studies included in each review. The primary studies included in the current and each of the identified published systematic review and health technology assessment reports are listed in Table 22.

Table 22 Studies included in the systematic reviews and health technology assessment reports

Current review	Jarrett et al (2004a)	Matzel et al (2004b)	ASERNIP-S (2003) Rapid Review	NICE (2004)	Mowatt et al (2003)
Alltomare et al (2004a) Ganio et al (2001a) Ganio et al (2002) Jarrett et al (2004b) Matzel et al (2004a) Rasmussen et al (2004) Ripetti et al (2002) Rosen et al (2001) Uludag et al (2004) Vaizey et al (2000)[a]	Ganio et al (2002) Jarrett et al (2004b) Leroi et al (2001) Matzel et al (2003) Rosen et al (2001) Uludag et al (2002) Vaizey et al (2000)[a]	Altomare et al (2004b) Ganio et al (2001a) Ganio et al (2001b) Kenefick et al (2002a) Leroi et al (2001) Malouf et al (2000b) Matzel et al (2001) Matzel et al (2003) Matzel et al (2004a) Rasmussen & Christiansen (2002) Ripetti et al (2002) Rosen et al (2001) Uludag et al (2002)	Ganio et al (2002) Kenefick et al (2002a) Matzel et al (2001) Rosen et al (2001) Vaizey et al (2000)[a]	Primary studies[b] Ganio et al (2002) Jarrett et al (2004b) (unpublished at time of inclusion in review) Leroi et al (2001) Matzel et al (2003) Matzel et al (2004a) (unpublished at time of inclusion in review – MDT-301 2003) Rosen et al (2001) Uludag et al (2002) Vaizey et al (2000)[a]	NA – protocol for systematic review

Abbreviations NA, not applicable
[a] Crossover study of 2 participants
[b] Related references also reported

The results of the effectiveness as derived from the published systematic reviews and health technology assessment reports are summarised. Fifty-six per cent of participants (149/266; NICE 2004) who were eligible for, and undertook, PNE went on to receive permanent implantation of the SNS device (range 26.7–100 per cent, Jarrett et al 2004a). The studies did not define particular subgroups or characteristics of participants—for example the aetiology or severity of faecal incontinence— who were likely to benefit from SNS during PNE and subsequently continue to CTS.

Following permanent device implantation, 41–75 per cent of participants achieved complete faecal continence and 75–100 per cent of participants achieved at least a 50 per cent improvement in the number of faecal incontinence episodes per week (Jarrett et al 2004a, Matzel et al 2004b, NICE 2004). Most studies reported an improvement in the

ability to defer defecation, and in studies where the Cleveland Clinic Incontinence Score was used, all showed statistically significant improvements (Jarrett et al 2004a, Matzel et al 2004b, NICE 2004). The MDT-301 study (Matzel et al 2004a) also reported a significant decrease in faecal incontinence episodes and an improvement in the ability to defer defecation (NICE 2004). The crossover study (Vaizey et al 2000) reported an improvement in the number of faecal episodes per week from 2 and 10 with the device off to 1 and 0 when the device was on, the study also demonstrated a reversible benefit at nine months (NICE 2004, Jarrett et al 2004a). Ganio et al (2002) reported increased usage of incontinence pads per day, but no explanation for the increase is given in the publication (NICE 2004).

Quality of life instruments used in the studies included the ASCRS form and the Short Form-36 (SF-36) Health Survey. In the five studies using the ASCRS, all reported improvements in all categories, with three studies reaching statistical significance. In the two studies using SF-36, all categories of the survey remained unchanged or improved. One study showed statistically significant improvements in general health, vitality, social functioning, role-emotional and mental health (Jarrett et al 2004a, NICE 2004). The MDT-301 study (Matzel et al 2004a) also reported significant improvement in social function and mental health (NICE 2004).

The ASERNIP-S (2003) review found that good results were achieved with SNS when the incontinence was due to a functional deficit and that the study participants perceived an improved quality of life.

Discussion of systematic reviews and health technology assessment reports

The studies included in the systematic review and health technology assessment reports have shown that SNS is effective in reducing the number of faecal incontinence episodes per week, decreasing urgency to defaecate and improving quality of life. Participants included in the primary studies had faecal incontinence due to a variety of conditions, however the manner in which the data were reported in each of the studies does not allow comparison between patient groups.

The identified limitations include:

- Data are from case series, so the results may reflect a spontaneous improvement or placebo effect. However, the results of the crossover study (Vaizey et al 2000) and the magnitude of improvements observed make this unlikely.
- Possible bias due to:
  - selective reporting – two of the six studies reported prospective data collection (Jarrett et al 2004a, NICE 2004)
  - selection of participants – two of the six studies explicitly reported consecutive enrolment of participants (Jarrett et al 2004a, NICE 2004)
  - withdrawals and losses to follow-up – one study had significant losses to follow-up (Jarrett et al 2004a, NICE 2004).
- Too few participants studied to observe rare complications or adverse events (Jarrett et al 2004a, NICE 2004).

- The units of measure by which faecal incontinence episodes were reported were not standardised across studies. Some studies reported mean and standard deviation and others reported median and range (Jarrett et al 2004a, NICE 2004). This needs to be considered when analysing and interpreting results.

- Changes to the methods used for device implantation during PNE may reduce the incidence of lead dislodgement. This requires further long-term follow-up (Jarrett et al 2004a, NICE 2004).

The maximum length of follow-up was 99 months. There is a lack of long-term evidence for the safety and efficacy of SNS (ASERNIP-S 2003, Jarrett et al 2004a, NICE 2004).

The guidance issued in November 2004 as a result of the NICE (2004) health technology assessment was as follows:

> "Current evidence on the safety and efficacy of SNS for faecal incontinence appears adequate to support the use of this procedure, provided that the normal arrangements are in place for consent, audit and clinical governance".
>
> "The procedure should only be performed in specialist units by clinicians with a particular interest in the assessment and treatment of faecal incontinence".

Expert opinion

As the procedure will be performed by appropriately trained professionals in a tertiary care setting and an individual's eligibility for the procedure would be assessed following appropriate initial investigations, this will further limit the number of patients that will undergo sacral nerve stimulation. It is anticipated that approximately one to two tertiary centres per capital city in Australia will perform the procedure. Approximately 100 individuals nationally may be considered for peripheral nerve evaluation annually.

Summary of the effectiveness of sacral nerve stimulation for the treatment of faecal incontinence

The results of the effectiveness of sacral nerve stimulation for the treatment of faecal incontinence were similar between the current review and those reported in the identified systematic reviews and health technology assessment reports, despite differences in the primary studies included in each of the reviews. Sacral nerve stimulation appears to be effective in reducing the number of faecal incontinence episodes per week, decreasing urgency to defecate and improving quality of life. However, the effectiveness of sacral nerve stimulation for the treatment of faecal incontinence is difficult to determine due to:

- small number of individuals analysed.

- limited follow-up of the included studies (up to 99 months).

Stoma

A systematic search of the literature identified a number of articles that assessed the effectiveness of stoma formation for the treatment of faecal incontinence, however, none of these articles met the *a priori* inclusion criteria. Many of the identified studies reported the combined results of children and adults and those series that included only adults

enrolled fewer than 20 participants. These studies did not meet inclusion criteria due to fewer than 20 participants with faecal incontinence being enrolled. Information regarding the effectiveness of stoma formation (including ileal neoappendicostomy for antegrade colonic irrigation) for the treatment of faecal incontinence as extracted from these excluded studies is summarised in Appendix F.

What are the economic considerations?

The nominated comparators for SNS for the treatment of faecal incontinence are:

- continued use of conservative, non-surgical treatments
- stoma formation.

The Application acknowledges deficiencies in the data for economic evaluation of SNS versus stoma formation (Section 11), but provides a cost-analysis of the procedure based upon an expert statement. The Applicant estimates a cost per year/patient "sustained response" of $3,250 over the expected life of the generator batteries.

However, costs considered by the Applicant appear to represent a financial analysis of costs to the Commonwealth Government and are thus incomplete as an economic analysis. Notably, they include medical fees, but not all inpatient costs. Nor does the Applicant consider the cost-offsets (savings) from substituting another therapy for conservative management (or stoma formation). Furthermore, it is not evident from the description of methods that all resource consequences of expected adverse events have been costed.

A review of the literature failed to identify any studies of the relative cost-effectiveness of SNS compared to conservative, non-surgical treatment or stoma formation. This is not surprising as the data necessary for economic evaluation are difficult to collect, given the variation in aetiologies of faecal incontinence, variation in 'standard' treatment regimens and procedures and small patient numbers.

The economic evaluation for this assessment report addresses these issues from a societal perspective to the extent possible given the available data. To assess the cost-effectiveness of SNS versus conservative management, this report extends the Applicant's analysis of costs and relates these to an evidence-based estimate of surrogate, or intermediate, health outcomes. It has not been possible to prepare an economic evaluation of SNS versus stoma formation.

