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Sacral Nerve Stimulation For Urinary Urge Incontinence, Urgency-Frequency, Urinary Retention, and Fecal Incontinence

An Evidence-Based Analysis

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Executive Summary

Objective

The aim of this review was to assess the effectiveness, safety, and cost of sacral nerve stimulation (SNS) to treat urinary urge incontinence, urgency-frequency, urinary retention, and fecal incontinence.

Background: Condition and Target Population

Urinary urge incontinence, urgency-frequency, urinary retention, and fecal incontinence are prevalent, yet rarely discussed, conditions. They are rarely discussed because patients may be uncomfortable disclosing their symptoms to a health professional or may be unaware that there are treatment options for these conditions. Briefly, urge incontinence is an involuntary loss of urine upon a sudden urge. Urgency-frequency is an uncontrollable urge to void, which results in frequent, small-volume voids. People with urgency-frequency may or may not also experience chronic pelvic pain. Urinary retention refers to the inability to void despite having the urge to void. It can be caused by a hypocontractile detrusor (weak or no bladder muscle contraction) or obstruction due to urethral overactivity. Fecal incontinence is a loss of voluntary bowel control.

The prevalence of urge incontinence, urgency-frequency, and urinary retention in the general population is 3.3% to 8.2%, and the prevalence of fecal incontinence is 1.4% to 1.9%. About three-quarters of these people will be successfully treated by behaviour and/or drug therapy. For those who do not respond to these therapies, the options for treatment are management with diapers or pads, or surgery. The surgical procedures are generally quite invasive, permanent, and are associated with complications. Pads and/or diapers are used throughout the course of treatment as different therapies are tried. Patients who respond successfully to treatment may still require pads or diapers, but to a lesser extent.

The Technology Being Reviewed: Sacral Nerve Stimulation

Sacral nerve stimulation is a procedure where a small device attached to an electrode is implanted in the abdomen or buttock to stimulate the sacral nerves in an attempt to manage urinary urge incontinence, urgency-frequency, urinary retention, and fecal incontinence. The device was originally developed to manage urinary urge incontinence; however, it has also been used in patients with urgency-frequency, urinary retention, and fecal incontinence. SNS is intended for patients who are refractory to behaviour, drug, and/or interventional therapy.

There are 2 phases in the SNS process: first, patients must undergo a test stimulation phase to determine if they respond to sacral nerve stimulation. If there is a 50% or greater improvement in voiding function, then the patient is considered a candidate for the next phase, implantation.

Review Strategy

The standard Medical Advisory Secretariat search strategy was used to locate international health technology assessments and English-language journal articles published from 2000 to November 2004. The Medical Advisory Secretariat also conducted Internet searches of Medscape (1)and the manufacturer's website (2) to identify product information and recent reports on trials that were unpublished but that were presented at international conferences. In addition, the Web site Current Controlled Trials (3) was searched for ongoing randomized controlled trials (RCTs) investigating the role of sacral nerve stimulation in the management of voiding conditions.

Summary of Findings

Four health technology assessments were found that reviewed SNS in patients with urge incontinence, urgency-frequency, and/or urinary retention. One assessment was found that reviewed SNS in patients with fecal incontinence. The assessments consistently reported that SNS was an effective technology in managing these voiding conditions in patients who did not respond to drug or behaviour therapy. They also reported that there was a substantial complication profile associated with SNS. Complication rates ranged from 33% to 50%. However, none of the assessments reported that they found any incidences of permanent injury or death associated with the device.

The health technology assessments for urge incontinence, urgency-frequency, and urinary retention included (RCTs (level 2) as their primary source of evidence for their conclusions. The assessment of fecal incontinence based its conclusions on evidence from case series (level 4). Because there was level 2 data available for the use of SNS in patients with urinary conditions, the Medical Advisory Secretariat chose to review thoroughly the RCTs included in the assessments and search for publications since the assessments were released. However, for the health technology assessment for fecal incontinence, which contained only level 4 evidence, the Medical Advisory Secretariat searched for studies on SNS and fecal incontinence that were published since that assessment was released.

Urge Incontinence

Two RCTs were identified that compared SNS to no treatment in patients with refractory urge incontinence. Both RCTs reported significant improvements (> 50% improvement in voiding function) in the SNS group for number of incontinence episodes per day, number of pads used per day, and severity of incontinence episodes.

Urgency-Frequency (With or Without Chronic Pelvic Pain)

One RCT was identified that compared SNS to no treatment in patients with refractory urgency-frequency. The RCT reported significant improvements in urgency-frequency symptoms in the SNS group (average volume per void, detrusor pressure). In addition to the RCT, 1 retrospective review and 2 prospective case series were identified that measured pelvic pain associated with urgency-frequency in patients who underwent SNS. All 3 studies reported a significant decrease in pain at median follow-up.

Urinary Retention

One RCT was identified that compared SNS to no treatment in patients with refractory urinary retention. The RCT reported significant improvements in urinary retention in the SNS group compared to the control group for number of catheterizations required and number of voids per day. In addition to this RCT, 1 case series was also identified investigating SNS in women with urinary retention. This study also found that there were significant improvements in urinary retention after the women had received the SNS implants.

Fecal Incontinence

Three case series were identified that investigated the role of SNS in patients with fecal incontinence. All 3 reported significant improvements in fecal incontinence symptoms (number of incontinent episodes per week) after the patients received the SNS implants.

Long-Term Follow-up

None of the studies identified followed patients until the point of battery failure. Of the 6 studies identified describing the long-term follow-up of patients with SNS, follow-up periods ranged from 1.5 years to over 5 years. None of the long-term follow-up studies included patients with fecal incontinence. All of the studies reported that most of the patients who had SNS had at least a 50% improvement in voiding function (range 58%–77%). These studies also reported the number of patients who had their device explanted in the follow-up period. The rates of explantation ranged from 12% to 21%.

Safety, Complications, and Quality of Life

A 33% surgical revision rate was reported in an analysis of the safety of 3 RCTs comparing SNS to no treatment in patients with urge incontinence, urgency-frequency, or urinary retention. The most commonly reported adverse effects were pain at the implant site and lead migration. Despite the high rate of surgical revision, there were no reports of permanent injury or death in any of the studies or health technology assessments identified. Additionally, patients consistently said that they would recommend the procedure to a friend or family member.

Economic Analysis

One health technology assessment and 1 abstract were found that investigated the costing factors pertinent to SNS. The authors of this assessment did their own "indicative analysis" and found that SNS was not more cost-effective than using incontinence supplies. However, the assessment did not account for quality of life. Conversely, the authors of the abstract found that SNS was more cost-effective than incontinence supplies alone; however, they noted that in the first year after SNS, it is much more expensive than only incontinence supplies. This is owing to the cost of the procedure, and the adjustments required to make the device most effective. They also noted the positive effects that SNS had on quality of life.

Conclusions and Implications

In summary, there is level 2 evidence to support the effectiveness of SNS to treat people with urge incontinence, urgency-frequency, or urinary retention. There is level 4 evidence to support the effectiveness of SNS to treat people with fecal incontinence.

To qualify for SNS, people must meet the following criteria:

- Be refractory to behaviour and/or drug therapy
- Have had a successful test stimulation before implantation; successful test stimulation is defined by a 50% or greater improvement in voiding function based on the results of a voiding diary. Test stimulation periods range from 3 to 7 days for patients with urinary dysfunctions, and from 2 to 3 weeks for patients with fecal incontinence.
- Be able to record voiding diary data, so that clinical results of the implantation can be evaluated.

Patients with stress incontinence, urinary retention due to obstruction and neurogenic conditions (such as diabetes with peripheral nerve involvement) are ineligible for sacral nerve stimulation.

Physicians will need to learn how to use the InterStim System for Urinary Control. Requirements for training include these:

- Physicians must be experienced in the diagnosis and treatment of lower urinary tract disorders and should be trained in the implantation and use of the InterStim System for Urinary Control.
- Training should include the following:
  - Participation in a seminar or workshop that includes instructional and laboratory training on SNS. This seminar should include a review of the evidence on SNS with emphasis on techniques to prevent adverse events.
  - Completion of proctoring by a physician experienced in SNS for the first 2 test stimulations and the first 2 implants

Abbreviations

ASERNIP-S	Australian Safety and Efficacy Register of New Interventional Procedures – Surgical
CI	Confidence interval
MSAC	Medical Services Advisory Committee
NICE	National Institute for Clinical Excellence
OAB	Overactive bladder
RCT	Randomized controlled trial
SNS	Sacral nerve stimulation

Objective

The objective of this review was to systematically review the evidence of the effectiveness, safety, and costing of sacral nerve stimulation (SNS) to treat urinary urge incontinence, urgency-frequency, urinary retention, and fecal incontinence.

Background

Clinical Need: Target Population and Condition

This report focuses on the management of patients with urinary urge incontinence, urgency-frequency, urinary retention, or fecal incontinence. Urge incontinence is an involuntary loss of urine upon a sudden urge. Urgency-frequency is an uncontrollable urge to void, resulting in frequent, small volume voids. Urgency-frequency is often associated with interstitial cystitis and chronic pelvic pain. Urinary retention refers to the inability to void despite having the urge to void, it can be caused by a hypocontractile detrusor (weak or no bladder muscle contraction) or obstruction due to urethral overactivity. Fecal incontinence is a loss of voluntary control of the passage of liquid or solid stool. There is some evidence to suggest that people with a history of sexual abuse are more likely to suffer from urinary and fecal incontinence than the general population. (4;5)

Urge Incontinence

Urinary incontinence is often misinterpreted as a natural part of aging; however, this is not the case.. (6) Incontinence can be temporary, due to conditions such as urinary tract infections, vaginal infections, constipation; or due to an adverse effect from medications. Alternatively, incontinence can be chronic and affect patients indefinitely. Urinary incontinence is a symptom, not a disease. There are 3 types of urinary incontinence:

- *Urge incontinence* is when there is an involuntary loss of urine upon a sudden urge, ranging from mild leaking to uncontrollable wetting. It is also called hyperactive or irritable incontinence.
- *Stress incontinence* is characterized by leaking associated with laughing, coughing, jumping, and similar activities.
- *Overflow incontinence* is constant leaking or dribbling. It happens when the bladder does not empty completely.

A person may have a combination of the 3 types of incontinence. This is called *mixed incontinence*. The Canadian Continence Foundation (7) estimates that 25% of women over 40 years and 15% of men and women over 60 years have some type of incontinence.

The social implications of urinary incontinence include low self-esteem, restriction of social and sexual activities, and depression. Furthermore, urinary incontinence is often an important factor in deciding when to place elderly people in nursing homes. This has economic implications.

This report focuses on urge incontinence, because the device used during SNS is designed to manage urge incontinence only. There are 3 broad categories of urge incontinence (8):

- Motor urgency (most common) is overactivity of the bladder detrusor muscle on urodynamic testing.

- Detrusor hyperreflexia may be caused by a central neurologic deficit (e.g., a stroke or multiple sclerosis), a spinal cord injury, or a peripheral neurologic deficit, like sacral nerve root impingement syndrome (neurogenic).
- Idiopathic detrusor instability is diagnosed when there is no underlying cause identified. Postulated causes include congenital abnormalities, parasympathetic hypersensitivity, or an imbalance of neurotransmitters (non-neurogenic).
- Sensory urgency (functional incontinence) is when no overactivity of detrusor muscle can be demonstrated during urodynamic testing (non-neurogenic).
- Urethral instability is when a spontaneous reduction in pressure occurs in association with urgency (non-neurogenic).

It is important to note that SNS is indicated for people with non-neurogenic urge incontinence.

Urgency-Frequency

Urgency-frequency is characterized by the uncontrollable urge to urinate, resulting in frequent small-volume voids. One symptom of urgency-frequency is the feeling of not being able to void completely, which may or may not be associated with chronic pelvic pain. People who have urgency-frequency may void as often as every half hour and more than 4 times per night. This frequency can substantially interfere with people's quality of life and daily activities. For example, people cannot drive long distances without stopping, or attend meetings, or socialize normally. Sleep patterns are disrupted due to nocturia To cope, some people will limit the consumption of liquids and dehydrate themselves. People will also use diapers or pads to prevent accidental wetting from leaking through their clothing.

Urinary Retention

People with urinary retention are diagnosed as having complete retention (the inability to initiate a void), or partial retention (> 50 mL of residual urine in bladder after voiding). They may or may not have the sensation of fullness (i.e., feel the need to void). If they cannot sense bladder fullness, they are likely to suffer from overflow incontinence (constant leaking). The potential causes of urinary retention include weak or no bladder muscle contraction, obstruction of urethra (due to cancer, benign prostatic hypertrophy, or urethral overactivity), pelvic floor dysfunction, or an adverse effect of drug therapy. Most patients who receive SNS for urinary retention have urinary retention due to pelvic floor dysfunction (Personal communication, February 2005). Those who have urinary retention due to an obstruction will not benefit from SNS; therefore, they are not candidates for the procedure.

Urinary retention has several effects, including psychosocial implications that affect quality of life and self-esteem. There are also secondary health conditions due to increased abdominal pressure (resulting in hemorrhoids, urinary reflux, and/or kidney infection); poor fluid management; and repeated catheterizations (resulting in urinary tract infections, kidney stones, and impaired renal function).

Fecal Incontinence

Fecal incontinence refers to incontinence of flatus as well as the involuntary loss of stool. (9) Fecal incontinence can be passive or active. Passive fecal incontinence is when the person is unaware of the incontinence (i.e., has no urge). Active incontinence refers to a situation where the person is aware of the incontinence; however, he or she is unable to prevent it. Fecal incontinence may be caused by damage to the anal sphincter mechanism (through direct trauma or damage to the nerve supply), idiopathic degeneration of the sphincter, spinal injury, or other neurological conditions (e.g., multiple sclerosis). Obstetric trauma is the most important etiological factor in non-neurogenic fecal incontinence. (10) A study (11) investigating fecal incontinence found a significant association between fecal incontinence and

episiotomy ($P < .01$), forceps delivery ($P < .01$), perineal tears ($P < .01$) and hysterectomy ($P < .05$).

Existing Treatments Other Than Technology Being Reviewed

Treatments for Urge Incontinence

Generally, there are 4 broad areas of treatment for urge incontinence: behaviour modification, drug therapy, interventional therapy (including external electrical stimulation or intravesical electrical stimulation), and surgery. Diapers or pads are used throughout treatment and may be used in conjunction with the treatments. Patients who are treated successfully may still require diapers, but to a lesser extent.

Behaviour modification therapies include diet modification (avoiding caffeine, alcohol, dairy products and spices), toileting assistance (scheduled voiding), bladder training or retraining (to increase voiding volume and interval between voids), pelvic muscle rehabilitation (Kegel exercises), and biofeedback. Behaviour modification is sometimes overlooked as the first treatment option for patients with urge incontinence. (12) In a study (13) assessing the treatment of 372 patients with urge incontinence, drug therapy was the first-line treatment for 50% of the patients, and only 13% were treated with behaviour therapy first.

