NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of percutaneous posterior tibial nerve stimulation for overactive bladder syndrome

The symptoms of overactive bladder syndrome include the need to urinate often and without much warning (frequency), and urge incontinence (the strong need to urinate followed by an inability to stop passing urine). It is caused by the bladder muscle contracting before the bladder is full. Percutaneous posterior tibial nerve stimulation (PTNS) for overactive bladder involves inserting a fine needle into a nerve just above the ankle. A mild electric current is passed through the needle and carried to the nerves that control bladder function.

Introduction

The National Institute for Health and Clinical Excellence (NICE) has prepared this overview to help members of the Interventional Procedures Advisory Committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in March 2010.

Procedure name

- Percutaneous posterior tibial nerve stimulation for overactive bladder syndrome.

Specialty societies

- British Association of Urological Surgeons
- British Society of Urogynaecology
- Royal College of Obstetrics and Gynaecologists

Description

Indications and current treatment

Overactive bladder syndrome (OAB; also known as urgency-frequency syndrome) is defined as urinary urgency, with or without urge incontinence, usually with frequency and nocturia. OAB that occurs with urge urinary incontinence is known as ‘OAB wet’. OAB that occurs without urge urinary incontinence is known as ‘OAB dry’. In most cases, the cause of the overactive bladder is unknown. In some cases, it is associated with a neurological condition such as multiple sclerosis or Parkinson’s disease.

First-line treatments for OAB include bladder training, pelvic floor muscle training and anticholinergic drugs. In patients for whom conservative treatments have been unsuccessful, intravesical botulinum toxin injections and/or sacral nerve stimulation are sometimes used. More extensive surgical options for treating OAB include bladder reconstruction (such as augmentation cystoplasty) and urinary diversion.

What the procedure involves

Stimulation of the posterior tibial nerve delivers retrograde stimulation to the sacral nerve plexus. The posterior tibial nerve contains mixed sensory motor nerve fibres that originate from the same spinal segments as the innervations to the bladder and pelvic floor. The exact mechanism of action of neuromodulation is unclear. The potential benefit of percutaneous posterior tibial nerve stimulation is that it may achieve the same neuromodulatory effect as sacral nerve stimulation through a less invasive route.

Percutaneous posterior tibial nerve stimulation is performed while the patient is seated or reclined in a comfortable position. A fine gauge needle or needle electrode is inserted percutaneously just above and medial to the ankle, next to the tibial nerve, and a surface electrode is placed near the arch of the foot. The needle and electrode are connected to a low-voltage stimulator. Stimulation of the posterior tibial nerve produces a typical motor (plantar flexion or fanning of the toes) and sensory (tingling in the ankle, foot or toes) response. The current can be adjusted as necessary during the treatment. Initial treatment usually consists of 12 outpatient sessions lasting 30 minutes each, typically a week apart.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to percutaneous posterior tibial nerve stimulation for OAB. Searches were conducted of the following databases, covering the period from their commencement to 17 February 2010: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with overactive bladder syndrome.
Intervention/test	Percutaneous posterior tibial nerve stimulation for overactive bladder syndrome.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the overview

This overview is based on approximately 665 patients from 2 randomised controlled trials (RCTs) and 6 case series[1–8.]

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Table 2 Summary of key efficacy and safety findings on percutaneous posterior tibial nerve stimulation for overactive bladder syndrome

Abbreviations used: CI, confidence interval; HRQL, health-related quality of life; NS, not significant; OAB, overactive bladder; OAB-q, overactive bladder questionnaire; OR, odds ratio; PTNS, percutaneous tibial nerve stimulation; QoL, quality of life; SANS, Stoller afferent nerve stimulation

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Peters KM (2010)[1]

Randomised controlled trial

USA

Recruitment period: 2008–9

Study population: ambulatory adults with OAB symptoms

n = 220 (110 PTNS vs 110 sham)

Mean age (years): PTNS = 62.5, sham = 60.2
Sex: PTNS = 78% female, sham = 80% female

Patient selection criteria: ambulatory adults with OAB symptoms, age ≥ 18 years, score ≥ 4 on OAB-q short form for urgency, average urinary frequency ≥ 10 voids per day, bladder symptoms ≥ 3 months, self-reported failed conservative care, discontinued all antimuscarinics for ≥ 2 weeks. Exclusion criteria included pregnancy, neurogenic bladder, botulinum toxin in bladder or pelvic floor muscles within past year, pacemakers, current urinary tract or vaginal infection, use of sacral nerve stimulation, current use of TENS in pelvic region, back or legs, and previous PTNS treatment.

Technique: In the active treatment group, PTNS was delivered using the Urgent® PC neuromodulation system. Two inactive sham surface electrodes were also placed on the foot. In the sham group, a placebo needle was used (it gives the sensation of a slight prick but does not actually puncture the skin) and 2 active TENS surface electrodes were placed on the foot along with an inactive PTNS surface electrode.</td>
<td>Number of patients analysed: 220 (110 vs 110)

Moderate or marked improvement in overall bladder symptoms at 13 weeks (global response assessment - intent to treat analysis)
• PTNS = 54.5% (60/110)
• Sham = 20.9% (23/110), p < 0.001

Global response assessment improvement at 13 weeks compared to baseline
<table>
<tr><th></th><th>PTNS n (%)</th><th>Sham n (%)</th><th>p value</th></tr>
<tr><td>Urinary urgency</td><td>44/103 (42.7%)</td><td>24/105 (22.9%)</td><td>0.003</td></tr>
<tr><td>Urinary frequency</td><td>49/103 (47.6%)</td><td>23/105 (21.9%)</td><td>< 0.001</td></tr>
<tr><td>Urinary urge incontinence</td><td>39/103 (37.9%)</td><td>23/104 (22.1%)</td><td>0.02</td></tr>
</table>
Voiding diary OAB symptom episode data (mean ±SD)
<table>
<tr><th></th><th>Baseline</th><th>13 weeks</th><th>p value</th></tr>
<tr><td>PTNS</td><td></td><td></td><td></td></tr>
<tr><td>Mean voids/day</td><td>12.3 ± 3.2</td><td>9.8 ± 2.8</td><td>< 0.001</td></tr>
<tr><td>Night time voids</td><td>2.9 ± 1.6</td><td>2.1 ± 1.4</td><td>< 0.001</td></tr>
<tr><td>Voided volume (ml)</td><td>169.5 ± 78.9</td><td>183.0 ± 75.6</td><td>0.01</td></tr>
<tr><td>Median number of urge incontinence episodes</td><td>3.0</td><td>0.3</td><td>< 0.0001</td></tr>
<tr><td>Moderate to severe urgency</td><td>8.3</td><td>3.7</td><td>< 0.0001</td></tr>
</table>
</td>
<td>Treatment-related adverse events:
• Ankle bruising= 0.9% (1/110)
• Discomfort at needle site = 1.8% (2/110)
• Bleeding at needle site = 2.7% (3/110)
• Tingling in the leg = 0.9% (1/110)

No local treatment related adverse events were reported in the sham group.

No systemic adverse events were reported in either group.</td>
<td>Follow-up issues:
• 12 patients withdrew prior to 13-week follow-up: 5 patients withdrew consent (4 PTNS, 1 sham), 4 were lost to follow-up (2 in each group), and 3 withdrew for ‘other reasons’ (1 PTNS, 2 sham).

Study design issues:
• Patients were randomised using a random block design stratified by site.
• Subjects and study coordinators who administered questionnaires and reviewed voiding diary outcome measures were blinded to treatment assignment.
• Validated sham intervention.
• An intent to treat analysis was done, which counted any patient not assessed at 13 weeks as a failure.
• The OAB-q is validated for use in both continent and incontinent OAB patients. It consists of an 8-item symptom ‘bother’ scale (lower score means less symptoms) and 25 HRQL) items, comprising 4 subscales (concern, coping, social interaction, sleep) and a total HRQL score. For the HRQL items, a higher score indicates better HRQL.

