Urinary incontinence in women: the management of urinary incontinence in women

National Collaborating Centre for Women's and Children's Health

Commissioned by the National Institute for Health and Care Excellence

September 2013

This guideline was partially updated in April 2019. The sections that are no longer current are marked as 'Updated 2019' and grey shaded. See https://www.nice.org.uk/guidance/ng123 for the updated guidance.

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This guideline has been fully funded by NICE. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient.

Implementation of this guidance is the responsibility of local commissioners and/or providers

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Appendices A–V are in a separate file.

1 Guideline summary

1.1 Guideline development group membership, NCC-WCH staff and acknowledgements (Original 2006 guideline)

GDG members

Elisabeth Adams	Subspecialist in Urogynaecology
Alison Bardsley	Continence adviser/Service manager
Linda Crumlin	Patient/carer representative
Ian Currie	Consultant gynaecologist (with an interest in urogynaecology)
Lynda Evans	Patient/carer representative
Jeanette Haslam	Women's health physiotherapist
Paul Hilton	Consultant gynaecologist and urogynaecologist (GDG leader)
Margaret Jones	General practitioner
Malcolm Lucas	Consultant urological surgeon
Julian Spinks	General practitioner
Joanne Townsend	Urogynaecology nurse specialist
Adrian Wagg	Consultant geriatrician

National Collaborating Centre for Women's and Children's Health (NCC-WCH)

Martin Dougherty	Executive director
Beti Wyn Evans	Research fellow
Paul Jacklin	Senior health economist
Irene Kwan	Research fellow
Debbie Pledge	Information specialist
Samantha Vahidi	Work programme co-ordinator

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1.2 Guideline development group membership, NCC-WCH staff and acknowledgements (2013 partial update)

GDG members

Tony Smith	GDG chair
Paul Abrams	Urologist
Elisabeth Adams	Urogynaecologist
Kate Anders	Urogynaecology nurse
Rosie Benneyworth	General practitioner
Stephanie Knight	Physiotherapist
Catherine Linney	Lay member

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Susie Orme	Geriatrician
June Rogers	Lay member
Amanda Wells	Continence adviser

National Collaborating Centre for Women's and Children's Health (NCC-WCH)

David Bevan	Project manager
Liz Bickerdike	Research assistant
Hannah Rose Douglas	Associate director, Health Economics
David James	Clinical co-director
Juliet Kenny	Project manager (until March 2012)
Rosalind Lai	Information specialist
Hugh McGuire	Senior research fellow
Nitara Prasannan	Research assistant

Peer reviewers

Bob Freeman
Paul Hilton
Linda Cardozo
NICE Technical Support Unit (TSU)

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Additional support was received from: Wahab Bello, Julie Hodge Allen, Edmund Peston, Wendy Riches, Rupert Franklin and Paul Jacklin at the NCC-WCH and Sofia Dias and Tony Ades at the TSU.

1.2 Foreword

This guidance is a partial update of National Institute for Health and Care Excellence (NICE) clinical guideline 40 (published October 2006) and will replace it. For further information refer to Appendices A and D.

New and updated recommendations have been included based on evidence of the clinical and cost effectiveness of:

- Antimuscarinic drugs:
  - darifenacin
  - darifenacin – extended release
  - fesoterodine – modified release
  - oxybutinin
  - oxybutynin – modified release
  - oxybutynin – transdermal
  - oxybutynin – topical gel
  - propiverine
  - propiverine – extended release
  - solifenacin
  - tolterodine
  - tolterodine – extended release
  - trospium
  - trospium – extended release

- Percutaneous sacral nerve stimulation (P-SNS) compared with either no active treatment or placebo
- Percutaneous posterior tibial nerve stimulation (P-PTNS) compared with either no active treatment or placebo
- Transcutaneous posterior tibial nerve stimulation (T-PTNS) compared with either no active treatment or placebo
- Transcutaneous sacral nerve stimulation (T-SNS) compared with either no active treatment or placebo
- A comparison of T-SNS, T-PTNS and P-PTNS (if these treatments are found to be effective compared with no treatment or placebo)
- Botulinum toxin A compared with placebo in women with overactive bladder (OAB) caused by detrusor overactivity
- Pharmacological treatment compared with neuromodulation in all women with overactive bladder
- Pharmacological treatment compared with neuromodulation and botulinum toxin A in women with OAB caused by detrusor overactivity only
- Surgical approaches for mid-urethral procedures in women undergoing their primary surgical tape procedure:
    - retropubic bottom up
    - retropubic top down
    - transobturator inside out
    - transobturator outside in
    - single incision
- Interventions for women for whom the primary tape procedure has failed:
    - conservative management, looking only at:
        - lifestyle interventions, specifically weight loss, fluid management and smoking cessation
        - physical therapy, specifically pelvic floor muscle training
    - repeat tape procedure
    - fascial sling
    - colposuspension.

Recommendations are marked to indicate the year and type of review:

- **[2006]** if the evidence has not been reviewed since the original guideline.
- **[2006**, amended **2013]** if the evidence has not been reviewed, but an essential change has been made that affects the meaning of the recommendation.
- **[2013]** if the evidence has been reviewed but no change has been made to the recommendation.
- **[new2013]** if the evidence has been reviewed and the recommendation has been updated or added.

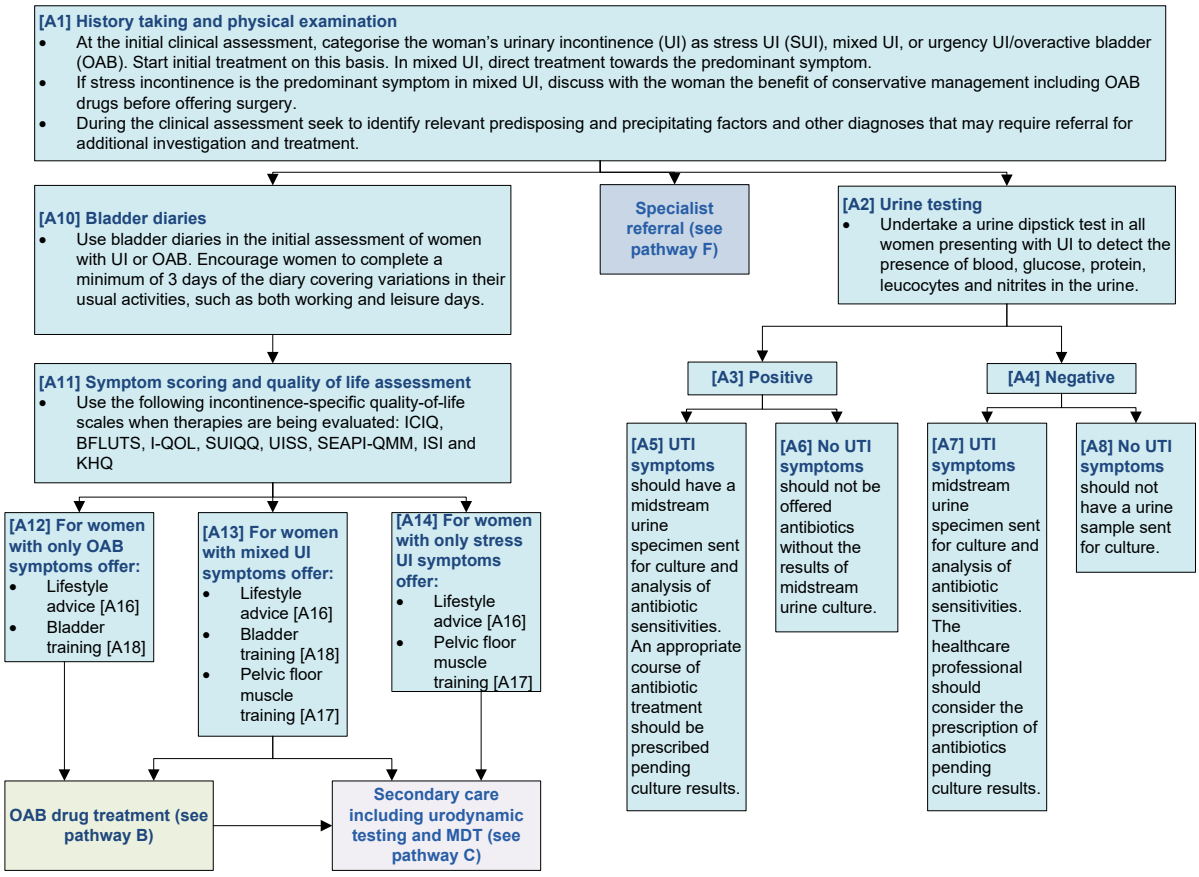
Appendix L contains recommendations from the 2006 guideline that the guideline development group (GDG) has removed or amended for clarification in the 2013 update. This is because the evidence has been reviewed and the recommendation has been updated or because NICE has updated other relevant guidance and has replaced the original recommendations. Where recommendations have

been replaced, details are provided. Where there is no replacement recommendation, an explanation for the proposed deletion is given.

A grey bar down the side of the page indicates those sections of the guideline which are new or have been updated. Material from the original guideline which has been deleted can be found in Appendix K.

1.3 Care pathway

A – Initial advice and conservative treatments



[A15] Do not offer: assessments
- Cystoscopy in the initial assessment
- Pad tests
- Q-tip, Bonney, Marshall and Fluid-Bridge tests
- Magnetic resonance imaging, computed tomography, X-ray is not recommended for the routine assessment of women with UI. Ultrasound is not recommended other than for the assessment of residual urine volume.

[A9] Assessment of residual urine
- Measure post-void residual volume by bladder scan or catheterisation in women with symptoms suggestive of voiding dysfunction or recurrent UTI.
- Use a bladder scan in preference to catheterisation on the grounds of acceptability and lower incidence of adverse events.
- Refer women who are found to have a palpable bladder on bimanual or abdominal examination after voiding to a specialist.

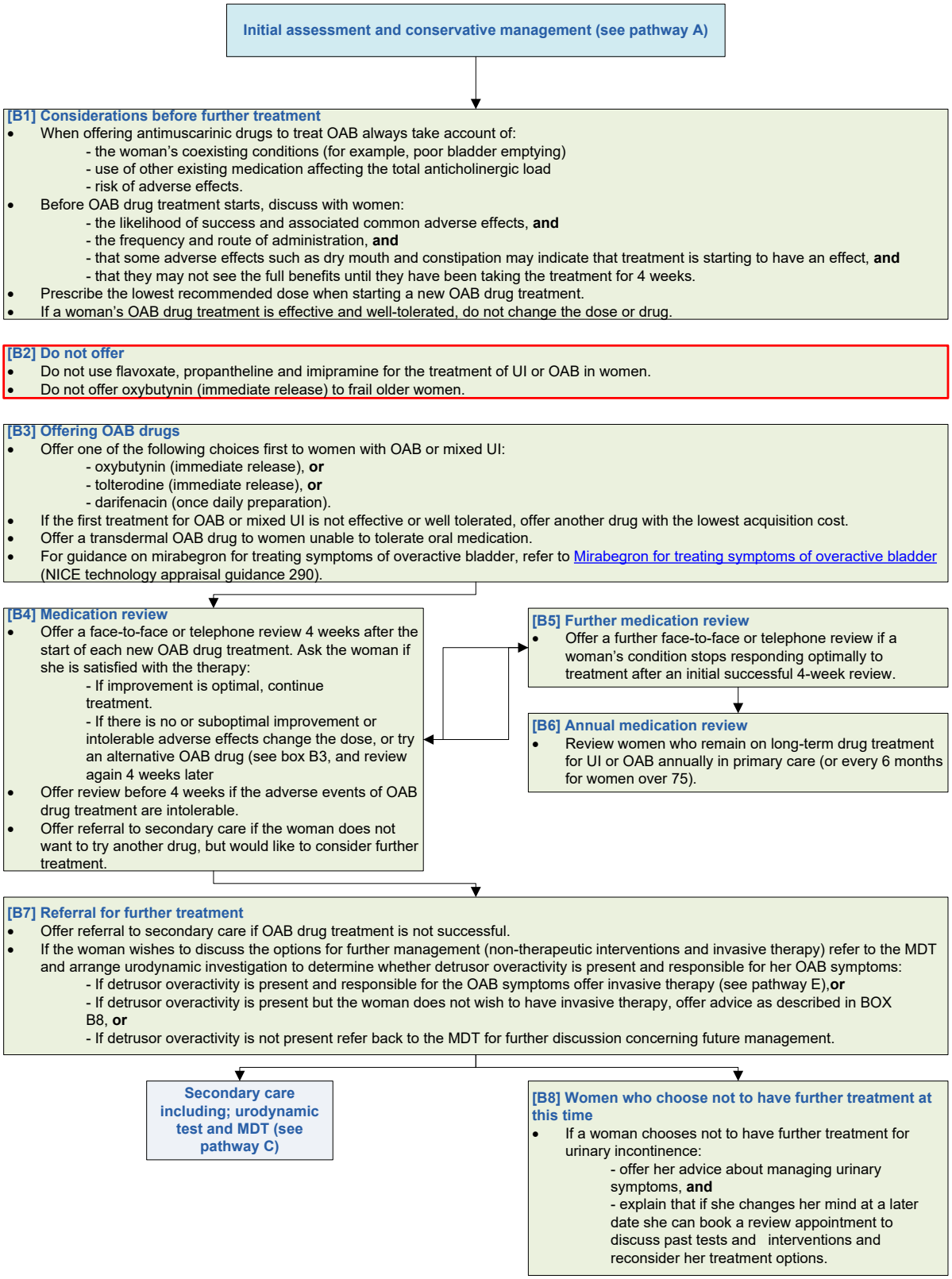
[A16] Lifestyle advice
- Recommend a trial of caffeine reduction to women with OAB.
- Consider advising modification of high or low fluid intake in women with UI or OAB.
- Advise women with UI or OAB who have a BMI greater than 30 to lose weight.

[A17] Pelvic floor muscle training
- Undertake routine digital assessment to confirm pelvic floor muscle contraction before the use of supervised pelvic floor muscle training for the treatment of UI.
- Offer a trial of supervised pelvic floor muscle training of at least 3 months' duration as first-line treatment to women with stress or mixed UI.
- Pelvic floor muscle training programmes should comprise at least 8 contractions performed 3 times per day.
- Continue an exercise programme if pelvic floor muscle training is beneficial.
- Electrical stimulation and/or biofeedback should be considered in women who cannot actively contract pelvic floor muscles in order to aid motivation and adherence to therapy.
- Offer pelvic floor muscle training to women in their first pregnancy as a preventive strategy for UI.

[A18] Bladder training
- Offer bladder training lasting for a minimum of 6 weeks as first-line treatment to women with urgency or mixed UI.
- If women do not achieve satisfactory benefit from bladder training programmes, the combination of an OAB drug with bladder training should be considered if frequency is a troublesome symptom.

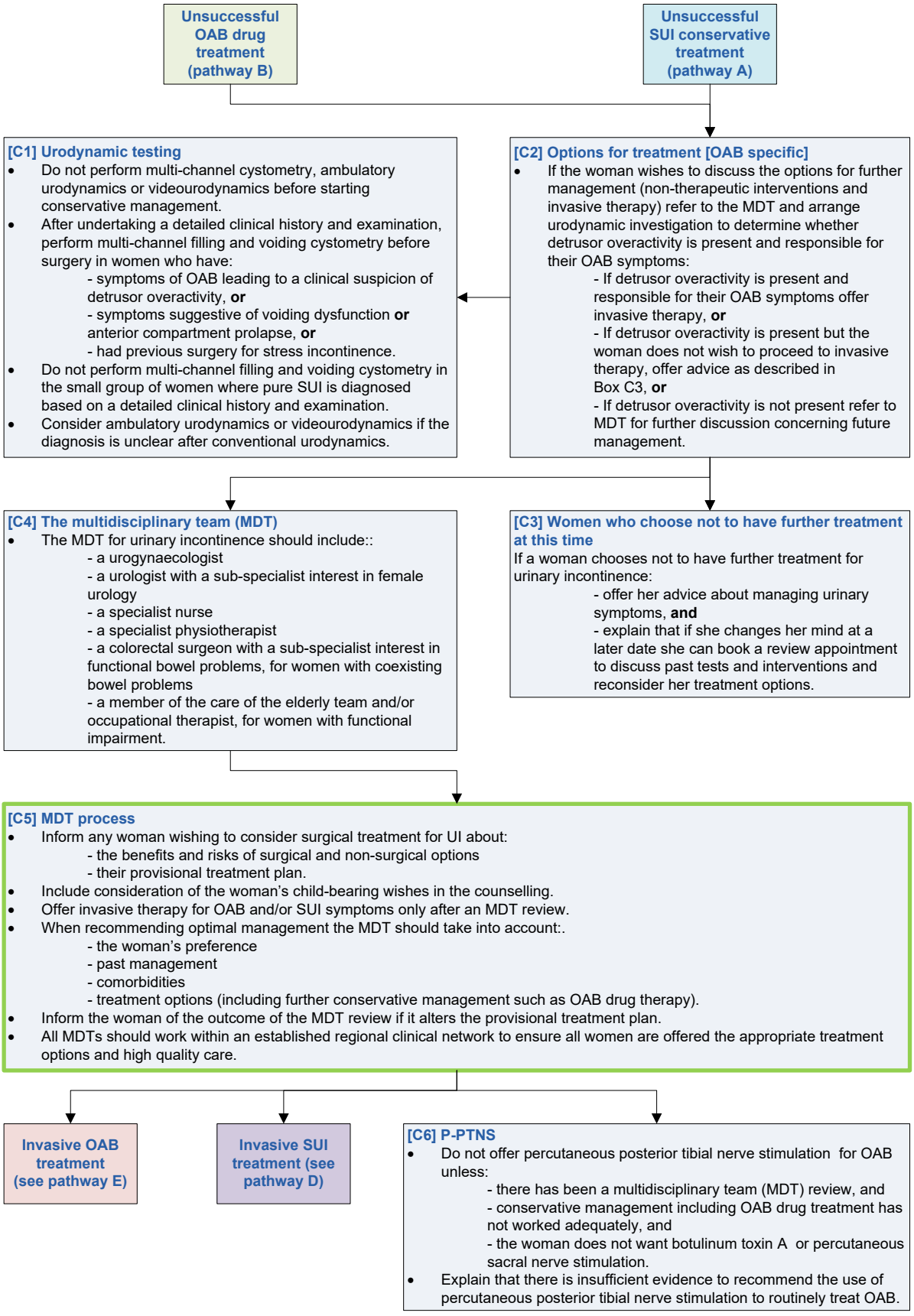
[A19] Do not offer: interventions
- Do not routinely use electrical stimulation in the treatment of women with OAB.
- Do not routinely use electrical stimulation in combination with pelvic floor muscle training.
- Do not use perineometry or pelvic floor electromyography as biofeedback as a routine part of pelvic floor muscle training.
- Do not offer transcutaneous sacral nerve stimulation to treat OAB in women.
- Explain that there is insufficient evidence to recommend the use of transcutaneous posterior tibial nerve stimulation to treat OAB.
- Do not offer transcutaneous posterior tibial nerve stimulation for OAB.

B – Drug treatment for OAB and mixed UI

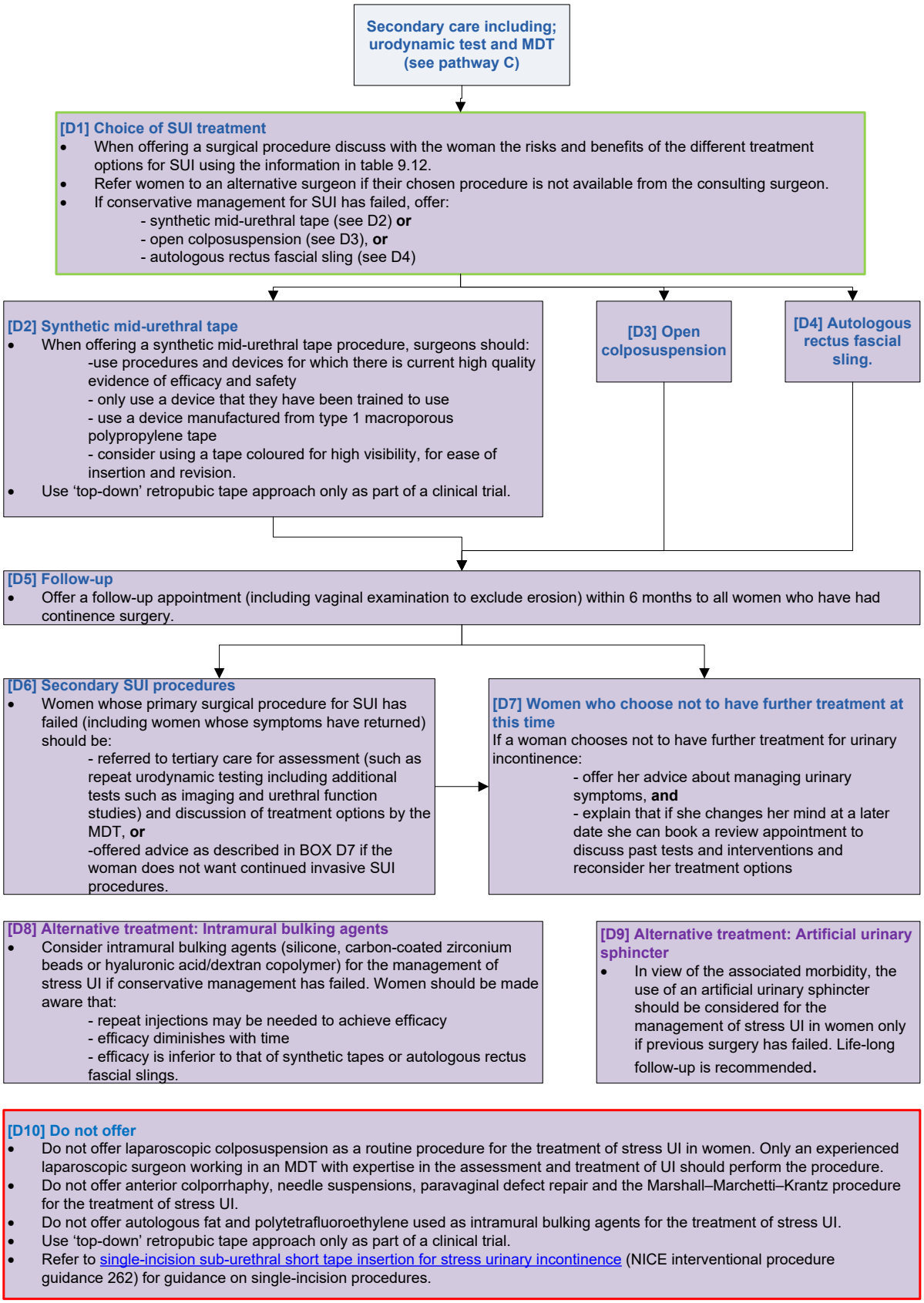


2013 Update

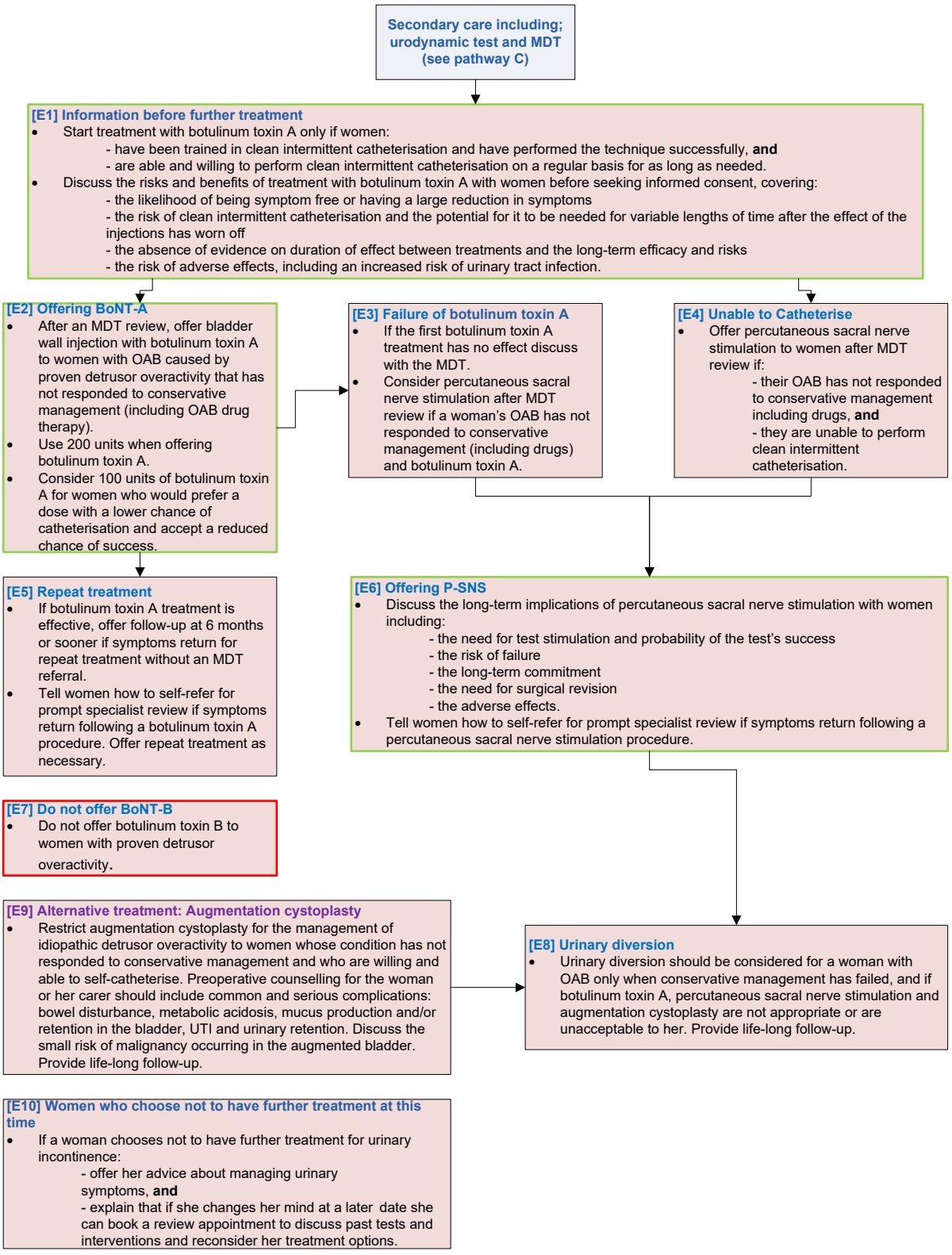
C – Secondary care including urodynamic testing and MDT



D – Surgical approaches for SUI



E – Invasive approaches to OAB



F – Referral for specialist intervention and surgeon standards

[F1] Urgent referral

- Refer women with UI who have symptomatic prolapse that is visible at or below the vaginal introitus to a specialist.
- Urgently refer women with UI who have any of the following:
  - microscopic haematuria in women aged 50 years and older
  - visible haematuria
  - recurrent or persisting UTI associated with haematuria in women aged 40 years and older
  - suspected malignant mass arising from the urinary tract.
- In women with UI, further indications for consideration for referral to a specialist service include:
  - persisting bladder or urethral pain
  - clinically benign pelvic masses
  - associated faecal incontinence
  - suspected neurological disease
  - symptoms of voiding difficulty
  - suspected urogenital fistulae
  - previous continence surgery
  - previous pelvic cancer surgery
  - previous pelvic radiation therapy

[F2] Maintaining and measuring expertise and standards for practice

- 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 an MDT with this training, and who regularly carry out surgery for UI in women.
- Training should be sufficient to develop the knowledge and generic skills documented below. Knowledge should include the:
  - specific indications for surgery
  - required preparation for surgery including preoperative investigations
  - outcomes and complications of proposed procedure
  - anatomy relevant to procedure
  - steps involved in procedure
  - alternative management options
  - likely postoperative progress.
- Generic skills should include
  - the ability to explain procedures and possible outcomes to patients and family and to obtain informed consent
  - the necessary hand–eye dexterity to complete the procedure safely and efficiently, with appropriate use of assistance
  - the ability to communicate with and manage the operative team effectively
  - the ability to prioritise interventions
  - the ability to recognise when to ask for advice from others
  - a commitment to MDT working.
- Training should include competence in cystourethroscopy.
- Operative competence of surgeons undertaking surgical procedures to treat UI or OAB in women should be formally assessed by trainers through a structured process.
- Surgeons who are already carrying out procedures for UI should be able to demonstrate that their training, experience and current practice equates to the standards laid out for newly trained surgeons.
- Only surgeons who carry out a sufficient case load to maintain their skills should undertake surgery for UI or OAB in women. An annual workload of at least 20 cases of each primary procedure for stress UI is recommended. Surgeons undertaking fewer than 5 cases of any procedure annually should do so only with the support of their clinical governance committee; otherwise referral pathways should be in place within clinical networks.
- There should be a nominated clinical lead within each surgical unit with responsibility for continence and prolapse surgery. The clinical lead should work within the context of an integrated continence service.
- A national audit of continence surgery should be undertaken.
- Surgeons undertaking continence surgery should maintain careful audit data and submit their outcomes to national registries such as those held by the British Society of Urogynaecology (BSUG) and British Association of Urological Surgeons Section of Female and Reconstructive Urology (BAUS-SFRU).