The evidence supporting or refuting the use of behaviour therapy to manage urge incontinence is limited. Four systematic reviews (12;14-16) have been identified that investigated behaviour therapy to manage urinary incontinence. A Cochrane review (16) of bladder training in adults with urinary incontinence reported that the studies that investigated bladder training were of variable quality and reported various outcome measures, which makes comparing the studies difficult. Wallace et al. (16) concluded that bladder training seemed effective in the management of urinary incontinence; however, they could not comment on if bladder training was better than other available treatments.

A Cochrane review by Haye-Smith et al. (14) [AU: The authors' names in text and in the citation do not match.] investigating behaviour therapy in people with urinary incontinence specifically focused on pelvic floor muscle exercises in women. They reported that pelvic floor exercises were effective to manage stress and mixed incontinence; however, the evidence supporting or refuting the use of pelvic floor exercises in women with urge incontinence was unclear. Similar to the conclusions by Wallace et al., Hay-Smith et al. reported that the studies included in their review reported various outcomes with little consistency between studies.

The authors of a systematic review (12) of randomized controlled trials (RCTs) on conservative management options for urge incontinence concluded that there was insufficient evidence to indicate that behaviour therapy, or drug therapy, or external electrical stimulation was the superior treatment. Another systematic review (15) that compared behaviour therapy with drug therapy in older patients (aged at least 55 years) with urinary incontinence (including stress, urge, and mixed incontinence) reported that drug therapy was less effective than behaviour therapy. They based their conclusion on 8 studies: 4 RCTs and 4 crossover studies. Three of the studies found that biofeedback significantly reduced the number of urge incontinence episodes compared with either drugs or placebo ($P < .05$). The other studies did not find a significant difference between treatments. None of the studies reported that drug therapy was significantly better than biofeedback.

Based on the results of these systematic reviews, it is not possible to understand fully the role of behaviour therapy in the management of urinary incontinence. Behaviour therapy seems to be effective in some groups of patients, but not in others. The success of a behaviour therapy intervention depends largely on the infrastructure supporting the intervention (Personal communication, February 2005). In other words, behaviour therapy requires resources such as staff (i.e. administrative staff, nurse continence

advisors and other specialists) and clinic space in order to effectively teach patients the behaviours. The underlying factors that predict a patient's success with behaviour therapy still need to be identified.

If behaviour modification is unsuccessful, drug therapy is prescribed. (13) There are 4 general types of drugs used to treat patients with urinary urge incontinence:

- Anticholinergic medications (e.g., oxybutynin, tolterodine): these reduce feelings of urgency.
- Smooth muscle relaxants (e.g., flavoxate): these discourage bladder muscles from tightening before the bladder is full.
- Tricyclic antidepressants (e.g., imipramine): these exert an anticholinergic effect by blocking norepinephrine or serotonin amine uptake.
- Combined anticholinergics and smooth muscle relaxants (e.g., oxybutynin chloride).

(See also Table 1, which lists some of the drugs used for managing urge incontinence and their possible adverse effects.)

There have been some relatively recent advances in the development of drug therapies for managing urge incontinence. Two drugs, tolterodine and oxybutynin, have "long-acting" or "extended release" formulations. With these, a patient needs to take only 1 pill per day, and there may be fewer adverse effects because the long-acting formulations are more stable than the original versions (Personal communication, February 2005). Dry mouth is the most common side effect in patients taking anticholinergics.

In a systematic review of tolterodine, Garely and Burrows (17) reported the results of a RCT that compared tolterodine (original version) to a placebo. They found that 35% of 986 patients in the tolterodine group reported dry mouth compared with 10% of the 683 patients in the placebo group. Garely and Burrows also reported results of a RCT that compared tolterodine long acting (Detrol LA) to a placebo and found that 24% of 505 patients in the treatment group reported dry mouth compared with 8% of the 507 patients in the placebo group. Based on these results, it seems that the new long-acting formulation may be associated with fewer adverse effects than the original; however, it is important to recognize that a trial comparing original tolterodine to tolterodine long-acting is needed for confirmation.

Before the release of these new drugs, poor compliance rates had been reported among patients using drug therapy to manage the symptoms of urinary urge incontinence because of the adverse effects of the drugs. The adverse effects reported included dry mouth, blurred vision, dry eyes, decreased sweating, and gastrointestinal effects. (18)

In 1999, Desgagne and LeLorier (18) did a retrospective study on the use of oxybutynin and flavoxate among Quebec residents aged 65 years or older (N = 6,690). They found that only 11.4% of the patients who were prescribed oxybutynin and 5.7% of the patients prescribed flavoxate were still taking the drug at 6 months. Oxybutynin has been associated with a higher adverse effect profile than tolterodine, (17;19) and according to an Ontario urologist who treats patients who have urge incontinence, flavoxate is rarely prescribed as first-line drug therapy for urge incontinence (Personal communication, February 2005). Harvey et al. (19) did a meta-analysis to compare tolterodine to oxybutynin (original versions) in patients with urge incontinence. They found oxybutynin was significantly more efficacious than tolterodine (weighted mean difference 0.41; 95% confidence interval [CI] 0.04–0.77, no *P*-value reported); however, tolterodine was associated with fewer adverse effects and lower drop-out rates. In an RCT comparing tolterodine (original version) to oxybutynin extended-release (Ditropan XL), Appell et al. (20) reported that oxybutynin extended-release was significantly more effective than tolterodine, and both drugs had similar toxicity profiles.

Herbison et al. (21) did a systematic review that compared anticholinergic drugs with a placebo in patients with urge incontinence found that there was an improvement in voiding function in patients receiving anticholinergic drugs ($P < .0001$), but that they also suffered from substantial adverse effects. Herbison et al. noted that patients receiving the anticholinergic drugs suffered from worse dry mouth ($P < .0001$). They concluded that the difference in effectiveness between the treatment and control group may not be clinically significant when combined with the adverse effects of the anticholinergic drugs. It is important to note that Herbison et al. included studies reporting on various anticholinergic drugs in their systematic review, and they included studies from 1978 in their meta-analyses of effectiveness. Drug technology has changed substantially over the past 25 years, and as mentioned previously, drugs for urinary incontinence have changed substantially over the past few years. The results of this study would be more intriguing if they had limited the scope of drugs included in their analysis and had limited the search strategy to studies less than 5 years old.

A 2004 systematic review by Siddiqui et al. (22) reported that 3 multicentre RCTs that compared oxybutynin with placebo treatment found that 28% to 51% of patients receiving oxybutynin achieved continence. Thus, between 49% and 72% failed to respond to the drug and required alternate treatments. Thus, drug therapy is effective and safe for many patients with urge incontinence, and with advances in drug technology, ideally the adverse effects of these drugs will continue to decline. Nonetheless, there is still a subset of patients for whom drug therapy does not work to control their urge incontinence.

If drug therapy is ineffective, interventional therapies are the next option. Interventional therapies for urge incontinence include external electrical stimulation, which stimulates the pelvic floor muscles, and intravesical electrical stimulation, which stimulates the inside of the bladder wall in an attempt to control micturition. Little information is available on the effectiveness of these therapies. It is important to recognize that behaviour, drug, and interventional therapies may be used together, and that the therapies are not necessarily independent of one another.

If behavioural, drug, and interventional therapies are all unsuccessful, then surgery is the next alternative. Possible surgical interventions include these:

- Enterocystoplasty, where a portion of intestine is used to reconstruct and enlarge the bladder. It is associated with complications like disturbance of bowel habit and recurrent urinary tract infections. (23)
- Bladder denervation, which involves disrupting the nerves supplying the bladder wall.
- Detrusor myomectomy, which involves removing a portion of the detrusor muscle from the dome of the bladder.
- Permanent indwelling catheterization, which involves surgically placing a catheter.
- Artifical urinary sphincter, which involves surgically placing an artificial urinary sphincter to control the flow of urine from the bladder.

These surgeries are considered a final attempt to manage urge incontinence, because they are invasive and irreversible. It is important to note that even though surgery may be able to control the voiding dysfunction, it may not lead to an overall improvement in quality of life, because of the associated adverse effects and complications (Personal communication, December 2004). The surgical revision rate for patients with artificial urinary sphincter is 50% up to 5 years after implantation. (24) Patients who fail conservative treatment and are ineligible for surgery (e.g., for various reasons, including comorbid conditions and frailty) manage their urge incontinence with diapers.

Table 1: Drugs Prescribed To Treat Urge Incontinence in Ontario

Drug	Drug Type	Typical Dosing	Adverse Effects
Frequently Used			
Oxybutynin Extended release: Ditropan XL Skin patch: Oxytrol	Anticholinergic/ Spasmolytic	2.55 mg bid to tid Ditropan XL 5–30mg daily Oxytrol Patch twice weekly (3.9 mg/day)	• Dry mouth ▪ Sensitivity to light ▪ Blurred vision ▪ Dry eyes ▪ Decreased sweating ▪ Flushing ▪ Drowsiness
Tolterodine Extended release	Anticholinergic	2 mg bid (4 mg daily for extended release)	▪ Dry mouth ▪ Abnormal vision ▪ Sensitivity to light
Imipramine (sometimes prescribed in combination with oxybutynin or tolterodine)	Anticholinergic/ Antidepressant	25–75 mg daily	▪ Gastrointestinal effects ▪ Drowsiness ▪ Weakness/tiredness ▪ Dry mouth ▪ Excitement/anxiety
New drugs To Be Approved			
Darifenacin (Enablex)	Anticholinergic (selective M3 blocker)	7.5–15 mg once daily	▪ Dry mouth ▪ Constipation ▪ Blurred vision
Solifenacin (Vesicare)	Anticholinergic (selective M3 blocker)	5–10 mg once daily	▪ Dry mouth ▪ Constipation ▪ Blurred vision
Trospium (Sanctura)	Anticholinergic	20 mg once or twice daily	▪ Dry mouth ▪ Constipation ▪ Dyspepsia ▪ Headac

Treatments for Urgency-Frequency

Non-surgical treatment options for patients with urgency-frequency are diet modification, drug therapy, and behavioural techniques (e.g., timed voiding, pelvic muscle exercises, and biofeedback). Hydrodistention is an interventional therapy for patients with urgency-frequency, in which the bladder is stretched with fluid. Stretching the bladder is thought to alter neurologic function, resulting in decreasing the transmission of pain. (25) In addition, stretching the bladder wall may stimulate production of bladder surface mucin, the normal protective coating of the bladder surface. Patients who experience chronic pelvic pain in association with urgency-frequency are sometimes prescribed narcotics to manage the pain. (26)

Surgical treatments for urgency-frequency include augmentation cystoplasty to increase the size of the bladder and bladder removal/urinary diversion. If non-surgical procedures do not work, and patients refuse or are ineligible to have surgery, then they manage their voiding condition by voiding frequently, using diapers or pads, and/or restricting fluids.

Treatments for Urinary Retention

No drug therapies were identified that effectively treated urinary retention. However, patients who have urinary retention due to benign prostatic hypertrophy are often prescribed alpha-blockers. These relax the periurethral portion of the external urethral sphincter to relieve some obstruction. Catheterization is used to reduce the volume of residual urine. Intermittent catheterization is associated with a lower infection rate than is permanent indwelling catheterization (inserting a catheter into the bladder, where it remains). Indwelling catheterization is recommended for people who are severely impaired or terminally ill.

Surgical treatments for urinary retention include urethrolysis, the removal of an anatomic obstruction in women; transurethral prostatectomy; stent placement or sphincterectomy to treat bladder neck obstruction); and urinary diversion continent pouch or orthotopic neobladder, to increase bladder size or divert urine from the bladder.

Treatments for Fecal Incontinence

Initially, the treatment options for fecal incontinence are diet change, antidiarrheal medication, and physical and behavioural therapy (such as pelvic floor exercises). Absorbent pads and anal plugs may also be used. Pads and diapers may be used throughout the course of treatment. If these treatments are not effective, then surgical interventions are the next option. These comprise sphincter repair, dynamic graciloplasty (transposition of the gracilis muscle [from upper leg] to the anus with the implantation of stimulating electrodes), and implantation of an artificial bowel sphincter. The most extreme management option for fecal incontinence is colostomy.

A Cochrane systematic review (27) investigated studies of drugs to manage fecal incontinence in adults. They found 11 trials that met their inclusion criteria; however, they noted that the studies included patients with diarrhea and/or fecal incontinence. Based on the results of the 11 small trials, there was little evidence indicating that drugs (antidiarrheal drugs and drugs that enhance anal sphincter tone) improved fecal incontinence.

The authors (28) of a systematic review of 14 studies evaluating the role of implanting an artifical bowel sphincter to manage fecal incontinence found that the benefit of the procedure is uncertain and associated with many potentially harmful side effects. A multisite case series (29) evaluating the safety and efficacy of implanting an artifical bowel sphincter for fecal incontinence reported 449 adverse effects among the 115 patients who had the procedure. Surgical intervention was required to manage 36% of these. Infection and erosion of the implanted artificial bowel sphincter were the complications that most frequently required surgical revision. Forty-one (36%) patients had their devices explanted. Despite the adverse events, the procedure was effective in 85% of the patients who still had the device implanted after 12 months.

In summary, if dietary changes, drug therapy, and physical and behavioural therapy are unsuccessful in the management of fecal incontinence, then the next option is invasive surgery, which is associated with considerable adverse effects. If a patient refuses or is ineligible for surgery, then the incontinence is managed with diapers.

New Technology Being Reviewed: Sacral Nerve Stimulation

Overview of Sacral Nerve Stimulation

During SNS, a device is implanted to stimulate electrically the sacral nerves in an attempt to manage voiding conditions. It is a reversible procedure, in that the device can be removed without permanent injury. The device was originally developed to manage urinary urge incontinence; however, it has also been used in patients with urgency-frequency, urinary retention, and fecal incontinence. According to Medtronic Inc. (Minneapolis, MN, United States), the manufacturer of the InterStim System for Urinary Control, the role of SNS is to manage patients who have not been treated successfully with behaviour therapy, drug therapy, or external stimulation.

The sacral nerves play an integral role in micturition (process for discharging urine), because the sacral nerves from the spinal cord control the bladder. The micturition reflex is a 2-part cycle consisting of: filling (storage) and emptying. For the reflex to function properly, 2 systems must be intact. First, the receptors and neurotransmitters must be balanced for the muscles to operate properly. Second, the neurosensory pathway along the brain, spinal cord, and bladder must be intact. The receptors in the bladder signal the sacral nerves that the bladder is full or empty. An interruption in this process causes voiding difficulties. SNS aims to correct the disruption between the nervous system and the bladder so that normal voiding can resume. By stimulating the sacral nerve with electrical pulses, the device mimics the signals required for normal micturition.

The level of nerve stimulation is determined by the amplitude (strength of the stimulation, measured in volts), the pulse width (duration of pulse, measures in microseconds), and the rate (the number of pulses per second).