Study population issues:
• Baseline characteristics were homogenous across treatment groups.

Other issues:
• This study was published after the search date specified in the overview.</td>
</tr>
</table>

Abbreviations used: CI, confidence interval; HRQL, health-related quality of life; NS, not significant; OAB, overactive bladder; OAB-q, overactive bladder questionnaire; OR, odds ratio; PTNS, percutaneous tibial nerve stimulation; QoL, quality of life; SANS, Stoller afferent nerve stimulation

Study details	Key efficacy findings	Key safety findings	Comments

Follow-up: 13 weeks
Conflict of interest/source of funding: supported by Uroplasty Inc.

episodes/day			
Sham			
Mean voids/day	12.4± 3.0	11.0 ± 3.1	< 0.001
Night time voids	2.9 ± 1.7	2.6 ± 1.6	0.02
Voided volume (ml)	168.7 ± 84.0	172.6 ± 90.6	0.13
Median number of urge incontinence episodes	1.8	1.0	< 0.0001
Moderate to severe urgency episodes/day	8.0	5.0	< 0.0001

The difference between the groups was statistically significant for all outcomes except voided volume.

OAB-q change from baseline at 13 weeks (mean change ± SD)

	PTNS	**Sham**	**Difference (PTNS – sham)**
Symptom severity score	-36.7 ± 21.5	-29.2 ± 20.0	-7.5 p = 0.01
HRQL score	34.2 ± 21.3	20.6 ± 20.6	8.2 p = 0.006

52% of patients in the PTNS group and 58% of patients in the sham group correctly identified their randomised intervention assignment.

Abbreviations used: CI, confidence interval; HRQL, health-related quality of life; NS, not significant; OAB, overactive bladder; OAB-q, overactive bladder questionnaire; OR, odds ratio; PTNS, percutaneous tibial nerve stimulation; QoL, quality of life; SANS, Stoller afferent nerve stimulation

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Peters KM (2009)[2]

Randomised controlled trial

USA

Recruitment period: 2006–8

Study population: ambulatory adults with OAB symptoms

n = 100 (50 PTNS vs 50 extended-release tolterodine)

Mean age (years): PTNS = 57.5, tolterodine = 58.2
Sex: PTNS = 96% female, tolterodine = 92% female

Patient selection criteria: ambulatory adults with OAB symptoms, with or without a history of previous anticholinergic drug use, with ≥ 8 voids per 24 hours. Exclusion criteria were OAB pharmacotherapy within the previous month, primary complaint of stress urinary incontinence, demonstrated sensitivity to tolterodine, pacemakers or implantable defibrillators, excessive bleeding, urinary or gastric retention, nerve damage or neuropathy, uncontrolled narrow angle glaucoma, positive urinalysis for infection or pregnancy.

Technique: PTNS was delivered using the Urgent® PC neuromodulation system. Parameters were maximised based on patient motor and sensory responses. Patients on tolterodine received a 90-day prescription for 4 mg daily with a subsequent decrease to 2 mg daily if the higher dose could not be tolerated.

Follow-up: 12 weeks
Conflict of interest/source of funding: supported by Uroplasty Inc.</td>
<td>Number of patients analysed: 87 (44 vs 43)

Global response assessment of OAB symptom improvement after 12 weeks of therapy
<table>
<tr><th></th><th>PTNS
n (%)</th><th>Tolterodine
n (%)</th></tr>
<tr><td>Subject assessment:</td><td>n = 44</td><td>n = 42</td></tr>
<tr><td>Cured</td><td>1 (2.3)</td><td>2 (4.8)</td></tr>
<tr><td>Improved</td><td>34 (77.3)</td><td>21 (50)</td></tr>
<tr><td>Cured or improved*</td><td>35 (79.5)</td><td>23 (54.8)</td></tr>
<tr><td>No improvement/ worsening</td><td>9 (20.5)</td><td>19 (45.2)</td></tr>
<tr><td>Investigator assessment:</td><td>n = 44</td><td>n = 43</td></tr>
<tr><td>Cured</td><td>2 (4.5)</td><td>2 (4.7)</td></tr>
<tr><td>Improved</td><td>33 (75)</td><td>24 (55.8)</td></tr>
<tr><td>Cured or improved**</td><td>35 (79.5)</td><td>26 (60.5)</td></tr>
<tr><td>No improvement/ worsening</td><td>9 (20.5)</td><td>17 (39.5)</td></tr>
</table>
* p = 0.01, ** p = 0.05

Voiding diary OAB symptom episode data (mean ± SD)
<table>
<tr><th></th><th>Baseline</th><th>12 weeks</th><th>p value</th></tr>
<tr><td colspan="4">PTNS (n = 41)</td></tr>
<tr><td>Voids/day</td><td>12.1 ± 3.1</td><td>9.8 ± 3.0</td><td>< 0.001</td></tr>
<tr><td>Nocturia</td><td>2.5 ± 1.2</td><td>1.7 ± 1.1</td><td>< 0.001</td></tr>
<tr><td>Urge incontinence</td><td>2.2 ± 2.3</td><td>1.2 ± 1.6</td><td>0.007</td></tr>
<tr><td>Moderate to severe urgency episodes/day</td><td>6.0 ± 4.1</td><td>3.9 ± 2.8</td><td>0.002</td></tr>
</table>
</td>
<td>Proportion of patients with at least 1 moderate adverse event reported to be related to the treatment:
• PTNS = 16.3% (8/49)
• Tolterodine = 14.3% (7/49)

In the PTNS arm, there was 1 report each of generalised swelling, worsening of incontinence, headache, haematuria, inability to tolerate stimulation, leg cramps, intermittent foot/toe pain and vasovagal response to needle placement.

Adverse events in the tolterodine arm included constipation, infection, dizziness, headache, vision disturbance, diarrhoea, increased frequency, fatigue, ear pain and abdominal pain.

In a repeated measures regression analysis during 12 weeks, constipation and dry mouth were reported less frequently in the PTNS arm compared to the tolterodine arm (p < 0.05).</td>
<td>Follow-up issues:
• Of the 100 patients randomised, 8 withdrew consent prior to 12-week follow-up (5 PTNS, 3 drug therapy). Four additional patients in the drug therapy group were withdrawn prior to 12-week follow-up: 3 because the treatment was unsuccessful and 1 for ‘other reasons’.
• One patient was lost to follow-up (allocated to PTNS).
• Three patients in the PTNS group were excluded from the analysis of the primary endpoint because the 12-week voiding diary was not completed.

Study design issues:
• Patients were randomised using a random block design stratified by site.
• The primary endpoint was mean reduction in number of voids per 24 hours (1-sided t test used with a non-inferiority margin of 20%).
• Secondary endpoints were analysed with 2-sided t tests.
• Two-day voiding diaries were collected at baseline and at 12 weeks, and were analysed by an independent biostatistician.
• The OAB-q is validated for use in both continent and incontinent OAB patients. It consists of an 8-item symptom ‘bother’ scale and 25 HRQL items, comprising 4 subscales (concern, coping, social interaction, sleep) and a total HRQL score. For the HRQL items, a higher score indicates better HRQL.