G – Alternative conservative management and pharamacological options

[G1] Catheters
- Bladder catheterisation (intermittent or indwelling urethral or suprapubic) should be considered for women in whom persistent urinary retention is causing incontinence, symptomatic infections, or renal dysfunction, and in whom this cannot otherwise be corrected. Healthcare professionals should be aware, and explain to women, that the use of indwelling catheters in urgency UI may not result in continence.

[G2] Intermittent urethral catheters
- Offer intermittent urethral catheterisation to women with urinary retention who can be taught to self-catheterise or who have a carer who can perform the technique.

[G3] Indwelling urethral catheters
- Give careful consideration to the impact of long-term indwelling urethral catheterisation. Discuss the practicalities, benefits and risks should be discussed with the patient or, if appropriate, her carer. Indications for the use of long-term indwelling urethral catheters for women with UI include:
  - chronic urinary retention in women who are unable to manage intermittent self-catheterisation
  - skin wounds, pressure ulcers or irritations that are being contaminated by urine
  - distress or disruption caused by bed and clothing changes
  - where a woman expresses a preference for this form of management.

[G4] Indwelling suprapubic catheters
- Indwelling suprapubic catheters should be considered as an alternative to long-term urethral catheters. Be aware, and explain to women, that they may be associated with lower rates of symptomatic UTI, 'bypassing', and urethral complications than indwelling urethral catheters.

[G5] Absorbent products, urinals and toileting aids
- Absorbent products, hand held urinals and toileting aids should not be considered as a treatment for UI. Use them only as:
  - a coping strategy pending definitive treatment
  - an adjunct to ongoing therapy
  - long-term management of UI only after treatment options have been explored.

[G6] Do not use
- Do not recommend complementary therapies for the treatment of UI or OAB.
- Do not use intravaginal and intraurethral devices for the routine management of UI in women. Do not advise women to consider such devices other than for occasional use when necessary to prevent leakage, for example during physical exercise.

[G7] Desmopressin
- The use of desmopressin may be considered specifically to reduce nocturia in women with UI or OAB who find it a troublesome symptom. Use particular caution in women with cystic fibrosis and avoid in those over 65 years with cardiovascular disease or hypertension.

[G8] Oestrogens
- Do not offer systemic hormone replacement therapy for the treatment of UI.
- Offer intravaginal oestrogens for the treatment of OAB symptoms in postmenopausal women with vaginal atrophy.

[G9] Duloxetine
- Do not use duloxetine as a first-line treatment for women with predominant stress UI. Do not routinely offer duloxetine as a second-line treatment for women with stress UI, although it may be offered as second-line therapy if women prefer pharmacological to surgical treatment or are not suitable for surgical treatment. If duloxetine is prescribed, counsel women about its adverse effects.

This guideline recommends some drugs for indications for which they do not have a UK marketing authorisation at the date of publication, if there is good evidence to support that use. Many drugs do not have a license for use specifically in pregnant women, reflecting the fact that this group is often excluded from studies. Unlicensed drugs are indicated with a footnote.

1.4 Key priorities for implementation

Number	Recommendation	See section
1	At the initial clinical assessment, categorise the woman's urinary incontinence (UI) as stress UI (SUI), mixed UI, or urgency UI/overactive bladder (OAB). Start initial treatment on this basis. In mixed UI, direct treatment towards the predominant symptom. **[2006]**	4.2
4	Undertake routine digital assessment to confirm pelvic floor muscle contraction before the use of supervised pelvic floor muscle training for the treatment of UI. **[2006, amended 2013]**	4.3
17	Use bladder diaries in the initial assessment of women with UI or OAB. Encourage women to complete a minimum of 3 days of the diary covering variations in their usual activities, such as both working and leisure days. **[2006]**	4.9
41	Do not offer percutaneous posterior tibial nerve stimulation for OAB unless: • there has been a multidisciplinary team (MDT) review, **and** • conservative management including OAB drug treatment has not worked adequately, **and** • the woman does not want botulinum toxin A* or percutaneous sacral nerve stimulation. **[new 2013]**	5.5
43	Absorbent products, hand held urinals and toileting aids should not be considered as a treatment for UI. Use them only as: • a coping strategy pending definitive treatment • an adjunct to ongoing therapy • long-term management of UI only after treatment options have been explored. **[2006]**	5.6
53	Before OAB drug treatment starts, discuss with women: • the likelihood of success and associated common adverse effects, **and** • the frequency and route of administration, **and** • that some adverse effects such as dry mouth and constipation may indicate that treatment is starting to have an effect, **and** • that they may not see the full benefits until they have been taking the treatment for 4 weeks. **[new 2013]**	6.1

2013 Update

* At the time of publication (September 2013), most Botulinum toxin type A preparations did not have a UK marketing authorisation for this indication. Evidence was only available for the licensed Botulinum toxin A (BOTOX, Allergan) preparation

Number	Recommendation	See section
58	Offer one of the following choices first to women with OAB or mixed UI: • oxybutynin (immediate release), **or** • tolterodine (immediate release), **or** • darifenacin (once daily preparation). **[new 2013]**	6.1
59	If the first treatment for OAB or mixed UI is not effective or well-tolerated, offer another drug with the lowest acquisition cost*. **[new 2013]**	6.1
74	Offer invasive therapy for OAB and/or SUI symptoms only after an MDT review. **[new 2013]**	7.2
94	When offering a surgical procedure discuss with the woman the risks and benefits of the different treatment options for SUI using the information in table 9.12. **[new 2013]**	9.2

2013 Update

1.5 Recommendations

Number	Recommendation	See section
	Assessment and investigation	
	History-taking and physical examination	
1	At the initial clinical assessment, categorise the woman's urinary incontinence (UI) as stress UI (SUI), mixed UI, or urgency UI/overactive bladder (OAB). Start initial treatment on this basis. In mixed UI, direct treatment towards the predominant symptom. **[2006]**	4.2
2	If stress incontinence is the predominant symptom in mixed UI, discuss with the woman the benefit of conservative management including OAB drugs before offering surgery. **[new 2013]**	4.2
3	During the clinical assessment seek to identify relevant predisposing and precipitating factors and other diagnoses that may require referral for additional investigation and treatment. **[2006]**	4.2
	Assessment of pelvic floor muscles	
4	Undertake routine digital assessment to confirm pelvic floor muscle contraction before the use of supervised pelvic floor muscle training for the treatment of UI. **[2006, amended 2013]**	4.3
	Assessment of prolapse	
5	Refer women with UI who have symptomatic prolapse that is visible at or below the vaginal introitus to a specialist. **[2006]**	4.4

2013

* This could be any drug with the lowest acquisition cost from any of the drugs reviewed, including an untried drug from recommendation 58. The evidence review considered the following drugs: darifenacin, fesoterodine, oxybutynin (immediate release), oxybutynin (extended release), oxybutynin (transdermal), oxybutynin (topical gel), propiverine, propiverine (extended release), solifenacin, tolterodine (immediate release), tolterodine (extended release), trospium and trospium (extended release). See chapter 6.

Number	Recommendation	See section
	Urine testing	
6	Undertake a urine dipstick test in all women presenting with UI to detect the presence of blood, glucose, protein, leucocytes and nitrites in the urine. **[2006]**	4.5
7	If women have symptoms of urinary tract infection (UTI) and their urine tests positive for both leucocytes and nitrites send a midstream urine specimen for culture and analysis of antibiotic sensitivities. Prescribe an appropriate course of antibiotic treatment pending culture results. **[2006]**	4.5
8	If women have symptoms of UTI and their urine tests negative for either leucocytes or nitrites send a midstream urine specimen for culture and analysis of antibiotic sensitivities. Consider the prescription of antibiotics pending culture results. **[2006]**	4.5
9	If women do not have symptoms of UTI, but their urine tests positive for both leucocytes and nitrites, do not offer antibiotics without the results of midstream urine culture. **[2006]**	4.5
10	If a woman does not have symptoms of UTI and her urine tests negative for either leucocytes or nitrites do not send a urine sample for culture because she is unlikely to have UTI. **[2006]**	4.5
	Assessment of residual urine	
11	Measure post-void residual volume by bladder scan or catheterisation in women with symptoms suggestive of voiding dysfunction or recurrent UTI. **[2006]**	4.6
12	Use a bladder scan in preference to catheterisation on the grounds of acceptability and lower incidence of adverse events. **[2006]**	4.6
13	Refer women who are found to have a palpable bladder on bimanual or abdominal examination after voiding to a specialist. **[2006]**	4.6
	Referral	
14	Urgently refer women with UI who have any of the following*: • microscopic haematuria in women aged 50 years and older • visible haematuria • recurrent or persisting UTI associated with haematuria in women aged 40 years and older • suspected malignant mass arising from the urinary tract. **[2006]**	4.7
15	In women with UI, further indications for consideration for referral to a specialist service include: • persisting bladder or urethral pain • clinically benign pelvic masses • associated faecal incontinence • suspected neurological disease • symptoms of voiding difficulty • suspected urogenital fistulae	4.7

* NICE's 'Referral guidelines for suspected cancer' define urgent referral as the patient being seen within the national target for urgent referrals (currently 2 weeks).

Number	Recommendation	See section
	• previous continence surgery • previous pelvic cancer surgery • previous pelvic radiation therapy*. **[2006]**	
	Symptom scoring and quality-of-life assessment	
16	Use the following incontinence-specific quality-of-life scales when therapies are being evaluated: ICIQ, BFLUTS, I-QOL, SUIQQ, UISS, SEAPI-QMM, ISI and KHQ. **[2006]**	4.8
	Bladder diaries	
17	Use bladder diaries in the initial assessment of women with UI or OAB. Encourage women to complete a minimum of 3 days of the diary covering variations in their usual activities, such as both working and leisure days. **[2006]**	4.9
	Pad testing	
18	Do not use pad tests in the routine assessment of women with UI. **[2006]**	4.10
	Urodynamic testing	
19	Do not perform multi-channel cystometry, ambulatory urodynamics or videourodynamics before starting conservative management. **[2006, amended 2013]**	4.11
20	After undertaking a detailed clinical history and examination, perform multi-channel filling and voiding cystometry before surgery in women who have: • symptoms of OAB leading to a clinical suspicion of detrusor overactivity, **or** • symptoms suggestive of voiding dysfunction **or** anterior compartment prolapse, **or** • had previous surgery for stress incontinence. **[2006, amended 2013]**	
21	Do not perform multi-channel filling and voiding cystometry in the small group of women where pure SUI is diagnosed based on a detailed clinical history and examination. **[2006, amended 2013]**	4.11
22	Consider ambulatory urodynamics or videourodynamics if the diagnosis is unclear after conventional urodynamics. **[2006, amended 2013]**	4.11
	Other tests of urethral competence	
23	Do not use the Q-tip, Bonney, Marshall and Fluid-Bridge tests in the assessment of women with UI. **[2006]**	4.12
	Cystoscopy	
24	Do not use cystoscopy in the initial assessment of women with UI alone. **[2006]**	4.13

* For further indications for consideration for referral, see recommendations 5 and 13.

Number	Recommendation	See section
	### Imaging	
25	Do not use imaging (MRI, CT, X-ray) for the routine assessment of women with UI. Do not use ultrasound other than for the assessment of residual urine volume. **[2006]**	4.14
	## Lifestyle interventions	
	### Caffeine	
26	Recommend a trial of caffeine reduction to women with OAB. **[2006]**	5.2
	### Fluid intake	
27	Consider advising modification of high or low fluid intake in women with UI or OAB. **[2006]**	5.2
	### Weight	
28	Advise women with UI or OAB who have a BMI greater than 30 to lose weight. **[2006]**	5.2
	## Physical therapies	
	### Pelvic floor muscle training	
29	Offer a trial of supervised pelvic floor muscle training of at least 3 months' duration as first-line treatment to women with stress or mixed UI. **[2006]**	5.3
30	Pelvic floor muscle training programmes should comprise at least 8 contractions performed 3 times per day. **[2006]**	5.3
31	Do not use perineometry or pelvic floor electromyography as biofeedback as a routine part of pelvic floor muscle training. **[2006]**	5.3
32	Continue an exercise programme if pelvic floor muscle training is beneficial. **[2006]**	5.3
	### Therapeutic stimulation	
33	Do not routinely use electrical stimulation in the treatment of women with OAB. **[2006]**	5.3
34	Do not routinely use electrical stimulation in combination with pelvic floor muscle training. **[2006]**	5.3
35	Electrical stimulation and/or biofeedback should be considered in women who cannot actively contract pelvic floor muscles in order to aid motivation and adherence to therapy. **[2006]**	5.3
	## Behavioural therapies	
	### Bladder training	
36	Offer bladder training lasting for a minimum of 6 weeks as first-line treatment to women with urgency or mixed UI. **[2006]**	5.4
	### Multicomponent behavioural therapy	
37	If women do not achieve satisfactory benefit from bladder training programmes, the combination of an OAB drug with bladder training should be considered if frequency is a troublesome symptom. **[2006]**	5.4

Number	Recommendation	See section
	Neurostimulation	
	Transcutaneous sacral nerve stimulation	
38	Do not offer transcutaneous sacral nerve stimulation* to treat OAB in women. **[new 2013]**	5.5
	Transcutaneous posterior tibial nerve stimulation	
39	Explain that there is insufficient evidence to recommend the use of transcutaneous posterior tibial nerve stimulation to treat OAB. **[new 2013]**	5.5
40	Do not offer transcutaneous posterior tibial nerve stimulation for OAB. **[new 2013]**	5.5
	Percutaneous posterior tibial nerve stimulation	
41	Do not offer percutaneous posterior tibial nerve stimulation for OAB unless: • there has been a multidisciplinary team (MDT) review, **and** • conservative management including OAB drug treatment has not worked adequately, **and** • the woman does not want botulinum toxin A† or percutaneous sacral nerve stimulation. **[new 2013]**	5.5
42	Explain that there is insufficient evidence to recommend the use of percutaneous posterior tibial nerve stimulation to routinely treat OAB. **[new 2013]**	5.5
	Alternative conservative management options	
	Absorbent products, urinals and toileting aids	
43	Absorbent products, hand held urinals and toileting aids should not be considered as a treatment for UI. Use them only as: • a coping strategy pending definitive treatment • an adjunct to ongoing therapy • long-term management of UI only after treatment options have been explored. **[2006]**	5.6
	Catheters	
44	Bladder catheterisation (intermittent or indwelling urethral or suprapubic) should be considered for women in whom persistent urinary retention is causing incontinence, symptomatic infections, or renal dysfunction, and in whom this cannot otherwise be corrected. Healthcare professionals should be aware, and explain to women, that the use of indwelling catheters in urgency UI may not result in continence. **[2006]**	5.6
	Intermittent urethral catheters	
45	Offer intermittent urethral catheterisation to women with urinary retention who can be taught to self-catheterise or who have a carer who can perform the technique. **[2006]**	5.6
	Indwelling urethral catheters	

2013 Update

* This is often known as transcutaneous electrical nerve stimulation (TENS).
† At the time of publication (September 2013), most Botulinum toxin type A preparations did not have a UK marketing authorisation for this indication. Evidence was only available for the licensed Botulinum toxin A (BOTOX, Allergan) preparation

Number	Recommendation	See section
46	Give careful consideration to the impact of long-term indwelling urethral catheterisation. Discuss the practicalities, benefits and risks with the patient or, if appropriate, her carer. Indications for the use of long-term indwelling urethral catheters for women with UI include: • chronic urinary retention in women who are unable to manage intermittent self-catheterisation • skin wounds, pressure ulcers or irritations that are being contaminated by urine • distress or disruption caused by bed and clothing changes • where a woman expresses a preference for this form of management. **[2006]**	5.6
	### Indwelling suprapubic catheters	
47	Indwelling suprapubic catheters should be considered as an alternative to long-term urethral catheters. Be aware, and explain to women, that they may be associated with lower rates of symptomatic UTI, 'bypassing', and urethral complications than indwelling urethral catheters. **[2006]**	5.6
	### Products to prevent leakage	
48	Do not use intravaginal and intraurethral devices for the routine management of UI in women. Do not advise women to consider such devices other than for occasional use when necessary to prevent leakage, for example during physical exercise. **[2006]**	5.6
	### Complementary therapies	
49	Do not recommend complementary therapies for the treatment of UI or OAB. **[2006]**	5.6
	## Preventive use of conservative therapies	
50	Offer pelvic floor muscle training to women in their first pregnancy as a preventive strategy for UI. **[2006]**	5.8
	## Women who choose not to have further treatment	
51	If a woman chooses not to have further treatment for urinary incontinence: • offer her advice about managing urinary symptoms, **and** • explain that if she changes her mind at a later date she can book a review appointment to discuss past tests and interventions and reconsider her treatment options. **[new 2013]**	5.10
	## Pharmacological treatment	
	### General principles when using OAB drugs	
52	When offering antimuscarinic drugs to treat OAB always take account of: • the woman's coexisting conditions (for example, poor bladder emptying) • use of other existing medication affecting the total anticholinergic load • risk of adverse effects. **[new 2013]**	6.1

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Number	Recommendation	See section
53	Before OAB drug treatment starts, discuss with women: • the likelihood of success and associated common adverse effects, **and** • the frequency and route of administration, **and** • that some adverse effects such as dry mouth and constipation may indicate that treatment is starting to have an effect, **and** • that they may not see the full benefits until they have been taking the treatment for 4 weeks. **[new 2013]**	6.1
54	Prescribe the lowest recommended dose when starting a new OAB drug treatment. **[new 2013]**	6.1
55	If a woman's OAB drug treatment is effective and well-tolerated, do not change the dose or drug. **[new 2013]**	6.1
	Choosing OAB drugs	
56	Do not use flavoxate, propantheline and imipramine for the treatment of UI or OAB in women. **[2006]**	6.1
57	Do not offer oxybutynin (immediate release) to frail older women*. **[new 2013]**	6.1
58	Offer one of the following choices first to women with OAB or mixed UI: • oxybutynin (immediate release), **or** • tolterodine (immediate release), **or** • darifenacin (once daily preparation). **[new 2013]**	6.1
59	If the first treatment for OAB or mixed UI is not effective or well-tolerated, offer another drug with the lowest acquisition cost.† **[new 2013]**	
60	Offer a transdermal OAB drug to women unable to tolerate oral medication. **[new 2013]**	6.1
61	For guidance on mirabegron for treating symptoms of overactive bladder, refer to Mirabegron for treating symptoms of overactive bladder (NICE technology appraisal guidance 290). **[new 2013]**	
	Reviewing OAB drug treatment	
62	Offer a face-to-face or telephone review 4 weeks after the start of each new OAB drug treatment. Ask the woman if she is satisfied with the therapy: • If improvement is optimal, continue treatment. • If there is no or suboptimal improvement or intolerable adverse effects change the dose, or try an alternative OAB drug (see recommendations 59 – 60), and review again 4 weeks later. **[new 2013]**	6.1

* The Guideline Development Group defined 'frail older women' as those with multiple comorbidities, functional impairments such as walking or dressing difficulties and any degree of cognitive impairment.
† This could be any drug with the lowest acquisition cost from any of the drugs reviewed, including an untried drug from recommendation 58. The evidence review considered the following drugs: darifenacin, fesoterodine, oxybutynin (immediate release), oxybutynin (extended release), oxybutynin (transdermal), oxybutynin (topical gel), propiverine, propiverine (extended release), solifenacin, tolterodine (immediate release), tolterodine (extended release), trospium and trospium (extended release). See chapter 6.

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Number	Recommendation	See section
63	Offer review before 4 weeks if the adverse events of OAB drug treatment are intolerable. **[new 2013]**	6.1
64	Offer referral to secondary care if the woman does not want to try another drug, but would like to consider further treatment. **[new 2013]**	6.1
65	Offer a further face-to-face or telephone review if a woman's condition stops responding optimally to treatment after an initial successful 4-week review. **[new 2013]**	6.1
66	Review women who remain on long-term drug treatment for UI or OAB annually in primary care (or every 6 months for women over 75). **[new 2013]**	6.1
67	Offer referral to secondary care if OAB drug treatment is not successful. **[new 2013]**	6.1
68	If the woman wishes to discuss the options for further management (non-therapeutic interventions and invasive therapy) refer to the MDT and arrange urodynamic investigation to determine whether detrusor overactivity is present and responsible for her OAB symptoms: • If detrusor overactivity is present and responsible for the OAB symptoms offer invasive therapy (see recommendations in chapter 8). • If detrusor overactivity is present but the woman does not wish to have invasive therapy, offer advice as described in recommendation 51. • If detrusor overactivity is not present refer back to the MDT for further discussion concerning future management. **[new 2013]**	6.1
	Desmopressin	
69	The use of desmopressin may be considered specifically to reduce nocturia* in women with UI or OAB who find it a troublesome symptom. Use particular caution in women with cystic fibrosis and avoid in those over 65 years with cardiovascular disease or hypertension. **[2006, amended 2013]**	6.2
	Duloxetine	
70	Do not use duloxetine as a first-line treatment for women with predominant stress UI. Do not routinely offer duloxetine as a second-line treatment for women with stress UI, although it may be offered as second-line therapy if women prefer pharmacological to surgical treatment or are not suitable for surgical treatment. If duloxetine is prescribed, counsel women about its adverse effects. **[2006]**	6.4
	Oestrogens	

* At the time of publication (September 2013), desmopressin did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

Number	Recommendation	See section
71	Do not offer systemic hormone replacement therapy for the treatment of UI. **[2006]**	6.5
72	Offer intravaginal oestrogens for the treatment of OAB symptoms in postmenopausal women with vaginal atrophy. **[2006]**	6.5
	The multidisciplinary team	
73	Inform any woman wishing to consider surgical treatment for UI about: • the benefits and risks of surgical and non-surgical options • their provisional treatment plan. Include consideration of the woman's child-bearing wishes in the counselling. **[2006, amended 2013]**	7.2
74	Offer invasive therapy for OAB and/or SUI symptoms only after an MDT review. **[new 2013]**	7.2
75	When recommending optimal management the MDT should take into account: • the woman's preference • past management • comorbidities • treatment options (including further conservative management such as OAB drug therapy). **[new 2013]**	7.2
76	The MDT for urinary incontinence should include: • a urogynaecologist • a urologist with a sub-specialist interest in female urology • a specialist nurse • a specialist physiotherapist • a colorectal surgeon with a sub-specialist interest in functional bowel problems, for women with coexisting bowel problems • a member of the care of the elderly team and/or occupational therapist, for women with functional impairment. **[new 2013]**	7.2
77	Inform the woman of the outcome of the MDT review if it alters the provisional treatment plan. **[new 2013]**	7.2
78	All MDTs should work within an established regional clinical network to ensure all women are offered the appropriate treatment options and high quality care. **[new 2013]**	7.2
	Invasive procedures for OAB	
	Botulinum toxin A	
79	After an MDT review, offer bladder wall injection with botulinum toxin A* to women with OAB caused by proven detrusor overactivity that has not responded to conservative management (including OAB drug therapy). **[new 2013]**	8.2

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Number	Recommendation	See section
80	Discuss the risks and benefits of treatment with botulinum toxin A††† with women before seeking informed consent, covering: • the likelihood of being symptom free or having a large reduction in symptoms • the risk of clean intermittent catheterisation and the potential for it to be needed for variable lengths of time after the effect of the injections has worn off • the absence of evidence on duration of effect between treatments and the long-term efficacy and risks • the risk of adverse effects, including an increased risk of urinary tract infection. **[new 2013]**	8.2
81	Start treatment with botulinum toxin A††† only if women: • have been trained in clean intermittent catheterisation and have performed the technique successfully, **and** • are able and willing to perform clean intermittent catheterisation on a regular basis for as long as needed. **[new 2013]**	8.2
82	Use 200 units when offering botulinum toxin A†††. **[new 2013]**	8.2
83	Consider 100 units of botulinum toxin A††† for women who would prefer a dose with a lower chance of catheterisation and accept a reduced chance of success. **[new 2013]**	8.2
84	If the first botulinum toxin A††† treatment has no effect discuss with the MDT. **[new 2013]**	8.2
85	If botulinum toxin A††† treatment is effective, offer follow-up at 6 months or sooner if symptoms return for repeat treatment without an MDT referral. **[new 2013]**	8.2
86	Tell women how to self-refer for prompt specialist review if symptoms return following a botulinum toxin A††† procedure. Offer repeat treatment as necessary. **[new 2013]**	8.2
87	Do not offer botulinum toxin B to women with proven detrusor overactivity. **[2006]**	8.2
	Percutaneous sacral nerve stimulation	
88	Offer percutaneous sacral nerve stimulation to women after MDT review if: • their OAB has not responded to conservative management including drugs, **and** • they are unable to perform clean intermittent catheterisation. **[new 2013]**	8.4
89	Consider percutaneous sacral nerve stimulation after MDT review if a woman's OAB has not responded to conservative management (including drugs) and botulinum toxin A*. **[new 2013]**	8.4
90	Discuss the long-term implications of percutaneous sacral nerve stimulation with women including:	8.4

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Number	Recommendation	See section
	• the need for test stimulation and probability of the test's success • the risk of failure • the long-term commitment • the need for surgical revision • the adverse effects. **[new 2013]**	
91	Tell women how to self-refer for prompt specialist review if symptoms return following a percutaneous sacral nerve stimulation procedure. **[new 2013]**	8.4
	### Augmentation cystoplasty	
92	Restrict augmentation cystoplasty for the management of idiopathic detrusor overactivity to women whose condition has not responded to conservative management and who are willing and able to self-catheterise. Preoperative counselling for the woman or her carer should include common and serious complications: bowel disturbance, metabolic acidosis, mucus production and/or retention in the bladder, UTI and urinary retention. Discuss the small risk of malignancy occurring in the augmented bladder. Provide life-long follow-up. **[2006, amended 2013]**	8.5
	### Urinary diversion	
93	Urinary diversion should be considered for a woman with OAB only when conservative management has failed, and if botulinum toxin A‡‡‡, percutaneous sacral nerve stimulation and augmentation cystoplasty are not appropriate or are unacceptable to her. Provide life-long follow-up. **[2006, amended 2013]**	8.6
	## Surgical approaches for SUI	
94	When offering a surgical procedure discuss with the woman the risks and benefits of the different treatment options for SUI using the information in table 9.12. **[new 2013]**	9.2
95	If conservative management for SUI has failed, offer: • synthetic mid-urethral tape (see recommendations 96–101) **or** • open colposuspension (see also recommendation 102), **or** • autologous rectus fascial sling (see also recommendation 103). **[new 2013]**	9.2
	### Synthetic tapes	
96	When offering a synthetic mid-urethral tape procedure, surgeons should: • use procedures and devices for which there is current high quality evidence of efficacy and safety*	9.2

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* The guideline only recommends the use of tapes with proven efficacy based on robust RCT evidence. However, technological advances are frequent, therefore the choice of tape should include devices that are shown in future clinical trials to have equal or improved efficacy at equal or lower cost. At the time of publication (September 2013) the following met the Guideline Development Group criteria:

- TVT or Advantage for a 'bottom-up' retropubic approach
- TVT-O for an 'inside-out' transobturator approach
- Monarc and obtryx halo for an 'outside-in' transobturator approach.