Cost-effectiveness of sacral nerve stimulation versus conservative, non-surgical treatment

The logical time frame for an evaluation of SNS compared to conservative management is the average battery-life of the implantable device, after which the device is replaced. The Applicant estimated this to be seven years.

TreeAge Pro (2005) software was used to develop the model for this evaluation (Figure 3). The values contained in the model are based as far as possible on the case series results reported in the NICE (2004) review. This systematic review of SNS specifically

for faecal incontinence was considered to be the most reliable source of data for evaluation.

Health care resource costs of sacral nerve stimulation versus conservative, non-surgical treatment

Costs of conservative, non-surgical treatment

Conservative, non-surgical treatments for faecal incontinence have been described herein as comprising dietary modifications, medications to change stool consistency, pelvic floor physiotherapy, biofeedback and 'toileting' strategies. In a review of dynamic graciloplasty for the treatment of faecal incontinence, the Royal Australasian College of Surgeons similarly described conservative treatment of faecal incontinence as comprising a high-fibre diet or bulk-forming agents to improve stool volume and consistency or the use of cleansing enemas, and biofeedback to increase the voluntary contraction amplitude of the EAS and the pelvic floor, recto-anal sensitivity and the coordination of the IAS and EAS responses to rectal distension (ASERNIP-S 2001). Pharmacotherapy is also routinely offered (expert advice).

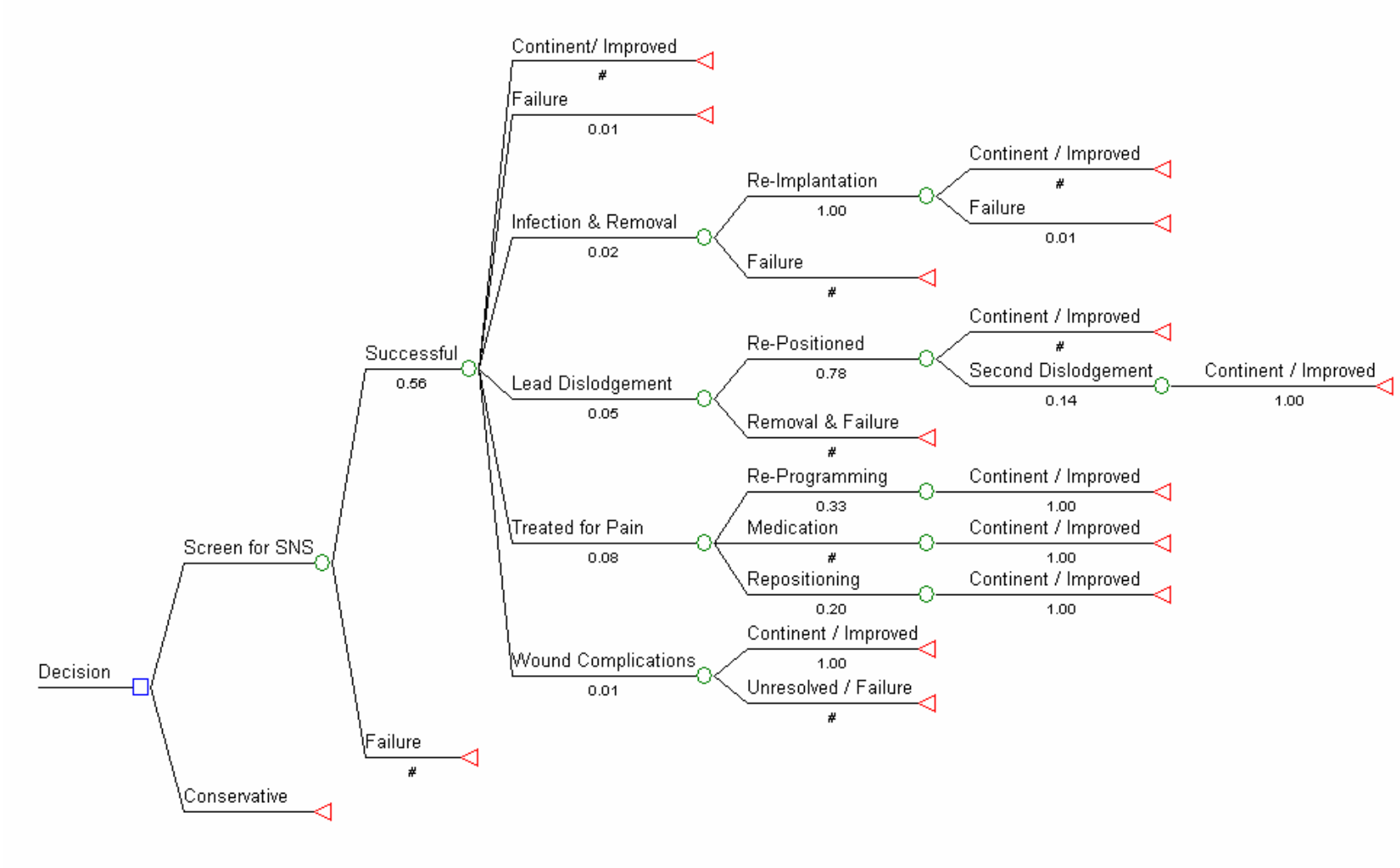

Figure 3 Structure of cost-effectiveness model: SNS versus conservative management

Conservative management therefore comprises lifestyle changes combined with a selection of health care for symptom relief. Unfortunately, the average use of this health care for the treatment of faecal incontinence could not be quantified from the literature. Although two studies of the cost of treating faecal incontinence were identified, they reported average costs for all patients, including the cost of surgeries (Borrie & Davidson 1992; Mellgren et al 1999). Results for non-surgical therapies were not reported separately.

However, to the extent that therapy entails lifestyle change, it may be inferred that the impacts on resources are negligible. This observation does not preclude patients perceiving significant reductions in their quality of life from imposed changes to lifestyle, but such impacts would be captured in the denominator (health outcomes) of the incremental cost-effectiveness ratio (ICER), rather than the numerator (costs).

At baseline, individuals eligible for SNS are defined as failing conservative management. Therefore, it was assumed for this evaluation that at the very least:

- continued use of pads is required
- pharmacotherapy with loperamide hydrochloride is prescribed for symptom relief (Table 25).

The Applicant's estimate of the costs of sacral nerve stimulation

The Application provides the cost of devices and related equipment necessary for SNS and suggests appropriate item numbers from the existing Medicare Benefits Schedule. The capital costs are given as:

PNE kit	$389.00
Test stimulation lead	$130.00
External stimulation power source	$550.00
Total device costs, PNE stage	$1,069.00

An economic evaluation requires estimation of the average cost per patient which in turn requires attribution of the expense of the re-usable capital item—the external stimulation power source—across the number of patients screened for SNS over the life of that item. The Applicant states that experience with SNS for chronic back pain shows the expected life of the external stimulation power source to be seven years, and assumes that 11 individuals will be screened. The basis of these estimates could not be verified; however, the cost during PNE using these parameters was estimated by the Applicant to be $600.00 per patient. The calculations for this estimate are not provided but it is assumed to be a rounded approximation of the costs of the external stimulation power source after attribution.

The costs of the stimulation device contained in the Application comprise:

Tined lead	$4,240.00
Lead introducer kit	$525.00
Quadripolar extension kit	$1,800.00
Interstim IPG Itrel 3	$9,226.00
Foramen needles	$130.00
Total device costs, SNS stage	$17,273.00

The Applicant suggests the following Medicare Items apply:

- Medical cost of PNE: Item No.39133 Epidural stimulator or intrathecal infusion device be applied ($101.10). Anaesthetist costs are not estimated.
- Medical cost of SNS: Item No.39139 Epidural electrode be applied ($850.65).

Health care costs applied in the model

The costs provided by the Applicant are insufficient to allow an economic evaluation. Therefore, the evaluation of costs was extended by including an estimate of inpatient costs, use of pads and pharmacotherapy for individuals either failing treatment, or not fully continent (described as 'improved'). Additionally, the Advisory Panel identified more appropriate Medicare Item numbers. Tables 23–25 summarise the results for patients undergoing PNE, for those successfully undergoing SNS and for those failing SNS and/or being conservatively managed, respectively.