There are 2 phases in the SNS process. Patients first must have a test stimulation to determine if they respond to the stimulation. If there is a 50% or more improvement in voiding function, then the patient is a candidate for the next phase, implantation. These phases are described in detail later in this section

Components of the Sacral Nerve Stimulator

The Medtronic InterStim System for Urinary Control is designed to stimulate the sacral nerve to control bladder function. The device creates an electrical current that flows between the negative and positive electrode lead (which is placed adjacent to a sacral nerve, most commonly S3). The electrical current requires a power source and a complete electrical circuit. These components comprise the system:

- A power source (implantable pulse generator)
- An extensive and lead system to deliver the electrical pulses
- A console programmer
- A patient programmer (with optional antenna)
- A control magnet
- A memory module software cartridge
- A test stimulation lead, foramen needles, cables, and ground pads
- A test stimulator

Phase 1: Test Stimulation

Test stimulation is the first phase. The purpose of this phase is to determine the effectiveness of the InterStim implant. During this outpatient procedure, a needle is inserted into the sacral foramen (usually S3) under local anesthesia. Once the needle is in place, the physician attempts to identify appropriate nerve stimulation responses. If nerve stimulation responses are identified, a temporary, percutaneous lead is inserted through the needle and placed near the sacral nerve. The lead is attached to an external test stimulator that attaches to the patient's waistband. The patient wears the test stimulator for 3 to 7 days if he or she has a urinary dysfunction, and for 2 to 3 weeks if he or she has fecal incontinence. Patients must keep a voiding diary while wearing the device to track their responses to it. If they have a 50% or more improvement in symptoms during this phase, then they are eligible for the implantation phase. Between one-third and one-half of patients who undergo test stimulation are successful and proceed to the implantation phase. (30-32)

Phase 2: Implantation

After a patient completes a successful test stimulation, he or she is considered for surgical implantation of the InterStim System. The device is implanted under general anesthesia in an operation that lasts about 2 hours. The surgeon makes 3 incisions: one on the lower back to place the lead next to the sacral nerve and anchor it, one in the lower abdomen or upper buttock to place the implant device, and one on the flank to connect the ends of the lead and extension. The lead is passed under the skin to the implant device. Patients are usually hospitalized for 1 to 2 days postoperatively. The device is programmed up to 1 week after the surgery. The physician and the patient each have control over the device. The physician has a programmer that adjust the device. Typically, it is programmed with a pulse width of 210 μsec, and a pulse rate of 10 pulses per second. The amplitude is normally set at 0.1 volts, but can be adjusted in 0.1-volt increments by the physician. (33) Patients can turn the device on or off, and can control the amplitude in a preset range defined by the physician. Some patients must turn the device off to void.

Regulatory Status

Health Canada licensed Medtronic's InterStim System for Urinary Control in February 2002 (Class IV, licence 14962). (All medical devices are grouped into 1 of 4 classes. Class I devices present the lowest potential risk, and Class IV devices present the greatest potential risk.) Health Canada approved the device for "the management of chronic intractable (functional) disorders of the pelvis and lower urinary or intestinal tract" (Personal communication, December 2004).

In 1998, the United States Food and Drug Administration (FDA) approved Medtronic's InterStim System for Urinary Control to treat urinary urge incontinence in patients who had failed or could not tolerate conservative treatments. Subsequently, in 1999, the FDA approved the device for the treatment of urinary retention and the symptoms of urgency-frequency in patients who had failed or could not tolerate conservative treatments. The FDA reported that about 20% of patients with urinary urge incontinence would benefit from SNS. The FDA has not approved the device for patients with fecal incontinence; however, clinical trials are underway in the United States to apply for approval for this indication.

Sacral Nerve Stimulation Use in Ontario and Canada

As of January 2005, 6 health centres in 4 provinces across Canada were using Medtronic's InterStim System for Urinary Control: Alberta, Ontario, Quebec, and Nova Scotia. On a per capita basis, Alberta is the most active province for the SNS procedure. One hospital in Ontario does SNS. It funds 12 SNS procedures per year. In January 2005, it reported that they had a waiting list of 47 people (Personal communication, January 2005).

The Toronto Western Hospital estimated that in the Metro Toronto catchment area (population about 5 million), there would be 50 new patients per year with urge incontinence, 12 new patients with urinary retention, and 20 new patients with urgency-frequency that would be identified as candidates for SNS (i.e., 80–85 SNS procedures in Metro Toronto per year) (Personal communication, December 2004).

Prevalence of Urge Incontinence

The prevalence of urge incontinence, urgency-frequency, urinary retention, and fecal incontinence is difficult to estimate, because people with these conditions may not tell their health practitioner about their symptoms due to embarrassment, or because they don't know there are treatment options available.

For this review, 6 studies were identified that examined the prevalence of urge incontinence (Table 2). Corcos and Schick (34) recently reported the results of a Canadian survey that assessed the prevalence of overactive bladder (OAB) and incontinence among Canadians aged 35 years or older. OAB is characterized by urinary urgency or the presence of involuntary bladder contractions, with or without urge incontinence. They reported that the prevalence of OAB was 18.1%. The prevalence of urge incontinence (or "wet" OAB) was 2.3% overall: 2.0% for men and 2.6% for women. They reported that 0.32% of the respondents had "severe wet OAB." The prevalence of mixed OAB (wet and dry OAB) was 0.3% for men and 2.1% for women. Corcos and Schick did not report what proportion of the patients with OAB had urge incontinence that could be managed through behavioural or drug therapies (i.e., the current standard treatment for urge incontinence).

The other Canadian study on the list was done in 2004 by Iron from the Medical Advisory Secretariat (unpublished). Iron surveyed women in Ontario on a variety of issues, including incontinence (stress and urge). Iron found that, based on the results of the survey, the prevalence of urge incontinence among women in Ontario is 6.2% and increases with age.

Table 2: Prevalence of Urge Incontinence in Men and Women by Age

Study, Year	Age, Years											
	Men						Women					
	30–39	40–49	50–59	60–69	≥ 70	All	30–39	40–49	50–59	60–69	≥ 70	All
	Prevalence of Urge Incontinence, %											
Corcos and Schick, 2004 (34)					NR	2.3					NR	6.5
Iron (MAS study), 2004						N/A		19.3		31.5	39.6	6.2*
McGrother et al., 2004 (35) (daily leaking)	NR	0.3	0.6	0.9	4.7	0.8	NR	2.0	2.9	3.3	13.8	3.5
Stewart et al., 2003 (36)	1.1	1.7	2.5	8.2	10.2	2.6	4.7	4.8	12.2	19.1	19.0	9.3
Milsom et al., 2000 (37)	NR	2.4	3.6	8.9	21.3	4.0	NR	7.8	12.3	15.2	22.8	7.4
Simeonova et al., 1999 (38)						N/A	2.2	4.5	4.8	7.8	23.9	NR
Range	1.1	0.3–2.4	0.6–3.6	0.9–8.9	4.7–21.3	0.8–4.0	2.2–4.7	2.0–7.8	2.9–12.3	3.3–19.1	13.8–23.9	3.5–9.3

*This study included women older than 15 years. The prevalence of urge incontinence was lowest among the youngest respondents.

Prevalence of Urgency-Frequency (With or Without Chronic Pelvic Pain)

In 2004, McGrother et al. (35) published the results of a survey in the United Kingdom on storage symptoms of the bladder. They surveyed 162,533 residents of the United Kingdom aged 40 years or older. They found that 1.5% of women and 1.0% of men voided at least once per half hour. They also reported that 5.5% of women and 5.3% of men voided at least 3 times per night. They did not report the incidence of pelvic pain in this population.

No studies were identified that reported the prevalence of chronic pelvic pain associated with urgency-frequency. Table 3 shows the prevalence of urgency-frequency according to age and gender.

Table 3: Prevalence of Urgency-Frequency in Women and Men by Age

Study, Year		Age, Years					
		Prevalence of Urgency Frequency, %					
		40–49	50–59	60–69	70–79	80–89	All
McGrother et al., 2004 (35)	Men	0.5	0.8	1.3	1.3	1.7	1.0
	Women	1.3	1.3	1.5	1.7	2.9	1.5
	Overall	1.8	2.1	2.8	3.0	4.6	1.3

Prevalence of Urinary Retention

It is unclear what the prevalence of chronic urinary retention is in Canada or throughout the world. Based on a study by Evans et al. (39) that investigated the prevalence and costs of long-term catheterization in patients with chronic urinary retention, they estimated that the prevalence of chronic urinary retention ranges from 0.03% to 0.07% in the general population, and is 0.5% of the population over 75 years.

Prevalence of Fecal Incontinence

Like with the other conditions described, the prevalence of fecal incontinence is difficult to estimate, because affected individuals may not consult a physician regarding the issue. Also, there are varying definitions of fecal incontinence. For the purposes of this assessment, fecal incontinence is defined as 1 or more incontinence episodes per week. This definition was chosen because this is the eligibility criterion specified in the studies (described further) investigating SNS in patients with fecal incontinence.

Three studies were found that reported prevalence for fecal incontinence using the definition above. A cross-sectional study by Perry et al. (40) of residents aged over 40 years in the United Kingdom found that among the 10,116 respondents to their survey, 1.4% reported fecal incontinence. Perry et al. also reported that 52% of the patients with fecal incontinence said their incontinence had an important impact on their quality of life. The prevalence of incontinence increased with age, but did not differ by sex. Lam et al. (11) surveyed 955 Australians regarding urinary and fecal incontinence. They reported that 1.8% of the population suffered from fecal incontinence. The other study was by Walter et al., (41) who surveyed 2000 Swedes on their bowel habits. They reported that 1.9% of the population had fecal incontinence. Thus, the prevalence of fecal incontinence across the 3 studies was relatively consistent, ranging from 1.4% to 1.9%.

Summary of Existing Health Technology Assessments

The Medical Advisory Secretariat identified 5 health technology assessments (8;10;42-44) on the role of SNS in the management of urge incontinence, urgency-frequency, urinary retention, or fecal incontinence (Table 4). One of the assessments focused specifically on fecal incontinence. (10) The others described SNS in the management of urinary dysfunctions.

National Institute for Clinical Excellence, 2004

Systematic review for the efficacy and safety of sacral nerve stimulation for faecal incontinence

The National Institute for Clinical Excellence (NICE) (10) identified 7 prospective case series (1 unpublished, 2 non-English–language) and 1 double-blind crossover trial (N = 2) that met the inclusion criteria.

Among the 6 of the 7 case series, 266 patients underwent test stimulation, and 149 (56%) of those patients had the implant procedure to manage their fecal incontinence. The main eligibility criterion for each of the 6 studies was that patients had to have failed conservative therapy. Among the 149 patients who had the SNS device implanted, there were18 adverse events. Three patients (from the same centre) had infections at the site of the implantation, 8 leads were dislodged in 7 patients, 6 patients complained of pain, and 1 patient had superficial wound dehiscence that healed uneventfully.

The authors concluded that there are several adverse effects (all manageable) associated with SNS for the treatment of fecal incontinence, and that there are limited data on the long-term effectiveness and safety of SNS. NICE supports the use SNS for fecal incontinence provided that "the normal arrangements are in place for consent, audit and clinical governance."

National Institute for Clinical Excellence, 2004

Systematic review for the efficacy and safety of sacral nerve stimulation for urinary urge incontinence and urgency-frequency

This health technology assessment by NICE National Institute for Clinical Excellence, 2004 (42) described the use of SNS for patients with urge incontinence or urgency-frequency. One RCT was included in the assessment. It was by Weil et al. (45) and compared SNS to no treatment in patients with refractory urge incontinence. They reported that SNS was an effective treatment for managing urge incontinence. This RCT will be described in more detail later in this report.

NICE concluded that the risk of patient harm was probably low, but that there were no data on the long-term effects of the device. They recommended more long-term studies to determine the long-term effectiveness, complications, and battery life. They also noted that hospital staff required adequate training and support to treat patients effectively with refractory urge incontinence.

In 2004, NICE released an Interventional Procedure Guidance relating to the evidence in its assessments. It stated that NICE supports the use of SNS for urge incontinence and urgency-frequency provided that "the normal arrangements are in place for consent, audit and clinical governance." (46)

Australian Safety and Efficacy Register of New Interventional Procedures–Surgical, 2003

Sacral nerve stimulation for treatment of urge incontinence

Australian Safety and Efficacy Register of New Interventional Procedures–Surgical (ASERNIP–S) (43) released a rapid review in the same year as the NICE assessment. Both of the publications were similar in terms of their literature searches (including sources searched and that both searched up until October 2002) and the number of eligible studies identified. However, because the ASERNIP-S publication was a rapid review, it had substantially fewer details than did the NICE assessment. Nonetheless, both reached similar conclusions – that SNS seems to manage chronic urge incontinence effectively, but that there are

substantial surgical revision and complication rates associated with it.

Medical Services Advisory Committee, 2000

Sacral nerve stimulation for refractory urinary urge incontinence or urinary retention

The Medical Services Advisory Committee in Australia (MSAC) (44) published a health technology assessment on SNS for refractory urge incontinence or urinary retention in 2000. It included studies investigating SNS in patients with refractory urge incontinence or urinary retention. Their assessment was based primarily on 2 RCTs: one by Schmidt et al. (32) comparing SNS to no treatment in patients with refractory urge incontinence and an abstract of an RCT by Grunewald et al. (47) comparing SNS to no treatment in patients with refractory urinary retention. (The full study was published in 2001 by Jonas et al. (31))

The MSAC reported that both of the RCTs had "methodological deficiencies" that limited the strength of the results. These included not describing the method of randomization or concealment of allocation. Furthermore, more than 20% of the sample was omitted from the analysis of the results without any explanation. Tthe same group of investigators did both of the RCTs, which were thus subject to the same flaws in methods. They are described in detail further in this review.

The MSAC recommended that "public funding for sacral nerve stimulator implantation should not be supported at this time" based on a lack of long-term efficacy data and the high rate of adverse events.

Blue Cross and Blue Shield Association, 2000

Sacral nerve stimulation for the treatment of refractory urge incontinence

The RCT by Schmidt et al. (32) formed the basis of the evidence for the Blue Cross and Blue Shield Association's assessment.(8) The RCT compared SNS to no treatment in patients with refractory urge incontinence. Whereas the authors of the MSAC assessment noted that this RCT neglected to indicate what happened to the 20% of the patients omitted from the analysis, the Blue Cross and Blue Shield Association assessment reported that the patients were omitted because there was insufficient follow-up data. It is unclear where the Blue Cross obtained this information because it is not reported in the study.

Table 4: Summary of Health Technology Assessments and Systematic Reviews on Sacral Nerve Stimulation*

Study, Year	Condition	Sources	Years	Studies Found	Conclusions
NICE, 2004 (10)	Fecal incontinence	MEDLINE, EMBASE, Science Citation Index, Cochrane Library, CINAHL, BIOSIS, and Current Controlled Trials	1966–May 2003	7 case series and 1 double-blind crossover study (N = 2)	▪ No reports of longstanding complications from SNS implantation ▪ "SNS appears to be efficacious in patients with a range of causes of incontinence."
NICE, 2004 (42)	Urge incontinence, and urgency-frequency	MEDLINE, PreMEDLINE, EMBASE, Current Contents, PubMed, Cochrane Library, and Science Citation Index	Up to October 2002	3 RCTs 22 case series	▪ Effectiveness is uncertain over long-term (> 10 years). ▪ If the procedure is to be undertaken, hospitals need adequate training and support. ▪ One-third of patients with implant report complications.
ASERNIP-S, 2003 (43)	Urge incontinence	MEDLINE, PreMEDLINE, EMBASE, Current Contents, PubMed, Cochrane Library, Science Citation Index	Up to October 2002	1 HTA (MSAC) 1 RCTs 2 case series	▪ The overall clinical results are positive for patients with chronic urge incontinence. ▪ The rates of surgical revisions and complications are high.
MSAC, 2000 (44)	Urge incontinence, and urinary retention	MEDLINE, HealthStar	1988–October 1999	2 RCTs 17 case series	▪ Intervention is associated with a relatively high rate of adverse events (51.6% experienced adverse event). ▪ Long-term effectiveness is uncertain. ▪ Cost-effectiveness ratios associated with the intervention are unfavourable. ▪ Public funding for SNS should not be supported at this time.
Blue Cross and Blue Shield, 2000 (8)	Urge incontinence	MEDLINE, Current Contents	1966-March 2000	1 RCT	▪ High rate of adverse events. ▪ It is likely that SNS is a more effective treatment option than available alternatives. ▪ There are not enough long-term data on battery life and replacement.