Number	Recommendation	See section
	• only use a device that they have been trained to use (see recommendations in chapter 11) • use a device manufactured from type 1 macroporous polypropylene tape • consider using a tape coloured for high visibility, for ease of insertion and revision. **[new 2013]**	
97	If women are offered a procedure involving the transobturator approach, make them aware of the lack of long-term outcome data. **[new 2013]**	9.2
98	Refer women to an alternative surgeon if their chosen procedure is not available from the consulting surgeon. **[new 2013]**	9.2
99	Use 'top-down' retropubic tape approach only as part of a clinical trial. **[new 2013]**	9.2
100	Refer to single-incision sub-urethral short tape insertion for stress urinary incontinence (NICE interventional procedure guidance 262) for guidance on single-incision procedures. **[new 2013]**	9.2
101	Offer a follow-up appointment (including vaginal examination to exclude erosion) within 6 months to all women who have had continence surgery. **[new 2013]**	9.2
	Colposuspension	
102	Do not offer laparoscopic colposuspension as a routine procedure for the treatment of stress UI in women. Only an experienced laparoscopic surgeon working in an MDT with expertise in the assessment and treatment of UI should perform the procedure. **[2006]**	9.2
	Biological slings	
103	Do not offer anterior colporrhaphy, needle suspensions, paravaginal defect repair and the Marshall–Marchetti–Krantz procedure for the treatment of stress UI. **[2006]**	9.2
	Intramural bulking agents	
104	Consider intramural bulking agents (silicone, carbon-coated zirconium beads or hyaluronic acid/dextran copolymer) for the management of stress UI if conservative management has failed. Women should be made aware that: • repeat injections may be needed to achieve efficacy • efficacy diminishes with time • efficacy is inferior to that of synthetic tapes or autologous rectus fascial slings. **[2006, amended 2013]**	9.3
105	Do not offer autologous fat and polytetrafluoroethylene used as intramural bulking agents for the treatment of stress UI. **[2006]**	9.3
	Artificial urinary sphincter	
106	In view of the associated morbidity, the use of an artificial urinary sphincter should be considered for the management of stress UI in women only if previous surgery has failed. Life-long follow-up is recommended. **[2006]**	9.3

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Number	Recommendation	See section
	Considerations following unsuccessful invasive SUI procedures or recurrence of symptoms	
107	Women whose primary surgical procedure for SUI has failed (including women whose symptoms have returned) should be: • referred to tertiary care for assessment (such as repeat urodynamic testing including additional tests such as imaging and urethral function studies) and discussion of treatment options by the MDT, **or** • offered advice as described in recommendation 51 if the woman does not want continued invasive SUI procedures. **[new 2013]**	9.5
	Maintaining and measuring expertise and standards for practice	
108	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 an MDT with this training, and who regularly carry out surgery for UI in women. [**2006]**	10.3
109	Training should be sufficient to develop the knowledge and generic skills documented below. Knowledge should include the: • specific indications for surgery • required preparation for surgery including preoperative investigations • outcomes and complications of proposed procedure • anatomy relevant to procedure • steps involved in procedure • alternative management options • likely postoperative progress. Generic skills should include • the ability to explain procedures and possible outcomes to patients and family and to obtain informed consent • the necessary hand–eye dexterity to complete the procedure safely and efficiently, with appropriate use of assistance • the ability to communicate with and manage the operative team effectively • the ability to prioritise interventions • the ability to recognise when to ask for advice from others • a commitment to MDT working. **[2006]**	10.3
110	Training should include competence in cystourethroscopy. **[2006]**	10.3
111	Operative competence of surgeons undertaking surgical procedures to treat UI or OAB in women should be formally assessed by trainers through a structured process. **[2006]**	10.3
112	Surgeons who are already carrying out procedures for UI should be able to demonstrate that their training, experience and current practice equates to the standards laid out for newly trained surgeons. **[2006]**	10.3
113	Only surgeons who carry out a sufficient case load to maintain their skills should undertake surgery for UI or OAB in women. An annual	10.3

Number	Recommendation	See section
	workload of at least 20 cases of each primary procedure for stress UI is recommended. Surgeons undertaking fewer than 5 cases of any procedure annually should do so only with the support of their clinical governance committee; otherwise referral pathways should be in place within clinical networks. **[2006]**	
114	There should be a nominated clinical lead within each surgical unit with responsibility for continence and prolapse surgery. The clinical lead should work within the context of an integrated continence service. **[2006]**	10.3
115	A national audit of continence surgery should be undertaken. **[2006]**	10.3
116	Surgeons undertaking continence surgery should maintain careful audit data and submit their outcomes to national registries such as those held by the British Society of Urogynaecology (BSUG) and British Association of Urological Surgeons Section of Female and Reconstructive Urology (BAUS-SFRU). **[2006]**	10.3

1.6 Key research recommendations

Number	Research recommendation	See section
RR6	How effective are different pelvic floor muscle training regimens in the management of women with overactive bladder (OAB) symptoms and to whom should it be offered? Why this is important For many women with urinary incontinence symptoms, management of their condition will take place predominantly in primary and community care. Pelvic floor muscle training may be their only experience of therapeutic intervention. It is not currently known whether different pelvic floor muscle training regimens have an impact on treatment outcomes. It is also not known whether other factors also have an impact on its effectiveness. These factors include the way that the training is offered, the technique that is taught, the intensity and frequency of training, and the length of time that pelvic floor muscle training is continued. Because pelvic floor muscle training is widely used in clinical practice, robust evaluation is needed to identify whether these or other factors have an important impact on patient-centred outcomes.	4.3
RR9	What is the comparative effectiveness and cost-effectiveness of transcutaneous stimulation of the sacral nerve roots, and transcutaneous and percutaneous posterior tibial nerve stimulation for the treatment of OAB?	5.5

Number	Research recommendation	See section
	Why this is important Transcutaneous neurostimulation can be applied either over the sacrum or over the posterior tibial nerve to modulate the sacral nerve supply to the bladder. The treatment uses surface electrodes and the woman can carry it out in her own home. Percutaneous posterior tibial nerve stimulation involves the introduction of a needle in the region of the posterior tibial nerve near the ankle, and at present is carried out in clinics in secondary care. Currently, it is offered widely as a conservative treatment for OAB without adequate evidence that it is effective. Although this is a relatively low cost treatment, both the equipment and staff time have a cost implication, and because it has been widely used in conservative management this has large resource consequences for the NHS. Robust evidence is needed to establish whether it is a cost-effective option relative to other conservative therapies for all women or for a selected group of patients who are unsuitable for or have unsuccessful botulinum toxin A, percutaneous sacral nerve stimulation or OAB drug treatment.	
RR11	What is the long-term effectiveness, optimal dose and optimal frequency of repeat therapy of botulinum toxin A in women with OAB based on detrusor overactivity including risk of adverse events such as urinary infection and intermittent catheterisation? **Why this is important** There are currently no trials looking at long-term outcomes, quality of life, satisfaction, optimal dose, optimal frequency and long-term adverse effects of botulinum toxin A for women with OAB. Further research into these outcomes will have an impact on future updates of key recommendations within the guideline and would impact on how resources are used within urinary incontinence services. Effective treatment with botulinum toxin A may need repeated injections to remain effective but the frequency of these is not reported in the current evidence. Botulinum toxin A has the potential to cause incomplete bladder emptying resulting in the need for women to perform catheterisation indefinitely. This not only has financial implications but catheterisation and the morbidity associated with it will not always be acceptable to women. Additionally, there are currently no data on whether repeated botulinum toxin A injections alter bladder function.	8.3
RR15	What is the effectiveness and optimum sequence of treatment with botulinum toxin A and percutaneous sacral nerve stimulation for the treatment of OAB after failed conservative (including drug) management? **Why this is important** It is not currently known which treatment option, either botulinum toxin A or percutaneous sacral nerve stimulation, is the most effective in the medium- and long-term for women with OAB in	8.3

Number	Research recommendation	See section
	whom initial treatment, including OAB drugs, has failed. The initial outlay for percutaneous sacral nerve stimulation is high but when successful it appears to be effective. Botulinum toxin A also has a high failure rate but a lower outlay and it is not yet understood the cost threshold (in terms of treatment cycles or length of follow-up) at which botulinum toxin A is likely to be the less cost-effective option compared with percutaneous sacral nerve stimulation. Currently, funding for percutaneous sacral nerve stimulation is on an individual basis because of its high cost, leading to geographical inequalities in access. A head-to-head longitudinal study of these 2 treatments would determine both which should be offered first and at what point in the treatment pathway. Such studies have not been done. This evidence could reduce inequalities in access to treatment. In subsequent NICE guidance, evidence would be available to inform recommendations on the treatment pathway and at which point in the treatment pathway for OAB each of these options should be offered. It would also provide more robust information to patients about the risk of adverse events and support women's choice about whether to proceed with treatment.	
RR18	What are the effects of the following predictors on tape failure? • Age per decade • Lower maximum urethral closure pressure • Secondary surgery versus primary surgery • Higher maximal flow rate • Concurrent pelvic organ prolapse surgery • Nocturia versus no nocturia • Urgency versus no urgency • Pad weight (per 10 g) • Previous urinary incontinence surgery versus no surgery • Q-tip maximum straining less than 30 degrees, yes versus no • Urge score (per 10 points) • Urgency symptoms versus no urgency symptoms • More than 20 procedures for each surgeon versus first 10 procedures for each surgeon • General anaesthesia versus local anaesthesia • BMI over 35 versus 30 or less • Maximum urethral closure pressure of 31 or more versus 30 or less • Primary surgery versus secondary surgery • Preoperative anticholinergic medication use versus no use **Why this is important** The factors identified for this research question are thought anecdotally by surgeons to have an impact on the outcome of tape surgery but there is little robust evidence in the literature. Certain patient factors such as older age and increased weight are thought to produce a higher chance of recurrent symptoms. Similarly, the effect of previous incontinence surgery,	9.3

Number	Research recommendation	See section
	concomitant prolapse surgery and the 'learning curve' of the surgeon are all thought to have adverse effects on outcome (including an increased chance of urgency incontinence). In addition there is little robust evidence regarding the effect of previous urgency incontinence, higher maximum flow rates, nocturia or preoperative use of anticholinergics on the occurrence of post-operative urgency and bladder overactivity. It would be useful to be able to individualise treatment by understanding these risks in more detail.	

1.7 Research recommendations

Number	Research recommendation	See section
RR1	The role of clinical pelvic floor muscle assessment prior to pelvic floor muscle training (PFMT) should be investigated to determine whether it enhances the therapeutic effect of the intervention.	4.3
RR2	Further research is needed to answer the question of whether the use of urodynamics, prior to initial or subsequent treatments, affects the outcomes and cost effectiveness of interventions in women with UI or OAB.	4.11
RR3	Further studies are required to clarify the role of ultrasound for the assessment of OAB.	4.14
RR4	There is a need for prospective interventional studies in all areas of lifestyle interventions to evaluate the effects of modifying these factors on UI and OAB.	5.2
RR5	Studies investigating different pelvic floor muscle training regimens are required to establish the optimum method of delivering and undertaking this intervention.	5.3
RR6	How effective are different pelvic floor muscle training regimens in the management of women with overactive bladder (OAB) symptoms and to whom should it be offered?	5.3
RR7	Research into the optimal electrical stimulation of the pelvic floor parameters is required, to inform future clinical practice. Studies investigating the role of electrical stimulation in women who cannot contract the pelvic floor muscle are required.	5.3
RR8	A direct comparison of single-component and multicomponent behavioural therapy is required.	5.4
RR9	What is the comparative effectiveness and cost-effectiveness of transcutaneous stimulation of the sacral nerve roots, and transcutaneous and percutaneous posterior tibial nerve stimulation for the treatment of OAB?	5.5

Number	Research recommendation	See section
R10	Further studies need to be undertaken to evaluate the role and effectiveness of physical and behavioural therapies and lifestyle modifications in the prevention of UI in women. Long-term outcomes in particular should be evaluated.	5.8
RR11	What is the long-term effectiveness, optimal dose and optimal frequency of repeat therapy of botulinum toxin A in women with OAB based on detrusor overactivity including risk of adverse events such as urinary infection and intermittent catheterisation?	8.2
RR12	What is the comparative effectiveness of all formulations of botulinum toxin A preparations for the treatment of OAB symptoms in women?	8.2
RR13	Further RCT evidence is required for drugs, Botulinum toxin A and P-SNS in women with OAB due to idiopathic detrusor overactivity	8.3
RR14	Further research is required to evaluate P-SNS test stimulation techniques, placement of leads on S3 and S4 root and the benefit of continuous nerve stimulation in comparison with an intermittent stimulation.	8.3
RR15	What is the effectiveness and optimum sequence of treatment with botulinum toxin A and percutaneous sacral nerve stimulation for the treatment of OAB after failed conservative (including drug) management?	8.3
RR16	Newer mid-urethral procedures and single incision procedures should be further investigated and compared with pelvic floor muscle training and accepted surgical interventions in the treatment of stress urinary incontinence.	9.2
RR17	What are long-term outcomes for 'top down' retropubic, transobturator proceedures?	9.2
RR18	What are the effects of the following predictors on tape failure? • Age per decade • Lower maximum urethral closure pressure • Secondary surgery versus primary surgery • Higher maximal flow rate • Concurrent pelvic organ prolapse surgery • Nocturia versus no nocturia • Urgency versus no urgency • Pad weight (per 10 g) • Previous urinary incontinence surgery versus no surgery • Q-tip maximum straining less than 30 degrees, yes versus no • Urge score (per 10 points) • Urgency symptoms versus no urgency symptoms • More than 20 procedures for each surgeon versus first 10 procedures for each surgeon • General anaesthesia versus local anaesthesia • BMI over 35 versus 30 or less • Maximum urethral closure pressure of 31 or more versus 30 or less • Primary surgery versus secondary surgery • Preoperative anticholinergic medication use versus no use	8.3

Number	Research recommendation	See section
RR19	What is the effectiveness of a repeat procedure following primary tape failure?	8.6
RR20	What is the effectiveness of re-suturing following vaginal tape erosion?	8.6
RR21	Which is the comparative effectiveness of a different procedure following failure of a primary tape, colposuspension and/or bulking agents intervention?	8.6
RR22	What is the efficacy of conservative treatments (including physiotherapy) following primary surgical procedure failure?	8.6

1.8 Other versions of the guideline

- Urinary incontinence in women: NICE guideline
- Urinary incontinence in wome: information for public

1.9 Schedule for updating the guideline

A formal review of the need to update a guideline is usually undertaken by NICE after its publication. NICE will conduct a review to determine whether the evidence base has progressed significantly to alter the guideline recommendations and warrant an update.

2 Introduction

2.1 Urinary incontinence

Urinary incontinence (UI) is a common symptom that can affect women of all ages, with a wide range of severity and nature. While rarely life-threatening, incontinence may seriously influence the physical, psychological and social wellbeing of affected individuals. The impact on the families and carers of women with UI may be profound, and the resource implications for the health service considerable.

The International Continence Society (ICS) has standardised terminology in lower urinary tract function: UI is defined as 'the complaint of any involuntary urinary leakage'.[1] This may occur as a result of a number of abnormalities of function of the lower urinary tract, or as a result of other illnesses, and these tend to cause leakage in different situations. Definitions for stress, mixed and urgency UI and overactive bladder (OAB) are given in the glossary. Other types of UI may be described by the situations that provoke urine loss, for example during sexual intercourse (coital intercourse), or on laughing or giggling. Some patients may simply report being 'wet all the time'. This may be a reflection of the severity of their condition, although may on occasions be due to other pathologies, for example fistula. There are currently approximately 80 cases of fistula between the urinary tract and genital tract treated each year in England and Wales and this condition is not considered further in this guideline. It is recognised that UI may be of a transient nature on occasion, reflecting acute health or environmental factors.

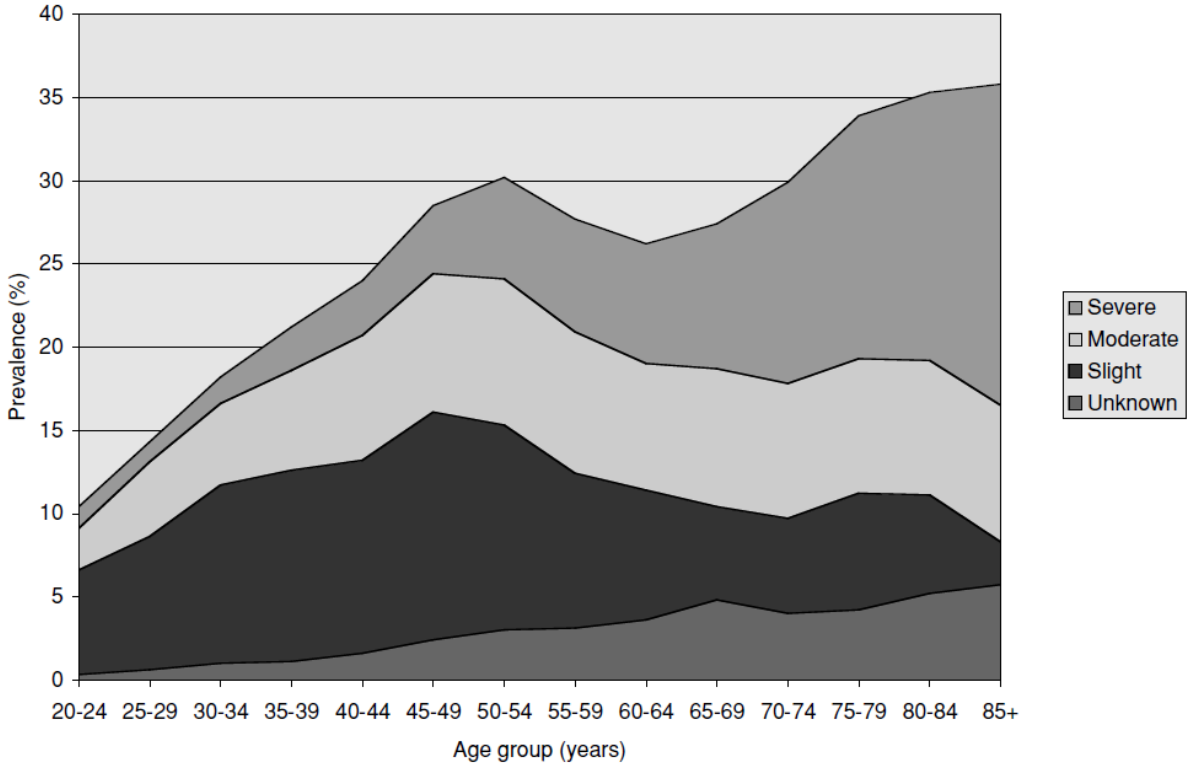
Prevalence and incidence

Urinary incontinence is an embarrassing problem to many women and thus its presence may be significantly underreported. In a UK community study, the prevalence of UI known to the health and social service agencies was 0.2% in women aged 15–64 years and 2.5% in those aged 65 and over.[2] A concurrent postal survey showed a prevalence of 8.5% in women aged 15–64 and 11.6% in those aged 65 and over. Incontinence was described as 'moderate' or 'severe' in one-fifth of those who reported it and, even among these, fewer than one-third were receiving health or social services for the condition.[2]

The Leicestershire MRC Incontinence Study, of individuals over 40 years of age, found that 33.6% of the population reported significant urinary symptoms but only 6.2% found these troublesome, and only 2.4% both bothersome and socially disabling. Of the population surveyed, 3.8% (one in nine of those with clinically significant symptoms) felt the need for help with their symptoms.[3,4] Some women may not see their UI as a major problem. For others, who do perceive a problem with which they would like help, there are often barriers to presentation. Women may take up to 10 years before seeking help.[5] They may be too embarrassed to seek advice, may not wish to bother their general practitioner (GP), may believe UI to be a normal consequence of the ageing process or may not appreciate that treatments are available.[6]

Differences in study populations, the definition and measurement of UI, and the survey method used result in a wide range of prevalence estimates.[7] Where the most inclusive definitions have been used ('ever', 'any', 'at least once in the last 12 months'), prevalence estimates in the general population range from 5% to 69% in women 15 years and older, with most studies in the range 25–45%.[7] There appears to be less variation in the prevalence of more severe UI and estimates in the general population range between 4% and 7% in women under 65 years, and between 4% and 17% in those over 65 for daily UI.[7] The Leicestershire MRC Incontinence Study found that, while 34.2% of women reported UI at times, only 3.5% experienced the symptom on a daily basis, 11.8% weekly, 7.3% monthly and 11.6% yearly.

Figure 2.1 Prevalence of incontinence by age group and severity



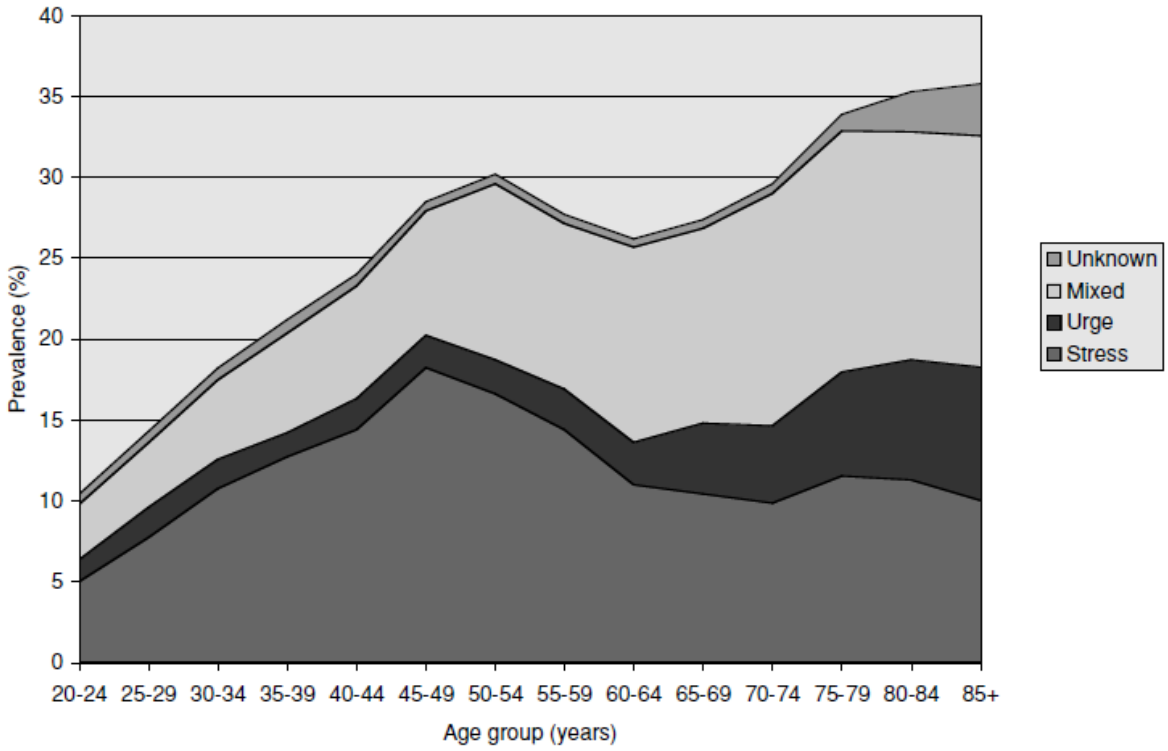
Several studies have shown that the prevalence of any UI tends to increase up to middle age, then plateaus or falls between 50 and 70 years, with a steady increase with more advanced age. The EPINCONT survey, of women aged over 20 years from Norway, illustrates this point (Figure 2.1). These data also show that slight to moderate UI is more common in younger women, while moderate and severe UI affects the elderly more often.[9,10]

Stress UI appears to be the most common UI type and overall 50% of incontinent women in the EPINCONT survey reported this as their only symptom; 11% described only urgency UI and 36% reported mixed UI.[9] This and other studies indicate that the trends in prevalence of UI at different ages reflect a reduction in the complaints of stress UI in those aged 50 years and over, with an increase in urge UI and mixed UI in women aged 60 years and above (Figure 2.2).[9,11] This study also found that the severity of incontinence varied between the different types: the proportion of incontinence that was regarded as being severe was 17%, 28% and 38% in the stress, urgency and mixed UI groups, respectively.[9]

There are relatively little epidemiological data on the prevalence of OAB syndrome. A telephone survey from the USA found an overall prevalence of OAB wet of 9.6% in women over 18 years of age, rising from 5% in those aged 18–44 to 19% in those over 65.[12] Survey data from Europe found prevalence of the same order.[13] The Leicestershire MRC Incontinence Study found an overall prevalence of OAB in women aged 40 and over of 21.4%.[14]

It has been estimated that, while not all may need or want help, 20.4% of people aged 40 years and over, representing around 5 million people in the UK, have a healthcare requirement.[8] In women aged 40 and over this figure increases from 20.5% aged 40–49 up to 35.6% at age 80 and over.