Study population issues:
• Baseline characteristics were homogenous across treatment groups.</td>
</tr>
</table>

Abbreviations used: CI, confidence interval; HRQL, health-related quality of life; NS, not significant; OAB, overactive bladder; OAB-q, overactive bladder questionnaire; OR, odds ratio; PTNS, percutaneous tibial nerve stimulation; QoL, quality of life; SANS, Stoller afferent nerve stimulation

Study details	Key efficacy findings	Key safety findings	Comments

Voided volume (ml)	152.7 ± 79.3	185.5 ± 81.1	0.001
Tolterodine (n = 43)			
Voids/day	12.5 ± 3.7	9.9 ± 3.8	< 0.001
Nocturia	2.5 ± 1.4	1.9 ± 1.6	0.03
Urge incontinence	3.5 ± 3.5	1.8 ± 2.5	0.006
Moderate to severe urgency episodes/day	7.4 ± 4.8	4.5 ± 3.6	< 0.001
Voided volume (ml)	141.2 ± 76.2	158.7 ± 99.8	0.06

There was no statistically significant difference between the groups.

OAB-q change from baseline at 12 weeks (mean change ± SD)

	PTNS (n = 44)	Tolterodine (n = 43)
Symptom severity score	-25.0 ± 20.8	-23.7 ± 25.5
HRQL score	25.3 ± 21.5	22.1 ± 20.7
Coping subscale	27.5 ± 26.2	26.9 ± 24.9
Concern subscale	30.0 ± 26.6	25.8 ± 24.6
Sleep subscale	26.3 ± 25.2	19.0 ± 26.0
Social subscale	14.2 ± 21.2	12.4 ± 19.1

$p < 0.001$ for all comparisons within each group. The differences between groups were not statistically significant.

Abbreviations used: CI, confidence interval; HRQL, health-related quality of life; NS, not significant; OAB, overactive bladder; OAB-q, overactive bladder questionnaire; OR, odds ratio; PTNS, percutaneous tibial nerve stimulation; QoL, quality of life; SANS, Stoller afferent nerve stimulation

Study details	Key efficacy findings	Key safety findings	Comments
Van Balken MR (2006)[3] **Case series (multicentre)** The Netherlands Recruitment period: not reported Study population: patients with OAB **n = 83** Mean age: 54.1 years Sex: 72% (60/83) female Patient selection criteria: inclusion and exclusion criteria were not described. Technique: PTNS was delivered using the Urgent® PC neuromodulation system. The current was set at a well-tolerable level. Patients underwent weekly 30-minute outpatient treatment sessions for 12 weeks. In case of sufficient improvement, patients were offered chronic treatment. Follow-up: 12 weeks Conflict of interest/source of funding: not reported	Number of patients analysed: **83** **Subjective response** = 55.4% (defined as a patient request for continuous chronic treatment to maintain the response) **Objective response** = 37.3% (defined as a decrease in symptoms [such as number of voids/24 hours and number of incontinence episodes/24 hours] of over 50%). A low total baseline score on the SF-36 questionnaire was predictive for not obtaining objective (OR 0.44, 95% CI 0.20 to 1.0) and/or subjective success (OR 0.42, 95% CI 0.20 to 0.89). In particular, PTNS was very likely to fail in patients with a low mental component score (≤ 30 out of a maximum of 50). Gender, age, weight, body mass index, duration of complaint, number and kinds of previous treatment, PTNS study centre and stimulation parameters were all statistically proved not to be of prognostic value.	No safety outcomes were reported.	**Study design issues**: • 8 study centres were involved. • All patients completed micturition or pain diaries as well as general and disease-specific QoL questionnaires. **Study population issues**: • The paper also reported results for an additional 16 patients with non-obstructive urinary retention and 33 patients with chronic pelvic pain. Data for these patients have not been included here.

Abbreviations used: CI, confidence interval; HRQL, health-related quality of life; NS, not significant; OAB, overactive bladder; OAB-q, overactive bladder questionnaire; OR, odds ratio; PTNS, percutaneous tibial nerve stimulation; QoL, quality of life; SANS, Stoller afferent nerve stimulation

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Vandoninck V (2003)[4]

Case series (multicentre)

The Netherlands and Italy

Recruitment period: 1999–2001

Study population: patients with OAB

n = 90
Median age: 51 years (range 19–82)
Sex: 74% female (67/90)

Patient selection criteria: patients with OAB. An increased urinary frequency was defined as 8 voids or more per 24 hours. Stress urinary incontinence was excluded through urodynamic investigation. Exclusion criteria were age < 18 years, symptoms < 6 months, pregnancy, urinary tract infection, carcinoma in situ, bladder malignancy, interstitial cystitis, bladder or kidney stone, severe cardiopulmonary disease, use of pentosan polysulphate sodium or bladder instillations, uncontrolled diabetes, diabetes with peripheral nerve involvement, neurological disease, change in parasympathetic medication, physiotherapy during the study, bladder outlet obstruction, transurethral instrumentation ≤ 4 weeks before or during the study.

Technique: treatment included 12 sessions of PTNS.

Follow-up: 12 weeks.
Conflict of interest/source of funding: sponsored by CystoMedix.</td>
<td>Number of patients analysed: 90

24-hour frequency volume chart data and QoL scores (mean values)
<table>
<tr><th></th><th>n</th><th>Base-line</th><th>n</th><th>12 wks</th><th>p value</th></tr>
<tr><td>Leakages</td><td>60</td><td>5</td><td>59</td><td>2</td><td>< 0.01</td></tr>
<tr><td>Incontinence severity</td><td>60</td><td>2</td><td>58</td><td>1</td><td>< 0.01</td></tr>
<tr><td>Urinary frequency</td><td>80</td><td>13</td><td>75</td><td>10</td><td>< 0.001</td></tr>
<tr><td>Mean voided volume (ml)</td><td>79</td><td>135</td><td>74</td><td>191</td><td>< 0.001</td></tr>
<tr><td>I-QoL</td><td>81</td><td>49</td><td>80</td><td>67</td><td>< 0.001</td></tr>
<tr><td>SF-36</td><td>79</td><td>57</td><td>82</td><td>67</td><td>< 0.001</td></tr>
</table>
Subjective response = 64.4% (58/90) (defined as a patient request for continuous chronic treatment to maintain the response)

Objective success rate (primary outcome - reduction in number of urinary leakage episodes of 50% or more per 24 hours) = 56.7% (34/60).

38% (23/60) of patients were considered to be dry after treatment. An additional 11 patients achieved at least 50% reduction in the number of leakage episodes.

Voiding frequency < 8 times per day = 25% (20/80)

Proportion of patients with daily incontinence:
• Baseline = 75% (60/80)
• After treatment = 44% (35/80)

50% or more reduction in severity of incontinence = 51.7% (31/60)</td>
<td>No safety outcomes were reported.</td>
<td>Study design issues:
• Prospective data collection.
• Consecutive patients.
• Quality of life was measured using I-QOL (incontinence specific) and the Short-Form health survey (SF-36). In both of these, a higher score denotes better quality of life.
• Incontinence severity was measured on a scale of 1 to 3 (1 = some drops, 2 = small amount, 3 = severe urine loss necessitating change of clothing).