* ASERNIP-S indicates Australian Safety and Efficacy Register of New Interventional Procedures-Surgical; HTA, health technology assessment; MSAC, Medical Services Advisory Committee; NICE, National Institute for Clinical Excellence; RCT, randomized controlled trial; SNS, sacral nerve stimulation.

Literature Review on Effectiveness

Objective

To assess the effectiveness, safety, and costing of SNS for refractory urinary urge incontinence, urgency-frequency, urinary retention, and fecal incontinence.

Questions Asked

- Is SNS effective in the management of refractory urinary urge incontinence, urgency-frequency, urinary retention, and/or fecal incontinence?
- Is SNS safe?
- Does SNS improve the quality of life of patients with refractory urinary urge incontinence, urgency-frequency, urinary retention, and/or fecal incontinence?
- What are the economic implications of SNS for any or all of the conditions?

Outcomes of interest

To address effectiveness, the following outcomes were examined:

- Urge incontinence: leakage episodes/day; number of diapers/day; severity of incontinence
- Urgency-frequency: number voids/day; volume/void; urgency before void; pelvic pain measurement
- Urinary retention: number of catheterizations/day; volume/catheterization
- Fecal incontinence: number of incontinent episodes per time period (day, week, month, etc); urgency (ability to defer defecation)

To evaluate safety, these outcomes were examined:

- Adverse effects
- Complication rate
- Number of explants
- Number of revision surgeries required

Quality of life was assessed as follows:

- Quality of life scores
- Patient satisfaction

Methods

Inclusion Criteria

Studies were included in this report if they met of the following criteria:

- Systematic reviews, non-RCTs, case series, or retrospective studies published since 2000, that were not previously reported in the health technology assessments
- RCTs comparing SNS to no treatment or an alternative treatment

- Included patients with refractory urge incontinence, urgency-frequency, urinary retention, and/or fecal incontinence
- Included patients with non-neurogenic conditions
- Reported at least one outcome of interest
- Included ≥10 patients who received an implant (not just test stimulation)
- English-language studies
- Abstracts or full reports

Exclusion Criteria

Studies were excluded from this report if any of the following applied:

- Duplicate publications (superseded by another publication by the same investigator group, with the same objective and data)
- They included patients with various voiding conditions and did not report results for each voiding condition separately
- Published in a language other than English
- Non-systematic reviews, letters, editorials, or case reports
- Animal or in-vitro studies
- Studies that did not report any of the outcomes of interest

Databases and Search Strategy

- Search date: November 6, 2004
- Databases searched: Cochrane Library International Agency for Health Technology Assessment (third quarter 2004); Cochrane Database of Systematic Reviews (third quarter 2004); Cochrane Central Register of Controlled Trials (third quarter 2004); MEDLINE (1966 to October 2004); MEDLINE In-Process and Other Non-indexed Citations (1966 to November 5, 2004); and EMBASE (1980 to 2004 week 44)
- Search terms: sacral nerve stimulation, sacral nerve neuromodulation, neuroprosthesis, urinary incontinence, urinary retention, urge incontinence, fecal incontinence

The Medical Advisory Secretariat also conducted Internet searches of Medscape and the manufacturer's Web site (2) to identify product information and recent reports on trials that were unpublished but were presented at international conferences. In addition, the Web site Current Controlled Trials (3) was searched for ongoing RCTs investigating the role of SNS in the management of voiding conditions.

The detailed literature search strategy is in Appendix 1.

Results of Literature Review

Summary of Medical Advisory Secretariat Review

Four RCTs were identified that met the inclusion criteria for this review. (30-32;45) Two compared SNS to no treatment in patients with urge incontinence, 1 compared SNS to no treatment in patients with urgency-frequency, and 1 compared SNS to no treatment in patients with urinary retention. In addition to the 4 RCTs, the Medical Advisory Secretariat identified 9 prospective case series, 4 retrospective studies, and 4 abstracts.

Table 5: Quality of Evidence of Included Studies

Study Design	Level of Evidence	Number of Eligible Studies*					
		UI	U-F	UR	FI	Long-Term Follow-up	Quality of Life
Large RCT, systematic reviews of RCT	1	---	---	---	---	---	---
Large RCT unpublished but reported to an international scientific meeting	1(g)†	---	---	---	---	---	---
Small RCT	2	2	1	1	---	---	---
Small RCT unpublished but reported to an international scientific meeting	2(g)	---	---	---	---	---	---
Non-RCT with contemporaneous controls	3a	---	---	---	---	---	---
Non-RCT with historical controls	3b	---	---	---	---	---	---
Non-RCT presented at international conference	3(g)	---	---	---	---	---	---
Surveillance (database or register)	4a	---	---	---	---	---	---
Case series (multisite)	4b	---	---	---	2	---	1
Case series (single site)	4c	---	2	---	1	3	---
Retrospective review, modeling	4d	---	1	1	---	---	---
Case series presented at international conference	4(g)	---	---	---	---	3	---
Total		2	4	2	3	6	1

*FI indicates fecal incontinence; HTA, health technology assessment; RCT, randomized controlled trial; U-F, urgency-frequency; UI, urge incontinence; UR, urinary retention
†g indicates grey literature.

Urge Incontinence

In 1999, Schmidt et al. (32) reported the results of a prospective, multicentre, non-blinded RCT that investigated the effectiveness of SNS compared with no treatment in patients with urge incontinence who were refractory to standard treatments (including behaviour modification and medications). One hundred and fifty-five patients were eligible for the trial, and underwent sacral nerve test stimulation. Ninety-eight patients had success with the test stimulation, and thus were randomized to receive either SNS or no treatment. Schmidt et al. did not note if they compared the treatment and control groups at baseline to ensure equivalency between groups on age, sex, previous treatments for incontinence, and duration of incontinence symptoms. After 6 months, the patients in the control group were offered the SNS procedure. Schmidt et al. (32) only reported 6-month follow-up data for 76 patients. They did not discuss what happened to the remaining 22 patients. Originally, 4 of these had been randomized to the control group, and 18 had been randomized to the treatment group.

Schmidt et al. also did not report an intent-to-treat analysis. That is, they conducted their analysis of the data based on 76 patients, rather than the whole randomized sample of 98 patients. This is problematic, because it is unclear from the study what happened to these patients, especially considering most of the missing patients were from the treatment group (n = 18). The patients could have been missing for a variety of reasons, including insufficient data at the time of analysis to include them in the 6-month follow-up; drop-out due to adverse effects or ineffectiveness; or living far away from the treatment centre. In their analysis of the 76 patients, Schmidt et al. reported that the number of daily incontinence episodes, the severity of the incontinence, and the number of pads used daily decreased for patients in the treatment group compared with those in the control group at 6 months ($P < .0001$).

The Medical Advisory Secretariat reanalyzed Schmidt et al.'s results and included all patients who were randomized (N = 98). Based on the data available in the study, the Medical Advisory Secretariat conservatively assumed that all 18 missing patients in the treatment group failed to respond to SNS, and the 4 missing patients in the control group showed no improvement at 6 months compared to baseline. Table 6 compares Schmidt et al.'s results with 76 patients to the Medical Advisory Secretariat's intent-to-treat results. Even when all of the missing patients were included in the analysis as having failed treatment, the results still indicate a significant improvement in the patients receiving SNS compared to no treatment ($P \leq .001$). Even though there were limitations in the design and reporting of this RCT, it seems that SNS is effective in patients with urge incontinence compared to no treatment.

Table 6: Comparison of Schmidt et al.'s (32) Results and the Medical Advisory Secretariat's Intent-to-Treat Analysis

Variable	Schmidt et al.'s (32) Analysis		Medical Advisory Secretariat's Intent-to-Treat Analysis*	
Daily incontinent episodes at 6 months	Treatment (n = 34)	Control (n = 42)	Treatment (n = 52)	Control (n = 46)
Zero leaks	16 (47%)	0 (0%)	16 (31%)	0 (0%)
Significant reduction	10 (29%)	2 (5%)	10 (19%)	2 (4%)
Slight reduction	5 (15%)	9 (21%)	5 (10%)	9 (20%)
No reduction	3 (9%)	31 (74%)	21 (40%)	35 (76%)
Chi-square		45.2		25.7
P		≤.0001		≤.001
Severity of heavy incontinence episodes at 6 months	Treatment (n = 26)	Control (n = 37)	Treatment (n = 52)	Control (n = 46)
Zero leaks	20 (77%)	3 (8%)	20 (38%)	3 (6%)
Significant reduction	4 (15%)	1 (3%)	4 (8%)	1 (2%)
Slight reduction	2 (8%)	6 (16%)	2 (4%)	6 (16%)
No reduction	0 (0%)	27 (73%)	26 (50%)	36 (79%)
Chi-square		42.7		17.7
P		≤ .001		≤ .001
Pads or diapers replaced daily at 6 months	Treatment (n = 30)	Control (n = 42)	Treatment (n = 52)	Control (n = 46)
Zero leaks	15 (50%)	1 (2%)	15 (29%)	1 (2%)
Significant reduction	11 (37%)	2 (5%)	11 (21%)	2 (4%)
Slight reduction	2 (7%)	10 (24%)	2 (4%)	10 (22%)
No reduction	2 (7%)	29 (69%)	24 (46%)	33 (72%)
Chi-square		46.6		25.0
P		≤ .001		≤ .001

*This analysis assumed the patients whose results were not reported failed to respond to treatment.

The RCT by Weil et al. (45) randomized 44 patients with refractory urge incontinence to receive either SNS (treatment) or to continue their prior conservation management (control). At 6 months, the patients in the control group also underwent SNS. At 6 months, Weil et al. reported that the mean number of

incontinent episodes per day, mean leakage severity, and the mean pad usage was significantly lower in the treatment group than the control group ($P < .05$). It is not clear whether the study was powered to detect a significant difference in the outcomes between the treatment and the control group. Table 7 describes the characteristics of the 2 RCTs.

Table 7: Patient Characteristics in Randomized Controlled Trials on Urge Incontinence*

Study	Successful Test Stimulation† N (%Total)	Eligibility criteria	Dropped Out/Not Enough Data at 6 months to Include	Mean Incontinence Episodes/ Day, Baseline	Mean Incontinence Episodes/ Day, 6 Months	*P*
Weil et al., 2000 (45)	44/88 (50%)	▪ > 16 years ▪ refractory to std treatment ▪ 100 mL bladder capacity ▪ good surgical candidate ▪ able to complete study documentation and return for follow-up evaluation ▪ no neurogenic conditions or stress incontinence	6/44 (14%)	Treatment 13.5 (95% CI 10.3–16.7) Control 10.0 (95% CI 7.5–12.5)	Treatment 1.4 (95% CI 0.0–3.2) Control 11.2 (95% CI 8.9–13.5)	Treatment baseline vs. 6 months < .0005 Treatment vs. control at 6 months < .0005
Schmidt et al., 1999 (32)	98/155 (63%)	▪ > 16 years ▪ refractory to std treatment ▪ 100 mL bladder capacity ▪ good surgical candidate ▪ able to complete study documentation and return for follow-up ▪ no neurogenic conditions, stress incontinence, or pelvic pain	43/98 (43%)	Treatment 9.7 (SD, 6.3) Control 9.3 (SD, 4.8)	Treatment 2.6 (SD, 5.1) Control 11.3 (SD, 5.9)	Treatment baseline vs. 6 months < .0001‡ Treatment vs. control at 6 months < .0001‡

*CI indicates confidence interval; NR, not reported; pts, patients; RCT, randomized controlled trial; std, standard.
†Patients who had successful test stimulation results: they had ≥50% reduction in baseline voiding symptoms.
‡Does not account for patients lost to follow-up.

Urgency-Frequency

Hassouna et al. (30) investigated the role of SNS among patients with urgency-frequency. This study was done by the same group who did the RCT for urge incontinence (32) and the RCT for urinary retention (31).

Hassouna et al. did not indicate how many patients underwent the test stimulation procedure. Rather, they reported that 51 patients had successful test stimulation results and thus were randomized to receive either SNS or no treatment. A study by Siegel et al. (48) on the long-term results of this study noted that 220 patients with urgency-frequency underwent test stimulation. This suggests that only 23% of the patients had successful test stimulations and therefore were eligible for inclusion in Hassouna et al.'s RCT. Of note is that Hassouna et al. did not compare the treatment and control groups at baseline to ensure their demographic information was similar. Like the other RCTs, patients in the control group were offered SNS after 6 months.

Hassouna et al. compared the mean volume per void between the treatment and the control group at 6 months, and found that it significantly increased among patients in the treatment group compared with those in the control group ($P < .0001$). They also compared outcomes of patients in the treatment group at baseline to those of patients in the treatment group at 6 months, and found that there was a significant improvement in the amount voided at 6 months compared to baseline ($P < .01$). Based on the data in the study, the Medical Advisory Secretariat calculated unpaired t-tests for the treatment and control groups at 6 months for all outcomes, assuming a normal distribution of outcomes (Table 8). All of the outcomes were significant, with the exception of detrusor pressure at first sensation of fullness.

Table 8: Trial Outcomes for Randomized Controlled Trail Comparing Treatment to Control Group at 6 months (30)

Variable	Treatment Mean at 6 months (95% Confidence Interval)		Control Mean at 6 months (95% Confidence Interval)		*P*
	n		n		
At first sensation of fullness: Bladder volume, mL	23	161 (42–280)	25	92 (23–161)	< .0001
Detrusor pressure, cm H_2O	23	4.6 (0–9.5)	24	4.5 (0–9.7)	.89
At maximum fill volume or just before void: Bladder volume, mL	24	325 (140-510)	25	227 (123–331)	< .0001
Detrusor pressure, cm H_2O	23	11.8 (0–29)	24	7.0 (0–15.1)	.02
Peak detrusor pressure during cystometry, cm H_2O	22	16.5 (0–38.3)	23	9.8 (0–20.0)	.01
Volume at peak detrusor pressure, mL	21	302 (137–467)	24	212 (98–326)	< .0001

Hassouna et al. did not measure pelvic pain in association with urgency-frequency in their study; however, 3 studies (1 retrospective review (49), 2 case series (26;50)) were identified that examined the use of SNS in patients with chronic pelvic pain associated with urgency-frequency. Table 9 briefly outlines these studies.