Figure 2.2 Prevalence of UI types by age group



Risk factors

In addition to the effect of age, cross-sectional studies suggest other associations and possiblerisk factors for UI. These include pregnancy, parity, obstetric factors, menopause, hysterectomy, obesity, lower urinary tract symptoms, functional impairment, cognitive impairment, smoking, family history, diet and genetics. Urinary incontinence may be a presenting symptom of neurological disease.

Costs and implications for health services

Costs to patients and carers

Urinary incontinence is distressing and socially disruptive. It may be the cause of personal health and hygiene problems. It may restrict employment and educational or leisure opportunities, and lead to embarrassment and exclusion. Furthermore, for some, it may result in abuse of adults in the workplace and older people in residential care or nursing homes. In adult women with UI, 60% avoid going away from home, 50% feel odd or different from others, 45% avoid public transport and 50% report avoiding sexual activity through fear of incontinence.[15] Serious psychiatric morbidity has been reported in one-quarter of women attending hospital for investigation of UI.[16] For carers, UI is often a major reason for the breakdown of the caring relationship which can lead to admission to residential or nursing home care; incontinence is second only to dementia as an initiating factor for such moves.[17] Financial costs to patients and carers, including the cost of absorbent products, laundry, etc., may also be considerable.

Costs to the health services

There is limited information on the cost of managing UI in the UK although the estimated total cost in the USA in 1995 was $12.4bn (£7bn), with the vast majority of this relating to community or nursing home care ($8.6bn and $3.8bn [£5bn and £2.2bn], respectively).[18] These costs are of a similar order to those associated with gynaecological cancers, osteoporosis, pneumonia and influenza, and arthritis,[18] and in the USA and Sweden are equivalent to approximately 2% of the total healthcare budget.[19] With current UK health spending of £90bn, this would approximate to £1.8bn annually in England and Wales, or perhaps £600 per incontinent individual. Data from the Leicestershire MRC Incontinence Study estimates the annual cost to the NHS of treating clinically significant UI at £536m (£233m for women). The total annual service costs (including costs borne by individuals) were estimated at £743m.[20]

A study of the costs of care for women seeking treatment for UI across Europe (the PURE study), determined that the mean UI-related costs per year ranged from €359 (£248) in the UK/Ireland (where patients were predominantly treated by their GPs) to €515 (£355) in Germany and €655 (£452) in Spain (where the initial referral may sometimes be to specialists and sometimes to GPs).[5]

Health-related costs of managing OAB in the USA have been estimated at around $9bn (£5bn), the cost patterns raising the possibility that treating OAB at an early stage may both improve patient care and minimise overall use of healthcare resources.[21]

2.2 Aim of the guideline

This clinical guideline concerns the management of UI in adult women. It includes:

- stress UI
- OAB UI (with or without urgency)
- mixed UI.

It has been developed with the aim of providing guidance on:

- initial and ongoing assessments and investigations
- appropriate use of conservative and surgical treatment options
- the competence required by surgeons performing the primary and subsequent operative procedures.

2.3 Areas outside the remit of the guideline

This guideline does not address:

- the management and treatment of co-morbidities, such as pelvic organ prolapse (POP), except where they relate to the treatment of UI and/or OAB syndrome
- incontinence caused by neurological disease
- incontinence in men
- incontinence in children
- faecal incontinence.

2.4 For whom is the guideline intended?

This guideline is of relevance to those who work in or use the NHS in England and Wales, in particular:

- all healthcare professionals who are involved in the care of women who have UI or OAB syndrome (including GPs, nurses, physiotherapists, gynaecologists, urologists and occupational therapists). The healthcare professionals providing care for women with UI or OAB may vary depending on geographical service provision.
- those responsible for commissioning and planning healthcare services, including primary care trust commissioners, Health Commission Wales commissioners, and public health, trust and care home managers
- women with UI and/or OAB syndrome, their families and other carers.

Urinary incontinence in neurological disease

The guideline is not intended for women with neurological disease related incontinence. A separate guideline should be used in the treatment and management of this condition:

- Urinary incontinence in neurological disease. NICE clinical guideline 148 (August 2012).

2013 Update

2.5 Who has developed the guideline?

The guideline was developed by a multi-professional and lay working group (the guideline development group [GDG]) convened by the National Collaborating Centre for Women's and Children's Health (NCC-WCH). The membership is listed above. Staff from the NCC-WCH provided support for the guideline development process by undertaking systematic searches, retrieval and appraisal of the evidence and health economic modelling, and wrote successive drafts of the guideline.

All GDG members' potential and actual conflicts of interest were recorded on a declaration form provided by NICE and are shown in Appendix C. The form covered consultancies, fee-paid work, shareholdings, fellowships, and support from the healthcare industry. The GDG leader and NCC-WCH executive director consider that the declarations made did not influence the recommendations developed.

2.6 Other relevant documents

This guideline is intended to complement other existing and proposed works of relevance, including related NICE guidance:

- Guidelines:
  - Infection Control: Prevention of Healthcare-Associated Infection in Primary and Community Care[22]
  - Referral Guidelines for Suspected Cancer[23]
  - Routine Postnatal Care of Women and Their Babies[24]
- Cancer service guidance:
  - Improving Outcomes in Urological Cancer: the Manual.[25]
- Interventional procedures:
  - Sacral Nerve Stimulation for Urge Incontinence and Urgency-Frequency.[26]
  - Intramural Urethral Bulking Procedures for Stress Urinary Incontinence in Women[27]
  - Insertion of Extraurethral (Non-Circumferential) Retropubic Adjustable Compression
  - Devices for Stress Urinary Incontinence in Women[28]
  - Insertion of Biological Slings for Stress Urinary Incontinence in Women[29]
  - Bone-Anchored Cystourethropexy.[30]
- Other than NICE guidance, relevant works are:
  - the third International Consultation on Incontinence (ICI) (2005)[31,32]
  - the Royal College of Physicians report on incontinence (1995)[33]
  - the Department of Health's Good Practice in Continence Services (2000)[34]
  - the National Service Framework for Older People (2001).[35]

2.7 Related NICE guidance

- Urinary incontinence in neurological disease. NICE clinical guideline 148 (August 2012).
- Lower urinary tract symptoms. NICE clinical guideline 97 (May 2010).
- Patient experience in adult NHS services. NICE clinical guideline 138 (February 2012).
- Infection control. NICE clinical guideline 139 (March 2012).

- Percutaneous posterior tibial nerve stimulation for overactive bladder syndrome. NICE interventional procedure guidance 362 (2010).
- Sacral nerve stimulation for urge incontinence and urgency-frequency. NICE interventional procedure guidance 64 (2004).
- Insertion of biological slings for stress urinary incontinence. NICE interventional procedure guidance 154 (2006).
- Laparoscopic augmentation cystoplasty (including clam cystoplasty). NICE interventional procedure guidance 326 (2009).
- Single-incision sub-urethral short tape insertion for stress urinary incontinence in women. NICE interventional procedure guidance 262 (2008).
- Faecal incontinence. NICE clinical guideline 49 (2007).
- Insertion of extraurethral (non-circumferential) retropubic adjustable compression devices for stress urinary incontinence in women. NICE interventional procedure guidance 133 (2005).
- Intramural urethral bulking procedures for stress urinary incontinence. NICE interventional procedure guidance 138 (2005).

3 Guideline development methodology

3.1 2006 Guideline method

This guideline was commissioned by NICE and developed in accordance with the guideline development process outlined in the NICE technical manual.[36]

Literature search strategy

Initial scoping searches were executed to identify relevant guidelines (local, national and international) produced by other development groups. The reference lists in these guidelines were checked against subsequent searches to identify missing evidence.

Relevant published evidence to inform the guideline development process and answer the clinical questions was identified by systematic search strategies. The questions are shown in Appendix B. Additionally, stakeholder organisations were invited to submit evidence for consideration by the guideline development group (GDG) provided it was relevant to the clinical questions and of equivalent or better quality than evidence identified by the search strategies.

Systematic searches to answer the clinical questions formulated and agreed by the GDG were executed using the following databases via the 'Ovid' platform: Medline (1966 onwards), Embase (1980 onwards), Cumulative Index to Nursing and Allied Health Literature (1982 onwards), British Nursing Index (1985 onwards) and PsycINFO (1967 onwards). The most recent search conducted for the three Cochrane databases (Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and the Database of Abstracts of Reviews of Effects) was Quarter 1, 2006. The Allied and Complementary Medicine Database (AMED) was also used for alternative therapies (1985 onwards via the Datastar platform). Searches to identify economic studies were undertaken using the above databases and the NHS Economic Evaluations Database (NHS EED).

Search strategies combined relevant controlled vocabulary and natural language in an effort to balance sensitivity and specificity. Unless advised by the GDG, searches were not date specific. Language restrictions were not applied to searches. Both generic and specially developed methodological search filters were used appropriately.

There was no systematic attempt to search grey literature (conferences, abstracts, theses and unpublished trials). Hand searching of journals not indexed on the databases was not undertaken.

Towards the end of the guideline development process, searches were updated and re-executed, thereby including evidence published and included in the databases up to 17 March 2006. Any evidence published after this date was not included. This date should be considered the starting point for searching for new evidence for future updates to this guideline.

Further details of the search strategies, including the methodological filters employed, are available in the appendix.

Synthesis of clinical effectiveness evidence

Evidence relating to clinical effectiveness was reviewed using established guides[37–43] and classified using the established hierarchical system shown in Table 3.1.[36] This system reflects the susceptibility to bias that is inherent in particular study designs.

The type of clinical question dictates the highest level of evidence that may be sought. In assessing the quality of the evidence, each study receives a quality rating coded as '++', '+' or '−'. For issues of

therapy or treatment, the highest possible evidence level (EL) is a well-conducted systematic review or meta-analysis of randomised controlled trials (RCTs; EL = 1++) or an individual RCT (EL = 1+). Studies of poor quality are rated as '−'. Usually, studies rated as '−' should not be used as a basis for making a recommendation, but they can be used to inform recommendations. For issues of prognosis, the highest possible level of evidence is a cohort study (EL = 2). A level of evidence was assigned to each study, and to the body of evidence for each question.

For each clinical question, the highest available level of evidence was selected. Where appropriate, for example if a systematic review, meta-analysis or RCT existed in relation to a question, studies of a weaker design were not included. Where systematic reviews, meta-analyses and RCTs did not exist, other appropriate experimental or observational studies were sought. For diagnostic tests, test evaluation studies examining the performance of the test were used if the efficacy of the test was required, but where an evaluation of the effectiveness of the test in the clinical management of patients and the outcome of disease was required, evidence from RCTs or cohort studies was optimal.

Table 3.1 Levels of evidence for intervention studies

Level	Source of evidence
1++	High-quality meta-analyses, systematic reviews of randomised controlled trials (RCTs) or RCTs with a very low risk of bias
1+	Well-conducted meta-analyses, systematic reviews of RCTs or RCTs with a low risk of bias
1−	Meta-analyses, systematic reviews of RCTs or RCTs with a high risk of bias
2++	High-quality systematic reviews of case–control or cohort studies; high-quality case–control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal
2+	Well-conducted case–control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal
2−	Case–control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not causal
3	Non-analytical studies (for example case reports, case series)
4	Expert opinion, formal consensus

The system described above covers studies of treatment effectiveness. However, it is less appropriate for studies reporting diagnostic tests of accuracy. In the absence of a validated ranking system for this type of test, NICE has developed a hierarchy for evidence of accuracy of diagnostic tests that takes into account the various factors likely to affect the validity of these studies (Table 3.2).[36]

For economic evaluations, no standard system of grading the quality of evidence exists. Economic evaluations that are included in the review have been assessed using a quality assessment checklist based on good practice in decision-analytic modelling.[44]

Table 3.2 'Levels of evidence for studies of the accuracy of diagnostic tests

Level	Type of evidence
Ia	Systematic review (with homogeneity)[a] of level-1 studies[b]
Ib	Level-1 studies[b]
II	Level-2 studies[c]; systematic reviews of level-2 studies
III	Level-3 studies[d]; systematic reviews of level-3 studies
IV	Consensus, expert committee reports or opinions and/or clinical experience without explicit critical appraisal; or based on physiology, bench research or 'first principles'

[a] Homogeneity means there are minor or no variations in the directions and degrees of results between individual studies that are included in the systematic review.

[b] Level-1 studies are studies that use a blind comparison of the test with a validated reference standard ('gold' standard) in a sample of patients that reflects the population to whom the test would apply.

[c] Level-2 studies are studies that have only one of the following:

- narrow population (the sample does not reflect the population to whom the test would apply) use a poor reference standard (defined as that where the 'test' is included in the 'reference', or where the 'testing' affects the 'reference')
- the comparison between the test and reference standard is not blind
- case–control studies.

[d] Level-3 studies are studies that have at least two or three of the features listed above.

Table 3.3 MHRA classification of adverse effect frequency

Classification	Frequency of occurrence
Very common	more than 1 in 10 (> 10%)
Common	between 1 in 10 and 1 in 100 (≥ 1% and ≤ 10%)
Uncommon	between 1 in 100 and 1 in 1000 (≥ 0.1% and < 1%)
Rare	between 1 in 1000 and 1 in 10 000
Very rare	fewer than 1 in 10 000

Evidence was synthesised qualitatively by summarising the content of identified papers in evidence tables and agreeing brief statements that accurately reflected the evidence. Quantitative synthesis (meta-analysis) was performed where appropriate. Where confidence intervals were calculated, this was done in accordance with accepted methods.[45] Summary results and data are presented in the guideline text. More detailed results and data are presented in the evidence tables in the appendix, where a list of excluded studies is also provided.

Specific considerations for this guideline

It was anticipated that some evidence relevant to this guideline would not be specific to women with urinary incontinence (UI) and thus studies with mixed populations (men and women, and/or with UI of different aetiology) were considered if the majority of the population was women with idiopathic UI or overactive bladder (OAB).

Published guidance from the NICE Interventional Procedures (IP) Programme was considered, alongside all relevant evidence in women with UI or OAB when an interventional procedure was approved for use. Where the IP guidance states that an interventional procedure is not for routine use, the procedure was not considered within this guideline.

The NICE health technology appraisal on tension-free vaginal tape (2003) was updated within this guideline by addressing a question on the intervention. The associated NICE guidance will be withdrawn on publication of this guideline.

The classification of adverse effect frequency used by the Medicines and Healthcare products Regulatory Agency (MHRA) was adopted within the guideline, as shown in Table 3.3.

Health economics

The aims of the economic input into the guideline were to inform the GDG of potential economic issues relating to UI in women and to ensure that recommendations represent a cost-effective use of healthcare resources.

The health economist helped the GDG by identifying topics within the guideline that might benefit from economic analysis, reviewing the available economic evidence and, where necessary, conducting economic analysis. Reviews of published health economic evidence are presented alongside the reviews of clinical evidence, and modelling is presented in the appendices, with cross references from the relevant chapters.

Outcome measures used in the guideline

For this guideline, treatment has been assessed against a number of outcome domains, as follows:

- the woman's observations, including changes in symptoms and satisfaction
- generic and incontinence-specific aspects of quality of life (QOL)
- the clinician's observations including urodynamic investigation and quantification of incontinence
- harm (adverse effects, surgical complications)
- health economic outcomes, for example quality-adjusted life years (QALYs).

Table 3.4 Classification (grading) of recommendations for intervention studies

Grade	Evidence
A	• At least one meta-analysis, systematic review or randomised controlled trial (RCT) that is rated as 1++, and is directly applicable to the target population, or • a systematic review of RCTs or a body of evidence that consists principally of studies rated as 1+, is directly applicable to the target population and demonstrates overall consistency of results, or • evidence drawn from a NICE technology appraisal.
B	• A body of evidence that includes studies rated as 2++, is directly applicable to the target population and demonstrates overall consistency of results, or • extrapolated evidence from studies rated as 1++ or 1+.
C	• A body of evidence that includes studies rated as 2+, is directly applicable to the target population and demonstrates overall consistency of results, or • extrapolated evidence from studies rated as 2++.
D	• Evidence level 3 or 4, or • extrapolated evidence from studies rated as 2+, or • formal consensus.
D (GPP)	• A good practice point (GPP) is a recommendation for best practice based on the experience of the guideline development group.

Forming and grading recommendations

For each guideline question, recommendations were derived using, and explicitly linked to, the evidence that supported them. In the first instance, informal consensus methods were used by the GDG to agree evidence statements and recommendations. Additionally, in areas where no substantial evidence existed, the GDG considered other guidelines or consensus statements to identify current best practice. Shortly before the consultation period, formal consensus methods were used to agree guideline recommendations (modified Delphi technique) and to select five to ten key priorities for implementation (nominal group technique).

Each recommendation was graded according to the level of evidence upon which it was based, using the established systems shown in Tables 3.4 and 3.5. For issues of therapy or treatment, the best possible level of evidence (a systematic review or meta-analysis or an individual RCT) equates to a grade A recommendation. For issues of prognosis, the best possible level of evidence (a cohort study) equates to a grade B recommendation. However, this should not be interpreted as an inferior grade of recommendation because it represents the highest level of relevant evidence.

In addition, the GDG made research recommendations in areas where evidence is lacking.

External review

This guideline has been developed in accordance with the NICE guideline development process. This has included giving registered stakeholder organisations the opportunity to comment on the scope of the guideline at the initial stage of development and on the evidence and recommendations at the concluding stage. In addition, the guideline was peer reviewed by nominated individuals. The developers have carefully considered all of the comments during the consultation periods by registered stakeholders with validation by NICE.

Table 3.5 Classification (grading) of recommendations for intervention studies

Grade	Level of evidence
A (DS)	Studies with level of evidence Ia or Ib
B (DS)	Studies with level of evidence of II
C (DS)	Studies with level of evidence of III
D (DS)	Studies with level of evidence of IV

3.2 Schedule for updating the guideline

A formal review of the need to update a guideline is usually undertaken by NICE after its publication. NICE will conduct a review to determine whether the evidence base has progressed significantly to alter the guideline recommendations and warrant an update.

3.3 Methodology for 2013 Update

This guidance was commissioned by NICE and developed in accordance with the guideline development process outlined in the 2009 edition of The Guidelines Manual.

In accordance with NICE's Equality Scheme, ethnic and cultural considerations and factors relating to disabilities have been considered by the GDG throughout the development process and specifically addressed in individual recommendations where relevant. Further information is available from: www.nice.org.uk/aboutnice/howwework/NICEEqualityScheme.jsp.

Developing review questions and protocols and identifying evidence

The GDG formulated review questions based on the topics agreed with the stakeholders and included in the scope (see Appendix A) and prepared a protocol for each review question (see Appendix D). These formed the starting point for systematic reviews of relevant evidence. Published evidence was identified by applying systematic search strategies (see Appendix E) to the following databases: Medline (1950 onwards), Embase (1980 onwards), Cumulative Index to Nursing and Allied Health Literature (CINAHL; 1982 onwards), and three Cochrane databases (Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and the Database of Abstracts of Reviews of Effects). Searches to identify economic studies were undertaken using the above databases, the NHS Economic Evaluation Database (NHS EED) and the Health Technology Assessment (HTA) database. None of the searches were limited by date. Searches in Embase were limited to English language, and searches in Medline were limited to English language and studies in

humans. None of the other searches were limited by language of publication (although publications in languages other than English were not reviewed). Validated search filters were used to identify particular study designs, such as RCTs. There was no systematic attempt to search grey literature (conference abstracts, theses or unpublished trials), nor was hand searching undertaken of journals not indexed on the databases.

Towards the end of the guideline development process, the searches were updated and re-executed to include evidence published and indexed in the databases by 30 November 2012.

Reviewing and synthesising evidence

Evidence relating to clinical effectiveness was reviewed and synthesised according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach. In the GRADE approach, the quality of the evidence identified for each outcome in the review protocol is assessed according to the factors listed below, and an overall quality rating (high, moderate, low or very low) is assigned by combining the ratings for the individual factors.

- Risk of bias (in study design using either NICE or CASP methodological checklists; see http://www.nice.org.uk/guidelinesmanual and http://www.casp-uk.net/). This also includes limitations in the design or execution of the study (including concealment of allocation, blinding, loss to follow up; these can reduce the quality rating).
- Inconsistency of effects across studies – occurs when there is variability in the treatment effect demonstrated across studies (heterogeneity). (This can reduce the quality rating.)
- Indirectness – the extent to which the available evidence fails to address the specific review question (this can reduce the quality rating).
- Imprecision – present when there is uncertainty around the estimate of effect, for example when the confidence intervals are wide and cross the 'imaginary' lines of clinically significant effect (see 'Outcome measures' below). This reflects the confidence in the estimate of effect. (This can reduce the quality rating.)
- Other considerations (including large magnitude of effect, evidence of a dose–response relationship, or confounding variables likely to have reduced the magnitude of an effect; these can increase the quality rating in observational studies, provided no downgrading for other features has occurred).

The type of review question determines the highest level of evidence that may be sought. For issues of therapy or treatment, the highest possible evidence level is a well-conducted systematic review or meta-analysis of RCTs, or an individual RCT. In the GRADE approach, a body of evidence based on RCTs has an initial quality rating of high, but this may be downgraded to moderate, low or very low if the factors listed above are not addressed adequately. For issues of prognosis, the highest possible level of evidence is a controlled observational study (a cohort study or case–control study), and a body of evidence based on such studies would have an initial quality rating of low, which might be downgraded to very low or upgraded to moderate or high, depending on the factors listed above.

For each review question the highest available level of evidence was sought. Where appropriate, for example, if a systematic review, meta-analysis or RCT was identified to answer a question directly, studies of a weaker design were not considered. Where systematic reviews, meta-analyses and RCTs were not identified, other appropriate experimental or observational studies were sought.

Within the full guideline, summary GRADE tables are presented. The full GRADE tables can be found in Appendix I.

For the review in this update we used the study types and methodology checklists shown in Table 3.6.

Table 3.6 Study types per question and corresponding NICE methodological checklist used

Question	Study type	Checklist
Botulinum toxin A	Randomised controlled trials	NICE checklist for randomised controlled trials
Neuromodulation	Randomised controlled trials	NICE checklist for randomised controlled trials
Antimuscarinics	Systematic review	NICE checklist for systematic reviews and meta-analyses
Surgical interventions	Randomised controlled trials	NICE checklist for randomised controlled trials
	Observational studies	CASP checklist for observational studies

NICE National Institute for Health and Care Excellence, CASP critical appraisal skills programme

We used the CASP checklist for observational studies as none of the NICE checklists were appropriate for non-comparative studies.

The quality items for each study are reported the study's evidence table and are summarised in the footnotes of each GRADE profile. For this guideline, we inserted footnotes to explain the choice we made while assessing the quality of evidence for each outcomes. These footnotes indicated if we upgraded the evidence level, downgraded the evidence level or left the evidence level unchanged, and gave the rationale for doing this.

Some studies were excluded from the guideline reviews after obtaining copies of the publications because they did not meet inclusion criteria specified by the GDG (see Appendix G). These studies are listed in alphabetical order for each question and the reason for exclusion provided for each one.

Basic characteristics of each included study were summarised in evidence tables for each review question (see Appendix H) along with the quality assessment. Where outcome data were presented, results were entered in text-boxes exactly as reported in the full-text report of the study. The data grids in the 'Results' column contain data we exported to Revman 5.1 (see http://ims.cochrane.org/revman) for meta-analysis. Where the standard deviation of the mean change from baseline was not reported, we imputed this using either the baseline standard deviation (SD) from the control group or theSD from a similar group.

Where possible, dichotomous outcomes were presented as relative risks (RRs) with 95% confidence intervals (CIs), and continuous outcomes were presented as mean differences with 95% CIs or SDs.

The body of evidence identified for each therapy or treatment review question (or part of a review question) was presented in the form of a GRADE evidence profile summarising the quality of the evidence and the findings (pooled relative and absolute effect sizes and associated CIs). Where possible, the body of evidence corresponding to each outcome specified in the review protocol was subjected to quantitative meta-analysis. In such cases, pooled effect sizes were presented as pooled risk ratios (RRs), pooled odds ratios (ORs), or mean differences. By default, meta-analyses were conducted using a random effects models as this is regarded as a more conservative method.

Where quantitative meta-analysis could not be undertaken, the range of effect sizes reported in the included studies was presented in a GRADE profile.

Outcome measures

For this guideline update, the effectiveness of interventions to treat urinary incontinence has been assessed against a variety of outcomes. The justification for using these outcomes is based on their relevance to women with the condition, to stakeholders involved in the consultation for this guideline and the expert consensus opinion of members of the multidisciplinary GDG. Outcomes included those that were felt to be desirable states (for example improvement in continence status) and the unwanted side-effects of treatment (for example the need for self-catheterisation). When assessing the effectiveness of a particular treatment, information about the effect of that treatment on one or more primary outcomes was sought.

Primary outcomes agreed in stakeholder consultation were:

- continence status (zero episodes per day)
- self-reported rate of absolute symptom reduction; for example number of episodes of incontinence per day
- adverse effects; for example tolerability of drugs, development of new OAB symptoms after surgery for stress urinary incontinences, need for self-catheterisation after botulinum toxin A
- incontinence-specific quality of life; for example Incontinence – Quality of Life, Bristol Female Lower Urinary Tract Symptoms questionnaire (BFLUTS) or the King's Health Questionnaire
- psychological outcomes; such as anxiety and depression
- clinical measures; such as cystometric capacity, post-void residual volume.