Other issues:
• Urodynamic investigations were only performed at baseline and after 12 treatment sessions in 51% (46/90) of patients.
• The success rate is quoted as 56% but 34/60 rounds up to 57%.
• The percentage of patients with detrusor instability was reported as 70% but 34/46 is 74%.</td>
</tr>
</table>

Abbreviations used: CI, confidence interval; HRQL, health-related quality of life; NS, not significant; OAB, overactive bladder; OAB-q, overactive bladder questionnaire; OR, odds ratio; PTNS, percutaneous tibial nerve stimulation; QoL, quality of life; SANS, Stoller afferent nerve stimulation

Study details	Key efficacy findings	Key safety findings	Comments
	24-hour frequency volume chart data and Qol scores (mean values) in 46 patients who had urodynamic investigations at baseline and after 12 PTNS sessions		

	Base-line	12 wks	p value
24 hour frequency/volume chart			
Leakages	4	3	0.001
Incontinence severity	2	1.88	< 0.001
Urinary frequency	13	9	< 0.001
Mean voided volume (ml)	135	205	< 0.001
Quality of life scores			
I-QoL	39	66	< 0.001
SF-36	54	64	0.003
Cystometric data			
Cystometric capacity (ml)	243	340	0.043
Patients with detrusor instability*	74% (34/46)	74% (34/46)	
Volume at detrusor instability (ml)	133	210	0.012
Detrusor pressure at detrusor instability	35	41	0.67

*Detrusor instability was eliminated in 3 patients and de novo detrusor instability was noted in 3 patients.

The presence of detrusor instability at baseline (n = 48) was found to be a strong predictive factor for therapeutic failure.

Abbreviations used: CI, confidence interval; HRQL, health-related quality of life; NS, not significant; OAB, overactive bladder; OAB-q, overactive bladder questionnaire; OR, odds ratio; PTNS, percutaneous tibial nerve stimulation; QoL, quality of life; SANS, Stoller afferent nerve stimulation

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Congregado Ruiz B (2004)[5]

Case series

Spain

Recruitment period: 1999–2002

Study population: women with lower urinary tract dysfunction who had not responded to anticholinergic drugs

n = 51 (26 frequency-urgency, 22 urge incontinence, 3 interstitial cystitis)

Mean age: 55 years (range 18–74)
Sex: 100% (51/51) female

Patient selection criteria: lower urinary tract dysfunction, no response to anticholinergic drugs, age 18 years or over, sterile urine culture, no active cystitis or urethritis, no previous history of continence surgery, no history of current bladder malignancy, high-grade dysplasia or carcinoma.

Technique: Electrical current was increased until the flexor muscle of the first toe contracted. The voltage was then maintained 1 point below the stimulus that generated the muscular contraction. The treatment was administered weekly for a 30-minute period over 10 weeks.

Mean follow-up: 21 months (range 6–36)

Conflict of interest/source of funding: not reported</td>
<td>Number of patients analysed: 51

Frequency, voiding volume, leakage episodes and hypogastric pain in 26 women with frequency or urgency
<table>
<tr><th></th><th>Before treatment</th><th>After treatment</th><th>p value</th></tr>
<tr><td>Daytime frequency</td><td>9.6 ± 2.8</td><td>6.5 ± 2.0</td><td>< 0.001</td></tr>
<tr><td>Daytime voiding volume</td><td>148 ± 58</td><td>231 ± 71</td><td>< 0.001</td></tr>
<tr><td>Night time frequency</td><td>2.9 ± 2.0</td><td>1.4 ± 1.0</td><td>< 0.001</td></tr>
<tr><td>Night time voiding volume</td><td>198 ± 128</td><td>234 ± 105</td><td>NS</td></tr>
<tr><td>Hypogastric pain</td><td>11</td><td>4</td><td>< 0.05</td></tr>
</table>
Frequency, voiding volume, leakage episodes and hypogastric pain in 22 women with urge incontinence
<table>
<tr><th></th><th>Before treatment</th><th>After treatment</th><th>p value</th></tr>
<tr><td>Daytime frequency</td><td>8.7 ± 4.3</td><td>7.1 ± 3.2</td><td>< 0.05</td></tr>
<tr><td>Daytime voiding volume</td><td>133 ± 72</td><td>218 ± 88</td><td>< 0.001</td></tr>
<tr><td>Daytime leakage episodes</td><td>3.7 ± 3.6</td><td>1.7 ± 2.0</td><td>< 0.01</td></tr>
<tr><td>Night time frequency</td><td>2.5 ± 2.1</td><td>1.3 ± 1.3</td><td>< 0.05</td></tr>
<tr><td>Night time voiding volume</td><td>193 ± 122</td><td>272 ± 210</td><td>NS</td></tr>
<tr><td>Night time leakage episodes</td><td>1.2 ± 1.8</td><td>0.4 ± 0.8</td><td>< 0.01</td></tr>
</table>
</td>
<td>There were no infections, mechanism failures or pain detected during the treatment.</td>
<td>Study design issues:
• Prospective data collection.
• The study states that data were collected before, during and after the study but no timescales are defined in the results. Although the mean follow-up is 21 months, it is not clear if the ‘after treatment’ results relate to this follow-up or to the period immediately after treatment.

Study population issues:
• Patients were only included if they had not responded to anticholinergic drugs.

Other issues:
• The percentages for the patient evaluation of results have been re-calculated as those presented were incorrect.</td>
</tr>
</table>

Abbreviations used: CI, confidence interval; HRQL, health-related quality of life; NS, not significant; OAB, overactive bladder; OAB-q, overactive bladder questionnaire; OR, odds ratio; PTNS, percutaneous tibial nerve stimulation; QoL, quality of life; SANS, Stoller afferent nerve stimulation

Study details	Key efficacy findings	Key safety findings	Comments

Hypogastric pain	6	2	<0.05

Quality of life (26 women with frequency or urgency)

	Before treatment	After treatment
Felt bad	23 (88.4%)	3 (11.5%)
Felt indifferent	3 (11.5%)	5 (9.8%)
Felt happy	0	16 (61.5%)
Felt pleased	0	2 (7.7%)

$p < 0.05$

Patient evaluation of results (26 women with frequency or urgency)

- Excellent = 11.5% (3/26)
- Favourable = 65.4% (17/26)
- Fair = 15.4% (4/26)
- No difference = 7.7% (2/26)

Quality of life (22 women with urge incontinence)

	Before treatment	After treatment
Felt unhappy	3 (13.6%)	0
Felt bad	17 (77.3%)	5 (22.7%)
Felt indifferent	2 (9.1%)	5 (22.7%)
Felt happy	0	9 (40.9%)
Felt pleased	0	3 (13.6%)

$p < 0.05$

Patient evaluation of results (22 women with urge incontinence)

- Excellent = 18.2% (4/22)
- Favourable = 36.4% (8/22)
- Fair = 22.7% (5/22)
- No difference = 22.7% (5/22)

Abbreviations used: CI, confidence interval; HRQL, health-related quality of life; NS, not significant; OAB, overactive bladder; OAB-q, overactive bladder questionnaire; OR, odds ratio; PTNS, percutaneous tibial nerve stimulation; QoL, quality of life; SANS, Stoller afferent nerve stimulation