A retrospective study of 21 women suffering from interstitial cystitis (a symptom complex of urinary urgency-frequency and pelvic pain) who underwent SNS reported that these women significantly decreased their intake of narcotics to manage pelvic pain. (49) Four patients stopped using narcotics after implantation, and the mean reduction in morphine dose was 36%. The authors of the study did not indicate how long the women were followed-up and if the reduction in morphine dose was maintained over time. The prospective case series by Comiter et al. (50) reported a significant decrease in pelvic pain in patients who underwent SNS at median follow-up ($P < .01$). The other prospective case series did not report statistical significance values; however, they did report that on a scale of 0 to 10 (10 being the most painful), patients scores fell from a mean of 9.7 before implantation to 4.4 at median follow-up. (26)

Table 9: Non-Randomized Studies of Pelvic Pain Associated With Urgency-Frequency

Study	Type of study	N (% Female)	Mean Age, Years	Mean Follow-up, Months	Pain Score at Baseline	Pain Score at Median Follow-up	*P*
Peters and Konstandt, 2004 (49)	Retrospective	21 (81)	45.5 (17–68)	15.4 (7.4–23.1)	7-point scale (no values reported). Mean follow-up versus baseline		*P* < .05
Comiter et al., 2003 (50)	Prospective case series	25 (96)	46 (22–77)	14 (2–28)	5.8 (SD, 2.2) (0–10 scale)	1.6 (SD, 1.5)	< .01
Siegel et al., 2001 (26)	Prospective case series	10 (90)	Median 48 (22–60)	Median 19 (6–74)	9.7 (0–10 scale)	4.4	NR*

*NR indicates not reported.

Urinary Retention

One RCT (31)was identified that compared the role of SNS to no treatment in patients with urinary retention. (Patients with retention due to obstruction were excluded.) Jonas et al. reported that 177 patients with urinary retention underwent test stimulation; however, only 68 (38%) were successful. Thirty-seven patients were randomly assigned to have SNS, and 31 were randomized to receive no treatment. The patients in the control group were offered SNS after 6 months. Even though 68 patients were randomized, results were only reported for 51 patients. Of the missing 17 patients, Jonas et al. wrote, "6 [patients] were not yet enrolled for 6 months, 3 had been lost to follow-up and 8 were in the study but did not turn in a voiding diary." Jonas et al. did not account for these patients in their analysis, thus they did not report an intent-to-treat analysis. Of the missing patients, 8 were in the treatment group and 9 were in the control group. Jonas et al. did not report the reasons for missing patient data according to treatment group. Nor did they compare the treatment and control groups at baseline to ensure similarity across demographic characteristics.

In their analysis of the 51 patients, Jonas et al. reported that the number catheterizations per day significantly decreased in the treatment group compared with those in the control group at 6 months ($P < .0001$). The Medical Advisory Secretariat reanalyzed Jonas et al.'s results to include all patients who were randomized to the study originally (N = 68). Based on the data available, the Medical Advisory Secretariat conservatively assumed that the 8 missing patients in the treatment group failed to respond to SNS t, and the 9 missing patients in the control group showed no improvement in the number of daily catheterizations at 6 months compared to baseline. Table 10 shows the comparison. Even when all of the missing patients were included in the analysis as having failed treatment, there was still a significant improvement in the number of daily catheterizations at 6 months for the patients who had SNS ($P \leq .001$).

Table 10: Comparison of the Results From Jonas et al. (31) on Daily Catheterizations With the Medical Advisory Secretariat's Results

Variable	Jonas et al.'s analysis (31)		Medical Advisory Secretariat's Intent-to-Treat analysis	
Catheterizations per day at 6 months	Treatment (n = 29)	Control (n = 22)	Treatment (n = 37)	Control (n = 31)
Zero catheterizations	20 (69%)	2 (9%)	20 (54%)	2 (6%)
Significant reduction	4 (14%)	0 (0%)	4 (11%)	0 (0%)
Slight reduction	4 (14%)	12 (55%)	4 (11%)	12 (39%)
No reduction	1 (3%)	8 (36%)	9 (24%)	17 (55%)
Chi-square		27.7		24.9
P		$\leq$ .0001		$\leq$ .001

Jonas et al. reported the results of the RCT by comparing the outcomes of the treatment group at baseline to the outcomes of the treatment group at 6 months, rather than reporting the outcomes in the control group compared to the outcomes in the treatment group. Based on the data provided in the study, the Medical Advisory Secretariat has calculated unpaired t-tests, assuming a normal distribution of outcomes. Table 11 details the results of this analysis. All 6 outcomes measured were significantly improved after 6 months in the treatment group compared to the control group ($P < .0001$).

Table 11: Outcomes for Jonas et al.'s Randomized Controlled Trial: Treatment and Control Groups at 6 months (31)

Variable	Treatment Group (n = 29) Mean at 6 Months (95% Confidence Interval)	Control Group (n = 22) Mean at 6 Months (95% Confidence Interval)	*P*
Catheter volume/catheterization, mL	49 (0–155)	319 (124–514)	< .0001
Number of catheterizations/day	1.4 (0–4.0)	3.9 (1.7–6.1)	< .0001
Total catheter volume/day, mL	237 (0–801)	1305 (415–2195)	< .0001
Maximum catheter volume. mL	72 (0–217)	484 (192–776)	< .0001
Number of voids/day	6.5 (3.4–9.6)	2.9 (0–7.2)	< .0001
Total volume voided/day, mL	1808 (929–2687)	488 (0–1218)	.0001

In addition to the RCT by Jonas et al. (31), a retrospective study was identified that examined SNS in patients with urinary retention. Dasgupta et al. (51) reviewed the case records of 26 women with urinary retention who had undergone SNS between 1996 and 2002. Twenty-five (96%) of the 26 women regained voiding function immediately after surgery; however, after a mean follow-up of 37 months (range 2 to 73 months) 20 (77%) women were voiding spontaneously.

Fecal Incontinence

In July 2004, NICE published a thorough systematic review of the efficacy and safety of SNS in patients with fecal incontinence. (10) The review identified 6 prospective case series (1 unpublished, 2 non-English-language), 1 double-blind crossover trial (N = 2), and a prospective non-RCT that met the inclusion criteria. Since the release of the systematic review, 3 additional case series (52-54) were identified. No RCTs were identified that compared SNS to no treatment in patients with fecal incontinence. The case series are described in Table 12.

A multisite study (55) reported in the NICE systematic review was published in German in 2003. Since the publication of the systematic review, the multisite study has been published in English. (54) The multisite case series study by Jarrett et al. (53) reported that of the 46 patients who underwent SNS, all but 2 had improved continence functioning after a median follow-up of 12 months. Nineteen (41%) patients were fully continent at the median follow-up. In the 39 patients where there were measurements for the ability to defer defecation, all but 5 of them had improved in delaying defecation from a median of 1 minute at baseline to 10 minutes at median follow-up ($P < .001$). All 3 case series reported there was a significant decrease in weekly incontinence episodes at median follow-up in patients with fecal incontinence who had the SNS device.

Table 12: Case Series on the Role of Sacral Nerve Stimulation in the Management of Fecal Incontinence

Study, Year	Mean Age, Years (Range)	N (% Female)	N With Successful Test Stimulation† (% of total)	Median Follow-up, Months (Range)	Mean Incontinence Episodes Weekly (Range)		*P*
					Baseline	Median follow-up	
Jarrett, 2004 (53) (multisite)	Median 56 (35–68)	59 (87)	46 (78)	12 (1–72)	7.5 (1–78)	1 (0–39)	< .001
Matzel, 2004 (54) (multisite)	54.3 (NR)*	37 (89)	37 (100)	23.9 (NR)	16.4 (NR)	At 12 months: 3.1 (NR)	< .0001
Uludag, 2004 (52) (single site)	52 (26–75)	75 (88)	56 (75)	12 (NR)	7.5 (NR)	0.67 (NR)	< .001

* NR indicates not reported.
†Patients who had successful test stimulation results: they had ≥ 50% reduction in baseline voiding symptoms.

Long-Term Follow-up

There are still several unanswered questions about long-term follow-up. Medtronic Inc. reports that the battery should last 5 to 10 years depending on the use of the device, but no studies were identified that included patients to the point of battery failure. Six studies (including 3 abstracts) (48;51;56-59) were identified that reported long-term follow-up results for patients who had received SNS. The length of follow-up varied across the studies, ranging from 1.5 years to more than 5 years. The rate of explantation ranged from 11.5% to 20.5%. All of the studies reported that the implant was still effective in the majority of the patients at the time of follow-up. Table 13 provides an overview of these studies.

In the study by Dasgupta et al. (51) 26 women with urinary retention underwent SNS. Immediately after surgery, 25 women were voiding spontaneously. After a median follow-up of 37 months, 20 (77%) women were voiding spontaneously. Three women reported loss of efficacy and 2 had their stimulators deactivated because of pregnancy. Loss of efficacy was the most frequently reported complication. Dasgupta et al. reported 7 episodes of loss of efficacy. (They did not indicate the number of patients which experienced loss of efficacy.)

Siegel et al. (48) reported long-term follow-up of the patients included in the RCTs by Schmidt et al. (32), Hassouna et al. (30) and Jonas et al. (31) investigating the role of SNS in patients with urge incontinence, urgency-frequency, and urinary retention, respectively. This case series was included in previous health technology assessment, but the Medical Advisory Secretariat chose to include it because it reported on the 3 RCTs described in this systematic review. They reported long-term follow-up for 112 patients included in the 3 studies. They defined long-term follow-up as 1.5 to 3 years after SNS. Their analysis included 23 (20%) patients who had the device explanted. Despite the explantations, Siegel et al. reported that the patients had maintained significant improvements in bladder function in the 3 years since implantation. This was the case for the 3 subgroups of patients: those with urge incontinence; urgency-frequency; and urinary retention. The surgical revision rate was 33%. The most frequent revisions were relocation of the stimulator due to pain and readjustment of the lead after migration. Despite these revisions, 84% of the patients who had the implant said they were satisfied with it and would recommend it to a friend or family member.

Janknegt et al. (59) also reported long-term follow-up data from the patients in Schmidt et al.'s RCT (32). There is overlap between this study and the results reported by Siegel et al.; (48) however, it is not possible to tell how many patients were included in both analyses. They reported long-term (at least 12 months) follow-up results for 96 patients who had had SNS for refractory urge incontinence. Similar to the case series by Siegel et al., this study was reviewed in other health technology assessments; however, it was included in the review because it provided follow-up of the patients in one of the RCTs reported in this assessment. Eleven (11%) explants were reported among the 96 patients: 9 patients had explants because the device didn't work, 1 had an explant due to chronic leg pain, and 1 had an explant due to a bowel dysfunction. After a mean of 30.8 months (range, 12 to 60 months), 25 patients reported no daily incontinence episodes, and 35 reported daily incontinence episodes were lower by at least 50%, resulting in an overall success rate of 62%. At baseline, 90 patients reported using diapers or pads to manage leaks. At the mean follow-up, 30 patients said they no longer used pads, and 25 patients reported a reduction in diaper usage by at least 50%.

Additionally, Janknegt et al. attempted to establish factors that would predict success with SNS. They compared sex, age, psychological history, previous surgical procedures, duration of urinary symptoms, number of test stimulation procedures, lead location, medication use at 12 months and neurostimulator polarity (unipolar versus bipolar) in patients for whom SNS was successful, and in those for whom it was not. The significant difference in success with SNS was sex-based. They reported that 10 (91%) of the 11 men in the study had success with SNS compared to 50 (59%) of the 85 women in the study ($P = .048$). This result should be interpreted cautiously because the ratio of men to women was unbalanced. In all of the studies, there were more women than there were men.

In a 2004 abstract for the International Continence Society Conference, van Voskuilen et al. (56) reported follow-up results for 157 patients (82% women) who had SNS implants for urinary urge incontinence (70%) or urinary retention (30%). The mean age at implantation was 47.5 years. At a mean follow-up of 64 months (range 13–154 months), 61% of the patients had "good results." This was defined as "complete and lasting disappearance of symptoms or satisfactory symptom relief." Among the 157 patients, 118 (75%)reported at least 1 adverse event. Thirty-four patients had surgical revision to manage the adverse events. Thirty-one patients had their devices explanted. The length of time until the explantation was not reported in the abstract.

Table 13: Details of Long-Term Follow-up Data Across Studies on Sacral Nerve Stimulation*

Study, Year	Voiding Condition	N With Implant	Mean Follow-up (Range)	Patients With ≥ 50 Improvement at Follow-up, %	Explants, No. (%)
Dasgupta et al., 2004 (51)	UR	26	37 (2–73)	77	3 (11.5) lack of efficacy
van Voskuilen et al., 2004 (56)	UI, UR	157	64 (25.7–102.3)	Overall: 60.8UI: 57.6 UR: 71.7	31 (19.8) (lack of efficacy or adverse event)
van Voskuilen et al., 2004 (57)	UI, U-F, UR	93	NR Minimum 60 months	UI: 64.2 U-F: 66.7 UR: 76.0	14 (15.1) (lack of efficacy or adverse event)
Bemelmans et al. , 2002 (58)	U-F	57†	35 (23–47)	73	10 (13.5) (lack of efficacy or adverse event)
Janknegt et al., 2001 (59)‡	UI	96	30.8 (12–60)	62	11 (11.5) (9 lack of efficacy, 1 pain, 1 bowel dysfunction)
Siegel et al., 2000 (48)‡	UI, U-F, UR	112	NR Minimum 18 to 36 months	UI: 59 U-F: 69 UR: 70	23 (20.5) (no details provided)

*NR indicates not reported; U-F, urgency-frequency; UI, urge incontinence; UR, urinary retention
†74 patients received an implant; however, only 47 completed the voiding diary 12 months after implantation.
‡There is overlap in the patients included in Janknegt et al.'s (59) and Siegel et al.'s (48) studies.

Safety, Complications, and Quality of Life

To evaluate safety, complications, and quality of life associated with having SNS, studies for urge incontinence, urgency-frequency, urinary retention, and fecal incontinence, were combined. Table 14 shows the complications and adverse effects encountered by patients in the studies included in this review.

Siegel et al. (48) reported long-term follow-up results on the patients included in the RCTs by Schmidt et al. (32), Hassouna et al., (30) and Jonas et al. (31) on SNS in patients with urge incontinence, urgency-frequency and urinary retention, respectively. There was a 33% surgical revision rate among the 219 patients in the 3 studies. Nonetheless, 84% of the patients said they would repeat the procedure and would recommend it to a friend or family member.

Das et al.'s prospective case series (60) measured depression and health-related quality of life in patients who had SNS. The sample for this study comprised patients in the same RCTs noted above. Das et al. did not explain why they reported on depression and quality of life for only 89 patients, when there were 219 patients in the 3 studies. They found that 73% of the patients had some degree of depression at baseline. At 3 months, 41% of the patients in the treatment group had some degree of depression compared with 73% of patients in the control group ($P < .05$). These degrees of depression were consistent at 6 months and 12 months for both groups.