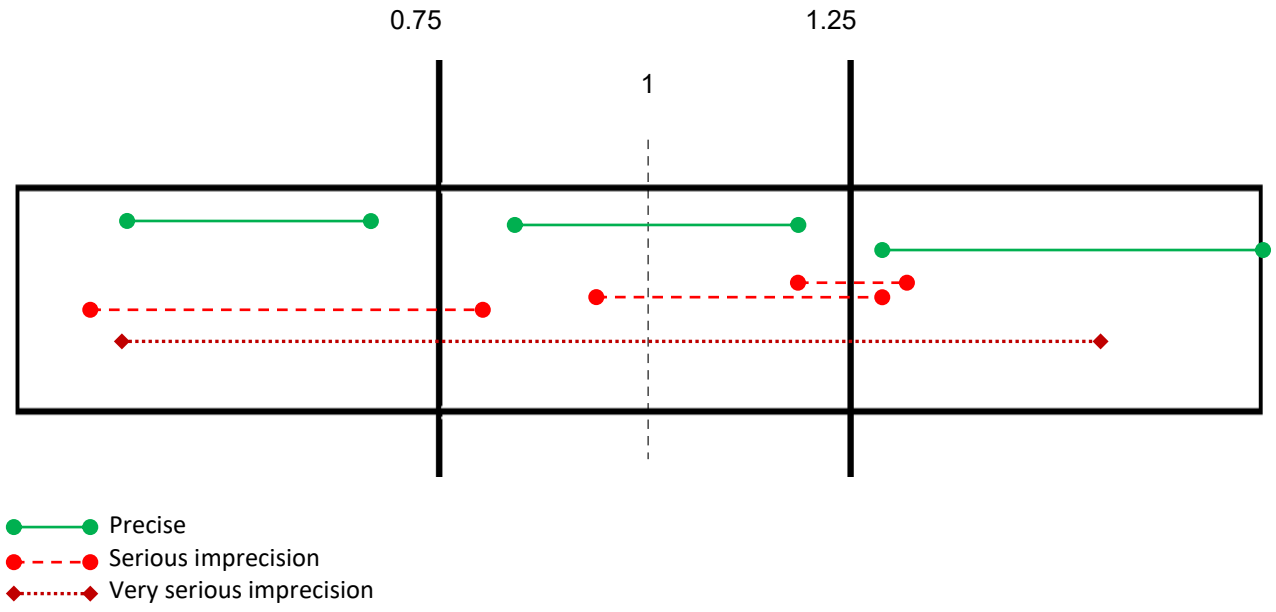
Once the GDG was convened, each member was surveyed to reach agreement on how to measure outcomes in a clinically meaningful way. The GDG members were asked individually to consider the time-point at which a specific outcome should be measured and the important adverse effects, and to prioritise the outcomes. (The questionnaire and feedback are available in Appendix V.)

Throughout the review we used the confidence intervals to decide imprecision, using a 'zone' rule.

The three zones, for example for the risk ratio, are less than 0.75, 0.75 to 1.25, and greater than 1.25. As demonstrated in Figure 1.1, if the confidence interval:

- was in a single zone, we rated the findings as precise and did not upgrade or downgrade
- crossed into two zones, we downgraded to 'serious imprecision'
- crossed into three zones, we downgraded to 'very serious imprecision'.

Figure 3.1 Zones approach to imprecision



Where the GDG selected a minimal important difference (MID) for a continuous outcome, this MID defined the three zones, for example for the OAB-Q quality of life scale the MID used in the literature was 10 points, so this was used to define the zones for imprecision. The mean number of episodes differed across studies at baseline so it was not feasible to define a study-based MID such as percentage reduction in symptoms. A default MID of 1 episode per day difference between the treatments was chosen to define the zones.

The GDG consensus was that patient satisfaction with treatment was the the best overall indicator of treatment success since it includes those women who, while not on optimal treatment, may nevertheless have improved quality of life compared with before treatment.

Network meta-analysis

A network meta-analysis (NMA) can be undertaken where there is a comparison of multiple treatments. The approach is an extension of meta-analysis that includes multiple different pairwise comparisons across a range of interventions to treat one condition.

For this guideline, a hierarchical Bayesian NMA was undertaken to evaluate the effectiveness of antimuscarinic drugs for the treatment of overactive bladder. Trial populations were sufficiently homogenous to allow indirect comparisons of treatments that had not been directly evaluated as trials were identified that compared treatments with a common comparator. The analysis was strengthened by incorporating direct evidence from head-to-head trials as well as indirect comparisons from placebo-controlled trials. The output of the NMA was odds ratios and median probabilities of effectiveness with 95% credible interval ratios (comparable with confidence intervals). The probabilities of effectiveness were used to parameterise a new health economic model developed for this guideline update.

The NMA was undertaken in WinBugs® with additional expert support provided by the Technical Support Unit at NICE.

Incorporating health economics

The aims of the health economic input to the guideline were to inform the GDG of potential economic issues relating to urinary incontinence and to ensure that recommendations represented a cost effective use of healthcare resources. Health economic evaluations aim to integrate data on benefits (ideally in terms of QALYs), harms and costs of different care options.

The GDG prioritised a number of review questions where it was thought that economic considerations would be particularly important in formulating recommendations. Systematic searches for published economic evidence were undertaken for these questions. For economic evaluations, no standard system of grading the quality of evidence exists and included papers were assessed using a quality assessment checklist based on good practice in economic evaluation. Reviews of the relevant published health economic literature are presented alongside the clinical effectiveness reviews.

Health economic considerations were aided by original economic analysis undertaken as part of the development process. For this guideline the areas prioritised for economic analysis were:

- The cost effectiveness of antimuscarinic drugs for overactive bladder after conservative management has been unsuccessful (incorporating a network meta-analysis of evidence of effectiveness).
- The cost effectiveness of Botulinum Toxin A versus sacral nerve stimulation in the treatment of overactive bladder once pharmacological treatment has been unsuccessful.

A third analysis comparing surgical approaches for mid-urethral procedures in women undergoing their primary surgical tape procedure was considered. However, there was insufficient evidence of difference in effectiveness or cost between each type of procedure to undertake a health economic analysis.

Evidence to recommendations

For each review question recommendations for clinical care were derived using, and linked explicitly to, the evidence that supported them. In the first instance, informal consensus methods were used by the GDG to agree short clinical and, where appropriate, cost effectiveness evidence statements which were presented alongside the evidence profiles.

Statements summarising the GDG's interpretation of the evidence and any extrapolation from the evidence used to form recommendations were also prepared to ensure transparency in the decision-making process. The criteria used in moving from evidence to recommendations were:

- relative value placed on the outcomes considered
- consideration of clinical benefits and harms

- consideration of net health benefits and resource use
- quality of the evidence
- other considerations (including equalities issues).

In areas where no substantial clinical research evidence was identified, the GDG members considered other evidence-based guidelines and consensus statements or used their collective experience to identify good practice. The health economics justification in areas of the guideline where the use of NHS resources (interventions) was considered was based on GDG consensus in relation to the likely cost effectiveness implications of the recommendations. The GDG members also identified areas where evidence to answer their review questions was lacking and used this information to formulate recommendations for future research.

Towards the end of the guideline development process, formal consensus methods (voting) were used to consider all the clinical care recommendations and research recommendations that had been drafted previously. The GDG identified ten 'key priorities for implementation' (key recommendations) and five high-priority research recommendations. The key priorities for implementation were those recommendations thought likely to have the biggest impact on clinical care and outcomes in the NHS as a whole. The priority research recommendations were selected in a similar way. Only a single round of voting was needed to reach consensus on the key priorities for implementation and the priority research recommendations.

Stakeholder involvement

Registered stakeholder organisations were invited to comment on the draft scope and the draft guideline. Stakeholder organisations were also invited to undertake a pre-publication check of the final guideline to identify factual inaccuracies. The GDG carefully considered and responded to all comments received from stakeholder organisations. The comments and responses, which were reviewed independently by NICE, are published on the NICE website.

Specific considerations for this guideline

Formal consensus voting

A formal consensus approach was used where it was agreed that a recommendation was required, but where the GDG was unable to reach a conclusion using discussion alone.

Methods

The formal consensus approach involved a series of action statements relating to management or treatment under review being drafted by the NCC-WCH technical team. These were collated into a consensus questionnaire. The GDG members were asked to independently complete the questionnaire stating their level of agreement ("strongly agree" to "strongly disagree") with each statement and provide comments on where statements should be amended. The results of the voting were collated by the technical team. If 70% or more of the GDG members agreed or disagreed with a statement then consensus was reached. If there was no consensus the statement could be adapted based on comments and presented for a second round of voting, applying the same majority threshold. This process would go on until consensus was reached, at which point the statements were then used to draft recommendations. These were discussed and ratified at a subsequent GDG meeting.

The GDG made 'a priori' decisions regarding outcomes. For each outcome it defined thresholds for clinically important differences (also known as 'minimal important difference' [MID]) for all outcome measures which are summarised here:

- For the outcome 'Patient satisfaction with treatment' the GDG agreed that, where possible, outcomes should be dichotomised into 'improved' and 'not improved' by combining categories, for example 'very improved' and 'improved'. The outcome statistic (RR) default definitions of MID were 0.75 and 1.25.
- For the outcome 'Self reported rate of absolute symptom reduction' the GDG agreed that a 50% reduction in symptoms constituted a clinically significant difference for both episodes of incontinence and episodes of urgency.

- For the outcome ‘Continence status (zero episodes per day)’ the GDG accepted that this was a valid definition in itself. Again, we used the default definitions of MID for RR as above.
- For the outcome ‘Incontinence-specific quality of life (QOL)’ the GDG agreed that only incontinence-specific quality of life should be used. The developers of these scales have published MIDs which can be used as the thresholds for clinically significant difference
- For the outcome ‘Adverse effects’ the GDG agreed that this should vary from question to question. For example, for BoNT-A, the need for self-catheterisation was specified as the single most important adverse effect. Default definitions of MID for relative risk were adopted as above.
- For the outcome ‘Psychological outcomes’ the GDG agreed that depression and anxiety were important outcomes. As with the I-QOL, an MID from the published literature would be used.
- For the outcome ‘Clinical measures’ the GDG agreed that post-void residual volume was the single most important of the different clinical measures used. In the absence of data, a default MID of 25% change in post-void residual volume was used. This meant that if the intervention or control led to an improvement or worsening of 25% of the baseline values then this was considered clinically meaningful for both patient and clinician.

4 Assessment and investigation

4.1 Introduction

Initial assessment when a woman comes into first contact with a health professional is important. It forms the basis for counselling, ongoing management and treatment. Categorisation of urinary incontinence (UI) by symptom profile may allow the patient to be directed to the most appropriate and effective resources. Further evaluation of severity of the condition, and ultimately the impact of treatment on that severity, will enable the healthcare professional to deliver the optimum care. Co-existing conditions (such as prolapse, diabetes or heart failure) or treatments (for example drug therapy) must be recognised and clinicians must be aware of their interaction with UI. Investigation should be used appropriately, taking into account the nature of the condition.

Studies considered for the assessment and investigation section

For history taking and physical examination, where primary research data were not available, published consensus statements and narrative reviews that discussed these issues were used as a basis for the guideline development group's (GDG's) statements and recommendations.[31,33,34]

For each investigation used in the assessment of UI in women, up to five questions were asked (refer to the assessment matrix in Appendix P):

- Does the investigation direct the woman to an alternative pathway?
- What is the diagnostic accuracy of the investigation?
- What is the test–retest reliability of the investigation?
- Does the use of the investigation affect outcomes?
- Does the use of the investigation predict outcomes of treatment?

For questions of diagnostic accuracy, the ideal study is one that makes blind comparison of the test with a validated reference standard in a sample of women reflective of the population to whom the test would apply. Within the clinical area of UI, there is no agreement as to what the reference standard is for the diagnosis of UI and thus studies that consider accuracy are limited by the standard against which they are compared.

4.2 History taking and physical examination

History taking of women with UI or overactive bladder (OAB) guides the investigation and management by evaluating symptoms, their progression and the impact of symptoms on lifestyle. Taking a history also allows the assessment of risk factors associated with the possible diagnoses. The relevant elements of history follow.

Urinary symptoms

In order to reach a clinical diagnosis, a urinary history is taken to determine storage and voiding patterns and symptoms. The major symptoms to consider include:

- Storage symptoms:
    - frequency (daytime), nocturia, urgency, urgency UI

- stress UI
- constant leakage (which may rarely indicate fistula).

- Voiding symptoms:
  - hesitancy, straining to void, poor or intermittent urinary stream.
- Post-micturition symptoms:
  - sensation of incomplete emptying, post-micturition dribbling.

Accompanying symptoms that may indicate the possibility of a more serious diagnosis and which require referral, such as haematuria, persisting bladder or urethral pain, or recurrent urinary tract infection (UTI), can also be identified when taking a urinary history.

How do urinary symptoms compare with urodynamic findings?

We found no studies in which clinical outcomes in women with UI diagnosed by clinical history alone were compared with those in women with UI diagnosed using urodynamics. However, several studies have evaluated the accuracy of the symptom of stress or urgency UI relative to findings on urodynamic (UD) investigations in women undergoing assessment of their urinary symptoms. Most of these studies have been considered in two reviews and a health technology assessment of diagnostic methods for UI.[46–48] Two of the publications included studies of women with symptoms of stress, mixed or urgency UI[46,48] and one included only studies evaluating women with stress UI.[47] The reviews that included women with stress, mixed or urgency UI calculated and combined sensitivity and specificity data for the symptom of stress (be it with or without mixed symptoms) and for the symptom of urgency UI (be it with or without mixed symptoms). The GDG considered that the mixed 'symptom' should be considered separately (because in practice women are categorised into those with stress, mixed or urgency UI) and that the important question in relation to the comparison of urinary history with urodynamic findings is whether urodynamics gives additional information to that obtained from the history alone. In considering this question, the GDG took the approach that a clinical history would be taken for every woman, and that a positive history for a particular type of UI would always be followed by treatment appropriate to that type of UI.

Overall, 25 relevant studies that compared the diagnosis based on history with urodynamic findings were considered by the GDG. These studies used cystometry as the reference standard for diagnosis of UI and therefore assumed that history taking had a lower diagnostic value in comparison. Fourteen studies included women with stress, mixed or urgency UI, and 11 presented raw data in a way that allowed sensitivity, specificity, positive predictive value (PPV) and negative predictive values (NPV) to be calculated.[49–62] Two of these studies only reported accuracy data for stress and mixed UI.[61,62] Five studies only investigated how a history of urgency UI or OAB compared with urodynamic findings of detrusor overactivity (DO).[63–67] Six studies only investigated how a history of stress UI compared with the finding of urodynamic stress incontinence,[68–73] four of which provided some but not all accuracy data.

Multichannel cystometry (with or without uroflowmetry, urethral pressure profilometry, or cystourethrography) was the urodynamic method used in 24 studies. The remaining study used single-channel cystometry for women with urgency UI (and suspected DO) and multichannel cystometry for women with stress UI.[50] All except four studies[62–64,70] stated that terminology used for urodynamic findings conformed to ICS standards.

With the exception of one study[49] which involved primary and secondary care, all studies were conducted in secondary or tertiary care.

The GDG focused on the 11 studies that provided diagnostic accuracy data for stress, mixed and urgency UI. Confidence intervals were calculated for each value, as this was considered to be more appropriate than pooling data from individual studies. Pooling the available data (by meta-analysis) or generating receiver operating characteristic curves was not considered to be appropriate because the population in each study varied in terms of the relative proportions of stress, mixed or urgency UI, the methods used to obtain a history varied, and the studies were considered to be of poor quality in terms of defining diagnostic accuracy because of unblended urodynamic testing.

The diagnostic accuracy data for the studies is summarised in Table 4.1. For further details refer to Appendix Q.

Table 4.1 Summary of diagnostic accuracy data

UI symptom	Sensitivity median (range)	Specificity median (range)	Positive predictive values median (range)	Negative median predictive values (range)
Stress UI	66% (17–83%)	83% (49–92%)	70% (41–95%)	69% (49–85%)
Mixed UI	68% (42–85%)	77% (34–89%)	35% (18–70%)	90% (80–97%)
Urgency UI	45% (14–86%)	96% (81–98%)	73% (25–81%)	91% (79–98%)

The overall conclusions are that the available studies comparing history of stress, mixed or urgency UI with findings of stress UI and/or DO on multichannel cystometry have poor internal and external validity. We consider that the NPV is of particular interest in terms of assessing whether urodynamic testing provides additional information compared with clinical history, because this quantity summarises the extent to which a negative history is associated with a negative finding on urodynamics (i.e. whether diagnosis based on urodynamics would alter the findings for women with no history of a particular type of UI). In addressing the question of whether urodynamics gives additional information to that obtained from history alone, with the limitations of the studies in mind, the following conclusions can be drawn:

- If a woman does not report mixed UI (i.e. if she reports pure stress UI or pure urgency UI), the probability of finding urodynamic stress incontinence (USI) plus DO on cystometry is small (around 10%), therefore urodynamic testing might be said to offer little additional diagnostic value. It is acknowledged that urodynamic investigation is not simply used to distinguish USI and DO, and that further information may be obtained about other elements of lower urinary tract function, such as the voiding pattern.
- If a woman does not report pure urgency UI, the probability of finding DO on cystometry is small (again around 10%), therefore urodynamic testing offers little added diagnostic value.

The situation for pure stress UI is less clear-cut. Here 15–51% (median 31%) of women who do not report pure stress UI may nevertheless be found to have USI on cystometry. However, the lack of consistency between the NPVs in the available studies together with the lack of detailed information about the method of obtaining a history and the poor quality of the studies limit the extent to which the evidence would support urodynamic testing for women who do not report stress UI. However, a limitation of dealing with stress, mixed and urgency UI as three separate entities is that the analysis ignores the interdependence between the different diagnoses.

History taking is regarded as the cornerstone of assessment of UI. Current practice is that women with UI are categorised according to their symptoms into those with stress, mixed or urgency UI; women with mixed UI are treated according to the symptom they report to be the most troublesome. In the absence of evidence that urodynamic testing improves the outcome of women treated conservatively (see Section 4.11), and without robust evidence that urodynamic testing provides additional valuable information to the history alone in the initial assessment of women with UI, the GDG concluded that urodynamic testing is not required before initiating conservative treatment.

Bowel symptoms

Constipation or problems with defecation may predispose to UI and adversely affect the outcome of any continence surgery. Straining can contribute to loss of bladder control by weakening pelvic floor muscles (refer to lifestyle interventions, Section 5.1). Faecal incontinence in association with UI or OAB may suggest the presence of cognitive impairment, neurological and/or anatomical damage. Women with faecal incontinence may require referral for management of that condition/

Medical history

Conditions that may exacerbate or co-exist with UI or OAB can be identified by taking a general history and are important contributory factors to exclude. These include mental health, cognitive impairment and disorders of the:

- neurological system (e.g. multiple sclerosis, spinal cord injury, Parkinson's disease,
- cerebrovascular accident, cauda equina syndrome, pelvic plexus injury)
- metabolic system (e.g. diabetes)
- cardiorespiratory system
- renal system.

Surgical history

Previous surgery for UI or for POP may complicate treatment and make diagnosis more difficult because of its interference with the normal support mechanisms of the vagina and urethra. Any surgery that might have interfered with normal nerve supply to the bladder or urethra may also be relevant; this could include low spinal surgery, radical hysterectomy, low rectal surgery, sympathectomy or complex pelvic surgery.

Obstetric and gynaecological history

The number and type of deliveries and their outcome would normally be documented. The woman's desire for further childbearing should also be established as this may have implications for the most appropriate treatment options. The menstrual history and menopausal status should be determined, and enquiry made into symptoms of uterovaginal prolapse. The woman's sexual function and her expectations from this point of view should also be considered.

Drug history

Some medications may be associated with UI and their use may need to be reviewed. These include drugs that affect:

- the central nervous system, for example sedatives, hypnotics, anxiolytics and smooth muscle relaxants
- the autonomic nervous system, for example drugs with antimuscarinic action, sympathomimetics and sympatholytics
- fluid balance, for example diuretics and alcohol.

A drug history should consider previous medication for UI symptoms, and any known allergies, which may affect future treatment choices.

Does history taking affect outcome?

No evidence was identified that addressed this question. Nevertheless, the fundamental importance of history taking within all aspects of clinical practice cannot be overemphasised.

Test–retest reliability of history taking

No evidence was identified that addressed this question.

General assessment

Assessment of the social and functional impact of UI, desire for treatment, expectations and motivation are important as these help to establish the woman's goals, and may influence the type and degree of intervention offered.

Social circumstances to consider include home environment, personal relationships, occupational history and lifestyle factors such as smoking and body mass index (BMI). Adjustment of these lifestyle factors may form part of the management of the condition in some women (refer to Section 5.1).

Functional assessment, which may include consideration of access and ease of use of toileting aids, mobility and dexterity, is important. Assessment of the home environment may be undertaken, for example by an occupational therapist.

Physical examination

Physical examination is carried out to guide the diagnosis and management of incontinence and the identification of any underlying, modifying or serious conditions that require treatment outside the scope of this guideline.

The assessment of cognitive impairment allows the effect of disease to be taken into account and allows modification of treatment. The Abbreviated Mental Test Score (AMTS) and the Mini Mental State Examination (MMSE) should be undertaken for women aged over 75 years with complex comorbidities. These scales should also be considered for younger women if clinically appropriate.

Abdominal examination can detect a significantly enlarged bladder or palpable pelvic mass. A palpable bladder may indicate the presence of chronic urinary retention. Palpation may detect a volume of 300 ml or more.[74] Urinary incontinence may occur in association with urinary retention (often called overflow incontinence).

Pelvic assessment is important and should include vaginal examination, and possibly also rectal examination if clinically indicated. Vaginal examination can assess pelvic organ prolapse (POP) and identify atrophic changes, infection and excoriation. Uterine and ovarian enlargement may be determined by bimanual examination. When rectal examination is undertaken, it is used to further evaluate posterior vaginal wall prolapse and, where indicated by a history of constipation, prolapse or faecal incontinence. Assessment of pelvic floor, prolapse and residual urine are considered in more detail in Sections 4.3, 4.4 and 4.6.

Neurophysiology

Neurophysiological tests include assessments of nerve conduction and electromyography (EMG).The former include sacral reflex latencies, pudendal terminal motor latencies and evoked potentials, which test the integrity of nerve pathways relating to voiding and continence. Abnormal results might indicate underlying neurological dysfunction. Electromyography tests the end organ function of somatic muscles of the pelvic floor, or sphincter complexes, but cannot be used to record activity from smooth muscle. No evidence was identified that addressed diagnostic accuracy of neurophysiological testing in relation to idiopathic UI. Where history suggests evidence of neurological disease, examination of lower limbs together with sacral sensation and sacral reflexes is required.

Evidence statements for history taking and physical examination

The reporting of stress, urgency or mixed UI is commonly used to direct treatment decisions. [EL = 4]

The diagnostic value of history taking has been compared with urodynamic testing in women with UI or OAB. In general, there is a low level of agreement between a history of urinary symptoms and urodynamic findings. [EL = DS III]

However, women who do not report mixed or urgency UI are unlikely to have findings of mixed UI or DO on urodynamics. [EL = DS III]

Recommendations

Number	Recommendation
1	At the initial clinical assessment, categorise the woman's urinary incontinence (UI) as stress UI (SUI), mixed UI, or urgency UI/overactive bladder (OAB). Start initial treatment on this basis. In mixed UI, direct treatment towards the predominant symptom. **[2006]**
2	If stress incontinence is the predominant symptom in mixed UI, discuss with the woman the benefit of conservative management including OAB drugs before offering surgery. **[new 2013]**
3	During the clinical assessment seek to identify relevant predisposing and precipitating factors and other diagnoses that may require referral for additional investigation and treatment. **[2006]**

4.3 Pelvic floor muscle assessment

Methods used to assess pelvic floor muscle contraction include digital palpation, EMG and perineometry. For digital palpation, grading scales have been used to quantify the strength of contraction, for example the Oxford grading system.[31]

Does pelvic floor muscle assessment affect outcome?

In randomised controlled trials (RCTs) that evaluated pelvic floor muscle training (PFMT) for the treatment of UI, both those studies that did and those that did not assess pelvic floor muscle contraction prior to treatment showed efficacy of active treatment compared with control (refer to physical therapies, Section 5.2). [EL = 3] No further evidence was identified in relation to the effects of undertaking pelvic floor assessment on outcomes of women with UI.

Test–retest reliability

Two case series evaluated the test–retest reliability of grading systems for digital assessment.[75,76] One assessed the test–retest and inter-rater reliability of a four-item pelvic floor muscle rating scale (covering pressure, duration of contraction and displacement; n = 37, about two-thirds of whom had urinary symptoms). Retest was done after 1–4 weeks. Significant inter- and intrarater correlations were reported for the rating scale, and for EMG, which was also performed.[75] [EL = 3] The second case series evaluated test–retest reliability of digital assessments of pelvic floor muscle power and endurance in women with UI, with power being assessed on a modified Oxford grading system. Retest was undertaken after 2–5 weeks. Significant correlations between test and retest results were reported for both parameters, with agreement seen in nine cases (n = 20).[76] [EL = 3]

Two case series considered the inter-rater (not test–retest) reliability of a modified Oxford grading system. In the first study (n = 20, seven of whom had stress UI), poor inter-rater reliability was found for the grading system undertaken by physiotherapists, with agreement in nine cases (r = 0.7, Kappa score 0.37).[77] [EL = 3] The second case series in women with UI compared results of three clinicians' assessments with that of an expert clinician's assessment. No agreement was found between one of the clinicians and the expert prior to training. After training, the percentage agreement between the three clinicians and the expert was 70%, 78% and 80% (n = 30).[78] [EL=3]

Evidence statements for pelvic floor muscle assessment

There is a lack of evidence as to whether digital assessment of pelvic floor muscle contraction affects the outcome of PFMT in women with UI. [EL = 3] Inter- and intra-observer reliability of grading systems for digital assessment of pelvic floor muscle contraction is poor. [EL = 3]

From evidence to recommendations

The GDG recognises that there is a lack of evidence for clinical utility of digital pelvic floor muscle assessment. However, expert opinion is that the determination of whether a woman can contract pelvic floor muscles will direct treatment decisions. [EL = 4]

Recommendations

Number	Recommendation
4	Undertake routine digital assessment to confirm pelvic floor muscle contraction before the use of supervised pelvic floor muscle training for the treatment of UI. **[2006, amended 2013]**

Number	Research recommendation
RR1	The role of clinical pelvic floor muscle assessment prior to pelvic floor muscle training (PFMT) should be investigated to determine whether it enhances the therapeutic effect of the intervention.

4.5 Urine testing

Urinalysis is used to detect infection, protein, blood and glucose in the urine. Protein may indicate infection and/or renal impairment, blood may indicate infection or malignancy, and glucose may indicate diabetes mellitus. Some findings on urine testing indicate referral (see Section 4.7).

Diagnostic accuracy of urine testing for urinary tract infection

One study evaluated the accuracy of urine reagent strips for the diagnosis of UTI in women with UI. Identification of leucocytes and/or nitrites on a reagent strip was indicative of a positive test for infection. Using urine culture as the reference standard, the reagent strips had sensitivity of 29%, specificity of 99%, and positive and negative predictive values of 82% and 92%, respectively (n = 265).[82] [EL = DS II]

Does urine testing affect outcome?

No evidence was identified that addressed this question. The GDG also considered whether treating a UTI affects UI symptoms. While no evidence was found in relation to treating an infection, one study in nursing home residents considered the impact of treating bacteriuria on UI. Half the patients had bacteriuria at baseline, which was removed in 81% of patients by antibiotic treatment. Eradication of bacteriuria appeared to have no effect on incontinence (n = 191; 71% women).[83] [EL = 2+]

Evidence statements for urine testing

Urine dipstick testing for leucocytes and nitrites has low sensitivity and high specificity for the diagnosis of UTI in women with UI. A negative urine dipstick test therefore excludes a UTI with a high degree of certainty. Only one-third of positive tests are associated with bacteriologically proven UTIs. [EL = DS II]

From evidence to recommendations

Although urine testing for leucocytes and nitrites has a high specificity, false negatives can arise when infection occurs with organisms that do not convert nitrates to nitrites. Hence, in symptomatic patients with a negative test, the clinician may wish to consider prescribing antibiotics once a urine sample has been collected but before results of midstream urine culture are available.