Study details	Key efficacy findings	Key safety findings	Comments
Govier FE (2001)[6] **Case series (multicentre)** USA Recruitment period: 1999 Study population: patients with urgency, frequency and/or pelvic floor dysfunction **n = 53** Mean age: 57.4 years (range 24–80) Sex: 90% female Patient selection criteria: patients with documented urgency, frequency, and/or pelvic floor dysfunction resulting in a mean frequency of at least 10 voids per day and/or 3 per night; age > 18 years. Medical therapy, Kegel exercises, biofeedback and pelvic floor stimulators had failed in all patients. Exclusion criteria included an active urinary tract infection, structural abnormality or urodynamically proved instability secondary to a known neurological condition. Technique: SANS (UroSurge Inc) device used for stimulation. Sessions lasted 30 minutes and were once a week for 12 weeks. **Follow-up: 12 weeks** Conflict of interest/source of funding: two authors have disclosed a financial interest and/or other relationship with several manufacturers, including UroSurge Inc.	Number of patients analysed: **53** Success rate (defined as patients with at least 25% reduction in daytime and/or night time frequency) = 71% Proportion of patients with at least a 25% reduction or improvement in daytime frequency = 55.2% ($p < 0.05$) Average reduction in or improvement in mean daytime voiding frequency = 25% ($p < 0.05$) Average reduction or improvement in mean 24-hour voiding frequency = 22% ($p < 0.05$) Average reduction in or improvement in mean night time voiding frequency = 21% ($p < 0.05$) Average reduction in or improvement in daytime and night time urge incontinence or leak episodes = 35% ($p < 0.05$) Improvement in incontinence QoL indices = 20% ($p < 0.05$) Improvements were noted in the Short Form health survey (SF-36) and the pelvic pain visual analogue score but they were not statistically significant.	No serious or unanticipated adverse events were reported. There was one case of cardiomyopathy but it was not considered to be related to PTNS in any way. **Adverse events:** • Moderate throbbing pain at needle site = 2% (1/51) • Moderate foot pain = 2% (1/51) • Stomach discomfort = 2% (1/51) All events resolved spontaneously and did not impact or preclude further treatment.	**Follow-up issues**: • A total of 89% (47/53) of patients completed the study. Two patients were excluded for noncompliance, 1 was started on anticoagulants (exclusion criteria) and 3 quit the study at 4, 5 and 6 weeks respectively (reason not stated). **Study design issues**: • Prospective data collection. • Primary outcome was the change in mean daytime voiding frequency from baseline to 12 weeks. **Study population issues**: • The report states that 'medical therapy' had failed in all patients, but does not specify further. **Other issues**: • Patients who responded to the initial 12-week course of treatment transferred into chronic treatment or tapering protocol. Treatment sessions were customised to the individual patient, with increasing intervals between visits.

Abbreviations used: CI, confidence interval; HRQL, health-related quality of life; NS, not significant; OAB, overactive bladder; OAB-q, overactive bladder questionnaire; OR, odds ratio; PTNS, percutaneous tibial nerve stimulation; QoL, quality of life; SANS, Stoller afferent nerve stimulation

Study details	Key efficacy findings	Key safety findings	Comments
Nuhoglu B (2006)[7] **Case series** Turkey Recruitment period: not reported Study population: women with OAB **n = 35** Mean age: 47.3 years (range 35–57) Sex: 100% (35/35) female Patient selection criteria: Exclusion criteria included neurogenic condition causing urinary incontinence; persistent or recurring urinary tract infection; history of interstitial cystitis; bladder cancer; previous bladder augmentation surgery; spinal injury; Alzheimer's disease or dementia; obstruction of the urinary tract; primary diagnosis of stress incontinence. No patients received anticholinergic therapy during PTNS treatment. Technique: SANS device used. Treatment course lasted 10 weeks. Stimulation was applied at the highest current where the patient did not feel discomfort. **Follow-up: 12 months (after end of treatment)** Conflict of interest/source of funding: not reported	Number of patients analysed: **35** **Symptom free after treatment** = 54% (19/35) **Symptom free at 1 year** = 23% (8/35) (in patients with recurrence, symptoms reappeared around 3 months after treatment) **Base-line (n = 35)** / **Post treatment (n = 35)** / **1 year follow-up (n = 32)** Urgency (/day): 3.5 ± 1.8 / 1.9 ± 1.3* / 2.5 ± 1.7* Urge incontinence (/day): 2.3 ± 1 / 0.8 ± 0.7* / 1.4 ± 0.9 Urine volume (ml): 148.3 ± 49.1 / 178 ± 53.2* / 156.2 ± 46.8* Frequency (/day): 11.2 ± 2.9 / 7.4 ± 1.5* / 9.4 ± 2.4 QoL (SEAPI questionnaire): 15.4 ± 6.3 / 6.1 ± 6.1* / 9.3 ± 6.4* First bladder sensation (ml): 77.4 ± 22.7 / 92.9 ± 25.2* / 82.9 ± 21.6 Normal cystometric capacity (ml): 143.2 ± 41.1 / 174.4 ± 45.5* / 165.6 ± 40.6* Maximum cystometric capacity (ml): 390.5 ± 30.7 / 419.1 ± 30.1* / 403.7 ± 27.3 Involuntary detrusor contraction volume (ml): 135.1 ± 47.1 / 161.3 ± 71.3* / 136.2 ± 54.1 Involuntary detrusor contraction pressure (cmH_2O): 35.5 ± 10.3 / 23.1 ± 8.9* / 31.2 ± 10.6 * $p < 0.01$	No safety outcomes were reported.	**Follow-up issues**: • Losses to follow-up = 8.6% (3/35) **Study design issues**: • Quality of life was measured using an incontinence specific questionnaire (SEAPI), in which lower scores denote a higher quality of life. **Study population issues**: • All patients had previously undergone pharmacological treatment (oxybutynin) but 24 had OAB recurrence or insufficient response. The remaining 11 patients had to stop treatment because of drug side effects.

Abbreviations used: CI, confidence interval; HRQL, health-related quality of life; NS, not significant; OAB, overactive bladder; OAB-q, overactive bladder questionnaire; OR, odds ratio; PTNS, percutaneous tibial nerve stimulation; QoL, quality of life; SANS, Stoller afferent nerve stimulation

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>MacDiarmid SA (2010)[8]

Case series

USA

Recruitment period: not reported

Study population: patients with OAB who responded to an initial course of 12 consecutive weekly PTNS sessions

n = 33

Mean age: 59 years
Sex: 94% (31/33) female

Patient selection criteria: patients who had a successful response to an initial course of PTNS. Patients were required to be OAB drug-free throughout the study.

Technique: Urgent ® PC device used for stimulation. The treatment interval was extended or shortened based on treatment efficacy and wishes of the patient (the mean interval was 21 days). Treatment sessions were 30 minutes in duration and the current level was based on patient sensory and motor response.

Follow-up: 12 months (from start of treatment)

Conflict of interest/source of funding: the study was supported by Uroplasty Inc.</td>
<td>Number of patients analysed: 25 (at 12 months)

Mean improvements at 12 months from baseline
<table>
<tr><th></th><th>Baseline</th><th>Mean decrease</th><th>p value</th></tr>
<tr><td>Frequency (voids per day)</td><td>12.4</td><td>2.8</td><td>< 0.001</td></tr>
<tr><td>Urge incontinence (daily episodes)</td><td>2.2</td><td>1.6</td><td>< 0.001</td></tr>
<tr><td>Moderate to severe urgency episodes</td><td>6.3</td><td>3.7</td><td>< 0.01</td></tr>
<tr><td>Nocturia</td><td>2.5</td><td>0.8</td><td>< 0.05</td></tr>
</table>
Voided volume improved by a mean of 39 ml ($p < 0.05$)

Global response assessment of OAB symptom improvement from baseline
<table>
<tr><th></th><th>Investigator assessment</th><th>Patient assessment</th></tr>
<tr><td>6 months</td><td></td><td></td></tr>
<tr><td>Cured</td><td>9% (3/32)</td><td>13% (4/32)</td></tr>
<tr><td>Improved</td><td>88% (28/32)</td><td>81% (26/32)</td></tr>
<tr><td>No improvement/ worsening</td><td>3% (1/32)</td><td>6% (2/32)</td></tr>
<tr><td>12 months</td><td></td><td></td></tr>
<tr><td>Cured</td><td>20% (5/25)</td><td>16% (4/25)</td></tr>
<tr><td>Improved</td><td>76% (19/25)</td><td>80% (20/25)</td></tr>
<tr><td>No improvement/ worsening</td><td>4% (1/25)</td><td>4% (1/25)</td></tr>
</table>
As time progressed, there was statistically significant improvement in the OAB-q symptom severity score observed at 12 months vs 12 weeks and 6 months ($p < 0.01$).</td>
<td>One patient had 2 events of abdominal pain classified as related to PTNS.