However, when the depression scores were analyzed according to bladder dysfunction, only patients with

urge incontinence who had SNS showed a significant improvement in depression scores at 3 months compared to the control group. There was no significant difference in depression among urge incontinence patients only at 6 months. Patients with urgency-frequency and urinary retention who received SNS did not report significantly improved depression scores compared with patients with the same diagnoses who did not receive SNS at 3 or 6 months. This could be because the study was not powered to detect differences among subgroups of patients.

Dasgupta et al. (51) did a retrospective study of 26 women who had had SNS for urinary retention. They found that 54% of the women required surgical revision after surgery, mostly due to loss of effectiveness (27%), pain at the implant site (23%), and leg pain (23%). No explants were reported; however, the authors did not indicate if the surgical revisions improved effectiveness or relieved pain.

Jarrett et al. (53) did a multisite case series of 46 patients who had SNS for fecal incontinence. They compared scores on quality of life at the last follow-up to scores at baseline and found that general health was significantly better ($P = .024$), as was mental health ($P = .008$), social function ($P = .013$), and vitality ($P = .009$).

t is interesting to note that Jarrett and colleagues compared the quality of life scores for the patients in the study to the mean scores of residents in the United Kingdom. Even though the scores improved from baseline to last follow-up, they were still lower than the national mean scores in the United Kingdom. For instance, the score for general health at baseline was 49 (out of 100), and it increased to 55 at last follow-up; however, the mean score in the United Kingdom was 72 for general health. They did not provide a statistical comparison between the mean scores of the United Kingdom and the patients in their study. Matzel et al. (54) also reported improvements in quality of life from baseline to 12 months after implantation in patients with fecal incontinence; however, the scores were still lower than in the general population of the United Kingdom. The only 2 variables where the patients improved enough to match the United Kingdom's general population score were social functioning ($P = .0002$) and mental health ($P = .0007$). The scores after implantation for physical functioning, vitality, bodily pain, and general health were substantially lower than the mean scores of the general population (no statistical analysis provided).

Jarrett et al. (53) reported no major complications among the 46 patients implanted with the device to manage fecal incontinence. Four patients had lead displacements. Three patients had their leads repositioned, and 1 patient wanted the device explanted. Three patients reported pain at the implant site shortly after the device was implanted in the abdomen. All 3 of these patients received a local anesthetic and steroids to manage the pain. Patients who subsequently received implants had them placed in their buttocks.

In the multicentre study by Matzel et al., (54) 8 severe adverse events were reported among the 37 patients. (The authors of the study did not indicate if a patient experienced more than 1 adverse event.) Pain was the most frequently reported adverse event. One patient had the device explanted due to a deterioration of bowel symptoms. The resolution rate among the severe adverse events was 100%.

Uludag et al. (52) in a case series that voiding function immediately improved after implantation in all 50 patients; however, after 1 year, 2 (4%) patients had decreased efficacy of the device, and subsequently had the devices explanted. Two others had their devices explanted due to infection at the site of implantation. Four patients required revision surgery due to technical problems with the device.

Thus, there is a relatively high rate of surgical revision (approximately 33%) reported in the studies examining the safety of SNS, however, no permanent injuries or deaths were reported in any of the studies identified. As a comparison, the permanent implantation of an artificial urinary sphincter is a surgical procedure that has been shown to treat incontinence (including urge, stress, and mixed)

effectively; however, the surgical revision rate associated with it is about 50%. (24)

Table 14: Details of Complications and Revision Surgery for Patients With Urge Incontinence, Urgency-Frequency, Urinary Retention, or Fecal Incontinence

Study, Year	N With Implant	Mean Follow-up (Range)	Details of Revision Surgery	Complications	No. Explants (%) (Reason)
Das et al., 2004 (60)*	89	NR	NR	NR	NR
Dasgupta et al., 2004 (51)	26	37 mos (2–73)	21 revisions in 14/26 pts (54%) ▪ Loss of efficacy (27%) ▪ Pain at implant site (23%) ▪ Pain in leg (23%) ▪ Other (20%)	▪ Loss of efficacy (27%) ▪ Pain at implant site (23%) ▪ Pain (leg) (23%) ▪ Other (20%)	3 (12%) (loss of efficacy)
Jarrett et al., 2004 (53)	46	Median 12 mos (1–72)	▪ Lead displacement (9%)	▪ Lead displacement (9%) ▪ Pain at implant (7%)	1 (2%) (lead displacement)
Matzel, 2004 (54)	37	Median 23.9 mos (NR)	▪ Pain at implant (8%) ▪ Lead breakage (3%)	19 adverse events in 12 pts (8 severe events) ▪ Pain at implant (24%) ▪ Lead breakage (3%) ▪ Infection (3%)	1 (3%) (deterioration of bowel symptoms)
Uludag, 2004 (52)	56	Median 12 mos (NR)	▪ Technical problems with device (7%)	▪ Infection (4%) ▪ Technical problems with device (7%)	2 (4%) (infection) 2 (4%) (loss of efficacy)
Janknegt et al., 2001 (59)†	96	31 mos (12–-60)	32/96 (33%) ▪ Most common was repositioning the device to decrease pain	▪ Pain at implant (14%) ▪ New pain (11%) ▪ Lead migration (9%) ▪ Infection (7%) ▪ Pain at lead site (6%) ▪ Transient electric shock (6%)	11 (11%) (9 ineffective, 2 adverse effect)
Siegel et al., 2000 (48)‡	112	Range 18–36 mos (mean NR)	At 12 months (73/219 pts) 33% ▪ most common reasons were pain at device site and lead migration ▪ No serious adverse effects or permanent injury	At 12 months (219 pts): ▪ Pain at implant (20%) ▪ New pain (9%) ▪ Lead migration (8%) ▪ Infection (6%) ▪ Transient electric shock (6%) ▪ Other (19%)	23 (10.5%)
Weil et al., 2000 (45)	44	18 mos (6–36)	21 revisions in 16/44 (33%) ▪ 8 pts had lead migration ▪ 8 pts had pain at implant site	▪ Actuarial treatment failure at 36 months 32.4% (17%–56%) ▪ 50% reported adverse events	1 (2%) (pain at implant site)

* The patients in this study may overlap with the patients in Schmidt et al.'s (32), Jonas et al.'s (31) and Hassouna et al.'s (30) studies.
†There is overlap between the patients in Janknegt et al.'s (59) and Siegel et al.'s (48) studies;, however, it is unclear specifically which patients overlap.
‡The data for complications was reported for Schmidt et al.'s (32), Jonas et al.'s (31) and Hassouna et al.'s (30) studies together.

Economic Analysis

Literature Review: Objectives and Methods

The Medical Advisory Secretariat did a cost analysis of SNS for the management of urinary urge incontinence, urgency-frequency, urinary retention, and fecal incontinence. Previous health technology assessments and the peer-reviewed literature from 2000 to January 2005 were searched using the keywords listed in the methods for the literature review.

Results of Literature Review on Economics

The health technology assessment by the MSAC in Australia (44) contained an "indicative analysis" of the cost of treatment and the reduction in personal costs (e.g., incontinence supplies). In addition to MSAC's analysis, the Medical Advisory Secretariat found an abstract by Cappellano et al. (61) that was presented at the International Continence Society conference in 2003, which described the economical and social impact of SNS.

The MSAC found that it was more economical for patients to continue paying for incontinence supplies rather than to receive SNS. They noted that the savings in costs for specialized appliances and laundry is between $277.70 (AU) and $574.20 (AU) per patient with urge incontinence over 6 months, and about $245 (AU) per patient with urinary retention over 6 months. The cost-effectiveness ratio for SNS treatment for urge incontinence was estimated at about $35,000 (AU) (about $32,000 Canadian) per additional patient free of incontinence at 6 months follow-up. (44) Importantly, the MSAC did not account for quality of life in its analysis.

The abstract by Cappellano et al. (61) compared 3-month health services utilization before implantation with 3-month health services utilization between 9 and 12 months after implantation in patients with urinary conditions. They found that visits to a general practitioner fell from 1.1 to 0.5 on average per patient ($P < .01$), while visits to the urologist were relatively unchanged (from 1.5 to 1.2). The number of diagnostic tests decreased, on average, from 2 to 0.8 per person ($P < .01$). There was also a reduction in the daily use of incontinence pads from 2.1 (3 months per patient expenses of 120.96 Euros) to 0.5 (3 months per patient expenses of 28.8 Euros) ($P = .08$). For urinary retention, the use of catheters decreased from 1.1 at baseline (3 months per patient expenses of 178.2 Euros) to 0.1 (3 months per patient expenses of 16.2 Euros). Cappellano et al. concluded that SNS improves the economic management of patients with lower urinary tract dysfunction by reducing the number of pads and catheters required and the number of physician visits. They acknowledged that the decrease in physician visits did not occur until about 1 year after implantation, mostly owing to refinements of the stimulation (e.g., altering voltage settings). They also cited studies that indicated that SNS improves quality of life.

One possible reason for the difference between the economic reports could be due to the different time periods covered by each: MSAC determined costs over 6 months; Cappellano and colleagues, 12 months.

Ontario-Based Economic Analysis

Disclaimer: This economic analysis represents an estimate only, based on assumptions and costing methodologies that have been explicitly stated. These estimates will change if different assumptions and costing methodologies are applied for the purpose of developing implementation plans for the technology.

Hospitalization Costs

In fiscal year (FY) 2003, 7 hospital separations were identified from the discharge abstracts database that could have been associated with SNS (A combination of ICD-10 CA diagnosis codes and CCI procedure codes were used. See Appendix 2 for a list.) No cases were identified in FY 2002. To determine the cost per case, the prospectively adjusted for complexity resource intensity weights (PAC-10 weights) were used based on a weight of 1.0 having a dollar value of $4,505 during FY 2003 (Personal Communication, May 2005). The median PAC-10 weight in FY 2003 was 0.63, which was used as a measure of central tendency of the distribution over the mean owing to heavy skewing to the right. The associated cost was $2,823 per hospital separation. The total cost based on the most current volume of 7 hospital separations was $19,763 (CDN).

Device Costs

The cost of a single-lead stimulation device is approximately $10,000, and a dual-lead device is approximately $14,000. As a result, the current annual device costs based on current volumes would be in the range of $70,000 - $98,000. The implantable device generally lasts 5 –10 years, at which point it must be replaced.

Professional (Ontario Health Insurance Policy) Costs

Treatment involves an exploratory trial surgery (phase 1) which leads to permanent insertion of the device (phase 2) in 33% to 50% of the patients. There are 3 postoperative visits with either an urologist or a gastroenterologist.

The following fees have been adjusted upward by 2% to reflect the new OMA agreement.

Physician Costs

Psychological assessment phase: (1 visit)

$73.64: (FSC G192) Video fluoroscopic multichannel urodynamic assessment

Phase 1:

$240.98: (FSC Z816) Implantation of electrode for peripheral nerve stimulation

Anesthetist costs

Note: 4 base units + 1 unit for each 15 minutes in first hour + 2 units per 15 minutes thereafter
Assumption: Up to 2-hour surgery for phase 1

14 units: expected units according to FY 2003 billing data
$12.01: unit for anesthetists
$168.08: expected anesthetist billings for phase 1

$409: total professional medical fees per case (Z816)

Phase 2:

$307.38: (FSC Z823) implantation or revision of stimulation pack or leads

Anesthetist costs

Note: 8 base units + 1 unit for each 15 minutes in first hour + 2 units per 15 minutes thereafter
Note: At most, 50% of patients who undergo preliminary trial qualify for full implant
Note: 33% of patients require revision of surgery due to pain at implant site, lead migration, or infection

18 units: expected number of units based on FY 2003 billings
$12.01: unit fee for anesthetists
$216.10: expected anesthetist billings for phase 2

$523: total professional medical fees per case for phase 2

Note: 13% of patients require an explant of device

Follow-up assessment/psychological visits and preliminary visit (3 postoperatively during the first year):

The following code is used for follow-up:

FSC G193 ($44): Complete multichannel urodynamic assessment

Note: Similar cost for follow-up for fecal incontinence

$132: total expected post-op physician reimbursement (Note: figure does not account for present value of installing replacement devices twice during the next 15 years)

$1,439: total professional medical fees per case (expected)
$10,073: total professional medical fees based on seven procedures

The estimated Ontario prevalence of people who might be eligible for the procedure with urge incontinence, urgency-frequency, urinary retention is between 1,268 - 6,283) (Table 15) and/or fecal incontinence is 274 - 2,895 (Table 16). It is important to note that the prevalence estimate for Ontario may be high because it is difficult to accurately predict the prevalence of urinary conditions (many people are embarrassed to talk about the condition), and it is also very difficult to estimate the number of people with urinary conditions whose symptoms are severe enough to consider undergoing surgery.

Table 15: Number of Ontario Residents With Urge Incontinence, Urgency-Frequency, and Urinary Retention Who Might Benefit From Sacral Nerve Stimulation

Population of Ontario (2001 census)		**12,088,275**
Prevalence of urge incontinence, urgency-frequency, urinary retention	3.3%–8.2%	295,567–732,221
Will seek treatment (62) (Personal communication, March 2005)	26%	76,847–190,377
Will not be successfully treated with conservative treatments (62) (personal communication)	25%–33%	19,212–62,824
Will qualify for sacral nerve stimulation (FDA)	20%	3,842–12,565
Will have successful test stimulation (Personal communication, (30-32))	33%-50%	1,268–6,283

Table 16: Number of Ontario Residents With Fecal Incontinence Who Might Benefit from Sacral Nerve Stimulation

Population of Ontario Older Than 20 Years (2001 census)		**8,962,784**
Prevalence of fecal incontinence (definition ≥1 incontinent episode/week) (11;40;41)	1.4%–1.9%	125,479–170,293
Will seek treatment (63;64)	5%–33%	6,274–56,197
Will not respond to treatment with behaviour or drug therapy (65)	28%	1,757–15,735
Will qualify for sacral nerve stimulation* (FDA)	20%	351–3,147
Will have ≥ 50% improvement with test stimulation (52-54)	78%–92%	274–2,895

*Those who are not excluded due to age (< 18 years), neurogenic condition, frailty, obesity, or refusal of treatment.

Downstream Cost Savings

The following is a list of prescription medicines. Although SNS does not eliminate the need for prescription medications for the underlying symptoms, some patients will combine SNS with drug therapy if drug therapy has been somewhat effective. Table 17 shows the drugs prescribed in Ontario to manage urge incontinence. One recent abstract suggests that drug-related expenditures will be reduced by over 75%. (61)

Table 17: Drugs Prescribed for the Management of Urge Incontinence in Ontario

Drug	Drug type	Typical Dose
Frequently Used		
Oxybutynin Extended release: Ditropan XL Skin patch: Oxytrol	Anticholinergic/ Spasmolytic	2.5–5 mg bid to tid Ditropan XL 5–30mg daily Oxytrol Patch 2x weekly (3.9 mg/day)
Tolterodine	Anticholinergic	2 mg bid (4 mg daily for extended release)
Imipramine (sometimes prescribed in combination with oxybutynin or tolterodine)	Anticholinergic/ Antidepressant	25–75 mg daily
Rarely Used		
Propantheline bromide	Anticholinergic	7.5 mg bid to tid
Hyoscyamine	Anticholinergic	0.15 mg tid to qid (0.375 mg bid to tid for extended release)

Evidence on Costs and Cost-Effectiveness

According to the MSAC, (44) the cost saving in specialized appliances and laundry per patient is between $277.70 (AU) and $574.20 (AU) over 6 months for urge incontinence and about $245 (AU) for urinary retention over 6 months. The cost-effectiveness ratio for SNS treatment for urge incontinence is estimated at about $35,000 (AU) (about $32,000 Canadian) per additional patient free of incontinence at 6 months follow-up. (44)

Total costs in the Ontario-Based Economic Analysis determined that total costs were approximately $2,823 for Hospitalization Costs + $10,000 to $14,000 for Device Costs + $1,439 for OHIP physician costs.