Table 23 PNE costs applied in the model

Health care resource	Value	Source of value
Capital cost	$519.00	Applicant's estimate (excluding cost of re-useable stimulation power source)
Medical fee	$572.05	MBS Item No. 39130 (SNS Advisory Panel)
Imaging fee	$28.05	MBS Item No.60503 Fluoroscopy
Inpatient cost	$711.00	Average same-day procedure cost for private hospitals; National Hospital Cost Data Collection Cost Weights from AR-DRG Version 4.2, Round 7, 2002–03
Total per evaluation	$1,830.00	

Table 24 SNS costs applied in the model

Health care resource	Value	Source of value
Capital cost	$17,273.00	Applicant's estimate
Medical Fee	$289.00	MBS Item No. 39134 (SNS Advisory Panel)
Inpatient Cost	$711.00	Average same-day procedure cost for private hospitals; National Hospital Cost Data Collection Cost Weights from AR-DRG Version 4.2, Round 7, 2002–03
Total per implantation	$18,273.00	

Table 25 Conservative management costs applied in the model

Health care resource	Value	Source of value
Pharmacotherapy (Loperamide)	$195.00 per year	Allowing for intolerance and patient preference, assumed that 85% of patients are prescribed loperamide hydrochloride, at an average dose of 2 mg x 2 tablets daily (http://www.douglas.com.au/products/otc/pdfs/NEGASTROPI.pdf). Price taken from PBS, Dec 2004
Incontinence pants	$1,041.00 per year	Unit price from retail pharmacy. An average cost of $2.28 each for Tena pants (a market leader). Frequency of use taken as baseline rate [NICE (2004), Table 9]
Total per year	$1,236.00	

Cost assumptions: sacral nerve stimulation versus conservative non-surgical treatment

Inevitably, a number of assumptions were necessary to estimate costs. Key assumptions used in the model (Figure 3) were:

- No device components are reusable except the external stimulation power source during PNE.
- Adverse events during PNE are minor and are assumed to be treated during normal consultations with minimal implications for resources and/or quality of life.
- The day-procedure cost for repositioning of leads is assumed to be the average cost of a same-day admission to a private hospital plus the appropriate Medicare item fee.
- The procedure cost for device implant or removal is a same day procedure (SNS Advisory Panel).
- No allowance has been made for any anaesthesiology or physiotherapy costs.
- The frequency of medical consultations is assumed to be approximately the same for both treatment arms with patients being seen regularly as part of normal care.
- Pad-use occurs at the baseline rate reported in Table 8 of NICE (2004) for the 52% of participants who are improved but not fully continent.

Health outcomes: sacral nerve stimulation versus conservative, non-surgical treatment

Effectiveness of SNS

The pivotal source of evidence for the economic evaluation, NICE (2004), reported:

- Patients as continent or improved, where improved was defined as ≥50% fewer incontinent episodes
- Change in episodes of faecal incontinence per week, both number and percentage change
- Ability to defer defecation

- Episodes of urgency per week
- Pad use per day
- Faecal incontinence score (Cleveland Clinic)
- Quality of life.

Of these, a suitable measure of quality of life is the clearly preferred outcome measure for evaluation of interventions for faecal incontinence. As noted in this report, quality of life results have been reported using a variety of instruments, including the SF-36 questionnaire, for study participants at baseline and after implantation with SNS. Whilst the direction of the reported results favours SNS, estimation of magnitude by the SF-36 questionnaire is not suitable for use in economic evaluations directly, nor are the disease specific instruments. It has therefore been necessary to use a surrogate, or intermediate, health outcome measure. The most readily interpreted outcome is considered to be the number of continent or improved patients (Table 26). NICE (2004) reported the study MDT-301 separately in the belief that at least some of the patients enrolled in that study would also have been enrolled in other studies.

Table 26 Continent and improved participants at last follow-up (NICE 2004)

Study	Continent		Improved	
	n/N	%	n/N	%
Jarrett unpublished[a]	19/46	41	44/46	96
Leroi et al (2001)	2/4	50	3/4	75
Matzel et al (2003)	12/16	75	16/16	100
Rosen et al (2001)	–	–	16/16	100
Total	32/66	48	79/82	96
MDT-301	15/33	45	29/33	88

[a] unpublished at time of writing NICE review, later published (Jarrett et al 2004b)

Adverse events including device failure associated with sacral nerve stimulation

Nineteen adverse events occurring in the implantation phase were reported from the 149 implants and have been included in the economic model (Figure 3 and Table 27).

The probabilities assigned to each event in the model were calculated directly from NICE (2004) and are included in Figure 3.

Table 27 Assignment of treatment costs by health outcomes in the economic model

Health outcome (end 'state')	Description (NICE 2004)	Action reported (NICE 2004)	Costs assigned in economic model
Continent or improved	Participants fully continent (cured) or achieve 50% reduction in incontinent episodes (improved)	None required	PNE costs comprising same day admission plus MBS Items 39130 and 60503 (fluoroscopy) followed by cost of implantation comprising cost of device plus inpatient costs plus MBS Item 39134. Improved patients only (52%) continue pad and pharmacotherapy costs
Failure due to loss of efficacy of SNS implanted device	Treatment failure due to either participant preference or loss of efficacy	(Not reported – assumed that device was removed)	PNE costs (as above) plus cost of implantation (as above) plus repeat inpatient costs and medical costs (as for implantation) for device removal. All patients continue pad and pharmacotherapy costs
Conservative management	-—	—	Cost of incontinence pants and pharmacotherapy (all candidates for SNS receive initial PNE costs)
Adverse event			
. Infection	3 participants developed infections from their implants within 3 months	Removal cost of implant. SNS was successfully repeated in 1 and 2 remained candidates for re-insertion at the time of follow-up	PNE (as above) plus implantation costs (as above) plus inpatient cost plus MBS Item 39134 for device removal and cost of anti-infective. Cost of subsequent replacement assigned device cost plus further cost of implantation
. Lead dislodgement	Lead dislodgement occurred 8 times in 7 participants	5 leads relocated, 1 dislodged a second time and was removed. Patient preference resulted in a second removal. Interruption of the lead necessitated replacement in a further participant	Participants requiring repositioning of lead assigned day-procedure costs plus medical cost (MBS Item 39131). Inpatient and medical costs (as for cost of implantation) assigned for instances of device removal
. Pain requiring treatment	Six participants complained of pain relating to their implant	Injection of a local anaesthetic and steroid resolved the pain in all 6 cases (In study MDT-301, 4 of 10 instances of pain were resolved with re-programming)	Patients assigned one incremental specialist consultation (MBS Item 39131) for treatment of pain. Patients requiring repositioning of lead assigned day-procedure costs
. Wound complications	Superficial wound dehiscence	Wound healed uneventfully	Patients assigned one additional specialist consultation (MBS Item 108, $67.35) for wound treatment

Study MDT-301 (Matzel et al 2004a) reported temporary loss of efficacy in one participant and sustained loss of efficacy in two participants, of whom one had the device removed and the other remained lost to follow-up. These results have been included in the model which is based upon the case series reported in NICE (2004) but are tested in the sensitivity analysis.

The results of the economic evaluation for SNS versus conservative, non-surgical treatment are shown in Table 28 in which the unit of effectiveness is patient-years of continence or improved continence. In conformity with convention in economic evaluation, costs and outcomes after the first year have been discounted at 5 per cent/annum.

Table 28 Results of the economic evaluation

Strategy	Costs[a]	Incremental costs[b]	Effect[c] (years)	Incremental effect	Cost/Effect	ICER
Conservative Management	$7,000	–	0	–	–	–
Screen for SNS	$18,000	$11,000	3.29	3.29	$5,411	$3,156

Abbreviations: ICER, incremental cost-effectiveness ratio
[a]Total average costs assigned per patient over 7 years
[b]Difference in cost between SNS and conservative management
[c]Average years of continence or improved continence per patient over 7 years

The model suggests that the ICER is approximately $3,200 per patient-year of continence or improved continence.

Sensitivity Analysis

Considerable uncertainty exists in relation to outcomes generally and to costs of treatment particularly under both treatment arms of the model. Parameters in the model tested for sensitivity to the results include:

Inpatient costs

The advice of the Health Information Unit, The Alfred Hospital, was that patients admitted for implantation of a device for SNS for treatment of faecal incontinence would be assigned to AR-DRGv4.2 G11Ba. The average total cost of this DRG is $1,719 per separation (plus a medical cost of $287) with an average length of stay of 1.7 days (National Hospital Cost Data Collection Cost Weights For AR-DRG Version 4.2, Round 7; 2002-03; AIHW).

The assignment of costs to AR-DRGv4.2 G11B is to some degree a convenience for hospital administrators in the absence of a specific DRG for SNS. The extent to which the cost-weight for this DRG is representative of true procedural costs is not known. If a hospital separation cost of $1,719 is substituted for the base-case value of $711, implantation costs increase to $19,281 (base case = $18,273).

This variation in the inpatient cost of implantation changes the ICER from $3,200 to $3,668 per patient-year of continence or improved continence.

Loss of efficacy

The MDT-301 study (Matzel et al 2004a) was reported separately in NICE (2004). It was noted that of the 34 participants permanently implanted for SNS, two participants (5.9%) lost efficacy for the duration of the follow-up period. One had the system removed and the other was lost to follow-up. Allowing for 5.9% of permanently implanted patients to become treatment failures due to loss of efficacy (base case = 1.0%) and assuming that both subsequently have the system removed changes the ICER to $3,362 per patient-year of continence or improved continence.