In patients with symptoms of UTI and a positive urine test for leucocytes and nitrites, infection is highly likely and immediate prescription of antibiotics is therefore justified. In single uncomplicated UTI it might be argued that this should be done without sending urine for laboratory analysis, depending on local knowledge of antibiotic resistance. In recurrent or complicated cases, however, this would not be appropriate. We therefore recommend that a midstream urine specimen be sent for culture and antibiotic sensitivities before prescribing in all cases.

Recommendations

Number	Recommendation
6	Undertake a urine dipstick test in all women presenting with UI to detect the presence of blood, glucose, protein, leucocytes and nitrites in the urine. **[2006]**
7	If women have symptoms of urinary tract infection (UTI) and their urine tests positive for both leucocytes and nitrites send a midstream urine specimen for culture and analysis of antibiotic sensitivities. Prescribe an appropriate course of antibiotic treatment pending culture results. **[2006]**
8	If women have symptoms of UTI and their urine tests negative for either leucocytes or nitrites send a midstream urine specimen for culture and analysis of antibiotic sensitivities. Consider the prescription of antibiotics pending culture results. **[2006]**
9	If women do not have symptoms of UTI, but their urine tests positive for both leucocytes and nitrites, do not offer antibiotics without the results of midstream urine culture. **[2006]**
10	If a woman does not have symptoms of UTI and her urine tests negative for either leucocytes or nitrites do not send a urine sample for culture because she is unlikely to have UTI. **[2006]**

4.6 Assessment of residual urine

Some findings on physical examination or from history taking in relation to emptying may indicate referral because of suspected voiding dysfunction. Abdominal examination can detect a significantly enlarged bladder, which may indicate the presence of chronic urinary retention. Palpation may detect a volume of 300 ml or more.[74] Large post-void residual urine may indicate the presence of underlying bladder outlet obstruction, neurological disease or detrusor failure. These would be a reason for referral to a specialist rather than progression through a path of conservative treatments. Large residual urine – in effect chronic retention of urine – may also present with renal failure although this is much less

likely in women than in men. However, there is no accepted definition for what constitutes a high or large residual volume in women with UI. Residual urine volumes may vary and thus repeat measurements may be required.

Methods used to measure post-void residual urine are abdominal palpation, ultrasound scanning and catheterisation.

Diagnostic accuracy

The diagnostic accuracy of bladder ultrasound for the measurement of post-void residual urine was evaluated in three studies, using a bladder scanner (portable bladder ultrasound).[84–86] The accuracy of bimanual examination was evaluated in one study.[87] Catheterisation was used as the reference standard in each. The residual urine volume indicative of a positive test result ranged from 50 to 200 ml across the studies.

Portable ultrasound (bladder scanner) versus catheterisation

Two studies enrolled men and women.[84,86] The first study, in nursing home residents, reported sensitivities of 90–95% with a portable bladder ultrasound device at residual volume cut-off of less than 50 or 100 ml, and 59–69% for residual volumes of more than 100, 150, or 200 ml. Specificity values were 63–71% and 95–99%, respectively. It was not possible to calculate positive and negative predictive values from the data given (n = 201; 74% women).[86] [EL = DS Ib] The second study reported sensitivities of 90% for a post-void residual of 100 ml or more, and 92% for 200 ml or more. Specificities were 88% and 83%, PPV 91% and 76%, and NPV 86% and 95%, respectively (n = 46; 74% women).[84] [EL = DS Ib] One study evaluated only women with UI. Based on a residual urine volume of 100 ml being a positive result, ultrasound had a sensitivity of 67% and specificity of 97%. It was not possible to calculate PPV or NPV from the data given (n = 95).[85] [EL = DS II]

Bimanual examination versus catheterisation

The diagnostic accuracy of bimanual examination relative to catheterisation in women was assessed in one study. Based on a residual urine volume of 50 ml being a positive result, bimanual examination had a sensitivity of 14%, specificity of 67%, PPV 7% and NPV 82% (n = 47).[87] [EL = DS Ib]

Does assessment of residual urine affect outcome?

No evidence was identified that addressed this question.

Test–retest reliability

One study reported test–retest reliability of portable ultrasound scanner measurements, with good correlation reported for both observers (r = 98 for one [187 pairs measured] and r = 97 for the second [143 pairs]).[86] [EL = DS Ib]

Evidence statements for assessment of residual urine

The sensitivity and specificity of ultrasound (using a bladder scanner) in the detection of post-void residual urine volume, in comparison with catheterisation, is within clinically acceptable limits. [EL = DS II] The former is less invasive with fewer adverse effects. [EL = 4] The sensitivity of bimanual examination to detect small post-void residual volumes is poor. [EL = DS Ib]

From evidence to recommendations

The GDG considers that the lack of evidence for what constitutes a clinically significant residual volume in women with UI precludes making a recommendation other than in women who have signs or symptoms suggestive of voiding dysfunction.

Recommendations

Number	Recommendation
11	Measure post-void residual volume by bladder scan or catheterisation in women with symptoms suggestive of voiding dysfunction or recurrent UTI. **[2006]**
12	Use a bladder scan in preference to catheterisation on the grounds of acceptability and lower incidence of adverse events. **[2006]**

13	Refer women who are found to have a palpable bladder on bimanual or abdominal examination after voiding to a specialist. **[2006]**

4.7 Referral

Evidence statement

Certain signs or symptoms on assessment indicate referral for further investigation by an appropriate specialist. The NICE guideline on referral for suspected cancer covers some indications for referral that are relevant to this guideline.[23] [EL = 4]

From evidence to recommendations

There are other women for whom referral for further advice or specialist intervention may be considered, because of either co-existent conditions or a history of prior interventions. The GDG recognises that not all such women may wish to be referred. However, referral should be considered in these cases. Owing to variations in service configuration, it is not possible to state to which service or healthcare professional women should be referred. Similarly, timescales are not specified for referral priorities because NICE recommends that trusts should work to local definitions of maximum waiting times. [EL = 4]

Recommendations

Number	Recommendation
14	Urgently refer women with UI who have any of the following*: • microscopic haematuria in women aged 50 years and older • visible haematuria • recurrent or persisting UTI associated with haematuria in women aged 40 years and older • suspected malignant mass arising from the urinary tract. **[2006]**
15	In women with UI, further indications for consideration for referral to a specialist service include: • persisting bladder or urethral pain • clinically benign pelvic masses • associated faecal incontinence • suspected neurological disease • symptoms of voiding difficulty • suspected urogenital fistulae • previous continence surgery • previous pelvic cancer surgery • previous pelvic radiation therapy†. **[2006]**

4.8 Symptom scoring and quality-of-life assessment

Symptom and quality of life (QOL) scoring is used to give some quantification of the impact of urinary symptoms and provides a measure that can be used to assess outcomes of treatment at a later stage. The International Consultation on Incontinence (ICI) uses three grades of recommendation for symptom scoring and QOL scales, based on the evidence available to support their use, as listed below:[31]

- highly recommended – validity, reliability and responsiveness established with rigour in several data sets ('Grade A'), or in one dataset with UI ('Grade A^{new}')

* NICE's 'Referral guidelines for suspected cancer' (http://guidance.nice.org.uk/CG27) define urgent referral as the patient being seen within the national target for urgent referrals (currently 2 weeks).
† For further indications for consideration for referral, see recommendations 5 and 13.

- recommended ('Grade B') – validity, reliability and responsiveness indicated but not with rigour; validity and reliability established with rigour in several data sets
- with potential ('Grade C') – questionnaires in early development.

The test–retest reliability of ICI 'Grade A' or 'Grade A^{new}' condition-specific scales for use in women are considered within this guideline because these are the questionnaires validated to the highest level. These are:[31]

- ICIQ, BFLUTS and SUIQQ (for combined evaluation of symptoms and QOL impact of UI)
- I-QOL, SEAPI-QMM, KHQ, IIQ, IIQ-7, UISS and CONTILIFE (for evaluation of QOL impact of UI)
- OAB-q, UDI, UDI-6, ISI and BFLUTS (for combined evaluation of symptoms and QOL impact of OAB).

Test–retest reliability of symptom scoring and quality-of-life scales

Test–retest reliability was generally reported within validation studies for these questionnaires, although in the case of CONTILIFE,[88] and the short forms of UDI and IIQ (UDI-6, IIQ-7),[89] no test–retest reliability data were presented. The available studies generally quoted correlation of test and retest findings, with some publications reporting actual scores or differences in test–retest scores. [EL = 3]

The results are shown in Table 4.2. For ICIQ, BFLUTS, I-QOL, SUIQQ, UISS, SEAPI-QMM, ISI and KHQ, either significant agreement or significant correlation between test and retest scores was reported (correlation was assessed using Spearman's, Pearson's, Cronbach's alpha, or the intraclass correlation coefficients). Few studies reported the actual test and retest scores. The available evidence for UDI, IIQ and OAB-q showed either a significant difference between test and retest scores and/or poor correlation between test and retest scores. [EL = 3]

Evidence statement for symptom scoring and quality-of-life

The test–retest reliability of ICIQ, BFLUTS, I-QOL, SUIQQ, UISS, SEAPI-QMM, ISI and KHQ is good. For other scores, the evidence is weak or absent. [EL = 3]

Recommendations

Number	Recommendation
16	Use the following incontinence-specific quality-of-life scales when therapies are being evaluated: ICIQ, BFLUTS, I-QOL, SUIQQ, UISS, SEAPI-QMM, ISI and KHQ. **[2006]**

4.9 Bladder diaries

Bladder diaries are used to document each cycle of filling and voiding over a number of days and can provide information about urinary frequency, urgency, diurnal and nocturnal cycles, functional bladder capacity and total urine output. They also record leakage episodes, fluid intake and pad changes and give an indication of the severity of wetness. They may also be used for monitoring the effects of treatment.

Table 4.2 Test–retest reliability of quality of life and symptom scoring scales

Questionnaire	Population	Test–retest interval	Level of agreement between test and retest
International Consultation on Incontinence Questionnaire (ICIQ)[90]	144 men and women (84% women); several samples in clinics and in the community	2 weeks	Significant agreement reported for each of the nine symptom items (percentage agreement ranging from 85% to 96%)

Questionnaire	Population	Test–retest interval	Level of agreement between test and retest
Bristol Female Lower Urinary Tract Symptoms (BFLUTS)[91]	50 women with UI	2 weeks	78% of answers identical on both occasions; Spearman's rank correlation for total symptom and problem scores 0.86 and 0.90
Stress and Urgency Incontinence and Quality of Life Questionnaire (SUIQQ)[92]	59 women with stress or mixed UI	Mean 22 days	No retest value significantly different from test value; Cronbach's alpha ranged from 0.72 to 0.77 for components
Incontinence Quality of Life (I-QOL)[93–95]	288 women with stress or mixed UI[93]	2 weeks	Cronbach's alpha 0.95, scores not reported
	62 patients (68% women)[94]	Mean 18 days	Intraclass correlation 0.93, scores not reported
	1901 women with stress UI enrolled in duloxetine trials	2 weeks	Median intraclass correlation score 0.87
SEAPI-QMM[96]	315 men and women with UI (68% women)	5 days	Cronbach's alpha correlation ranging from 0.73 to 0.88 for the three domains
King's Health Questionnaire (KHQ)[97]	110 women referred to a tertiary urogynaecology unit for urodynamic investigations	Mean days 9 (2–16)	Cronbach's alpha ranging from 0.73 to 0.89 for each domain
Urogenital Distress Inventory (UDI) and Incontinence Impact Questionnaire (IIQ)[98]	237 women with UI; 3 samples (community-dwelling with stable, unspecified UI; undergoing assessment for conservative treatment; on waiting list for colposuspension)	Median 3 days	A significant difference seen between test and retest scores for both UDI and IIQ, with poor agreement (Kappa ratings) for one question on UDI and for two questions on IIQ
IIQ[99]	69 women with UD stress UI or DO	1 week and 6 weeks	Pearson's correlation r = 0.73 at 1 week and r = 0.65 at 6 weeks; test–retest scores not reported
Urinary Incontinence Severity Score (UISS)[100]	51 women with UI	1 week	Spearman's rank correlation 0.88; no test–retest scores presented
Overactive Bladder Questionnaire (OAB-q)[101]	47 men and women (75% women) with a clinical diagnosis of OAB	2 weeks	Symptom bother scale scores fell significantly from test to retest; no significant differences in other items; Spearman's rank correlation between 0.8 and 0.93 for all items of the questionnaire
Incontinence Severity Index (ISI)[102]	237 women with UI	3 days	Kappa scores for the two questions of the instrument (leakage episodes and quantity) were significant (0.69 and 0.83); severity index scores not reported

BFLUTS Bristol Female Lower Urinary Tract Symptoms, DO detrusor overactivity, ICIQ International Consultation on Incontinence questionnaire, IIQ Incontinence Impact Questionnaire, I-QOL Incontinence Quality of Life, ISI Incontinence Severity Index, KHQ King's Health Questionnaire, OAB overactive bladder, OAB-q Overactive Bladder Questionnaire, r correlation

coefficient, SUIQQ Stress and Urgency Incontinence and Quality of Life Questionnaire, UD urodynamic, UDI Urogenital Distress Inventor, UI urinary incontinence, UISS Urinary Incontinence Severity Score

Test–retest reliability of bladder diaries

Five studies evaluated the test–retest reliability of bladder diaries or frequency–volume charts. One study evaluated a 1 day diary,[103] one a 3 day diary,[104] and three studies evaluated a 7 day diary.[105–107] Data captured in the charts were: frequency and voided volume;[103] frequency, leakage and urgency episodes, and voided volume;[104] frequency and leakage episodes;[105,106] and leakage episodes only.[107]

1 day diary

A case–control study reported some reproducibility data for the 1 day charts in women with stress UI. The 95% limits of agreement between the first and second days of measurement lay between 0.5 and 2.1 for frequency, and for total, mean and largest single voided volume measures (n = 80).[103] [EL = 3]

3 day diary

In a case series of men and women with stress, mixed or urgency UI, or OAB, the retest reliability of a 72 hour bladder diary and pad test was evaluated after an interval of 1 week (n = 106; 84% women). The authors' predefined minimum correlation coefficient for test–retest reliability of 0.7 was met for overall frequency, day frequency, leakage episodes, urgency episodes and mean voided volume (correlation coefficient 0.70–0.87), but not for night frequency (0.605). Correlation, but not actual results, was also reported for 24 and 48 hour results; the correlation appeared to improve at 72 hours compared with 24 hours for urgency episodes. Compliance with recording voided volume data fell with time.[104] [EL = 3]

Diaries of 7 days or longer

A case series evaluated the reproducibility of leakage episode and frequency data from a 7 day diary repeated after 4 weeks in women with urodynamic stress UI (n = 138). Minimal differences in test–retest results were seen for leakage episodes (mean 1.7/week, r = 0.906) and frequency (mean 0.03/(24 hours), r = 0.831). Correlation coefficients for the first 3 and last 4 days of the diary were also reported, which were 0.887 for leakage episodes and 0.908 for frequency.[105] [EL = 3]

A second case series reported test–retest variability and correlations of leakage episodes, and diurnal and nocturnal frequency, based on a 7 day diary in women aged 55 years or over (n = 50; 68% USI, 32% DO with or without stress UI). The test–retest reliability was reported to be significant for the three parameters, with correlation coefficients of 0.86–0.91. No significant differences were seen between any test and retest results.[106] [EL = 3]

The third case series investigated the reliability of a 14 day diary for the measurement of leakage episodes in women. Significant correlation was reported between the diary findings of weeks one and two, with 5 days' recording being necessary for internal consistency, for women with predominant urgency UI and 7 days for women with predominant stress UI (n = 214).[107] [EL = 3]

Does the use of bladder diaries affect outcome?

A considerable placebo effect has been reported in many placebo-controlled trials evaluating the effectiveness of conservative interventions for the treatment of UI or OAB, with this placebo effect being reflected in self-reported changes in voiding pattern, using bladder diaries. This placebo effect usually decreases over time. Several investigators suggest that completion of these diaries, together with the close monitoring, placebo medication, and therapeutic attention via interaction between them and their patients, induces a bladder training/retraining effect. However, none of the trials were designed to examine whether bladder diaries affect outcomes of women with UI or OAB, and therefore the conclusion that the diaries are the cause of a placebo effect is not proven. In addition, sufficient duration will be needed to allow the initial 'beneficial' placebo response to run its course so that true effects of interventions can be observed.

Evidence statements for bladder diaries

Bladder diaries are a reliable method of quantifying urinary frequency and incontinence episodes. [EL = 3] They are useful as a measure of outcome of treatments. The optimum duration of bladder diaries is unclear. [EL = 4]

Recommendations

Number	Recommendation
17	Use bladder diaries in the initial assessment of women with UI or OAB. Encourage women to complete a minimum of 3 days of the diary covering variations in their usual activities, such as both working and leisure days. **[2006]**

4.10 Pad testing

Pad tests are used to detect and quantify urine loss. Pad tests of varying duration have been evaluated: 1 hour or less, 24 hours, and 48 hours or longer.

Does pad testing affect outcome?

No studies were identified that addressed this question.

Test–retest reliability

Short pad tests

Fourteen studies considered the test–retest reliability of pad testing: eight studies considered short pad tests (1 hour or less), and six considered tests of longer duration (24–72 hours). The data reported generally were correlations of test and retest findings, with some publications reporting actual scores or differences in test–retest scores. Correlation was assessed using Spearman's, Pearson's or Lin's concordance correlation coefficients in five studies; the remaining nine studies did not state which test was used.

The results for the short pad tests are shown in Table 4.3. One study considered the reliability of a test of 12–15 minutes' duration.[108] The standardised 1 hour pad test was used in four studies.[109–113] Another three studies used a modified version where the test differed in the method of filling the bladder, or in the quantity of fluid instilled or consumed.[114–116] Across these studies, significant correlation or agreement was reported between test and retest urine loss, although the differences between test and retest results across studies varied widely (means of 2–23 g).

24, 48 and 72 hour pad tests

Six case series reported test–retest reliability for pad tests of 24–72 hours.[104,117–121] The results are shown in Table 4.4. These studies also reported significant correlation between test and retest results. One study noted that the number of pad-test days required for optimal reliability was 3 days (data only shown in graph in publication).[119] Another found that correlation appeared to improve at 72 hours compared with 24 hours, but compliance fell.[104] [EL = 3]

Evidence statements for pad testing

The evidence supporting the use of pad testing is contradictory and of poor quality. However, there appears to be good group correlation with test–retesting even though the amounts leaked may differ in individuals. It is possible that pad tests of longer duration (24 hours or longer) are more sensitive for measuring incontinence than a short standardised 1 hour test. There is a lack of evidence in relation to whether pad testing in the assessment of women with UI affects outcomes. [EL = 3]

While there is no evidence of diagnostic value or clinical utility for pad testing, the GDG's viewis that pad tests may be useful for evaluating therapies for incontinence. [EL = 4]

Recommendations

Number	Recommendation
18	Do not use pad tests in the routine assessment of women with UI. **[2006]**

Table 4.3 Test–retest reliability of short pad tests

Pad test duration	Population and any relevant test conditions	Test–retest interval	Level of agreement between test and retest
12–15 minutes[108]	33 women with stress UI; testing undertaken as part of cystometry, with the bladder filled to 75% of cystometric capacity	Same day	Significant correlation (r = 0.74) reported between test and retest; no numerical data reported
Standardised 1 hour test[109]	56 women with an unspecified type of UI; study aimed to ensure bladder volume at retest was similar to that at the first test, although median volumes were significantly different	3–10 days	Significant difference of 9.7 g between test and retest
Standardised 1 hour test[110,111]	18 women with stress or mixed UI	1–15 days	Mean test–retest difference of 23 g (median 4 g); significant correlation reported (r = 0.68)
Standardised 1 hour test[113]	20 women with stress, mixed or urgency UI	1 week	Difference in median pad weight gain of 3 g between tests; significant correlation r = 0.77
Standardised 1 hour test[112]	19 men and women with stress, mixed or urgency UI	1–36 days	Correlation of 0.96 reported for difference in urine loss; differences in test–retest results not reported
Modified Standardised 1 hour test[114]	67 women with stress and mixed UI; bladder filled to capacity with normal saline	Immediate	Significant test–retest difference in urine loss of 9 g and 12 g; correlations r = 0.97 and r = 0.84, respectively
Modified standardised 1 hour test[115]	16 women referred for PFMT; 1 litre rather than 500 ml fluid consumed	1–7 days	Mean difference in urine loss of 2 g on pad test; significant correlation r = 0.73
Modified standardised 1 hour test[116]	25 women with stress or mixed UI; bladder instillation of fluid to 50% of maximum cystometric capacity	1–85 days	Mean test–retest differences of up to 24 g; significant correlation r = 0.97

r = correlation coefficient, UI urinary incontinence

Table 4.4 Test–retest reliability of pad tests of at least 24 hours' duration

Pad test duration	Population and any relevant test conditions	Test–retest interval	Level of agreement between test and retest
24 hours[117]	13 women with stress or mixed UI	Consecutive days	Non-significant mean difference of 5 g between test and retest; retest results differed approximately three-fold from the first test
24 hours[118]	31 women with stress or urgency UI	Consecutive days	Significant correlation (r = 0.82)
24 hours[119]	104 women with UI; urodynamic finding: 65% stress UI, 29% mixed UI, 6% DO and 'others'	Consecutive days	Significant correlation between the first 24 hours and 7 days of data; authors also claimed that 3 pad-

Pad test duration	Population and any relevant test conditions	Test–retest interval	Level of agreement between test and retest
			test days optimal for reliability (data only shown in graph)
24 and 48 hours[120]	15 women with unspecified type of UI	6–28 days	Significant correlation for both tests: 24 hour (r = 0.66), 48 hour (r = 0.9)
24 and 48 hours[121]	112 women with lower urinary tract symptoms	1 week	Significant correlation for 24 hour (r = 0.9) and 48 hour (r = 0.94) tests; test–retest differences (percentage of the mean) 7% and 2%, respectively
72 hours[104]	106 patients (84% women) with stress, mixed or urgency UI or OAB	1 week	Mean test–retest difference 13 g; the predefined minimum correlation coefficient for test–retest reliability of 0.7 was met for pad weight gain (r = 0.935)

DO detrusor overactivity, OAB overactive bladder, r correlation coefficient, UI urinary incontinence

4.11 Urodynamic testing

The term 'urodynamics' encompasses a number of varied physiological tests, of bladder and urethral function, which aim to demonstrate an underlying abnormality of storage or voiding. The term is often used loosely to mean multichannel cystometry.

Cystometry is the measurement of intravesical pressure, which can be carried out through a single recording channel (simple cystometry) or, more commonly, by multichannel cystometry, which involves the synchronous measurement of both bladder and intra-abdominal pressures by means of catheters inserted into the bladder and the rectum or vagina. The aim is to replicate the woman's symptoms by filling the bladder and observing pressures changes or leakage caused by provocation tests.

Uroflowmetry entails a free-flow void into a recording device, which provides the practitioner with information about the volume of urine passed and the rate of urine flow.

There are also numerous tests of urethral function, including urethral pressure profilometry and leak point pressure measurement. These are used to derive values that reflect the ability of the urethra to resist urine flow, expressed most commonly as maximum urethral closure pressure (MUCP), or as abdominal, cough or Valsalva leak point pressures (ALPP, CLPP, VLPP).

Videourodynamics involves synchronous radiographic screening of the bladder with multichannel cystometry and is so called because originally the information was recorded to videotape. Ambulatory urodynamics involves multichannel cystometry carried out with physiological bladder filling rates and using portable recording devices, which enable the woman to remain ambulant during the test.

Diagnostic accuracy

The agreement between urinary history and urodynamic findings is considered in Section 4.2.

Does urodynamic testing affect outcome?

A systematic review considering this question has been published but it only included one fully published RCT.[122] The RCT was considered alongside other relevant, fully published data.[123]

The RCT compared conservative treatment tailored to urodynamic findings (PFMT or bladder retraining) with a multicomponent conservative treatment regimen (PFMT and bladder retraining), without prior urodynamic investigation in women with symptoms of UI or OAB (n = 60; 48 analysed). After 3 months of treatment, no significant differences were seen between groups in any outcome (leakage episodes, frequency, nocturia, subjective assessment, short pad test). Since the uninvestigated trial arm received

both treatments, the outcomes from treatment may be uninformative about the value of urodynamics.[123] [EL = 1–]

Two observational studies reported outcomes of continence surgery for stress UI in women who had preoperative urodynamic investigations (61% or 71%), compared with those who did not. Neither found significant differences between groups in cure/success rates or symptom severity scores at mean follow-up of 25 months (n = 109)[124] [EL = 2–] or at 1 year (n = 279).[125,126] [EL = 2+]

Do preoperative urodynamic findings predict post-surgical outcomes?

In a few case series of surgical interventions for stress UI in women, authors retrospectively explored whether certain preoperative findings on urodynamic testing (urethral pressure profilometry or uroflowmetry) predicted surgical success or complications. These studies cover a range of surgical procedures (suspension procedures, slings, intramural bulking agents), with some studies evaluating more than one procedure. Data were presented in various ways, with some studies comparing the mean urethral pressures in successful or failed groups and others considering the success or failure rates above certain urethral pressure thresholds. Generally, small numbers of women were involved in the individual studies (n range 45–375, with most studies including fewer than 100 women). Cure rates were reported at varying durations of follow-up, ranging from 3 to 26 months (most under 1 year). The impact of possible confounding factors was not generally considered within the study reports. The studies were neither designed nor powered to show differences in the outcomes evaluated. [EL = 3]

The majority of the identified studies considered whether urethral closure pressures or leak point pressures predicted success of surgical procedures.[127–139] Other studies considered whether urine flow rates or urethral closure pressures predicted complications (voiding dysfunction or *de novo* DO).[129,140–144]

Success

Five of eight case series reported that the urethral closure pressure was statistically significantly lower in women who failed surgery (colposuspension, tension-free vaginal tape [TVT], vaginal wall sling), or that the failure rate was higher in women with maximum urethral closure pressure (MUCP) of 20 cmH_2O or less.[127,131–133,139] Two case series found no significant association between preoperative MUCP and surgical success or failure.[128,129] One case series reported varying results according to the procedure undertaken, with mean MUCP significantly lower in women who failed colporrhaphy, with no differences found for MUCP in women who had successful or unsuccessful needle suspension or colposuspension procedures.[134]

A further two studies considered different pressure measurements. One reported that preoperative opening detrusor pressure and urethral pressure at closure were significantly lower in women who had objective failure of colposuspension.[129] Another reported that the preoperative 'index of urethral relaxation at stress' (ratio of highest intraurethral pressure between coughs in the stress urethral pressure profilometry to the MUCP at rest) in women undergoing a suspension procedure was significantly lower in cases of objective failure.[128]

Four studies considered success according to abdominal or Valsalva leak point pressures (VLPP). Three reported no difference in success rates after surgery (vaginal wall sling, polypropylene sling, polytetrafluoroethylene bulking) according to baseline leak point pressures.[130,131,135] One of these studies reported that the failure rate was significantly higher in women with both VLPP less than 50 cmH_2O and MUCP less than 30 cmH_2O, compared with both values above these thresholds.[131] The fourth case series reported a significantly lower cure rate with retropubic 'bottom-up' tapes in women with low VLPP (less than 60 cmH_2O).[138]

Complications

The preoperative maximum urine flow rate was significantly lower in women who had delayed voiding in three of four studies that considered this.[140,142,144] One reported that a maximum flow rate of less than 20 ml/second was associated with delayed voiding.[140] The third study found no significant association between preoperative peak urine flow rate or residual volume and delayed voiding.[141] The procedures undertaken were a fascia lata sling, retropubic 'bottom-up' tapes and colposuspension.