Three other events classified as unknown relationship with PTNS were reported – 1 case each of urinary tract infection, worsening hypertension and diarrhoea.

All other adverse events were reported as non-treatment related (not described).</td>
<td>Follow-up issues:
• Of the 8 patients who discontinued treatment, 1 withdrew due to lack of effectiveness, 1 switched back to drug treatment, 1 did not want further treatment, 2 withdrew to continue PTNS outside of the study, 1 was lost to follow-up and the remaining 2 left the study for other health reasons.

Study design issues:
• Patients were treated at individualised tapering intervals over the course of 9 months.

Study population issues:
• The study only included patients who responded to an initial 12-week course of PTNS (as part of the RCT reported by Peters et al, 2009).

Other issues:
• Patients were not counselled about fluid management and it is not known if fluid management habits changed during the study.</td>
</tr>
</table>

Efficacy

In an RCT of 220 patients comparing PTNS with sham, 55% (60/110) of patients in the PTNS group and 21% (23/110) of patients in the sham group had a moderate or marked improvement in overall bladder symptoms at 13 weeks ($p < 0.001$)[1].

In an RCT of 100 patients comparing PTNS with medication, 80% (35/44) of patients in the PTNS group and 55% (23/42) of patients in the medication group considered themselves to be cured or improved ($p = 0.01$)[2]. Both groups showed a similar statistically significant decrease in the number of voids per day, nocturia, urge incontinence and the number of moderate to severe urgency episodes per day. Quality of life was also significantly improved in both groups immediately after treatment.

A case series of 83 patients reported a subjective response of 55% (defined as a patient request for continuous chronic treatment to maintain the response) and an objective response of 37% (defined as a decrease in symptoms [such as number of voids per 24 hours and number of incontinence episodes per 24 hours] of over 50%)[3].

A second case series of 90 patients reported a subjective response of 64% (58/90) and an objective response of 57% (34/60) (defined as 50% or more reduction in urinary leakage episodes per 24 hours)[4].

A case series of 51 patients reported statistically significant improvements in daytime frequency, daytime voiding volume, night time frequency and hypogastric pain[5]. Of the 26 women with frequency or urgency, 12% (3/26) rated the results as excellent, 65% (17/26) favourable, 15% (4/26) fair and 8% (2/26) considered there to be no difference. A case series of 53 patients reported a success rate of 71% (defined as a reduction in daytime and/or night time frequency of 25% or more)[6].

In a case series of 35 patients, the proportion of patients who were symptom free decreased from 54% (19/35) immediately after treatment to 23% (8/35) at 1-year follow-up[7].

In another case series, 33 patients who responded to an initial 12 sessions of PTNS were offered additional treatment sessions at varying intervals for a further 9 months. 94% (30/32) of patients considered themselves to be cured or improved at 6 months and 96% (24/25) at 12 months[8].

Safety

Most studies reported that there were no serious adverse events associated with PTNS.

In the RCT comparing PTNS with anticholinergic medication, 16% (8/49) of patients in the PTNS group and 14% (7/49) of patients treated with medication reported at least 1 moderate adverse event that was considered to be related to the treatment. In the PTNS group, there was 1 report each of generalised swelling, worsening of incontinence, headache, haematuria, inability to tolerate stimulation, leg cramps, intermittent foot/toe pain and vasovagal response to needle placement. Constipation and dry mouth were reported less frequently in the PTNS group compared to the medication group ($p < 0.05$)[2].

The RCT of 220 patients comparing PTNS with sham reported 7 treatment-related adverse events in the PTNS group. These were bleeding at the needle site (3% [3/110]), discomfort at the needle site (2% [2/110]), ankle bruising (1% [1/110]) and tingling in the leg (1% [1/110]). There were no adverse events reported in the sham group[1].

The case series of 51 patients reported 1 case each of throbbing pain at the needle site, foot pain and stomach discomfort[6]. In another case series of 33 patients, there was 1 report each of abdominal pain, urinary tract infection, worsening hypertension and diarrhoea[8]. The abdominal pain was thought to be related to PTNS but it was unknown if the other events were related to the treatment.

Validity and generalisability of the studies

- Different outcome measures have been used to define success rates.
- Five studies listed neurological disease within the exclusion criteria[1,2,4,6,8].
- Different stimulation devices were used that had different stimulation parameters.
- Five studies did not follow the patients up beyond the end of the 12-week treatment cycle[1,2,3,4,6].
- The inclusion criteria in 2 studies stated that the OAB was refractory to medical treatment[5,6]. One study only included patients who reported that 'conservative care' had failed[1].
- Two case series reported results at 12 months[7,8]. In 1 of these, patients continued to be treated with PTNS at varying intervals over a 9-month period after an initial 12-week course of treatment[8]. In the other case series, no further treatments were given after the initial course of 10 weeks[7].

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B gives details of the recommendations made in each piece of guidance listed.

Interventional procedures

- Laparoscopic bladder augmentation cystoplasty (including clam cystoplasty). NICE interventional procedures guidance 326 (2009). Available from www.nice.org.uk/guidance/IPG326

- Sacral nerve stimulation for urge incontinence and urgency-frequency. NICE interventional procedures guidance 64 (2004). Available from www.nice.org.uk/guidance/IPG64

Clinical guidelines

- Urinary incontinence: the management of urinary incontinence in women. NICE clinical guideline 40 (2006). Available from www.nice.org.uk/guidance/CG40

Specialist Advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and does not represent the view of the society.

Mr M Drake, Mr P Dasgupta (British Association of Urological Surgeons)

Mr P Toozs-Hobson, Mr R Trochez (Royal College of Obstetricians and Gynaecologists).

- Three Specialist Advisers described PTNS as a minor variation of an existing procedure and one described it as established practice.
- For refractory OAB, PTNS would be compared against sacral nerve stimulation. For initial management of OAB it would be compared against anticholinergic drugs.

- One Specialist Adviser described an anecodotal adverse event of discomfort if the needle actually hits the tibial nerve.
- Adverse events reported in the literature include minor bleeding, pain and infection at the needle site.
- Subjective outcomes include symptom control: reduced episodes of urgency and urge incontinence, daily pad usage and quality of life outcomes.
- Objective outcomes of efficacy include urodynamic parameters such as detrusor overactivity and bladder capacity.
- The long term efficacy has not been established.
- There is no RCT against sacral nerve stimulation.
- Patient selection is important.
- The treatment carries a significant burden for the patient, initially requiring 12-weekly visits.
- One Specialist Adviser noted that intravesical botulinum injections are becoming increasingly available throughout the NHS for refractory OAB. However, this is unlicensed and evidence is awaited, so it is not certain that it will be a long-term option. The trajectory of intravesical botulinum injections will substantially affect PTNS.
- Two Specialist Advisers thought that the potential impact on the NHS is likely to be minor and two thought it would be moderate.

Patient Commentators' opinions

NICE's Patient and Public Involvement Programme was unable to obtain patient commentary for this procedure.

Issues for consideration by IPAC

None other than those listed above.

References

1. Peters KM, Carrico DJ, Perez-Marrero RA et al. (2010) Randomized trial of percutaneous tibial nerve stimulation versus sham efficacy in the treatment of overactive bladder syndrome: results from the SUmit trial. Journal of Urology 183: 1438–43.

2. Peters KM, MacDiarmid SA, Wooldridge LS et al. (2009) Randomized trial of percutaneous tibial nerve stimulation versus extended-release tolterodine: results from the overactive bladder innovative therapy trial. Journal of Urology 182: 1055–61.