Complete continence as the outcome

NICE (2004) reported that 48 per cent of the participants receiving permanent implants (56% of the intention-to-treat patients) gained complete continence. Thus, the average number of continent years per patient would be approximately 1.9 over the 7-year period. In this case, the ICER would be $5,334 per patient-year of complete continence according to the model.

Data limitations in the evaluation of sacral nerve stimulation versus stoma formation

Limitations of the published data prevented preparation of an economic evaluation of SNS compared to stoma formation. Procedures such as colostomy, ileostomy, cecostomy, appendicostomy and antegrade colonic enema were considered for stoma formation.

An economic evaluation of SNS versus stoma formation is only feasible if it is possible to estimate the difference in health outcomes and the difference in costs between the two treatments (SNS and stoma formation) over an appropriate time frame.

This entails assigning probabilities to each branch of the pathways shown in Figure 4 over the life of the device and the identification and estimation of:

- the relevant health care resources used (and the unit cost of each resource)
- the extent to which each health care resource is used expressed as the average number of units used per patient
- the average health outcomes per patient under the alternative treatments for faecal incontinence in a metric that is common to both SNS and stoma patients.

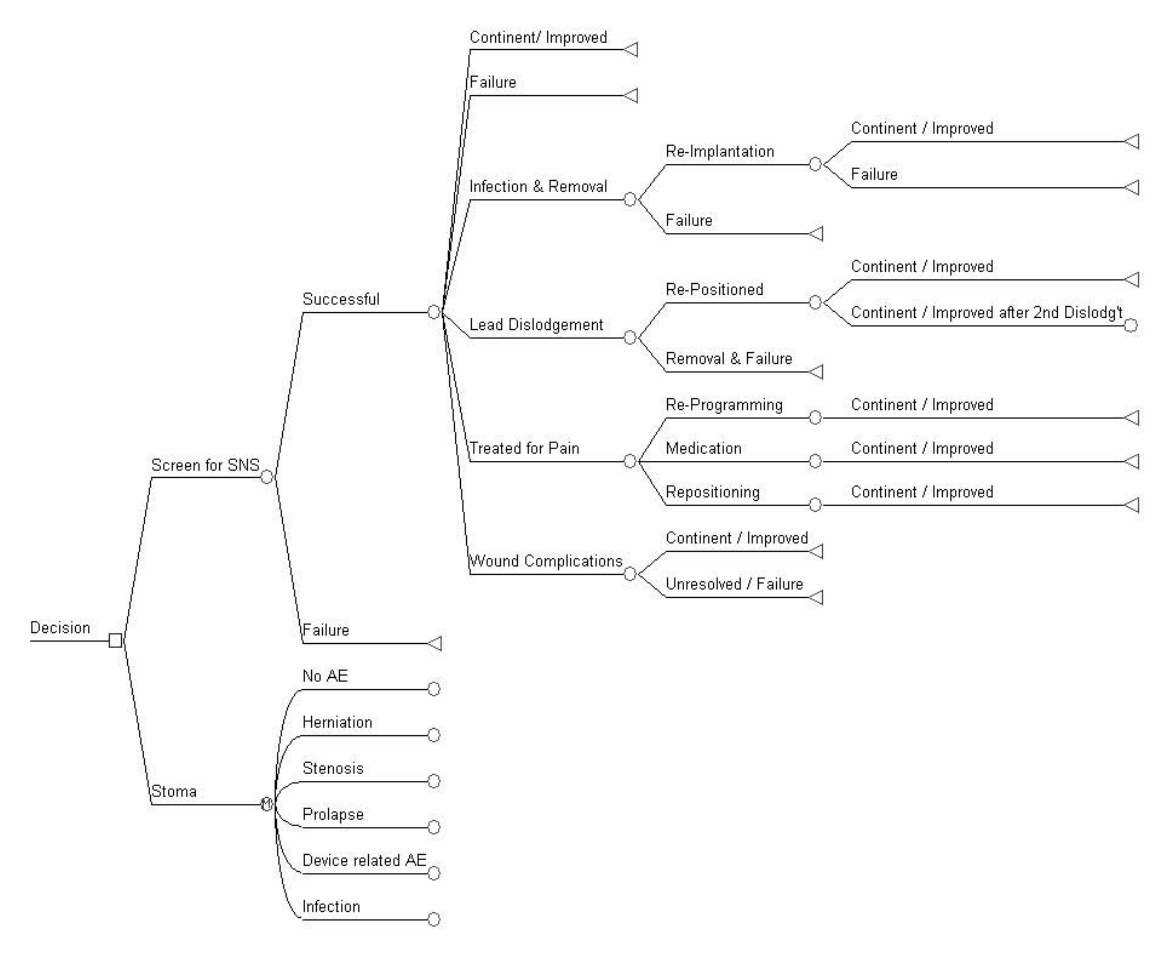

Figure 4 SNS versus stoma formation: Structure required for economic evaluation

Whilst the literature identifies the range and severity of adverse events following stoma formation, there are insufficient data relating to:

- the probabilities of each adverse event attributable to stoma formation
- the average resource use per patient and therefore treatment cost of these adverse events
- measurement of outcomes in a unit common to both treatments. For example, the use of surrogate measures of efficacy, such as incontinence episodes per week, pad-use and anorectal manometry results are redundant in the case of stoma formation. Effective comparison of SNS to stoma formation requires quantification of quality of life gains in the economic evaluation.

Conclusions

There is significant uncertainty in the estimates of the prevalence of faecal incontinence in Australia. Whilst the estimated prevalence of faecal incontinence in Australia is high, it is expected that only a small proportion of the 15 to 20 per cent of individuals who may be considered for surgical intervention of any type would proceed to have surgery. It is also important to clarify that patients who may be considered appropriate for SNS are a subset of the 15 to 20 per cent of individuals who may be considered for any type of surgical intervention. Therefore, the number of patients that may be considered for SNS for the treatment of faecal incontinence is unknown, but is likely to be considerably less than 15 to 20 per cent of individuals who may be appropriate for any type of surgical intervention.

Safety

The evidence available to date indicates that SNS for the treatment of faecal incontinence is safe as adverse events are not severe. This conclusion is based however on a small number of study participants, hence there is a compromised ability to detect rare adverse events and there is no long term follow-up.

Effectiveness

The effectiveness of SNS for the treatment of faecal incontinence was assessed from nine case series and one double blind crossover study, two systematic reviews of non-randomised studies and two health technology assessment reports.

Data from the identified case series and double blind crossover study demonstrate that SNS appears to be effective in reducing the number of faecal incontinence episodes per week, decreasing urgency to defecate and improving quality of life. The quality of life category of "social functioning" showed statistically significant improvements in three of four studies using the SF-36 questionnaire following SNS. In addition, all studies utilising disease-specific questionnaire showed a consistent, significant improvement in all four categories of lifestyle, coping/behaviour, depression/self perception and embarrassment. Whilst SNS appears to be effective, it is important to acknowledge that:

- a small number of individuals have been analysed;
- there is limited follow-up of participants in the included studies (up to 72 months) hence, the long term effectiveness of SNS is unknown;
- data is derived from case series - in the absence of a comparator arm, it cannot be ruled out that the improvements observed in participants following SNS occurred spontaneously;
- results may be biased due to: none of the studies included in this review stated that participants were consecutively enrolled; there may have been selective reporting of participants; participants withdrew and were lost to follow-up; and it

is unclear whether the participants enrolled in each of the series represented a spectrum of severity of faecal incontinence;

- participants enrolled in each of the series had faecal incontinence due to different aetiologies. Data were not reported in a way that allowed subgroup analyses to assess if one patient group would be more likely to benefit than another;

- differences in the reporting of faecal incontinence episodes per a given time frame between the included studies does not allow for easy comparison of results between studies or for an overall estimate of the effectiveness of sacral nerve stimulation to be estimated.

Similarly, the identified systematic reviews and health technology assessment reports concluded that SNS was effective in reducing the number of faecal incontinence episodes per week, decreasing urgency to defecate and improving quality of life. However, various limitations to the data have been identified:

- they were all from case series and the results may therefore represent a placebo effect

- there is potential bias due to selective reporting of results, the nature of selection of participants and the withdrawals and losses to follow-up

- too few participants were studied to observe rare adverse events

- heterogeneity in units of measure of faecal incontinence episodes made the data difficult to compare across studies

- the maximum length of follow-up was 99 months.

Cost-effectiveness

A review of the literature identified no studies of the relative cost-effectiveness of SNS compared to either conservative, non-surgical treatment or stoma formation for the treatment of faecal incontinence.