No association was found between preoperative MUCP or VLPP values and voiding dysfunction in the studies that considered this.[140,142,143]

Two studies considered factors associated with the development of *de novo* DO, following colposuspension. Preoperative opening detrusor pressure, urethral pressure at closure and acceleration of flow rate were significantly higher in women with *de novo* DO in one study, while preoperative MUCP was not found to be associated with *de novo* DO (n = 209).[129] The second study did not report an association between uroflowmetry and *de novo* DO (n = 77).[144] [EL = 3]

Different methods of urodynamic investigation

Single-channel versus multichannel cystometry

The findings of single-channel ('simple') and multichannel cystometry were compared in four studies (n range 70–179).[145–148] Two studies included elderly men and women, with data reported separately for women.[145,146] The tests were conducted on the same day in three studies[146–148] (in random order in one147) and after an interval of 1–4 weeks in the fourth study.145 Assessments or interpretation of the traces were performed blind in two of the studies[146,147] [EL = DS II] but not in the other two.[145,148] [EL = DS III] The diagnostic accuracy results, for simple compared with multichannel cystometry, for a diagnosis of DO (or detrusor hyperreflexia[145]) in the four studies were: sensitivity range 59–100%, specificity 68–89%, PPV 17–84%, NPV 79–100%.

A fifth study reported accuracy of single-channel cystometry with cough stress test, relative to multichannel cystometry, for a diagnosis of stress UI. The sensitivity, specificity, PPV and NPVs found were 84%, 84%, 87% and 81%, respectively (n = 145).[149] [EL = DS III]

Stress test versus multichannel urodynamics

Three studies evaluated the accuracy of a simple stress test for a diagnosis of stress UI.[150–152] In the first, the stress test was conducted with a fixed bladder volume (which requires catheterisation). Compared with videocystometry and leak point pressure findings, the stress test had sensitivity of 94%, specificity 90%, PPV 97% and NPV 82%.[150] [EL = DS II] In the second study, the stress test was conducted with an empty bladder and found sensitivity of 49%, specificity 95%, PPV 98% and NPV 29% compared with multichannel cystometry. These values changed to 65%, 76%, 66% and 76%, respectively, when the stress test was compared with MUCP of 20 cmH_2O or less.[151] [EL = DS III]

The third study compared the accuracy of urethral closure pressure profilometry during multichannel cystometry for a diagnosis of stress UI, relative to a diagnosis based on a clinical stress test. Urethral closure pressure profilometry had sensitivity of 93%, specificity of 83%, PPV 92% and NPV 86% (n = 981).[152] [EL = DS III]

Ambulatory versus conventional multichannel urodynamics

Six case series compared ambulatory urodynamics with conventional multichannel cystometry or videocystometry (n range 20–22).[153–158] In three studies, the populations evaluated were those in whom a diagnosis had not been reached on conventional cystometry or whose symptoms did not match the cystometric findings.[153,156,158] Three of the studies included men and women, the majority being women.[153,156,157]

The studies differed in the duration of ambulatory monitoring (3–24 hours) and in the interval between tests (from 1 week to a mean of 37 weeks in those that reported this). The studies considered agreement between the two methods with none reporting data in a way that allows calculation of sensitivity, specificity, PPV or NPV. Two studies reported the agreement for any type of UI,[153,154] and four for urgency UI or DO.[155–158]

The studies reported the following:

- 63% had additional findings on ambulatory urodynamics[153]
- significant difference in the proportions with DO or with normal findings on ambulatory versus conventional urodynamic testing[154]
- more patients were found to have DO on ambulatory than conventional urodynamic testing[155–158] [EL = 3]

Videocystourethrography versus other methods

Videocystourethrography (VCU) was compared with multichannel cystometry in one study (n = 159). VCU had sensitivity of 61%, specificity 70%, PPV 56% and NPV 74% for a diagnosis of stress UI, and

14%, 97%, 87% and 45%, respectively, for urgency UI.[159] [EL = DS III] Compared with clinical assessment (n = 37), the accuracy of VCU was: [160]

- sensitivity of 74%, specificity 78%, PPV 78% and NPV 74% for stress UI
- 0, 91%, 0 and 91%, respectively, for mixed UI (zero sensitivity and PPV because no women had both a clinical and urodynamic finding of mixed UI)
- 50%, 89%, 20% and 97%, respectively, for urgency UI.[160] [EL = DS III]

No studies were identified that compared the accuracy of leak point pressures with MUCP for the diagnosis of intrinsic sphincter deficiency.

Test–retest reliability of urodynamic testing

One case series evaluated the intra- and inter-observer reliability of voiding measurements (pressure flow parameters) in women. Repeat cystometry was done after 1 week. Differences in intra- and inter-rater findings for the parameters measured (opening and closure detrusor pressure, maximum flow rate, detrusor pressure at maximum flow rate) were reported to be small although no statistical analysis was reported (n = 554).[161] [EL = 3]

No studies were identified in relation to the test–retest reliability of the filling phase of cystometry.

In a series of men and women with OAB, cystometry was performed at baseline and repeated after 2–4 weeks' placebo treatment within an RCT. All parameters (volume at first desire to void, volume at first involuntary contraction, and maximum pressure of involuntary contraction) increased significantly at the second measurement, and therefore it seems this study evaluated the effects of placebo on cystometric parameters rather than reproducibility (n = 30; 40% women).[162] [EL = 3]

Health economics of urodynamic testing

Resource scarcity provides the rationale for undertaking any health economic analysis. Finite resources mean that expenditure on preoperative urodynamic testing, or anything else for that matter, carries an opportunity cost – that is, other possible uses of those resources and benefits from them are foregone. The efficiency issue is then whether that expenditure represents the best use of those scarce resources: could greater patient benefit be obtained if the resources used for preoperative urodynamic testing were employed elsewhere? The health economics of preoperative urodynamic testing is especially important to consider because its impact on outcomes has been questioned and yet it currently represents routine clinical practice, using actual NHS resources. Therefore, an economic analysis of preoperative urodynamic testing in women who failed conservative treatment has been undertaken for this guideline and the details are given in Appendix R.

Evidence statements for urodynamic testing

There is often inconsistency between the clinical history and the urodynamic findings. [EL = DS III] Multichannel cystometry, when it reproduces the woman's symptoms, may reveal the underlying pathophysiological explanation of incontinence. Single-channel cystometry is less reliable, although a simple clinical stress test may be as accurate as multichannel cystometry in the diagnosis of stress UI. [EL = 3] Although videocystourethrography has the benefit of simultaneous structural and functional assessment, it is not clear whether this adds any relevant diagnostic accuracy, compared with multichannel cystometry. Ambulatory monitoring demonstrates functional abnormalities more often than multichannel cystometry, but the significance of this is unclear. [EL = 3] There is no evidence that pretreatment multichannel cystometry will improve the outcomes of treatments for incontinence. [EL = 2–] Although some urodynamic parameters have been found to correlate with adverse outcomes of surgery such as voiding difficulty and OAB, no test has been shown to reliably predict beneficial or adverse outcomes of surgery. [EL = 3] Nevertheless, it is recognised that preoperative urodynamic testing is firmly established in clinical practice and widely believed to contribute to improved patient counselling with regard to the likely outcomes of surgery. [EL = 4]

Economic modelling shows the cost effectiveness of preoperative urodynamic testing to be highly sensitive to the proportion of women with pure stress incontinence who failed conservative treatment, but this is not clearly established.

From evidence to recommendations

The GDG considers that urodynamic testing does not assist in the assessment of a woman prior to conservative treatment. The GDG also maintains the view that urodynamics investigation is not essential in every woman prior to primary surgery for stress UI, and therefore is not routinely recommended.

While the evidence suggests that preoperative urodynamics are not necessary for women with pure stress incontinence, the GDG accepts that these tests may help where the clinical diagnosis is not clear or in those women where initial surgical therapy has failed. Complex reconstructive urological procedures such as augmentation cystoplasty have been developed for use in specific urodynamic abnormalities; they should only be undertaken where these abnormalities are shown to be present.

Evidence to recommendations (2013)

Although urodynamic testing was not reviewed within the 2013 guideline update, in order to improve the implementation of the recommendation the GDG has modified the recommendations to clarify the indications of its use.

Explanatory text was added to the recommendation on multi-channel filling and voiding cystometry particularly because establishing a diagnosis of pure SUI requires a detailed clinical history and examination. This has been added to the recommendation to avoid women being offered surgical treatment for SUI without the identification of any symptoms of OAB, which are present in most women who have stress incontinence.

The recommendations have been reordered to avoid misinterpretation of the recommendation, since the majority of women (following unsuccessful conservative management) are likely to require urodynamic testing because they have some symptoms of OAB.

Finally, the recommendations for ambulatory urodynamics have additional text to clarify that this procedure should take place following unclear outcomes from an initial urodynamic assessment.

Recommendations

Number	Recommendation
19	Do not perform multi-channel cystometry, ambulatory urodynamics or videourodynamics before starting conservative management. **[2006, amended 2013]**
20	After undertaking a detailed clinical history and examination, perform multi-channel filling and voiding cystometry before surgery in women who have: • symptoms of OAB leading to a clinical suspicion of detrusor overactivity, **or** • symptoms suggestive of voiding dysfunction **or** anterior compartment prolapse, **or** • had previous surgery for stress incontinence. **[2006, amended 2013]**
21	Do not perform multi-channel filling and voiding cystometry in the small group of women where pure SUI is diagnosed based on a detailed clinical history and examination. **[2006, amended 2013]**
22	Consider ambulatory urodynamics or videourodynamics if the diagnosis is unclear after conventional urodynamics. **[2006, amended 2013]**

Number	Research recommendation
RR2	Further research is needed to answer the question of whether the use of urodynamics, prior to initial or subsequent treatments, affects the outcomes and cost effectiveness of interventions in women with UI or OAB.

4.12 Other tests of urethral competence

Other than urodynamic studies, the Q-tip, POP-Q, Bonney, Marshall and Fluid-Bridge tests can assess urethral competence (hypermobility of the urethrovesical junction). The Q-tip test involves placing a sterile Q-tip in the urethra and the woman is asked to bear down. If the Q-tip moves more than 30° the test is considered positive. The Bonney and Marshall tests involve pressing either the index and middle finger of the examiner's hand (Bonney test) or the jaws of a forceps (Marshall test) against the anterior vaginal wall, without pressing on the urethra. The stress provocation test is repeated and if no leakage occurs the Bonney or Marshall test is said to be positive. The Fluid-Bridge test is designed to test bladder neck competence by testing for the presence of fluid within the urethra, by demonstrating continuity between two channels of a pressure-recording catheter (one in the bladder and the other in the urethra).

Diagnostic accuracy

Q-tip test

One study compared the accuracy of the Q-tip test for evaluating urethrovesical junction mobility against ultrasound, as the reference standard in women with prolapse or UI (93% UI). It reported that the Q-tip test (change of 30° or more between rest and straining angles from the horizontal) had sensitivity of 25%, specificity 78%, PPV 67% and NPV 37%, relative to a positive test on ultrasound (more than 10 mm movement, n = 114).[163] [EL = DS III]

Three studies compared visual assessment of the urethrovesical junction (POP-Q) with the Q-tip test.[164–166] One of these studies reported the accuracy of the POP-Q system for diagnosing urethral hypermobility, using the Q-tip test as the reference standard, in women with symptoms of prolapsed (70%) and/or UI (30%). Results were presented for different cut-off points of Aa descent. As the Aa point became more distal, specificity and PPV of visual assessment increased (from 36% to 100% and 80% to 100%, respectively), and sensitivity and NPV fell (from 94% to 2% and 67% to 26%, respectively) (n = 111).[164] [EL = DS III] The other studies evaluated the correlation between Q-tip and POP-Q measurements in women who had urethral hypermobility (maximum straining angle of 30° or more on Q-tip test). The proportions with urethral hypermobility for each stage of the POP-Q classification were:

- 62% for stage 0, 83% stage I, 95% stage II, 100% for stages III and IV, correlation coefficient r = 0.47 (n = 274)[165] [EL = 3]
- 6% for stage 0, 91% for stage II, 100% for stages II to IV, correlation coefficient r = 0.79.[166] [EL = 3]

Bonney and Marshall tests

Three studies reported findings of urodynamic testing with or without the Bonney test in women with stress UI.[167–169] None were truly diagnostic accuracy studies in that they did not report sensitivity, specificity, PPV or NPV.

One case series found that none of the women who had demonstrable leakage during urodynamic investigation leaked during the Bonney test (hence all had a positive Bonney test). Urethral closure pressure was approximately three-fold higher when conducting the test than when not (n = 61).[167] [EL = 3]

In a similar study, outcomes were measured at rest, when conducting the Bonney test, and with direct compression of the urethra and bladder neck. Urethral closure pressure, pressure profile area and cough pressure profile area increased significantly compared with resting profiles, when conducting the Bonney test, and when urethra and bladder neck were directly compressed. No significant differences in pressures were seen between the Bonney test and urethral compression. All women had urine leakage when coughing at rest; none leaked during the Bonney test or with urethral/bladder neck compression (n = 12).[168] [EL = 3]

A third study did not report complete numerical results for the outcomes assessed (urethroscopic observations, proximal urethral pressure changes, pressure transmission ratio). The authors noted that there was no overlap between the Bonney test and direct urethral compression in proximal urethral pressure changes (n = 37).[169] [EL = 3]

One study reported urethral closure pressure profile and cough pressure profile measurements in women with stress UI when undertaking the Marshall test, and with intentional urethral occlusion. The urethral closure and cough pressure profiles were not significantly different during the Marshall test or with urethral occlusion (n = 16).[170] [EL = 3]

Fluid-Bridge test

Three studies evaluated the accuracy of the Fluid-Bridge test for the diagnosis of stress UI in women.[171–173] In each study, fluid reaching a point 0.5 cm from the urethrovesical junction indicated a positive test. In two studies, the reference standards used were a clinical and a urodynamic diagnosis of stress UI.[171,172] The test was conducted with women in the supine position in both studies, and additionally in the erect position in one.[172] With women in the supine position, the Fluid-Bridge test had:

- sensitivity 74–86%, specificity 42–62%, PPV 66–72% and NPV 64–70% relative to urodynamic findings
- sensitivity 72–89%, specificity 35–53%, PPV 43–54%, and NPV 71–85% relative to a clinical diagnosis (n = 67, n = 76).[171,172] [EL = DS III]

With women in the erect position, the Fluid-Bridge test had:

- sensitivity 100%, specificity 24%, PPV 37% and NPV 100% relative to a urodynamic diagnosis (n = 76)[172]
- sensitivity 100%, specificity 16%, PPV 40% and NPV 100% relative to a clinical diagnosis (n = 76).[172] [EL = DS III]

A third study evaluated the accuracy of a 'modified' Fluid-Bridge test relative to a diagnosis of stress UI due to bladder neck incompetence based on findings on history or on the Marshall test (n = 66). The Fluid-Bridge test had:

- sensitivity 86%, specificity 87%, PPV 79% and NPV 93% relative to the Marshall test
- sensitivity 73%, specificity 88%, PPV 85% and NPV 80% relative to history.

Urethral pressure profilometry had sensitivity 50%, specificity 88%, PPV 69% and NPV 78% relative to the Marshall test.[173] [EL = DS III]

Do tests of urethral competence predict outcome?

Only one study reported any data relevant to this question. In a case series of women undergoing colposuspension or needle suspension, the failure rate was significantly higher in women with a negative Q-tip test, who formed 4% of the study population (n = 406).[174] [EL = 3]

Evidence statements for tests of urethral competence

The Q-tip, Bonney, Marshall and Fluid-Bridge tests have been developed to evaluate the mobility or competence of the urethrovesical junction. [EL = DS III] However, there is no evidence to support their role in the clinical assessment of UI. [EL = 4]

Recommendations

Number	Recommendation
23	Do not use the Q-tip, Bonney, Marshall and Fluid-Bridge tests in the assessment of women with UI. **[2006]**

4.13 Cystoscopy

Cystoscopy is the direct visualisation of the bladder and urethral lumen using either a rigid or flexible cystoscope. Examination is used to identify areas of inflammation, tumour, stones and diverticula, all of which are findings that will require management within a different clinical pathway.

Alternative pathway

One study aimed to determine whether multichannel cystometry, in combination with urethrocystoscopy, improved the 'diagnostic accuracy' of cystometry alone in women, 93% of whom presented with UI, the remainder with prolapse (6%) or retention (1%). The women's history as reported did not indicate that cystoscopy was necessary. Urethrocystoscopy indicated a new diagnosis, of different pathology, in six women (n = 84).[175] [EL = 3]

Diagnostic accuracy

Two studies evaluated the accuracy of dynamic urethroscopy (urethroscopy with simultaneous supine cystometry) relative to multichannel cystometry with or without urethral pressure profilometry, for the diagnosis of stress UI (one study)[176] or DO (one study).[148] For a diagnosis of stress UI, urethroscopy had sensitivity of 60%, specificity 79%, PPV 75% and NPV 66% (n = 99).[176] [EL = DS III] For a diagnosis of DO, urethrocystoscopy had sensitivity of 25%, specificity 94%, PPV 65% and NPV 74% (n = 218).[148] [EL = DS III]

Evidence statement for cystoscopy

The available evidence does not support the role of cystoscopy in the assessment of women with UI. [EL = 3]

From evidence to recommendation

The GDG felt that cystoscopy may be of value in women with pain or recurrent UTI following previous pelvic surgery, or where fistula is suspected; its place in recurrent stress UI without these additional features is less clear.

Recommendations

Number	Recommendation
24	Do not use cystoscopy in the initial assessment of women with UI alone. **[2006]**

4.14 Imaging

Imaging techniques that can be used in the assessment of the urinary tract include ultrasonography, X-ray, computed tomography (CT) and magnetic resonance imaging (MRI). Confirmation of alternative pelvic pathology, by means of cross-sectional imaging or ultrasound, would be an indication for referral to a specialist. In addition, imaging may be used to characterise the extent and anatomical contents of a POP, especially in the standing position with MRI.

Diagnostic accuracy

The use of ultrasound for the diagnosis of post-void residual urine is considered in Section 4.6.

Diagnosis of UI

No evidence was identified that considered the use of MRI or CT scanning in the assessment of women with UI. Studies considering the use of ultrasound and X-ray imaging are described below.

The sensitivity and specificity of ultrasound and the Q-tip test, relative to a urodynamic finding of stress UI in women, was reported in one case series. Ultrasound (a positive test defined as a 1 cm or greater drop in urethrovesical junction) had a sensitivity and specificity of 86% and 91%, respectively. The values were 90% and 55%, respectively, for a positive Q-tip test (change in angle of 35° or more) (n = 67).[177] [EL = DS II]

Other studies have investigated whether certain parameters that could be measured by imaging might be used in the assessment of women with UI. These parameters include bladder wall thickness, bladder neck positioning, specific urethral measurements and the posterior urethrovesical angle.

Bladder wall thickness for DO diagnosis

Two studies focused on bladder wall thickness measured by transvaginal ultrasound for the diagnosis of DO.[178,179] One reported significantly greater bladder wall thickness in women with DO than with any other diagnosis, and that bladder wall thickness of more than 5 mm had sensitivity of 84%, specificity 89% and PPV 94% for diagnosing DO, using videocystourethrography with or without ambulatory urodynamics as the reference standard (n = 180).[178] [EL = 3] The second study investigated bladder wall thickness in women in whom urodynamic findings and clinical diagnoses were equivocal. Compared with women with stress UI, and compared with women without UI on urodynamic testing, the bladder wall thickness in women with DO appeared to be significantly greater (n = 128).[179] [EL = 3]

Studies investigating correlation of anatomical shape or movement with stress UI

Another four studies considered whether anatomical shape or movement correlates with reporting of UI, or with urodynamic findings, but the clinical significance of the findings reported in these studies is not clear. The studies considered the following (see evidence tables for findings).

- A case series investigated whether urethral measurements, taken by intraurethral ultrasonography, could distinguish women with intrinsic sphincter deficiency (ISD) from those with urodynamic stress UI (n = 39).[180]
- Two studies considered whether the posterior urethrovesical angle measured using bead chain urethrocystography could be used to diagnose stress UI.[181,182] One of the studies aimed to determine how bladder neck descent and posterior urethrovesical angle correlated with urodynamic findings (n = 84).[181] [EL = 3] The other study considered the prevalence of several parameters, including posterior urethrovesical angle of 115° or more, in continent and incontinent groups (n = 59).[182] [EL = 3]
- One study evaluated two parameters measured on bead chain cystography (the urethra at the most dependent position in the bladder, and descent of the urethrovesical junction below the posterior edge of the symphysis pubis) compared with a 1 cm or greater drop in urethrovesical junction, measured on ultrasound in women with stress UI (n = 85).[183] [EL = 3]

Does imaging affect women's outcomes?

No evidence was identified that addressed this question.

Evidence statement for imaging

There is a lack of evidence regarding the use of MRI or CT scanning in the assessment of women with UI. The available data do not support the use of ultrasound or X-ray imaging in the assessment of UI. The correlation between anatomy and function is unclear. [EL = 3]

Recommendations

Number	Recommendation
25	Do not use imaging (MRI, CT, X-ray) for the routine assessment of women with UI. Do not use ultrasound other than for the assessment of residual urine volume. **[2006]**

Number	Research recommendation
RR3	Further studies are required to clarify the role of ultrasound for the assessment of OAB.

4.15 Information provision

No evidence was identified in relation to whether providing information to a woman has an impact in terms of her satisfaction with the outcomes of treatment for UI or OAB.

Despite this lack of evidence, women should receive the correct information, at the right time, with the support they need to use it. It is well recognised in the healthcare community that clear communication, the involvement of service users and the provision of timely evidence-based information are key elements in moving towards a genuinely patient-centred service.

Patients' desire for information may be underestimated in the majority of cases, although it is also recognised that individual patients' desire for information varies.[186] Information 'seekers' may cope better with more information, and information 'avoiders' cope better with less.

Women presenting with symptoms of UI need information that helps them to understand the various types of UI, their symptoms, investigations and the treatments recommended. They need to feel confident that the information provided is based on valid, systematic research into which clinical procedures, drug therapies and medical devices are most effective. However, patients and their families need information that is both scientifically valid and understandable. Since patients make important medical decisions with their clinicians (not separately from them), information provided must be designed for use by patients with their clinicians.

Women with UI should also be given information on where else to go for help and support.

5 Conservative management

5.1 Introduction

This chapter refers to those therapies used for urinary incontinence (UI) that do not involve surgery. These include lifestyle interventions, physical, behavioural, drug and complementary therapies, and non-therapeutic interventions (such as products that collect or contain leakage). The preventive use of physical and behavioural therapies and of lifestyle interventions is also considered.

The International Continence Society defines 'conservative treatment' as therapies that are usually low cost, and managed principally by the person with UI with instruction/supervision from a healthcare professional. They differ from other forms of incontinence management, in that they have a low risk of adverse effects and do not prejudice other subsequent treatments.

Overactive bladder (OAB) drug treatment is also considered to be a conservative management approach and is discussed in more detail in Section 6.1.

5.2 Lifestyle interventions

Studies considered for the lifestyle interventions question

Evidence described in this section is derived from studies that investigated the effects of modifying the specified lifestyle factors on UI- or OAB-related outcomes. Where no such interventional studies were identified, other study designs investigating how these lifestyle factors may affect the prevalence, or incidence, of UI or OAB were considered. Several observational studies have considered the possible association between lifestyle factors and UI, many of which include both men and women.