Existing Guidelines for Use of Technology

In 2004, NICE released an Interventional Procedure Guidance relating to the evidence in the health technology assessment that stated that NICE supports the use SNS for urge incontinence and urgency-frequency provided that "the normal arrangements are in place for consent, audit and clinical governance." (46) NICE released a similar statement on the use of SNS in patients with fecal incontinence. (66) No other guidelines were identified.

Appraisal

Policy Implications

Patient Outcomes – Medical, Clinical

- There is level 2 evidence supporting the effectiveness and safety of SNS for adults with refractory urge incontinence, urgency-frequency, and urinary retention.
- Compared with patients who receive no treatment, patients with the SNS implant have significantly improved voiding function in terms of leakage, pads used, and catheterizations.
- Qualify of life is also improved, especially among patients with urge incontinence.
- After mean follow-up of 5 years, about 61% of patients achieve at least a 50% improvement in voiding function.
- The surgical revision rate was 33% in 3 RCTs.. (30-32)
- There is level 4 evidence supporting the effectiveness and safety of SNS in adults with refractory fecal incontinence.
- No studies were found that followed-up patients to the point of battery failure. The longest follow-up was 5 years.
- SNS is designed for patients for whom behaviour and drug therapy have not worked.
- The following people will ***not*** benefit from SNS:

    - Patients with neurogenic conditions (e.g., spinal cord injuries, complete spinal lesions, spina bifida, multiple sclerosis, and diabetes with peripheral nerve involvement)
    - Children aged 16 years or younger
    - Patients who cannot operate patient programmer
    - Patients with other stimulation devices (e.g., pacemaker)
    - Patients with stress or mixed incontinence
    - Patients who have urinary retention due to obstruction

Patient Characteristics

To qualify for SNS, a person must meet the following criteria:

- Be refractory to drug and/or behaviour treatment.
- Have had successful test stimulation before implantation; successful test stimulation is defined by a 50% or greater improvement in voiding function based on the results of a voiding diary. Test stimulation periods range from 3 to 7 days for patients with urinary dysfunctions, and from 2 to 3 weeks for patients with fecal incontinence.
- Be able to record information on voiding in a diary, so that clinical results of the implantation can be evaluated.

Physician Training

Physicians will need to learn how to use the InterStim System for Urinary Control. Requirements for training include these:

- Physicians must be experienced in the diagnosis and treatment of lower urinary tract disorders and should be trained in the implantation and use of the InterStim System for Urinary Control.
- Training should include:
  - Participation in a seminar or workshop that includes instructional and laboratory training on SNS. This seminar should include a review of the evidence on SNS with emphasis on techniques to prevent adverse events.
  - Completion of proctoring by a physician experienced in SNS for the first 2 test stimulations and the first 2 implants.

Demographics

- The prevalence of urge incontinence, urgency-frequency, urinary retention, and fecal incontinence is difficult to estimate because people can have these conditions and never consult a physician, owing to a lack of awareness for treatments or to embarrassment in discussing the condition.
- The best available evidence suggests that the prevalence of urge incontinence, urgency-frequency, and urinary retention in the general population is 3.3% to 8.2%, and the prevalence of fecal incontinence is 1.4% to 1.9%. About three quarters of these people will be successfully treated by behaviour and/or drug therapy; however, for those who do not respond to these therapies, the options for treatment are management with diapers or pads, or surgery.
- Based on discussion with a physician who uses the SNS procedure in patients with urinary voiding conditions the following was noted:

  - His client base is aged 18 to 70 years.
  - 30% to 40% of his patients have chronic pelvic pain associated with their urinary dysfunction.
  - The majority of his clients are women.
  - Patients with the implant need to be followed-up every 6 months for 4 years, and then annually.

Ethical Considerations

The physician in Ontario who is currently performing SNS has funding from his hospital to perform 12 implant procedures per year. As noted in this review, the battery in the device lasts 5 to 10 years

depending on its use. The physician started implanting these devices in patients in the late 1990s, and now the batteries are beginning to fail. The physician is facing an ethical dilemma in deciding which patients will receive the 12 implants that he has funding to implant per year—new implants or replacement implants? The physician indicated that the waiting list works on a first come, first served basis, with some exceptions made for people whose well-being is severely compromised (e.g., people with chronic urinary tract infections that will not heal due to repeated irritation due to catheterization).

Currently, patients who fail behaviour or drug therapy and patients who do not seek treatment because they are unaware of treatments or are too embarrassed to seek treatment manage incontinence with diapers or pads. Currently, there is no funding or subsidy provided in Ontario to people who manage their incontinence with diapers. Diapers cost about $1 CDN each. Absorbent pads are slightly less expensive. According to Schmidt et al., (32) patients with urge incontinence used a mean of 6.2 (SD, 5.0) pads or diapers per day before they underwent SNS. Based on these data, the cost of diapers per year for 1 patient with urge incontinence is about $2,263.

Urge incontinence, urgency-frequency, urinary retention, and fecal incontinence are not readily discussed conditions in the general population. Having one of these conditions affects a person's ability to work, socialize, and interact with his or her community. SNS has the potential to treat a small proportion of these people. Nonetheless, there will still be many people suffering from urge incontinence, urgency-frequency, urinary retention, and fecal incontinence.

Diffusion – International, National, Provincial

SNS is done internationally (United States, Canada, Australia, Europe, Japan, Latin America). In Canada, it is done in 4 provinces: Ontario, Quebec, Nova Scotia, and Alberta.

Currently, one physician in Ontario does SNS. The physician has funding from one hospital to implant 12 devices a year. As of January 2005, there is a waiting list of 47 people. No physicians in Ontario do SNS for patients who have only fecal incontinence.

Stakeholder analysis

Patients

SNS has been proven effective and safe in patients with refractory urge incontinence, urgency-frequency, urinary retention, and fecal incontinence. Studies have reported significant improvements in quality of life and reduced depression.

Nurse Continence Advisors

Nurse continence advisors are distributed throughout the province and treat people with voiding conditions with conservative treatments. These advisors may be the first health care professionals that patients with these conditions see; thus, their knowledge about treatments is crucial.

Family physicians

Family physicians need to be aware of all treatment options for patients with urge incontinence, urgency-frequency, urinary retention, and fecal incontinence, and where to refer patients to.

Urologists, Uro-gynecologists, Gastroenterologists

Specialists need to be aware of treatments for urge incontinence, urgency-frequency, urinary retention, and fecal incontinence. Training will need to be offered to specialists if they want to learn how to perform the SNS procedure.

Conclusions

There is level 2 evidence to support the effectiveness and safety of SNS for patients with urge incontinence, urgency-frequency, or urinary retention. There is level 4 evidence to support the effectiveness and safety of SNS for patients with fecal incontinence. The long-term follow-up data is still emerging; however, it appears that SNS is effective up to at least 5 years. Despite a somewhat high complication profile, no permanent injuries or deaths have been attributed to SNS. Most patients who receive the implant report that they would undergo the procedure again or recommend it to a friend, regardless of the complications.

Currently, only about one-quarter of people with urge incontinence, urgency-frequency, urinary retention, or fecal incontinence seek treatment. Drug and behaviour therapy effectively treat about 75% of the patients with these conditions who seek treatment. SNS has the potential to treat about 5% of these patients. This leaves 20% of patients who seek treatment with few alternatives (surgery or diapers). There is also the three-quarters of the people with one of these conditions that do not seek help for their symptoms because they are embarrassed or unaware of treatments.

SNS undoubtedly plays a role in the treatment of a small proportion of people with urge incontinence, urgency-frequency, urinary retention or fecal incontinence; however, a broader overview of the management of these voiding conditions may be beneficial in being able to treat as many people as possible with these conditions.

Glossary

Anticholinergic	A drug that interferes with the effects of acetylcholine; it blocks the passage of impulses through the parasympathetic nerves
Biofeedback	A therapeutic technique that allows people, though using electronically displayed auditory or visual information, to gain voluntary control over unconscious, physiological variables, such as heart rate and blood pressure; for voiding problems, it helps people become aware of and control of their pelvic muscles
Bladder denervation	A procedure that disrupts the nerves supplying the bladder wall
Catheterization	The insertion of a catheter, a thin, flexible tube to drain urine away from the body
Detrusor	The smooth muscle in the wall of the bladder that contracts the bladder and expels urine; the bladder is often referred to as the detrusor muscle
Detrusor hyperreflexia	Involuntary detrusor contraction; may be caused by a central neurologic deficit, a spinal cord injury, or a peripheral neurologic deficit, like sacral nerve root impingement syndrome
Detrusor myomectomy	A surgical procedure that involves removing a portion of the detrusor muscle from the dome of the bladder
Enterocystoplasty	A procedure where a portion of intestine is used to reconstruct and enlarge the bladder; it is associated with complications like disturbed bowel habit and recurrent urinary tract infections
Fecal incontinence	A loss of voluntary control of the passage of liquid or solid stool; also refers to incontinence of flatus (gas)
Hydrodistention	An interventional therapy for patients with urgency-frequency, in which the bladder is stretched with fluid; it is thought to alter neurologic function, thereby decreasing the transmission of pain
Idiopathic detrusor instability	Diagnosed when no underlying cause for an unstable detrusor (bladder) is identified; postulated causes are congenital abnormalities, parasympathetic hypersensitivity, or an imbalance of neurotransmitters
Micturition	The medical term for urination, the discharge or passage of urine
Mixed incontinence	A combination of the 3 types of incontinence (urge, stress, and overflow)
Motor urgency	Overactivity of the bladder detrusor muscle on urodynamic testing
Overactive bladder	A form of urinary incontinence that results from sudden, involuntary contraction of the detrusor muscle; it causes a sudden and unstoppable need to urinate (also called urge incontinence)
Overflow incontinence	Constant leaking or dribbling; it happens when the bladder does not empty completely
Permanent indwelling catheterization	The permanent insertion of a catheter to treat urinary incontinence; recommended for people who are severely impaired or terminally ill
Prevalence	Total number of people with the disease at any one time
Sacral nerves	The 5 pairs of nerves (S1–S5) that arise from the sacral segments of the spinal cord
Sacral nerve stimulation	A procedure where a small device attached to an electrode is implanted in the abdomen or buttock to stimulate the sacral nerves in an attempt to manage urinary urge incontinence, urgency-frequency,

	urinary retention, and fecal incontinence
Sensory urgency	An involuntary loss of urine that happens when people have trouble reaching a bathroom in time, often because of a physical condition like arthritis. Also called functional incontinence, it is diagnosed when no overactivity of detrusor muscle is found during urodynamic testing.
Stress incontinence	Involuntary passage of urine that happens when body movements put strain on the bladder, for example, during exercise or sneezing
Urge incontinence	An involuntary loss of urine upon a sudden urge; also called hyperactive or irritable incontinence
Urgency-frequency	An uncontrollable urge to void, resulting in frequent, small volume voids; often associated with interstitial cystitis and chronic pelvic pain
Urinary retention	The inability to void despite having the urge to void, it can be caused by a hypocontractile detrusor (weak or no bladder muscle contraction) or obstruction due to urethral overactivity

Appendices

Appendix 1

Sacral Nerve Stimulation Literature Search Strategy

Search date: November 6, 2004
Databases searched: Ovid MEDLINE, MELINE In-Process and Other Non-indexed Citations, Cochrane DSR and CCTR, INAHTA

Database: Ovid MEDLINE(R) <1966 to October Week 4 2004>
Search Strategy:

1 sacral nerve stimulation.mp. (115)
2 sacral nerve neuromodulation.mp. (7)
3 sacral neuromodulation.mp. (79)
4 sacral nerve electrostimulation.mp. (3)
5 neuroprosthesis.mp. (98)
6 or/1-5 (276)
7 exp Electric Stimulation/ (92602)
8 exp Electrodes, Implanted/ (16992)
9 exp Urinary Incontinence/ (15794)
10 exp Urinary Retention/ (1717)
11 (7 or 8) and (9 or 10) (275)
12 6 and (9 or 10) (73)
13 11 or 12 (319)
14 limit 13 to (human and English language and yr=2000-2004) (72)
15 limit 14 to systematic reviews (5)
16 14 (72)
17 limit 16 to (case reports or comment or editorial or letter or news or "review literature" or review, multicase or "review of reported cases") (9)
18 16 not 17 (63)
19 from 18 keep 1-62 (62)
20 19 or 15 (62)
21 from 20 keep 1-62 (62)

Database: EMBASE <1996 to 2004 Week 44>
Search Strategy:

1 exp Nerve Stimulation/ (17942)
2 exp Electrostimulation/ (10913)
3 exp NEUROMODULATION/ (6122)
4 sacral nerve stimulation.mp. (98)
5 sacral nerve neuromodulation.mp. (7)
6 sacral neuromodulation.mp. (91)
7 sacral nerve electrostimulation.mp. (2)
8 neuroprosthesis.mp. (101)
9 or/1-8 (31951)
10 exp mixed incontinence/ or exp stress incontinence/ or exp urge incontinence/ or exp urine

incontinence/ or exp urine retention/ (10725)
11 9 and 10 (440)
12 limit 11 to (human and English language and yr=2000 - 2005) (261)
13 limit 12 to (editorial or letter or note or "review") (115)
14 Case Report/ (330179)
15 12 not (13 or 14) (131)
16 from 15 keep 1-131 (131)

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <November 05, 2004>
Search Strategy:

1 sacral nerve stimulation.mp. (3)
2 sacral nerve neuromodulation.mp. (1)
3 sacral neuromodulation.mp. (1)
4 sacral nerve electrostimulation.mp. (0)
5 neuroprosthesis.mp. (8)
6 incontinence.mp. [mp=title, original title, abstract, name of substance] (374)
7 or/1-5 (13)
8 6 and 7 (4)
9 limit 8 to (English language and yr=2000 - 2005) (3)
10 from 9 keep 1-3 (3)

Appendix 2

ICD10

Urge incontinence R32 or N39.4 (other specified urinary incontinence)
Urinary retention R33
Pelvic pain R10.2
Urgency-frequency R39.13
Fecal incontinence R15

CCI

1.BX.09.HA-DV for phase 2 of implantation

References

1. Medscape [homepage on the Internet].Web MD. 2006. [cited 2005 Jan. 24]. Available from: http://www.medscape.com/home

2. Medtronic I. Medtronic [homepage on the Internet]. 2005. [cited 2005 Feb. 2]. Available from: www.medtronic.com

3. Current Controlled Trials Ltd. Current Controlled Trials [homepage on the Intranet]. 2005. [cited 2005 Jan. 25]. Available from: www.controlled-trials.com

4. Davila GW, Bernier F, Franco J, Kopka SL. Bladder dysfunction in sexual abuse survivors. J Urol 2003; 170: 476-479

5. Scarinci I, McDonald-Haile J, Bradley LA, Richter JE. Altered pain perception and psychosocial features among women with gastrointestinal disorders and history of abuse: a preliminary model. Am J Med 1994; 97: 108-118

6. Sampselle CM, Palmer MH, Boyington AR, O'Dell KK, Wooldridge L. Prevention of urinary incontinence in adults: population-based strategies. Nurs Res 2004; 53((6 Supl)): S61-S67

7. Canadian Continence Foundation. Information about incontinence [Web page]. 2004. [cited 2005 Feb. 21]. Available from: http://www.continence-fdn.ca/indexeng.htm

8. Lefevre FV. Sacral nerve stimulation for the treatment of refractory urge incontinence [report on the Internet]. March 2000. Chicago: Blue Cross and Blue Shield Association. [cited 2005 Jan. 20]. Available from: http://www.cms.hhs.gov/coverage/download/id73b.pdf.