The Application (Section 11) included a cost-analysis of the procedure based upon an expert statement. However, costs considered by the Applicant appear to represent a financial analysis of costs to the Commonwealth Government and are thus incomplete as an economic analysis. The economic evaluation of SNS versus conservative, non-surgical treatment developed for this review addresses these issues from a societal perspective as far as possible, given the available data. It has not been possible to prepare an economic evaluation of SNS versus stoma formation.

The outcome measure applied in the evaluation is continence or improved continence. Ideally, a suitable measure of quality of life would have been used. As noted in the main body of the review, quality of life results have been reported in the literature for patients at baseline and after implantation with the SNS device, using a variety of instruments that included the SF-36 questionnaire. Whilst the direction of the reported results favours SNS, the SF-36 questionnaire is not suitable for direct estimation of the magnitude of

quality of life gains in an economic evaluation and neither are the disease-specific instruments.

The model presented is based on data from a published health technology assessment report on the outcomes and adverse events and provides brief commentary on the treatment of adverse events. The ICER was found to be $3,200 per patient-year of continence or improved continence.

This result from the economic evaluation is subject to many limitations such as the necessary use of case-series data reviewed for this report and the considerable uncertainty in relation to costs. However, sensitivity analysis shows some robustness in the result, most likely due to the dominance in the estimates of the cost of the device itself.

Recommendation

MSAC recommended that there is evidence of safety for sacral nerve stimulation in adults with faecal incontinence refractory to conservative, non-surgical treatment and who have an anatomically intact but functionally deficient anal sphincter. The total number of patients is small; there is some evidence of effectiveness and cost-effectiveness. MSAC supports public funding in these circumstances.

The Minister for Health and Ageing endorsed this recommendation on 4 July 2005.

Appendix A MSAC terms of reference and membership

MSAC's terms of reference are to:

- advise the Minister for Health and Ageing on the strength of evidence pertaining to new and emerging medical technologies and procedures in relation to their safety, effectiveness and cost-effectiveness and under what circumstances public funding should be supported;
- advise the Minister for Health and Ageing on which new medical technologies and procedures should be funded on an interim basis to allow data to be assembled to determine their safety, effectiveness and cost-effectiveness;
- advise the Minister for Health and Ageing on references related either to new and/or existing medical technologies and procedures; and
- undertake health technology assessment work referred by the Australian Health Ministers' Advisory Council (AHMAC) and report its findings to AHMAC.

The membership of the MSAC comprises a mix of clinical expertise covering pathology, nuclear medicine, surgery, specialist medicine and general practice, plus clinical epidemiology and clinical trials, health economics, consumers, and health administration and planning:

Member	Expertise or Affiliation
Dr Stephen Blamey (Chair)	general surgery
Associate Professor John Atherton	cardiology
Professor Syd Bell	pathology
Dr Michael Cleary	emergency medicine
Dr Paul Craft	clinical epidemiology and oncology
Dr Gerry FitzGerald	Australian Health Minister's Advisory Council representative
Dr Kwun Gong	thoracic medicine
Associate Professor Jane Hall	health economics
Dr Terri Jackson	health economics
Professor Brendon Kearney	health administration and planning
Dr Debra Graves	pathology
Dr Ray Kirk	health research
Dr Michael Kitchener	nuclear medicine
Dr Ewa Piejko	general practice
Mrs Sheila Rimmer	consumer representative
Professor Jeffrey Robinson	obstetrics and gynaecology
Professor John Horvath	medical advisor to the Department and Health Minister
Ms Rosemary Huxtable	Medicare Benefits Branch
Professor Ken Thomson	radiology
Dr Douglas Travis	urology
Professor Alan Lopez	epidemiology
Associate Professor Donald Perry-Keene	endocrinology
Professor Michael Solomon	colorectal medicine

http://www7.health.gov.au/msac/membership.htm#a [Last updated: 24 February, 2005]

Appendix B Advisory Panel

Advisory Panel for MSAC application 1077
Sacral nerve stimulation for faecal incontinence

Dr Ray Kirk (Chair) BSc, PhD Director New Zealand Health Technology Assessment Unit Clinical Senior Lecturer in Public Health Christchurch School of Medicine and Health Sciences University of Otago, New Zealand	MSAC Member
Ms Sheila Rimmer BSc Hons (Econ), MA (Political Science), AM Ranelagh	MSAC member
Dr Michael Whishaw MBBS, FRACP Consultant Physician in Geriatric Medicine Medical Director of Royal Melbourne Hospital, Royal Park Campus	Nominated by the Continence Foundation of Australia
Associate Professor Eric Guazzo MBBS, MD, FRACS, FRCS Neurosurgeon Vice-President for Neurosurgical Society of Australasia	Nominated by the Neurosurgical Society
Mr Stephen Bell MBBS, FRACS Consultant Colorectal Surgeon, Suite 27, Cabrini Medical Centre Senior Lecturer in Surgery, Monash University	Nominated by the Colorectal Surgical Society
Mrs Elizabeth Symons RN, GradDip AE&T, PGradDipEval Stomal Therapy Nurse Continence Nurse Advisor	Nominated by the Consumers' Health Forum

Associate Professor David Lubowski MB BCh FRACS Associate Professor, University of NSW Councillor, Colorectal Surgical Society of Australia Suite 6, Level 5, St George Private Medical Centre Kogarah, NSW	Nominated by the Colorectal Surgical Society

Evaluators

Monash Evaluation Group Evaluators	Monash University

Department of Health and Ageing

Ms Alex Lloyd Project Manager	Health Technology Section

Appendix C Search strategies

Table C1 SNS for the treatment of faecal incontinence terms for Medline

Number	Search term
1	InterStim.mp.
2	implantable pulse generator.mp.
3	sacral nerve stimulat$.mp.
4	pelvic floor stimulat$.mp.
5	sacral root stimulat$.mp.
6	or/1-5
7	sacral.mp.
8	(s2 or s3 or s4).mp.
9	sacrococcygeal region/
10	or/7-9
11	stimulat$.mp.
12	modulat$.mp.
13	neurostimulat$.mp.
14	neuromodulat$.mp.
15	(neural adj stimulat$).mp.
16	(neural adj modulat$).mp.
17	(nerve adj stimulat$).mp.
18	(nerve adj modulat$).mp.
19	neurotransmitter.mp. or Neurotransmitters/
20	neuroprostheses.mp.
21	electric stimulation therapy/
22	or/11-21
23	10 and 22
24	6 or 23
25	((faecal or fecal) adj incontinence).mp.
26	fecal incontinence/
27	(voiding adj dysfunction).mp.
28	((faecal or fecal) adj impaction).mp.
29	fecal impaction/
30	((faecal or fecal) adj urgency).mp.
31	urge incontinence.mp.
32	constipation.mp. or constipation/
33	anal incontinence.mp.
34	rectal incontinence.mp.
35	bowel incontinence.mp.
36	spurious incontinence.mp.
37	overflow incontinence.mp.
38	soiling.mp.
39	or/25-38
40	24 and 39

Table C2 SNS safety terms for Medline

Number	Search term
1	InterStim.mp.
2	implantable pulse generator.mp.
3	sacral nerve stimulat$.mp.
4	pelvic floor stimulat$.mp.
5	sacral root stimulat$.mp.
6	or/1-5
7	sacral.mp.
8	(s2 or s3 or s4).mp.
9	(sacrococcygeal adj2 region$).mp.
10	or/7-9
11	stimulat$.mp.
12	modulat$.mp.
13	neurostimulat$.mp.
14	neuromodulat$.mp.
15	(neural adj stimulat$).mp.
16	(neural adj modulat$).mp.
17	(nerve adj stimulat$).mp.
18	(nerve adj modulat$).mp.
19	neurotransmitter$.mp.
20	neuroprostheses.mp.
21	(electric adj2 stimulation adj2 therap$).mp. [mp=title, original title, abstract, name of substance, mesh subject heading]
22	or/11-21
23	10 and 22
24	6 or 23
25	safety.mp.
26	SAFETY/
27	exp RISK/
28	risk$.mp.
29	((adverse or side) adj5 (event$ or effect$)).mp.
30	ae.xs.
31	or/25-30
32	24 and 31

Table C3 Conservative, non-surgical treatment for faecal incontinence safety terms for Medline