3. Van Balken MR, Vergunst H, Bemelmans BL. (2006) Prognostic factors for successful percutaneous tibial nerve stimulation. European Urology 49: 360–5.

4. Vandoninck V, van Balken MR, Finazzi Agro E et al. (2003) Percutaneous tibial nerve stimulation in the treatment of overactive bladder: urodynamic data. Neurourology & Urodynamics 22: 227–32.

5. Congregado Ruiz B, Pena Outeirino XM, Campoy Martinez P et al. (2004) Peripheral afferent nerve stimulation for treatment of lower urinary tract irritative symptoms. European Urology 45: 65–9.

6. Govier FE, Litwiller S, Nitti V et al. (2001) Percutaneous afferent neuromodulation for the refractory overactive bladder: results of a multicenter study. Journal of Urology 165: 1193–8.

7. Nuhoglu B, Fidan V, Ayyildiz A et al. (2006) Stoller afferent nerve stimulation in woman with therapy resistant over active bladder; a 1-year follow up. International Urogynecology Journal 17: 204–7.

8. MacDiarmid SA, Peters KM, Shobeiri SA et al. (2010) Long-term durability of percutaneous tibial nerve stimulation for the treatment of overactive bladder. Journal of Urology 183: 234–40.

Appendix A: Additional papers on percutaneous posterior tibial nerve stimulation for overactive bladder syndrome

The following table outlines the studies that are considered potentially relevant to the overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Amarenco G, Ismael SS, Even-Schneider A et al. (2003) Urodynamic effect of acute transcutaneous posterior tibial nerve stimulation in overactive bladder. Journal of Urology 169: 210–5.	Case series n = 44	PTNS was associated with significant improvement in first involuntary detrusor contraction volume and maximum cystometric capacity.	Small case series with no follow-up.
Capitanucci ML, Camanni D, Demelas F et al. (2009) Long-term efficacy of percutaneous tibial nerve stimulation for different types of lower urinary tract dysfunction in children. Journal of Urology 182: 2056–61.	Case series n = 14 (with OAB)	Symptom improvement = 86% (12/14) Cure rate at 1 year = 41% Chronic stimulation was necessary to maintain results in 50% of patients.	Small case series.
De Gennaro M, Capitanucci ML, Mastracci P et al. (2004) Percutaneous tibial nerve neuromodulation is well tolerated in children and effective for treating refractory vesical dysfunction. Journal of Urology 171: 1911–3.	Case series n = 10 (with OAB)	Symptom improvement = 80%	Small case series.
Finezzi-Agro E, Campagna A, Sciobica F et al. (2005) Posterior tibial nerve stimulation: Is the once-a-week protocol the best option?. Minerva Urologica e Nefrologica 57: 119–23.	RCT (weekly sessions vs 3-weekly) n = 35	The periodicity of stimulation did not affect the results of PTNS treatment. In both groups, patients reported subjective improvement after 6–8 stimulation sessions. Success rate = 65%	Small study with no follow-up.
Finazzi-Agro E, Rocchi C, Pachatz C et al. (2009) Percutaneous tibial nerve stimulation produces effects on brain activity: study on the modifications of the long latency somatosensory evoked potentials. Neurourology & Urodynamics 28: 320–4.	RCT n = 24	Mean amplitude of P80 and P100 waves increased significantly after PTNS but not after sham stimulation.	Focus of study is to assess effects of PTNS on brain activity.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Kabay S, Kabay SC, Yucel M et al. (2009) The clinical and urodynamic results of a 3-month percutaneous posterior tibial nerve stimulation treatment in patients with multiple sclerosis-related neurogenic bladder dysfunction. Neurourology and Urodynamics 28: 964–8.	Case series n = 19	Statistically significant improvements in mean volume at first involuntary detrusor contraction and mean maximum cystometric capacity. 'PTNS is effective to suppress neurogenic detrusor overactivity in multiple sclerosis patients.'	Small case series with no follow-up.
Kabay SC, Kabay S, Yucel M et al. (2009) Acute urodynamic effects of percutaneous posterior tibial nerve stimulation on neurogenic detrusor overactivity in patients with Parkinson's disease. Neurourology & Urodynamics 28: 62–7.	Case series n = 32	Detrusor overactivity was suppressed and bladder capacity increased after PTNS, in patients with Parkinson's disease.	Small case series with no follow-up.
Kabay SC, Yucel M, Kabay S.(2008) Acute effect of posterior tibial nerve stimulation on neurogenic detrusor overactivity in patients with multiple sclerosis: urodynamic study. Urology 71: 641–5.	Case series n = 29	Detrusor overactivity was suppressed and bladder capacity increased after PTNS, in patients with multiple sclerosis.	Small case series with no follow-up.
Karademir K, Baykal K, Sen B et al. (2005) A peripheric neuromodulation technique for curing detrusor overactivity: Stoller afferent neurostimulation. Scandinavian Journal of Urology & Nephrology 39: 230–3.	RCT (PTNS alone vs PTNS and drug therapy) n = 43	Combining PTNS with drug therapy increased the success rate but the difference was not statistically significant.	Focus on combination of PTNS with drug therapy.
Klingler HC, Pycha A, Schmidbauer J et al. Use of peripheral neuromodulation of the S3 region for treatment of detrusor overactivity: a urodynamic-based study. Urology 56: 766–71.	Case series n = 15	Complete response (cure) = 47% (7/15) Significant improvement = 20% (3/15) Non responders = 33% (5/15)	Small case series.
MacDiarmid SA, Staskin DR (2009) Percutaneous tibial nerve stimulation (PTNS): a literature-based assessment. Current Bladder Dysfunction Reports 4: 29–33.	Meta-analysis n = 244	Overall, 71% of patients showed statistically significant improvement.	No description of statistical methods. It doesn't include the most recent RCT included in table 2.
Surwit EA, Campbell J, Karaszewski K (2009) Neuromodulation of the pudendal, hypogastric, and tibial nerves with pelvic floor muscle rehabilitation in the treatment of urinary urge incontinence. Neuromodulation 12: 175–9.	Case series n = 256 Median follow-up = 17 months	93% of patients were dry at 3 months.	Combined treatment (PTNS plus pelvic floor muscle rehabilitation).

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Svihra J, Kurca E, Luptak J et al. (2002) Neuromodulative treatment of overactive bladder--noninvasive tibial nerve stimulation. Bratislavske Lekarske Listy 103: 480–3.	RCT n = 28	There were similar statistically significant improvements in International Prostate Symptom Score, Incontinence quality of life and behavioural urge score with PTNS and drug therapy. There were no changes in the group without treatment.	Larger RCTs are included.
van Balken MR, Vergunst H, Bemelmans BL (2006) Sexual functioning in patients with lower urinary tract dysfunction improves after percutaneous tibial nerve stimulation. International Journal of Impotence Research 18: 470–5.	Case series n = 83	Sexual functioning improved after PTNS, in particular overall satisfaction, libido and the frequency of sexual activities.	Another study of the same patient group is included in table 2.
van Balken MR, Vandoninck V, Gisolf KW et al. (2001) Posterior tibial nerve stimulation as neuromodulative treatment of lower urinary tract dysfunction. Journal of Urology 166: 914–8.	Case series n = 37	Successful outcome = 59% (22/37) (defined as patients requesting to continue treatment)	Small case series with no follow-up.
van der Pal F, van Balken MR, Heesakkers JP et al. (2006) Correlation between quality of life and voiding variables in patients treated with percutaneous tibial nerve stimulation. BJU International 97: 113–6.	Case series n = 30	There was a statistically significant decrease in nocturia and incontinence episodes.	Small case series with no follow-up.
van der Pal F, van Balken MR, Heesakkers JP et al. (2006) Percutaneous tibial nerve stimulation in the treatment of refractory overactive bladder syndrome: is maintenance treatment necessary? BJU International 97: 547–50.	Case series n = 11	Continuous therapy is necessary in patients with OAB treated successfully by PTNS.	Small case series.
van der Pal F, van Balken MR, Heesakkers, J PFA et al. (2006) Implant-driven tibial nerve stimulation in the treatment of refractory overactive bladder syndrome: 12-Month follow-up. Neuromodulation 9: 163–71.	Case series n = 8 Follow-up = 12 months	4 out of 8 patients met the primary objective at 12 months. Implant-driven tibial stimulation appears to be feasible and safe.	Small case series.
Vandoninck V, van Balken MR, Finazzi Agro E et al. (2003) Posterior tibial nerve stimulation in the treatment of urge incontinence. Neurourology & Urodynamics 22: 17–23.	Case series n = 35	Subjective success = 63% (22/35) Complete cure = 46% (16/35)	Small case series with no follow-up.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Wooldridge LS (2009) Percutaneous tibial nerve stimulation for the treatment of urinary frequency, urinary urgency, and urge incontinence: results from a community-based clinic. Urologic Nursing 29: 177–85.	Case series n = 53	There was a statistically significant mean decrease in day and night voids and episodes of urge incontinence when compared to baseline.	Small case series with no follow-up.