9. Macmillan AK, Merrie AE, Marshall RJ, Parry BR. The prevalence of fecal incontinence in community-dwelling adults: a systematic review of the literature. Dis Colon Rectum 2004; 47(8): 1341-1349

10. Fraser C, Glazener C, Grant A, Mowatt G, Bravo Y, Cross L et al. Systematic review of the efficacy and safety of sacral nerve stimulation for faecal incontinence. Interventional Procedures Programme. Review body report [report on the Internet]. 2004. Aberdeen (Scotland): National Institute for Clinical Excellence (NICE). [cited 2005 Jan. 22]. Available from: http://www.nice.org.uk/page.aspx?o=ip123systematicreview.

11. Lam TCF, Kennedy ML, Chen FC, Lubowski DZ, Talley NJ. Prevalence of faecal incontinence: obstetric and constipation-related risk factors: a population-based study. Colorectal Dis 1999; 1: 197-203

12. Berghmans LCM, Hendriks HJM, De Bie RA, Van Waalwijk van Doorn ESC, Bo K, Van Kerrebroeck P. Conservative treatment of urge urinary incontinence in women: a systematic review of randomized clinical trials. BJU Int 2000; 85(3): 254-263

13. Gnanadesigan N, Saliba D, Roth CP, Solomon DH, Chang JT, Schnelle J et al. The quality of care provided to vulnerable older community-based patients with urinary incontinence. J Am Med Dir Assoc 2004; 5(3): 141-146

14. Hay-Smith E, Bo K, Bergmark M, Hendriks H, De Bie R, Van Waalwijk van Doorn ESC. Pelvic floor muscle training for urinary incontinence in women (Cochrane Review). Cochrane Database Syst Rev 2005; Issue 1(Art. No.: CD001407. DOI: 10.1002/14651858.CD001407.pub2.)

15. Teunissen TAM, de Jonge A, van Weel C, Lagro-Janssen ALM. Treating urinary incontinence in the elderly--conservatic measures that work: a systematic review. J Fam Pract 2004; 53: 25-32

16. Wallace SA, Roe B, Williams K, Palmer M. Bladder training for urinary incontinence in adults. Cochrane Database Syst Rev 2004; Issue 1(Art. No.: CD001308. DOI: 10.1002/14651858.CD001308.pub2)

17. Garely AD, Burrows L. Benefit-risk assessment of tolterodine in the treatment of overactive bladder in adults. Drug Saf 2004; 27: 1043-1057

18. Desgagne A, LeLorier J. Incontinence drug utilization patterns in Quebec, Canada. Value Health 1999; 2: 452-458

19. Harvey MA, Baker K, Wells GA. Tolterodine versus oxybutynin in the treatment of urge urinary incontinence: a meta-analysis. Am J Obstet Gynecol 2001; 185(1): 56-61

20. Appell R, Sand PK, Dmochowski R, Anderson R, Zinner N, Lama D et al. Prospective randomized controlled trial of extended-release oxybutynin chloride and tolterodine tartratein the treatment of overactive bladder: results of the OBJECT study. Mayo Clin Proc 2001; 76: 358-363

21. Herbison P, Hay-Smith J, Ellis G, Moore K. Effectiveness of anticholinergic drugs compared with placebo in the treatment of overactive bladder: systematic review. BMJ 2003; 326(7394): 841-844

22. Siddiqui MAA, Perry CM, Scott LJ. Oxybutynin extended-release. Drugs 2004; 64: 885-912

23. Hasan ST, Marshall C, Robson WA, Neal DE. Clinical outcome and quality of life following enterocystoplasty for idiopathic detrusor instability and neurogenic bladder dysfunction. Br J Urol 1995; 76(5): 561-567

24. Clemens JQ, Schuster TG, Konnak JW, McGuire EJ, Faerber GJ. Revision rate after artificial urinary sphincter implantation for incontinence after radical prostatectomy: actuarial analysis. J Urol 2001; 166(4): 1372-1375

25. Glemain P, Riviere C, Lenormand L, Karam G, Bouchot O, Buzelin JM. Prolonged hydrodistention of the bladder for symptomatic treatment of interstitial cystitis: efficacy at 6 months and 1 year. Eur Urol 2002; 41(1): 79-84

26. Siegel S, Paszkiewicz E, Kirkpatrick C, Hinkel B, Oleson K. Sacral nerve stimulation in patients with chronic intractable pelvic pain. J Urol 2001; 166: 1742-1745

27. Cheetham M, Brazzelli M, Norton C, Glazener CMA. Drug treatment for faecal incontinence in adults. Cochrane Database Syst Rev 2002; Issue 3(Art. No.: CD002116. DOI: 10.1002/14651858.CD002116.)

28. Mundy L, Merlin TL, Maddern GJ, Hiller JE. Systematic review of safety and effectiveness of an

artificial bowel sphincter for faecal incontinence. Br J Surg 2004; 91(6): 665-672

29. Wong WD, Congliosi SM, Spencer MP, Corman ML, Tan P, Opelka FG et al. The safety and efficacy of the artificial bowel sphincter for fecal incontinence: results from a multicenter cohort study. Dis Colon Rectum 2002; 45: 1139-1153

30. Hassouna MM, Siegel SW, Nyeholt AABL, Elhilali MM, Van Kerrebroeck PEV, Das AK et al. Sacral neuromodulation in the treatment of urgency-frequency symptoms: a multicenter study on efficacy and safety. J Urol 2000; 163(6): 1849-1854

31. Jonas U, Fowler CJ, Chancellor MB, Elhilali MM, Fall M, Gajewski JB et al. Efficacy of sacral nerve stimulation for urinary retention: results 18 months after implantation. J Urol 2001; 165(1): 15-19

32. Schmidt RA, Jonas U, Oleson KA, Janknegt R, Hassouna MM, Siegel SW et al. Sacral nerve stimulation for treatment of refractory urinary urge incontinence. J Urol 1999; 162: 352-357

33. Chancellor MB, Chartier-Kastler E. Principles of sacral nerve stimulation (SNS) for the treatment of bladder and urethral sphincter dysfunctions. Neuromodulation 2000; 3: 15-26

34. Corcos J, Schick E. Prevalence of overactive bladder and incontinence in Canada. Can J Urol 2004; 11: 2278-2284

35. McGrother CW, Donaldson MM, Shaw C, Matthews RJ, Hayward TA, Dallosso HM et al. Storage symptoms of the bladder: prevalence, incidence and need for services in the UK. BJU Int 2004; 93(6): 763-769

36. Stewart WF, Van Rooyen JB, Cundiff GW, Abrams P, Herzog AR, Corey R et al. Prevalence and burden of overactive bladder in the United States. World J Urol 2003; 20: 327-336

37. Milsom I, Stewart W, Thuroff J. The prevalence of overactive bladder. Am J Manag Care 2000; 6((11 Suppl)): S565-S673

38. Simeonova Z, Milsom I, Kullendorff AM, Molander U, Bengtsson C. The prevalence of urinary incontinence and its influence on the quality of life in women from an urban Swedish population. Acta Obstet Gynecol Scand 1999; 78(6): 546-551

39. Evans A, Pheby D, Painter D, Feneley R. The costs of long-term catheterization in the community. Br J Community Nurs 2000; 5(10): 477-488

40. Perry S, Shaw C, McGrother C, Matthews RJ, Assassa RP, Dallosso H et al. Prevalence of faecal incontinence in adults aged 40 years or more living in the community. Gut 50(4):480-4, 2002;

41. Walter S, Hallbook O, Gotthard R, Bergmark M, Sjodahl R. A population-based study on bowel habits in a Swedish community: prevalence of faecal incontinence and constipation. Scand J Gastroenterol 2002; 37: 911-916

42. Brazzelli M, Murray A, Fraser C, Grant A. Sacral nerve stimulation for urge incontinence and urgency-frequency [report on the Internet]. IP082. 2004. London: National Institute for Clinical Excellence (NICE). [cited 2005 Jan. 26]. Available from: http://www.nice.org.uk/cms/ip/ipcat.aspx?c=56779.

43. Australian Safety and Efficacy Register of New Interventional Procedures-Surgical. Sacral nerve stimulation for treatment of urge incontinence. Rapid Review. New and Emerging Techniques - Surgical [report on the Internet]. June 2003. Royal Australasian College of Surgeons. [cited 2004 Dec. 12]. Available from: http://www.surgeons.org/AM/Template.cfm?Section=Search_Asernips&section=Horizon_Scanning_Reports&template=/CM/ContentDisplay.cfm&ContentFileID=2115.

44. Medical Services Advisory Committee. Sacral nerve stimulation for refractory urinary urge incontinence or urinary retention [report on the Internet]. 2000. Canberra: Medical Services Advisory Committee (MSAC). [cited 2004 Dec. 10]. Available from: http://www.msac.gov.au/pdfs/reports/msac1009.pdf.

45. Weil EHJ, Ruiz-Cerda JL, Eerdmans PHA, Janknegt RA, Bemelmans BLH, Van Kerrebroeck P. Sacral root neuromodulation in the treatment of refractory urinary urge incontinence: a prospective randomized clinical trial. Eur Urol 2000; 37(2): 161-171

46. National Institute for Clinical Excellence. Sacral nerve stimulation for urge incontinence and urgency-frequency - guidance [report on the Internet]. 64. 2004. National Institute for Clinical Excellence (NICE). Interventional Procedure Guidance. [cited 2005 Jan. 15]. Available from: http://www.nice.org.uk/cms/ip/page.aspx?o=ipg064guidance.

47. Grunewald, V., Jonas, U., and MDT-103 Multicenter Study Group. Sacral electrical nerve stimulation for treatment of severe voiding dysfunction [abstract]. J Urol. 1999. 275

48. Siegel SW, Catanzaro F, Dijkema HE, Elhilali MM, Fowler CJ, Gajewski JB et al. Long-term results of a multicenter study on sacral nerve stimulation for treatment of urinary urge incontinence, urgency-frequency, and retention. Urology 2000; 56(6 Suppl 1): 87-91

49. Peters KM, Konstandt DB. Sacral neuromodulation decreases narcotic requirements in refractory interstitial cystitis. BJU Int 2004; 93: 777-779

50. Comiter CV. Sacral neuromodulation for the symptomatic treatment of refractory interstitial cystitis: A prospective study. J Urol 2003; 169: 1369-1373

51. Dasgupta R, Wiseman OJ, Kitchen N, Fowler CJ. Long-term results of sacral neuromodulation for women with urinary retention. BJU Int 2004; 94(3): 335-337

52. Uludag O, Koch SMP, van Gemert WG, Dejong CHC, Baeten C. Sacral neuromodulation in patients with fecal incontinence: A single-center study. Dis Colon Rectum 2004; 47: 1350-1357

53. Jarrett M, Varma JS, Duthie GS, Nicholls RJ, Kamm MA. Sacral nerve stimulation for faecal incontinence in the UK. Br J Surg 2004; 91: 755-761

54. Matzel K, Kamm M, Stosser M, Baeten C, Christiansen J, Madoff R et al. Sacral spinal nerve stimulation for faecal incontinence: multicentre study. Lancet 2004; 363: 1270-1276

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

56. van Voskuilen A, Weil E, van Koeveringe G, De Bie R, Van Kerrebroeck P. Long term results of sacral nerve stimulation for lower urinary tract symptoms: a single center study [abstract].

International Continence Society. 2004. [cited 2004 Dec. 15]. Available from: http://www.icsoffice.org/publications/2004/pdf/0236.pdf

57. van Voskuilen A, Van Kerrebroeck P, Van Den Hombergh U. Long-term efficacy, safety and quality of life results of sacral neuromodulation for the treatment of voiding dysfunctions:outcomes from a prospective, worldwide clinical study [abstract]. International Continence Society. 2004. [cited 2004 Dec. 20]. Available from: http://www.icsoffice.org/publications/2004/pdf/0054.pdf

58. Bemelmans BL, Heesakkers JP, Van Den Hombergh U. Long-term effects of sacral neuromodulation in patients suffering from urgency/frequency [abstract]. International Continence Society. 2002. [cited 2004 Dec. 2]. Available from: http://www.icsoffice.org/publications/2002/pdf/416.pdf

59. Janknegt RA, Hassouna MM, Siegel SW, Schmidt RA, Gajewski JB, Rivas DA et al. Long-term effectiveness of sacral nerve stimulation for refractory urge incontinence. Eur Urol 2001; 39(1): 101-106

60. Das AK, Carlson AM, Hull M. Improvement in depression and health-related quality of life after sacral nerve stimulation therapy for treatment of voiding dysfunction. Urology 2004; 64(1): 62-68

61. Cappellano F, Bertapelle P, Spreafico L, Del Popolo G, Kocjancic E, Donelli A et al. Economical and social impact of sacral nerve stimulation therapy in 62 patients with lower urinary tract dysfunction [abstract]. International Continence Society. 2003. [cited 2004 Dec. 22]. Available from: http://www.icsoffice.org/publications/2003/pdf/176.pdf

62. Herschorn S, Corcos J, Gajewski J, Schulz J, Ciu E. Canadian urinary bladder survey: population-based study of symptoms and incontinence [abstract]. International Continence Society. 2003. [cited 2004 Dec. 22]. Available from: http://www.icsoffice.org/publications/2003/pdf/049.pdf

63. Enck P, Bielefeldt K, Rathmann W, Purrmann J, Tschope D, Erckenbrecht JF. Epidemiology of faecal incontinence in selected patient groups. Int J Colorectal Dis 1991; 6: 143-146

64. Johanson JF, Lafferty J. Epidemiology of fecal incontinence: the silent affliction. Am J Gastroenterol 1996; 91: 33-36

65. Norton C, Kamm MA. Outcome of biofeedback for faecal incontinence. Br J Surg 1999; 86: 1159-1163

66. National Institute for Clinical Excellence. Sacral nerve stimulation for faecal incontinence-guidance [report on the Internet]. IPG099. 2004. London: National Institute for Clinical Excellence (NICE). Interventional Procedure Guidance. [cited 2005 Jan. 22]. Available from: http://www.nice.org.uk/page.aspx?o=IPG099guidance.