Number	Search term
1	((faecal or fecal) adj incontinence).mp.
2	fecal incontinence/
3	(voiding adj dysfunction).mp.
4	((faecal or fecal) adj impaction).mp.
5	fecal impaction/
6	((faecal or fecal) adj urgency).mp.
7	urge incontinence.mp.
8	constipation.mp. or constipation/
9	anal incontinence.mp.
10	rectal incontinence.mp.
11	bowel incontinence.mp.
12	spurious incontinence.mp.
13	overflow incontinence.mp.
14	soiling.mp.
15	or/1-14
16	safety.mp.
17	SAFETY/
18	exp RISK/
19	risk$.mp.
20	((adverse or side) adj5 (event$ or effect$)).mp.
21	ae.xs.
22	or/16-21
23	(Anti-incontinence devices, Pads and Pants).mp. [mp=title, original title, abstract, name of substance word, subject heading word]
24	anti-incontinence device$.tw.
25	(anti-incontinence adj device$).tw.
26	((diet or dietary) adj change).mp.
27	((diet or dietary) adj manipulation).mp.
28	((diet or dietary) adj treatment).mp.
29	((diet or dietary) adj therapy).mp.
30	((diet or dietary) adj management).mp.
31	((diet or dietary) adj fibre).mp.
32	*Dietary Fiber/ or dietary fibre.mp.
33	((diet or dietary) adj supplement$).mp.
34	((diet or dietary) adj education).mp.
35	pelvic floor exercise.tw.
36	Pelvic Floor Muscles Exercise$.tw.
37	Pelvic Floor Muscle$ Exercise$.tw.
38	physical muscle train$.tw.
39	Biofeedback.mp. or exp "Biofeedback (Psychology)"/
40	(Biofeedback adj therapy).mp. [mp=title, original title, abstract, name of substance word, subject heading word]
41	Physical Therapy Techniques.mp. or exp Physical Therapy Techniques/

Table C3 (cont'd) Conservative, non-surgical treatment for faecal incontinence safety terms for Medline

Number	Search term
42	(biofeedback adj train$).mp. [mp=title, original title, abstract, name of substance word, subject heading word]
43	(Lifestyle adj Intervention$).mp. [mp=title, original title, abstract, name of substance word, subject heading word]
44	anal retrain$.tw.
45	((faecal or fecal) adj retrain$).mp.
46	Medication.mp.
47	drug therapy.mp. or exp Drug Therapy/
48	Phenylephrine.mp. or exp PHENYLEPHRINE/
49	Loperamide.mp. or LOPERAMIDE/
50	toilet training.mp. or exp Toilet Training/
51	Antidiarrheals/ or constipating agents.mp.
52	or/23-51
53	15 and 22 and 52
54	limit 53 to humans
55	limit 54 to english language
56	limit 55 to "all adult (19 plus years)"

Table C4 Stoma search for Medline

Number	Search term
1	(cecostomy or caecostomy).mp. or CECOSTOMY/
2	appendicostomy.mp.
3	stoma.mp. or Stomas/
4	colostomy.mp. or COLOSTOMY/
5	ileostomy.mp. or ILEOSTOMY/
6	Ostomy.mp. or OSTOMY/
7	antegrade colonic enema.mp.
8	((faecal or fecal) adj incontinence).mp.
9	fecal incontinence/
10	(voiding adj dysfunction).mp.
11	((faecal or fecal) adj impaction).mp.
12	fecal impaction/
13	((faecal or fecal) adj urgency).mp.
14	urge incontinence.mp.
15	constipation.mp. or constipation/
16	anal incontinence.mp.
17	rectal incontinence.mp.
18	bowel incontinence.mp.
19	spurious incontinence.mp.
20	overflow incontinence.mp.
21	soiling.mp.
22	or/1-7
23	or/8-21
24	22 and 23

Appendix D HTA, clinical trial and other relevant websites

HTA websites

Agence d'Evaluation des Technologies et des Modes d'Intervention en Santé (Aetmis) http://www.aetmis.gouv.qc.ca/en/ [Accessed 17 November 2004]

Agencia de Evaluación de Tecnologias Sanitarias (AETS) http://www.isciii.es/aets/ [Accessed 17 November 2004]

Agency for Healthcare Research and Quality – technology assessments (AHRQ) http://www.ahcpr.gov/clinic/techix.htm [Accessed 17 November 2004]

Agenzia per I Servizi Sanitari Regionali [Italian] http://www.assr.it/ [Accessed 17 November 2004]

Alberta Heritage Foundation for Medical Research (AHFMR) http://www.ahfmr.ab.ca/hta/ [Accessed 17 November 2004]

Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP-S) http://www.surgeons.org/asernip-s/ [Accessed 17 November 2004]

BCBS Technology Evaluation Center http://www.bcbs.com/tec/index.html [Accessed 17 November 2004]

Bundesaertekammer HTA [German] http://www.bundesaerztekammer.de/30/HTA/ [Accessed 17 November 2004]

Canadian Coordinating Office for Health Technology Assessment (CCOHTA) http://www.ccohta.ca/ [Accessed 17 November 2004]

CEDIT: Comité d'Evaluation et des Diffusion des Innovations Technologiques http://cedit.aphp.fr/ [Accessed 17 November 2004]

Center for Health Services and Policy Research (CHSPR) http://www.chspr.ubc.ca/ [Accessed 17 November 2004]

Center for Medical Technology Assessment (CMT) http://www.cmt.liu.se/English/Engstartsida.html [Accessed 17 November 2004]

Danish Centre for Evaluation and Health Technology Assessment (DACEHTA) http://www.sst.dk/Planlaegning_og_behandling/Medicinsk_teknologivurdering.aspx?lang=en [Accessed 17 November 2004]

Deutsches Institut fur Medizinische Dokumentation und Information (DIMDI) http://www.dimdi.de/dynamic/en/index.html [Accessed 17 November 2004]

EUROSCAN: The European Information Network on New and Changing Health Technologies http://www.publichealth.bham.ac.uk/euroscan/ [Accessed 17 November 2004]

Finnish Office for Health Care Technology Assessment http://www.stakes.fi/finohta/ [Accessed 17 November 2004]

Health Council of the Netherlands http://www.gr.nl/ [Accessed 17 November 2004]

HSTAT : Health Services/Technology Assessment Text http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=hstat [Accessed 17 November 2004]

Health Technology Assessment (HTA) Database http://nhscrd.york.ac.uk/htahp.htm [Accessed 17 November 2004]

Health Technology Assessment Information Service (HTAIS) http://www.ecri.org/Products_and_Services/Membership_Programs/Health_Technology_Assessment_Information_Service/Default.aspx [Accessed 17 November 2004]

Health Technology Assessment International (HTAi) http://www.htai.org/ [Accessed 17 November 2004]

Institute for Clinical Systems Improvement (ICSI) http://www.icsi.org/index.asp [Accessed 17 November 2004]

Institute of Technology Assessment of the Austrian Academy of Science http://www.oeaw.ac.at/ita/welcome.htm [Accessed 17 November 2004]

International Network of Agencies for Health Technology Assessment (INAHTA) http://www.inahta.org/ [Accessed 17 November 2004]

International Society for Pharmacoeconomics and Outcomes Research http://www.ispor.org/ [Accessed 17 November 2004]

L'Agence Nationale d'Accreditation et d'Evaluation en Sante [French] http://www.anaes.fr/ANAES/anaesparametrage.nsf/HomePage?ReadForm [Accessed 17 November 2004]

Medical Technology Assessment Group (M-TAG) http://www.m-tag.net/flash_index.htm [Accessed 17 November 2004]

The National Coordinating Centre for Health Technology Assessment (NCCHTA) http://www.hta.nhsweb.nhs.uk/ [Accessed 17 November 2004]

National Horizon Scanning Centre http://www.publichealth.bham.ac.uk/horizon/ [Accessed 17 November 2004]

National Institute for Clinical Excellence (NICE) http://www.nice.org.uk/Cat.asp?pn=professional&cn=toplevel&ln=en [Accessed 17 November 2004]

NZHTA Clearing House http://nzhta.chmeds.ac.nz/ [Accessed 17 November 2004]

SBU Evaluates Health Care Technology http://www.sbu.se/www/index.asp [Accessed 17 November 2004]

Swiss Network for Health Technology Assessment (SNHTA)http://www.snhta.ch/home/portal.php [Accessed 17 November 2004]

Technology Assessment Unit at McGill University Health Centre http://www.mcgill.ca/tau/ [Accessed 17 November 2004]

West Midlands Health Technology Assessment Collaboration (WMHTAC) http://www.publichealth.bham.ac.uk/wmhtac/ [Accessed 17 November 2004]

Clinical trial register websites

CentreWatch clinical trials listing service http://www.centerwatch.com/ [Accessed 17 November 2004]

ClinicalTrials.com http://www.clinicaltrials.com/ [Accessed 17 November 2004]

ClinicalTrials.gov http://www.clinicaltrials.gov/ [Accessed 17 November 2004]

Current Controlled Trials http://www.controlled-trials.com/ [Accessed 17 November 2004]

NHMRC Clinical Trials Centre http://www.ctc.usyd.edu.au/trials/registry/registry.htm [Accessed 17 November 2004]

Society for Clinical Trials http://www.sctweb.org/ [Accessed 17 November 2004]

TrialsCentral http://www.trialscentral.org/ [Accessed 17 November 2004]

UK The National Research Register http://www.update-software.com/national/ [Accessed 17 November 2004]