Appendix B: Related NICE guidance for percutaneous posterior tibial nerve stimulation for overactive bladder syndrome

Guidance	Recommendations
Interventional procedures	**Laparoscopic augmentation cystoplasty (including clam cystoplasty). NICE interventional procedures guidance 326 (2009)** 1.1 Current evidence on the safety and efficacy of laparoscopic augmentation cystoplasty (including clam cystoplasty) is limited in quantity and quality but raises no major safety concerns, and the open procedure is well established. This procedure may therefore be used with normal arrangements for clinical governance, consent and audit. 1.2 Patient selection and treatment should be carried out by a multidisciplinary team with specialist expertise in the management of urinary incontinence and experience in complex laparoscopic reconstructive surgery. 1.3 Clinicians undertaking laparoscopic augmentation cystoplasty (including clam cystoplasty) should submit data on all patients undergoing the procedure to the Female and Reconstructive Urology database run by the British Association of Urological Surgeons (available from www.sarahfowler.org/bsfru.htm) to allow monitoring of safety outcomes in the long term. **Sacral nerve stimulation for urge incontinence and urgency-frequency. NICE interventional procedures guidance 64 (2004).** 1.1 Current evidence on the safety and efficacy of sacral nerve stimulation for urge incontinence and urgency-frequency appears adequate to support the use of this procedure provided that the normal arrangements are in place for consent, audit and clinical governance. 1.2 Patient selection is important. The diagnosis should be defined as clearly as possible and the procedure limited to patients who have not responded to conservative treatments such as lifestyle modifications, behavioural techniques and drug therapy. Patients should be selected on the basis of their response to peripheral nerve evaluation.

Clinical guidelines	**Urinary incontinence: the management of urinary incontinence in women. NICE Clinical Guideline 40 (2006).** • Bladder diaries should be used in the initial assessment of women with UI or OAB. Women should be encouraged to complete a minimum of 3 days of the diary, covering variations in their usual activities, such as both working and leisure days. • Bladder training lasting for a minimum of 6 weeks should be offered as first-line treatment to women with urge or mixed UI. • Immediate release non-proprietary oxybutynin should be offered to women with OAB or mixed UI as first-line drug treatment if bladder training has been ineffective. If immediate release oxybutynin is not well tolerated, darifenacin, solifenacin, tolterodine, trospium or an extended release or transdermal formulation of oxybutynin should be considered as alternatives. Women should be counselled about the adverse effects of antimuscarinic drugs. • Sacral nerve stimulation is recommended for the treatment of UI due to detrusor overactivity in women who have not responded to conservative treatments.Women should be offered sacral nerve stimulation on the basis of their response to preliminary percutaneous nerve evaluation. Life-long follow-up is recommended. • Surgery for UI should be undertaken only by surgeons who have received appropriate training in the management of UI and associated disorders or who work within a multidisciplinary team with this training, and who regularly carry out surgery for UI in women. **The following statements were also made about PTNS:** Data on posterior tibial nerve stimulation are mainly derived from case series of men and women with OAB, which show improvement in leakage episodes, frequency, voided volume and QOL with treatment for up to 3 months. Symptoms recur on treatment withdrawal. Adverse effects reported relate to needle insertion site (pain, tenderness, haematoma). Combining oxybutynin treatment with posterior tibial nerve stimulation did not lead to additional benefit. Overall the available data are inadequate to define the place of posterior tibial nerve stimulation for UI or OAB. [EL = 3] There is a need for a robust evaluation of transcutaneous electrical nerve stimulation and posterior tibial nerve stimulation for the treatment of UI.

Appendix C: Literature search for percutaneous posterior tibial nerve stimulation for overactive bladder syndrome

Databases	Date searched	Version/files	No. retrieved
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	16/02/2010	Issue 1, 2010	6
Database of Abstracts of Reviews of Effects – DARE (CRD website)	16/02/2010	N/A	0
HTA database (CRD website)	16/02/2010	N/A	1
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	16/02/2010	Issue 1, 2010	14
MEDLINE (Ovid)	16/02/2010	1950 to February Week 1 2010	114
MEDLINE In-Process (Ovid)	16/02/2010	February 11, 2010	9
EMBASE (Ovid)	16/02/2010	1980 to 2010 Week 05	122
CINAHL (NLH Search 2.0)	16/02/2010	N/A	39
BLIC (Dialog DataStar)	16/02/2010	N/A	10
• National Institute for Health Research Clinical Research Network Coordinating Centre (NIHR CRN CC) Portfolio Database	17/02/2010	None found	
Current Controlled Trials *meta*Register of Controlled Trials - *m*RCT	17/02/2010	Trial of Maintenance Therapy With Posterior Tibial Nerve Stimulation for Overactive Bladder 2009 Modified Extension Study to the SUmiT Trial: Evaluation of Long Term Therapy With Percutaneous Tibial Nerve Stimulation (PTNS) for Overactive Bladder Symptoms 2009 Posterior Tibial Nerve Stimulation vs. Sham 2007 Overactive Bladder Innovative Therapy Trial (OrBIT) 2007	
Clinicaltrials.gov	17/02/2010	Study of Urgent PC Versus Sham Effectiveness in Treatment of Overactive Bladder Symptoms Pulsed Electromagnetic Stimulation for Treatment of Overactive Bladder	

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1	exp Urinary Bladder, Overactive/
2	(overactiv* adj3 bladder*).tw.
3	OAB.tw.
4	exp urinary incontinence/ or exp urinary incontinence, urge/
5	(urge* adj3 incontinen*).tw.
6	exp Urination Disorders/
7	(urin* adj3 (disorder* or dysfunct*)).tw.
8	(detrus* adj3 (hyperreflexia* or instabilit*)).tw.
9	(void* adj3 (disorder* or dysfunct*)).tw.
10	(urin* adj3 (incontinen* or leak* or urgen* or frequen*)).tw.
11	or/1-10
12	PTNS.tw.
13	neurostimulat*.tw.
14	(urgen* adj3 pc adj3 neuromodulat*).tw.
15	SANS.tw.
16	(stoller* adj3 afferent* adj3 nerv*).tw.
17	urosurge.tw.
18	exp Electric Stimulation Therapy/ and exp Tibial Nerve/
19	(tibial* adj3 nerve* adj3 stimulat*).tw.
20	or/12-19
21	11 and 20
22	animals/ not humans/
23	21 not 22