Other relevant websites

The Cleveland Clinic http://www.clevelandclinic.org/colorectal/research.htm

Colorectal Eporediensis Center News http://www.colorep.it/Rivista%20CEC/

Mayo Clinic College of Medicine http://www.mayoclinic.org/colorectalsurgery-jax/clintrials.html

St Mark's Hospital and Academic Institute http://www.stmarkshospital.org.uk/

Appendix E Adverse events reported in individual primary studies

Table E1 **Complication rates in participants who have had sacral nerve stimulator implants for the treatment of faecal incontinence during PNE**

Study	N	Electrode/ lead replaced/ repositioned	Electrode/ lead explants	Generator problems	Electrode & lead problems	Pain	Infection
Ganio et al (2001a)	23	2	–	–	4	–	–
Jarrett et al (2004b)	59	–	–	–	–	–	1
Leroi et al (2001)	11	–	–	–	2	–	–
Matzel et al (2004a)	37	–	–	–	1	–	9
Rasmussen et al (2004)	45	–	3	–	7	–	3
Ripetti et al (2002)	16	1	–	–	1	–	–
Uludag et al (2004)	75	–	4	–	10	–	4
Vaizey et al (1999)	12	–	–	–	4	–	–
Total	**278**	**3**	**7**	**0**	**29**	**0**	**17**

Table E2 **Complication rates in participants who have had sacral nerve stimulator implants for the treatment of faecal incontinence during CTS**

Study	N	Re-operations	IPG/Electrode/ Lead replaced/ repositioned	Permanent explants	Generator problems	Electrode & lead problems	Pain	Infection	Seroma	Wound problems	Other
Altomare et al (2004a)	14	2	–	–	–	2	–	1	1	–	–
Ganio et al (2001b)	16	–	–	–	–	–	1	–	1	–	–
Ganio et al (2002)	31	2	1	–	–	1	1	–	–	–	–
Jarrett et al (2004b)	46	4	3	1	–	4	3	–	–	–	–
Leroi et al (2001)	6	1	–	–	–	1	–	–	–	1	–
Malouf et al (2000b)	5	2	1	–	–	1	–	–	–	–	–
Matzel et al (2001)	6	4	2	2	–	–	2	–	–	–	–
Matzel et al (2004a)	34	10	3	2	4	1	10	1	–	–	3[a]
Rasmussen et al (2004)	37	5	–	5	–	–	–	2	–	–	3[b]
Ratto et al (2003)	10	–	–	–	–	–	–	–	1	–	–
Rosen et al (2001)	16	6	2	4	–	2	–	3	–	–	–
Uludag et al (2004)	50	6	–	2	4[c]	–	–	2	8	–	–
Total	**271**	**42**	**12**	**16**	**8**	**12**	**17**	**9**	**11**	**1**	**6**

[a] Deterioration of bowel symptoms
[b] Cessation of clinical response at 3, 12 and 18 months
[c] Technical failure

Appendix F Information from excluded studies of outcomes of stoma formation for the treatment of faecal incontinence

Branagan et al (2003) reported on 35 patients with spinal cord injury who had a stoma formed between March 1986 and March 2002. The average patient age at injury was 28.9 (range 6-62) years, the mean time from injury to stoma formation was 17.1 (range 0-36.3) years and the mean time of poor bowel function prior to stoma formation was 8 (range 1.5-25) years. The mean age of the patients when the stoma was formed was not reported, hence this study may be reporting results for adults and children combined. The mean follow-up following stoma formation was 4.6 years (range 0.3-15.8). Twenty-three of 35 patients (65.7%) required stoma formation for constipation, four (11.4%) for faecal incontinence, two (5.7%) for sepsis, one (2.86%) for malignancy and one (2.9%) for perineal trauma at the time of injury. The average time patients spent on bowel care decreased from 10.3 hours (range 3.5-45) per week prior to stoma formation to 1.9 hours (range 0.5-7.8) per week following stoma formation, and all patients reported that bowel care was easier following stoma formation. Of the 31 patients questioned, 18 (58.1%) felt that the stoma had given them more independence, 12 (38.7%) felt that it made no difference and one (3.2%) patient felt that independence had decreased, despite a significant decrease in time spent on bowel care. Twenty-five (80.6%) patients described their quality of life as much better, five (16.1%) described their quality of life as better and one (3.2%) described quality of life as worse.

Bruce et al (1999) reported on the use of the antegrade continence enema in seven patients (four women and three men) with refractory neurogenic faecal incontinence. Patients were enrolled between October 1995 and September 1998 and had a mean age of 33.6 (range 23–54) years at the time of surgery. The causes of faecal incontinence included myelomeningocele in five (71.4%), multiple sclerosis in one (14.3%) and post-sacral rhizotomies for pelvic pain in one (14.3%). Mean post-operative follow-up was 22.4 months (range 3–34). All patients were continent at last follow-up and used antegrade continence enema irrigation every other day on average. Five patients performed their irrigations independently and two required assistance. Use of subjective patient administered questionnaires showed that all patients were satisfied with their outcomes and no patient required protective clothing for faecal soiling.

Christensen et al (2001) reported on the use of an ileal neoappendicostomy for antegrade colonic irrigation in nine patients with severe colorectal dysfunction enrolled from September 1999 to November 2000. Median patient age was 50 (range 29–69) years and all patients were women. Patients were followed prospectively for a median follow-up of 10 (range 3–20) months. At last follow-up, eight (88.9%) patients still used the ileal appendicostomy which was fully continent in two (22.2%) patients. In the eight patients still using the ileal appendicostomy, the stoma were reported to be easily catheterised in six (75.0%) patients and narrow in one (12.5%). One (12.5%) patient had stenosis of the ileal conduit. With regular irrigation, faecal incontinence was reported to be absent or reduced and constipation had been treated successfully in three of four (75.0%) patients. One patient was reported to have had an unsatisfactory result from the irrigation procedure. Overall, seven of nine (77.8%) patients reported a significant improvement in

bowel function, with satisfaction reported as very high in three (37.5%), high in four (50.0%) and very poor in one (12.5%).

Stone et al (1990) reported on stoma effectiveness in 20 spinal cord injury patients treated for chronic gastrointestinal problems (12, 60.0%), perineal ulcers (7, 35.0%) and low rectal cancer (1, 5.0%). The mean age of patients in the series was 51.6 years, the mean time since injury 15.7 years and patients were followed up for a mean of 4.5 (range 0.2–21.0) years following stoma formation. Stone et al (1990) stated that two patients with faecal incontinence as an indication were cured by colostomy. Of the 19 living patients, none would have elected for the colostomy to be reversed. Patients experiencing the greatest satisfaction from their colostomy were those treated for gastrointestinal problems. Seven patients (36.8%) rated their quality of life as much better, three (15.8%) as better, and one (5.3%) as unchanged.

Appendix G Included studies

Systematic reviews, systematic review protocol and health technology assessments

Australian Safety and Efficacy Register of New Interventional Procedures - Surgical (ASERNIPS) 2003, *Sacral nerve stimulation for treatment of faecal incontinence* [Internet]. Available from: http://www.surgeons.org/asernip-s/net-s/procedures/SNS_Faecal_Incontinence.pdf [Accessed 10 September 2004].

Jarrett, M.E., Mowatt, G., Glazener, C.M., Fraser, C., Nicholls, R.J., Grant, A.M. & Kamm, M.A. 2004a. 'Systematic review of sacral nerve stimulation for faecal incontinence and constipation', *British Journal of Surgery*, 91 (12), 1559–1569.

Matzel, K.E., Stadelmaier, U. & Hohenberger, W. 2004b. 'Innovations in fecal incontinence: sacral nerve stimulation', *Diseases of the Colon & Rectum*, 47 (10), 1720–1728.

Mowatt, G., Glazener, C. & Jarrett, M. 2003. 'Sacral nerve stimulation for faecal incontinence in adults (Protocol for a Cochrane Review)', *The Cochrane Library*, John Wiley & Sons Ltd, Chichester, UK, Issue 3, 2004.

NICE (National Institute for Clinical Excellence) 2004, *Systematic review of the efficacy and safety of sacral nerve stimulation for faecal incontinence* [Internet]. Aberdeen. Available from: www.nice.org.uk [Accessed 4 November 2004].

Primary studies

Case series

Altomare, D.F., Rinaldi, M., Petrolino, M., Monitillo, V., Sallustio, P., Veglia, A., De Fazio, M., Guglielmi, A. & Memeo, V. 2004a. 'Permanent sacral nerve modulation for fecal incontinence and associated urinary disturbances', *International Journal of Colorectal Disease*, 19 (3), 203–209.

Ganio, E., Luc, A.R., Clerico, G. & Trompetto, M. 2001a. 'Sacral nerve stimulation for treatment of fecal incontinence: a novel approach for intractable fecal incontinence', *Diseases of the Colon & Rectum*, 44 (5), 619–631.

Ganio, E., Luc, A.R., Ratto, L.C., Doglietto, G.B., Masin, A., Dodi, G., Altomare, D.F., Memeo, V., Ripetti, V., Arullani, A., Falletto, E., Gaetini, A., Scarpino, O., Saba, V., Infantino, A., La Manna, S., Ferulano, G.P. & Villani, R. 2002, *Sacral Nerve Modulation for fecal incontinence: Functional results and assessment of the Quality of Life* [Internet]. Available from: http://www.colorep.it/Rivista%20CEC/sacral_nerve_modulation_for_feca.htm [Accessed 24 September 2004].

Jarrett, M.E., Varma, J.S., Duthie, G.S., Nicholls, R.J. & Kamm, M.A. 2004b. 'Sacral nerve stimulation for faecal incontinence in the UK', *British Journal of Surgery*, 91 (6), 755–761.

Matzel, K.E., Kamm, M.A., Stoesser, M., Baeten, C.G.M.I., Christiansen, J., Madoff, R., Mellgren, A., Nicholls, R.J., Rius, J. & Rosen, H. 2004a. 'Sacral spinal nerve stimulation for faecal incontinence: multicentre study', *The Lancet*, 363 (9417), 1270–1276.

Rasmussen, O.O., Buntzen, S., Sorensen, M., Laurberg, S. & Christiansen, J. 2004. 'Sacral nerve stimulation in fecal incontinence', *Diseases of the Colon & Rectum*, 47 (7), 1158–1163.

Ripetti, V., Caputo, D., Ausania, F., Esposito, E., Bruni, R. & Arullani, A. 2002. 'Sacral nerve neuromodulation improves physical, psychological and social quality of life in patients with fecal incontinence', *Techniques in Coloproctology*, 6 (3), 147–152.

Rosen, H.R., Urbarz, C., Holzer, B., Novi, G. & Schiessel, R. 2001. 'Sacral nerve stimulation as a treatment for fecal incontinence', *Gastroenterology*, 121 (3), 536–541.

Uludag, O., Koch, S.M.P., Van Gemert, W.G., Dejong, C.H.C. & Baeten, C.G.M.I. 2004. 'Sacral neuromodulation in patients with fecal incontinence: A single-center study', *Diseases of the Colon & Rectum*, 47 (8), 1350–1357.

Double blind crossover study

Vaizey, C.J., Kamm, M.A., Roy, A.J. & Nicholls, R.J. 2000. 'Double-blind crossover study of sacral nerve stimulation for fecal incontinence', *Diseases of the Colon & Rectum*, 43 (3), 298–302.

Appendix H Excluded studies

Sacral nerve stimulation

Reported PNE results only

Altomare, D.F., Rinaldi, M., Petrolino, M., Ripetti, V., Masin, A., Ratto, C., Trerotoli, P., Monitillo, V., Lobascio, P., De Fazio, M., Guglielmi, A. & Memeo, V. 2004b. 'Reliability of electrophysiologic anal tests in predicting the outcome of sacral nerve modulation for fecal incontinence', *Diseases of the Colon & Rectum*, 47 (6), 853–857.

Ganio, E., Masin, A., Ratto, C., Altomare, D.F., Ripetti, V., Clerico, G., Lise, M., Doglietto, G.B., Memeo, V., Landolfi, V., Del Genio, A., Arullani, A., Giardiello, G. & de Seta, F. 2001c. '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*, 44 (9), 1261–1267.

Vaizey, C.J., Kamm, M.A., Turner, I.C., Nicholls, R.J. & Woloszko, J. 1999. 'Effects of short term sacral nerve stimulation on anal and rectal function in patients with anal incontinence', *Gut*, 44 (3), 407–412.

Case reports

Buntzen, S., Rasmussen, O.O., Ryhammer, A.M., Sorensen, M., Laurberg, S. & Christiansen, J. 2004. 'Sacral nerve stimulation for treatment of fecal incontinence in a patient with muscular dystrophy: Report of a case', *Diseases of the Colon & Rectum*, 47 (8), 1409–1411.

Matzel, K.E., Stadelmaier, U., Hohenfellner, M. & Gall, F.P. 1995. 'Permanent electrostimulation of sacral spinal nerves with an implantable neurostimulator in treatment of fecal incontinence', *Der Chirurg; Zeitschrift fur alle Gebiete der operativen Medizen*?' 66 (8), 813–817.

Matzel, K.E., Stadelmaier, U., Bittorf, B., Hohenfellner, M. & Hohenberger, W. 2002. 'Bilateral sacral spinal nerve stimulation for fecal incontinence after low anterior rectum resection', *International Journal of Colorectal Disease*, 17 (6), 430–434.

Case series enrolling fewer than 20 participants

Chia, Y.W., Lee, T.K., Kour, N.W., Tung, K.H. & Tan, E.S. 1996. 'Microchip implants on the anterior sacral roots in patients with spinal trauma: does it improve bowel function?', *Diseases of the Colon & Rectum*, 39 (6), 690–694.

Ganio, E., Ratto, C., Masin, A., Luc, A.R., Doglietto, G.B., Dodi, G., Ripetti, V., Arullani, A., Frascio, M., BertiRiboli, E., Landolfi, V., DelGenio, A., Altomare, D.F., Memeo, V., Bertapelle, P., Carone, R., Spinelli, M., Zanollo, A., Spreafico, L., Giardiello, G. & de Seta, F. 2001b. 'Neuromodulation for fecal incontinence: outcome in 16 patients with definitive implant. The initial Italian Sacral Neurostimulation Group (GINS) experience', *Diseases of the Colon & Rectum*, 44 (7), 965–970.

Kenefick, N.J., Vaizey, C.J., Cohen, R.C., Nicholls, R.J. & Kamm, M.A. 2002a. 'Medium-term results of permanent sacral nerve stimulation for faecal incontinence', *British Journal of Surgery*, 89 (7), 896–901.

Kenefick, N.J., Vaizey, C.J., Nicholls, R.J., Cohen, R. & Kamm, M.A. 2002b. 'Sacral nerve stimulation for faecal incontinence due to systemic sclerosis', *Gut*, 51 (6), 881–883.

Leroi, A.M., Michot, F., Grise, P. & Denis, P. 2001. 'Effect of sacral nerve stimulation in patients with fecal and urinary incontinence', *Diseases of the Colon & Rectum*, 44 (6), 779–789.

MacDonagh, R.P., Sun, W.M., Smallwood, R., Forster, D. & Read, N.W. 1990. 'Control of defaecation in patients with spinal injuries by stimulation of sacral anterior nerve roots', *British Medical Journal*, 300 (6738), 1494–1497.

Malouf, A.J., Vaizey, C.J., Nicholls, R.J. & Kamm, M.A. 2000. 'Permanent sacral nerve stimulation for fecal incontinence', *Annals of Surgery*, 232 (1), 143–148.

Matzel, K.E., Stadelmaier, U., Hohenfellner, M. & Gall, F.P. 1995. 'Electrical stimulation of sacral spinal nerves for treatment of faecal incontinence', *The Lancet*, 346 (8983), 1124–1127.

Matzel, K.E., Stadelmaier, U., Hohenfellner, M. & Hohenberger, W. 1998. 'Treatment of anal sphincter insufficiency by ?? with implantable sacral spinal nerve stimulators', *Langenbecks Archiv fur Chirurgie. Supplement. Kongressband. Deutsche Gesellschaft fur Chirurgie. Kongress*, 115, 494–497.

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

Matzel, K.E., Bittorf, B., Stadelmaier, U. & Hohenberger, W. 2003. 'Sacral nerve stimulation in the treatment of faecal incontinence', *Der Chirurg; Zeitschrift fur alle Gebiete der operativen Medizen*, CORRECT NAME? IE IS IT 'DER CHIRURG'? 74 (1), 26–32.

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Abbreviations

ABS	Australian Bureau of Statistics
ARTG	Australian Register of Therapeutic Goods
ASCRS	American Society of Colon and Rectal Surgeons
ASERNIP-S	Australian Safety and Efficacy Register of New Interventional Procedures – Surgical
CI	confidence interval
CNS	central nervous system
CTS	chronic therapeutic stimulation
EAS	external anal sphincter
FI	faecal incontinence
IAS	internal anal sphincter
IBD	inflammatory bowel disease
IBS	irritable bowel syndrome
ICER	incremental cost-effectiveness ratio
IPG	implantable pulse generator
IQR	interquartile range
MBS	Medicare Benefits Schedule
MS	multiple sclerosis
NICE	National Institute for Clinical Excellence
NNT(H)	number needed to treat to harm
PNE	peripheral nerve evaluation
RCT	randomised controlled trial
SD	standard deviation
SF-36	Short Form-36 Health Survey Quality of Life Questionnaire
SNS	sacral nerve stimulation

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