5.2.1 Bowel habit

No studies were identified that addressed the effects of modifying bowel habit on UI in women. Three observational studies in women considered whether bowel habit is a risk factor for UI. One observational study compared the history of bowel function in women with uterovaginal prolapse (n = 23, ten of whom had 'minor' stress UI symptoms), women with stress UI (n = 23) and a control group (n = 27). Straining at stool as a young adult was reported by significantly more women with prolapse or stress UI than the control group (61% versus 30% versus 4%), as was bowel frequency of less than twice a week as young adults in women with prolapse compared with control (48% versus 8%).[187][EL = 2+]

Another cohort study reported that bowel urgency was associated with risk of OAB at 1 year (n = 12 570).[14][EL = 2+]

A cross-sectional study considered the effects of constipation and straining at stool on lower urinary tract symptoms. Stress UI, urgency and hesitancy were associated with both constipation and straining at stool. Sensation of incomplete emptying, post-void dribble and straining were associated with straining at stool (n = 487).[188][EL = 3]

A further cross-sectional survey reported that constipation was associated with a risk of stress and urgency UI, although constipation was not defined (n = 6006).[189][EL = 3]

5.2.2 Dietary factors

No studies were identified that addressed the effects of modifying dietary factors, including alcohol consumption. A cohort study investigated the association between the intake of certain foods, energy,

minerals and vitamins and the 1 year incidence of stress UI or OAB in women aged 40 years or above. The data indicate that certain quantities of some foods may be associated with reduced risk of new-onset OAB (chicken, vegetables, bread, protein, vitamin D and potassium) or new-onset stress UI (bread), and some quantities may be associated with an increased risk of new-onset OAB or stress UI (carbonated drinks) or stress UI (high fat, cholesterol, vitamin B12 and zinc intake) n = 6424.[190–192][EL = 2+]

A cross-sectional study did not find an association between alcohol use and urgency (n = 1059; 50% women).[193][EL = 3]

5.2.3 Caffeine

One randomised controlled trial (RCT) evaluated the effects of reducing caffeine intake to a maximum of 100 mg/day in addition to bladder training compared with bladder training alone in men and women with OAB with or without UI (n = 74). At 1 month, significantly greater reductions in urgency episodes and frequency were seen in the caffeine reduction group, with no significant differences between groups in reductions in urgency UI episodes.[194][EL = 1+]

Four observational studies investigated the relationship between caffeine consumption and UI or OAB.[195–198] Two of these studies evaluated the effects of caffeine on urodynamic parameters in women, as follows:

- A case–control study reported that the risk of detrusor oversactivity (DO) was significantly higher with high versus minimal caffeine intake (odds ratio [OR] 2.4, 95% confidence interval [CI] 1.1 to 6.5). The risk with moderate versus minimal caffeine intake was not statistically significant (OR 1.5, 95% CI 0.1 to 7.2, n = 259).195 [EL = 2+]
- A significant increase in detrusor pressure rise on bladder filling was seen after 200 mg caffeine intake in women with DO. No significant changes were identified in other urodynamic parameters in either group (women with DO or asymptomatic women, n = 30).[196] [EL = 3]

The other two studies reported the effects of modifying caffeine intake on subjective or objective outcomes:[197,198]

- During the initial 2–4 week self-monitoring phase of a behaviour management programme in women,[199] daily intake of caffeine, urine loss, daytime leakage episodes, and frequency fell and daily fluid intake increased. None of the changes in outcomes was significantly associated with reduced caffeine intake (n = 34).[197] [EL = 3]
- In a series of older people with psychiatric conditions who underwent a 13 week programme of alternating caffeine intake or abstinence, day and night leakage episodes were higher during periods of caffeine intake (n = 14; eight women).[198][EL = 3]

Four cross-sectional studies investigated the association between caffeine intake and UI or OAB.[193,200–202] The findings in the individual studies were as follows:

- no association between coffee intake and urgency (n = 1059; 50% women)[193]
- increased risk of UI with tea intake (n = 6876)[200]
- nocturia was more common in women who drank tea in the evening (no numerical data presented; n = 3669)[201]
- the risks for difficulty in emptying the bladder and having a weak urinary stream were higher in women who drank coffee (n = 297).[202] [EL = 3]

Recommendations

Number	Recommendation
26	Recommend a trial of caffeine reduction to women with OAB. **[2006]**

5.2.4 Fluid intake

In one RCT in women with UI (type unspecified), no significant changes in leakage episodes were reported after modifying daily fluid intake for 5 weeks. Adherence to fluid intake protocols was reported to be poor (n = 32).[203][EL = 1−]

A further crossover RCT considered the effects of fluid manipulation over a 3 week period in women with stress UI or idiopathic DO. Fluid manipulation consisted of caffeine restriction for 1 week followed by increased or decreased fluid intake in association with continued caffeine restriction for 2 weeks. Caffeine restriction alone did not lead to statistically significant reductions in any outcome (leakage or urgency episodes, frequency, 24 hour pad test). Increasing fluid intake led to a significant increase in urgency episodes in women with DO, with no significant effects on other outcomes. After reducing fluid intake, significant reductions in leakage and urgency episodes, and in frequency, were seen (n = 84; 69 analysed).[204][EL = 1−]

Based on women with stress UI or DO enrolled in a study of behaviour management,[205] weak correlation between fluid intake and diurnal and nocturnal frequency and leakage episodes was reported over a 1 week period (n = 126).[206][EL = 3]

Recommendations

Number	Recommendation
27	Consider advising modification of high or low fluid intake in women with UI or OAB. **[2006]**

5.2.5 Smoking

No studies were identified that addressed the effects of smoking cessation on UI in women. One cohort study found significantly increased incidence of stress UI or OAB in current smokers compared with never smokers at 1 year (n = 6424).[190][EL = 2+] A case–control study reported significantly higher prevalence of smoking among women with UI than women who were continent (OR 4.2, 95% CI 2.2 to 8.2). In women with UI, the prevalence of urgency UI was significantly higher among smokers than non-smokers (n = 160).[207][EL = 2−]

Six cross-sectional surveys considered the relationship between smoking and UI in women. Three surveys reported no association (n = 297, n = 486, n = 6037; 56% women).[202,208,209] The others reported a positive association between current smoking and UI (one study, n = 6876)[200] or nocturia (one study, n = 3669),[201] and between former smoking and UI (two studies, n = 6876; 1059 [50% women]).[193,200] [EL = 3]

5.2.6 Weight

One RCT evaluated the effects of a 3 month weight reduction programme in overweight women with UI. Reductions in weight and leakage episodes and improvements in quality of life (QOL) were significantly greater in the group assigned weight reduction compared with no intervention. Beyond the randomisation phase, women were offered continued intervention for 6 months, after which symptoms were still improved compared with baseline (n = 48; 40 analysed).[210][EL = 1−]

Three case series reported the effects of surgically induced weight loss on UI in morbidly obese women:

- In 12 women with stress, urgency or mixed UI who had mean weight loss of 33% following gastric bypass surgery, nine were subjectively cured of UI with no significant change in frequency at mean follow-up of 14 months.[211][EL = 3]
- In women who had lost 50% or more of their excess weight following bariatric surgery, the prevalence of stress UI fell from 61% to 12% after stabilisation of weight loss (2–5 years) (n = 138).[212][EL = 3]

- In men and women who lost 46% of their excess bodyweight following laparoscopic adjustable gastric banding, 64% reported that their stress UI was better. Symptoms were unchanged in the remainder (n = 195; 83% women).[213]

A fourth case series evaluated the effects of a 3 month weight reduction programme on leakage episodes in ten women with UI (six urgency, three mixed, one stress). Seven women reported at least 50% reduction in leakage episodes (all those who lost at least 5% of their weight, and one-quarter of those who lost less than 5% of their weight).[214][EL = 3]

Two cohort studies[190,215] and five cross-sectional studies[188,200,201,208,209] investigated the relationship between BMI and UI or OAB. One cohort study found significantly increased 1 year incidence of stress UI or OAB in women with BMI more than 30, compared with a BMI of 20–25 (n = 6424).[190][EL = 2+] The second cohort study, which investigated the prevalence of stress or urgency UI in participants of high- or low-impact exercise, reported that BMI was associated with risk for regular stress and urgency UI but gave no specific detail (n = 104).[215][EL = 2+]

The cross-sectional studies found that the prevalence or risk of UI or OAB was higher with increased BMI, specifically:

- increased risk of UI with BMI greater than 25 (n = 6876)[200]
- women with regular UI had the highest mean BMI (n = 486)[208]
- significantly higher prevalence of UI in women with BMI greater than 29 (n = 6037; 56% women)[209]
- increased risk of two or more nocturia episodes versus one episode for women with BMI of 30 or more versus less than 20 (n = 3669)[201]
- increased risk of UI or urgency with increasing BMI, although BMI thresholds were not defined (n = 487)[188]
- increased risk of urgency UI and a trend towards increased risk of urgency in women within the highest versus lowest BMI quartiles (n = 297)[202]
- increased risk of both stress and urgency UI in women within the highest BMI quartile (n = 6006).[189][EL = 3]

Recommendations

Number	Recommendation
28	Advise women with UI or OAB who have a BMI greater than 30 to lose weight. **[2006]**

5.2.7 Physical exercise

No controlled studies were identified that addressed the effects of physical exercise on UI in women. A cohort study investigated the prevalence of stress or urgency UI in past US Olympians who had participated in long-term high-impact exercise (gymnastics or track and field) in the past compared with low-impact exercise (swimming). No significant difference in the prevalence of stress or urgency UI was identified between high- or low-impact exercise groups (n = 104).[215] [EL = 2+] Another cohort study evaluated the effects of physical activity before, during and after first childbirth; the analysis suggested that pre-pregnancy high-impact activity may be associated with risk of UI (n = 665).[216] [EL = 2+]

Three cross-sectional studies investigated the prevalence of UI in women who exercise compared with those who do not. The three studies found that the overall prevalence of UI was not significantly different between groups (total n = 1677).[217–219][EL = 3] A further cross-sectional study reported that urgency was less likely in women who exercise at least weekly (n = 6006).[189][EL = 3]

Evidence statements for lifestyle interventions

There is a lack of high-quality prospective controlled trials evaluating the effects of modifying lifestyle factors in women with UI or OAB. [EL = 4]

Observational studies suggest that an increased caffeine intake may be associated with OAB and UI. [EL = 3] There is some evidence that caffeine reduction leads to less urgency and frequency when used in addition to bladder training. [EL = 1+]

Only RCTs of poor quality exist for modifying fluid intake, which were inconclusive. [EL = 1−] There is evidence of an association between obesity and UI or OAB, and in obese women weight reduction of at least 5% is associated with relief of UI symptoms. [EL = 3]

Constipation (bowel frequency of less than twice a week), and increased straining at stool in early adult life, may be associated with an increased tendency to prolapse and UI but no evidence on the effect of modifying bowel habit on continence was identified. [EL = 2+] Some dietary factors may increase the risk of developing UI or OAB although there is no evidence in relation to the effects of modifying these factors. [EL = 2+] Most observational studies suggest that smoking is associated with an increased risk of UI and OAB although there is no evidence relating to smoking cessation in the management of these symptoms. [EL = 3] There are conflicting data in relation to the association between physical exercise and UI prevalence. [EL = 3]

From evidence to recommendations

Where there is consistent evidence that a lifestyle factor appears to increase the risk of UI or OAB, or where there is consistent evidence of benefit from modifying a lifestyle factor, the GDG has recommended interventions in relation to these (caffeine, weight). Both excessive and inadequate fluid intake may lead to lower urinary tract symptoms; this should be considered on an individual basis. The overall lack of consistency in findings indicates a need for further research in this area.

Recommendations

Number	Research recommendation
RR4	There is a need for prospective interventional studies in all areas of lifestyle interventions to evaluate the effects of modifying these factors on UI and OAB.

5.3 Physical therapies

A variety of physical therapies are used in the management of UI in women. Pelvic floor muscle training (PFMT) involves recruiting pelvic floor muscles for muscle strengthening and skill training. Contraction of pelvic floor muscles causes inward lift of the muscles, with resultant increase in urethral closure pressure, stabilisation and resistance to downward movement.[220] Biofeedback can promote awareness of the physiological action of pelvic floor muscles by visual, tactile or auditory means, for example, by manometry or electromyography (EMG).[221,222] Weighted vaginal cones are cone-shaped appliances of various weights that can be used to facilitate strengthening of pelvic floor muscles. Passive and active contraction of the pelvic floor muscles aims to prevent the cones from slipping out of the vagina.[222] Therapeutic electrical stimulation involves the application of electrical current, usually via vaginal/rectal surface electrodes, to stimulate the pelvic floor muscles via their nerve supply, or to alter reflex activity or inhibit detrusor contractions by a neuromodulatory effect on the nerve pathways.

Studies considered for the physical therapies question

Evidence described in this section is derived from RCTs. Two systematic reviews published on the Cochrane library (PFMT, and weighted vaginal cones) in women with UI collate much of the RCT data identified in the systematic searches.[224,225] Owing to overlap of studies within Cochrane reviews, and because they include abstracts that have not subsequently been published, the studies were considered individually alongside all other relevant primary data.

Overall, the studies of physical therapies are heterogeneous in terms of the treatment programmes used, duration of treatment and/or follow-up, the populations and number of individuals enrolled and the outcomes measured. Several studies considered more than one intervention.

5.3.1 Pelvic floor muscle training

A wide range of different PFMT programmes was used across the RCTs, varying in duration, in number and type of contractions and repetitions. Daily PFMT was used in most. Further detail of the PFMT programmes used is provided in the relevant subsections.

PFMT versus no treatment or sham PFMT

Six RCTs compared PFMT with no treatment in a total of 422 women (211 having either treatment). Four enrolled women with stress UI,[226–229]and one included women with stress or mixed UI (8.9%).[230] The remaining study included women with stress, mixed or urgency UI (urgency UI in 16%), in which those with urgency UI were treated with bladder training and those with mixed UI with bladder training plus PFMT; this study is considered in the behavioural therapies section (5.3).[231,232] Some results for the 60% of women from this study who had stress UI were reported separately and are considered here.[232] Other than one quasi-RCT,[231,232] the studies were considered to be of good quality. [EL = 1+]

Women were advised to undertake daily PFMT in five studies. The number of contractions instructed varied, other than one study that only evaluated the 'knack' over a 1 week period.[227] The lowest number of contractions across the other studies was 8–12 contractions three times a day (plus an exercise class every week) and the highest was 20 contractions four times a day, increasing to 200 per day.[226,228,230,231] In a comparison with duloxetine, PFMT involved a target of 200 contractions per week (over 4 days), and the 'knack'. Half the studies provided other support, including an audiotape plus group training once a week[226] or a leaflet in addition to initial instruction.[230,231] The woman's ability to contract the pelvic floor muscle (PFM) was checked by vaginal palpation in five studies,[226–229,231,232] one of which excluded women unable to contract the PFM.[227]

Duration of treatment was 3 months in most studies, although this varied from 1 week to 6 months. Most studies considered cure rates and changes in leakage episodes at the end of treatment, which showed significantly greater improvements with PFMT compared with no treatment, in the five studies that recommended daily PFMT. The results for PFMT groups versus no treatment were:

- subjective cure rates of 16% and 56% versus 3% (two studies)[226,230]
- success (combined subjective cure and improvement) in 85% versus 0% (one study)[232]
- objective cure rates (1 hour pad test or negative stress test) of 44% and 65% versus 0% and 7% (two studies)[226,232]
- reductions in leakage episodes of 54% or 72% versus 6% and an increase of 10% (three studies; no numerical data in one).[226,230,232]

Three studies also considered short pad test results, each of which showed significantly less leakage in women undergoing PFMT.[226–228] One RCT used a 24 hour pad test where no difference was identified.[226] Both those studies that did[226–228,231,232] and those that did not[230] assess PFM contraction prior to treatment showed efficacy of active treatment groups over control. [EL = 3]

Five year follow-up has been reported of women from a 3 month study during which the control group was offered PFMT.[233] At 5 years in women with stress, mixed or urgency UI (those with stress or mixed undergoing PFMT), 69% reported improvement or dryness compared with pretreatment. However, a non-significant increase in leakage episodes was seen in women with stress UI (n = 110).[233][EL = 3]

In a comparison of PFMT with sham PFMT (and with duloxetine 80 mg with or without PFMT), sham PFMT involved contracting hip abductor muscles. No significant differences were reported between PFMT and sham PFMT groups in any outcome (leakage episodes, global improvement, QOL) after 12 weeks' treatment. It is unique to this trial that PFMT apparently gave no significant benefit over sham treatment.[229][EL = 1+]

Adverse effects

The majority of studies comparing PFMT with no treatment did not consider adverse effects. One RCT reported isolated adverse effects (pain, and an 'uncomfortable feeling' during exercise).[231] Another RCT

reported that no adverse effects occurred.[226]Adverse effects occurring in the PFMT and no treatment arms of the duloxetine study were pooled, and therefore a distinction between these interventions is not possible.[229]

Different pelvic floor muscle training regimens

Several RCTs compared different PFMT regimens, or different methods of delivering PFMT.

Intensive versus standard regimens

Four RCTs compared 'intensive' with 'standard' PFMT. The PFMT programmes and the populations evaluated were as follows:

- an exercise class every week in addition to standard PFMT (individual instruction, clinic biofeedback, 8–12 contractions three times a day, contraction checked by palpation) versus standard PFMT alone; 6 months' treatment, women with stress UI (n = 52)[234,235][EL = 1+]
- a programme of PFMT with bladder training for women with frequency and urgency (PFMT consisting of individualised instruction, target 80–100 contractions/day) versus standard postnatal care (which could include information on pelvic floor exercises); in women with stress, urgency (15%) or mixed UI (31%) 3 months postpartum, assessed after 1 year's treatment,[236] and at 6 years (n = 747)[237][EL = 1++]
- PFMT with or without vaginal cones versus standard PFMT (antenatal and postnatal instruction) in women with UI 3 months postpartum, assessed after 1 year's treatment and at 24–44 months postpartum; awareness of contraction checked by perineometry (n = 145)[238][EL = 1−]
- one-to-one instruction while in hospital postnatally, with an option to attend two postnatal pelvic floor exercise classes, versus standard care (verbal promotion of exercises, plus explanatory leaflet); effects assessed at 6 months postpartum (n = 190)[239][EL = 1+]

The rate of subjective cure or improvement was significantly higher in the intensive group in the study that considered this outcome (96% versus 66%; cure rates alone9%versus 0%).[234,235] Two of three studies in postpartum women found significantly lower UI prevalence in the intensive groups (60% versus 69% and 50% versus 76%),[236,238] while the third reported no significant difference (60% versus 46%).[239] The findings of pad tests were inconsistent (two studies).[234,235,238]

Longer term follow-up is available from two studies. At 6 years, no significant differences were found between 'intensive' and 'standard' groups in UI prevalence, severity or leakage episodes in the 69% of women followed up.[236,237][EL = 1++] Five year follow-up of the intensive PFMT arm (23 women) of one RCT[234,235] has also been published,[240] and a 15 year follow-up of both treatment arms.[241] Data at 15 years show no differences in urinary outcomes or satisfaction between groups in the 91% of women followed up.[241]

Group versus individual training

Two RCTs of 3 months' duration compared groups with individual PFMT in women with stress, mixed or urgency UI (n = 530, n = 44).[242] [EL = 1+] [243][EL = 1−] Group sizes were eight to ten[242] or four to twelve.[243] In the smaller of the two RCTs (n = 44), women also underwent bladder training. Neither study found significant differences between the two methods in the outcomes evaluated (leakage, UI severity, self-reported change in symptoms, pad test, QOL or frequency).

None of the RCTs comparing different PFMT methods considered adverse effects.

PFMT and drug treatment

One RCT compared PFMT with intravaginal oestrogen in women with stress UI (3 months' treatment with follow-up at 12 months) but no between-group analyses were reported.[228] [EL = 1+] Three RCTs evaluated combined PFMT and drug therapy (estriol, tolterodine and duloxetine).[229,244,245]

The PFMT regimen varied across these studies: five contractions per hour,[228] 75 contractions per day,[245] 15 minutes per day,[244] and a target of 200 contractions per week over a 4 day period.[229] Pelvic floor muscle contraction was checked by vaginal palpation in two studies.[228,229]

Oral estriol 1 mg plus PFMT was compared with PFMT alone in postmenopausal women with stress UI (n = 73; 66 analysed). A higher cure rate was reported with estriol plus PFMT compared with PFMT alone, at 2 years (78% versus 68%); no other outcomes were reported.[244] [EL = 1−]

The effects of adding PFMT to tolterodine 2 mg b.d. compared with tolterodine alone was considered in men and women with frequency, urgency and urgency UI (n = 480; 75% women). After 6 months' treatment, no significant differences were seen between tolterodineplus PFMT versus tolterodine alone in changes in any outcome. The reductions in symptoms with combined therapy versus tolterodine alone were: urgency UI episodes 64% versus 70%, frequency 23% versus 27%, and urgency 79% versus 83%. Overall 82% versus 86% considered themselves improved. Adverse effects reported with tolterodine (with or without PFMT) were dry mouth, headache, constipation, nausea, dry eyes and dizziness.[245] [EL = 1++]

Duloxetine 80 mg daily (with or without PFMT) was compared with PFMT and with no active treatment (sham PFMT and placebo drug) in women with stress UI (n = 201). Significantly greater reductions in leakage episodes were reported with duloxetine (with or without PFMT) compared with PFMT alone after 3 months' treatment. Global improvement and I-QOL scores indicated greater improvement with duloxetine plus PFMT compared with no active treatment. Discontinuation and adverse effect rates (nausea, dizziness, dry mouth, constipation, insomnia, somnolence, asthenia) were significantly higher in duloxetine-treated groups compared with PFMT or no active treatment combined.[229] [EL = 1+]

Recommendations

Number	Recommendation
29	Offer a trial of supervised pelvic floor muscle training of at least 3 months' duration as first-line treatment to women with stress or mixed UI. **[2006]**
30	Pelvic floor muscle training programmes should comprise at least 8 contractions performed 3 times per day. **[2006]**
31	Do not use perineometry or pelvic floor electromyography as biofeedback as a routine part of pelvic floor muscle training. **[2006]**
32	Continue an exercise programme if pelvic floor muscle training is beneficial. **[2006]**

Number	Research recommendation
RR5	Studies investigating different pelvic floor muscle training regimens are required to establish the optimum method of delivering and undertaking this intervention.
RR6	How effective are different pelvic floor muscle training regimens in the management of women with overactive bladder (OAB) symptoms and to whom should it be offered? Why this is important For many women with urinary incontinence symptoms, management of their condition will take place predominantly in primary and community care. Pelvic floor muscle training may be their only experience of therapeutic intervention. It is not currently known whether different pelvic floor muscle training regimens have an impact on treatment outcomes. It is also not known whether other factors also have an impact on its effectiveness. These factors include the way that the training is offered, the technique that is taught, the intensity and frequency of training, and the length of time that pelvic floor muscle training is continued. Because pelvic floor muscle training is widely used in clinical practice, robust evaluation is needed to identify whether these or other factors have an important impact on patient-centred outcomes.

5.3.2 Vaginal cones

Ten RCTs evaluated the use of weighted vaginal cones in women with UI compared with PFMT or electrical stimulation, or in combination with PFMT.[226,238,246–253] Other than one study that enrolled women with stress, mixed or urgency UI (postnatally),[238] all studies included women with stress UI. Between 37 and 145 women were evaluated in each study.

The protocol for cone use differed across studies. Seven used a range of weights, increasing according to ability to retain the cone (20–70 g,[226,247,252,253] 20–100 g,[238,250] or 50–100 g[246]). One study used a fixed weight of 150 g,[251] while two studies did not specify weights used.[248,249] In five studies, women were instructed to hold the cones in place twice or three times a day for 10–15 minutes.[238,246–248,250] Once daily use for between 5 and 25 minutes was advised in another five studies.[226,249,251–253]

In studies involving PFMT, daily PFMT was undertaken. The number of contractions ranged from 24 (eight contractions three times a day) to 100 where specified.[226,238,246–248] PFMT was individually tailored in three studies,[247,249,252] and included the 'knack' in two.[247,252] Seven studies stated that ability to contract PFM was checked at baseline.[226,238,246–248,252,253]

Cones versus no active treatment

Cones were compared with no treatment within one RCT (total n = 107). Significantly greater improvement in leakage and social activity indices were seen with cones after 6 months' treatment. No significant differences were seen between groups in other outcomes (subjective or objective cure, leakage episodes).[226][EL = 1+]

Cones versus PFMT

Cones were compared with PFMT in four studies of 3–6 months' duration.[226,246,247,249] Two of these studies had other treatment arms (electrical stimulation and an untreated control,[226] biofeedback[249]). A further study, also described under the intensive versus standard PFMT section, compared 'intensive' PFMT (PFMT/cones/PFMT plus cones) with standard postnatal care but only analysed results for women who completed the study. Results were presented for the intensive group as a whole, except for the proportion cured, where there was no significant difference between cone and PFMT groups at 1 year postpartum.[238] [EL = 1−]

Two studies of 3 months' duration reported no significant differences between cones and PFMT in improvements in outcomes evaluated: leakage episodes, subjective improvement, subjective or objective cure rates (n = 60);[247] [EL = 1+] or leakage episodes, PFM strength or QOL (KHQ) (n = 101).[249][EL = 1−]

The third study found significantly greater improvement with PFMT versus cones in the short pad test, leakage episodes, leakage index and PFM strength, and a significant difference in subjective and objective cure rates (56% versus 7% and 44% versus 15%). No significant differences were seen in 24 hour pad test results after 6 months' treatment (n = 107).[226] [EL = 1+] The fourth study, which only analysed results for those who completed 4 months' treatment, found a significantly greater reduction in leakage on the stress pad test with cones versus PFMT. No significant differences were found in other outcomes (PFM strength and subjective assessment) (n = 37).[246] [EL = 1−]

Cones versus electrical stimulation

Cones were compared with electrical stimulation in three studies, none of which reported significant differences between groups in any outcome, whether assessed at 1 or 6 months. Women in one study also undertook PFMT.[250] Outcomes evaluated across two studies were: short and 24 hour pad tests, subjective cure, leakage episodes, leakage and social activity indexes, and pelvic floor muscle strength.[226,250][EL = 1+] The remaining study only considered urethral pressure and pad test results, and gave inadequate data and detail of methods for evaluation (n = 20).[253] [EL = 1−]

Cones in combination with PFMT

Cones and PFMT in combination were compared with PFMT alone in a 3 month study. Limited results were given (urodynamics only available for 59%), with no between-group analysis for subjective assessments; however, a similar proportion of women in both groups reported cure or improvement (n = 46).[252][EL = 1+]

Cones and PFMT in combination were compared with electrical stimulation in two studies of 6 weeks' duration. One reported no differences between groups in leakage episodes or frequency, while no

between-group analyses were reported for other outcomes (n = 40).[248][EL = 1−] The other study found no significant differences between groups in any outcome (urethral or vaginal pressures, PFM contraction and subjective assessment) (n = 120).[251][EL = 1+]

Adverse effects

One study reported adverse effects, which were four reports in 27 cone users (one abdominal pain, one bleeding, two vaginitis) and two reports in the electrical stimulation group (tenderness and bleeding; discomfort).[226] No adverse effects were reported in the PFMT or untreated control groups. Motivation problems were very common in the cone and electrical stimulation groups in one study (52% and 32%).[226]

The withdrawal rate from cone therapy was 47% in a study that noted this, compared with none with PFMT.[247] Differences in withdrawal rates between groups were not apparent in other studies.

5.3.3 Biofeedback

Most data regarding biofeedback relate its use in conjunction with PFMT, rather than as an isolated intervention. A variety of biofeedback methods were used across these studies, differing in the probes used (vaginal probes with EMG electrodes, pressure-sensitive intravaginal devices), in the feedback provided (visual and/or auditory) and the setting in which biofeedback was undertaken (home or clinic). Additionally, a few studies used electrodes/rectal catheters to monitor muscle activity or abdominal pressure.

Only one study compared biofeedback alone with PFMT (and with cones, n = 101). No significant differences were found between the three groups in improvements in outcomes evaluated at 3

Eleven RCTs compared biofeedback-assisted PFMT with PFMT alone, in women with stress UI (eight studies),[254–263] stress or mixed UI (one study),[230] stress or urgency UI (one study)[264] or OAB (one study).[265] Treatment duration ranged from 4 weeks to 6 months, with the number of women per study ranging from 22 to 103; most included fewer than 50 women. Of the 11 studies, four were considered to be of poor quality [EL = 1−][255,258,261–263] and seven of good quality.[230,254,256,257,259,260,264,265] [EL = 1+]

The majority of the studies found no significant differences between biofeedback-assisted PFMT groups and PFMT alone in the outcomes measured (subjective or objective cure, QOL [BFLUTS] or social activity index scores).[230,256,258–265] Cure rates in the seven studies that reported this outcome (though variously defined) ranged from 16% to 69% (median 30%) with PFMT and from 15% to 73% (median 50%) with biofeedback-assisted PFMT.[230,254,256,258,261,264,265] Significant additional benefit, in terms of leakage episodes, was reported in one study that alternated biofeedback with electrical stimulation,[262,263] and in PFM parameters in two studies.[259,260,262,263]

A further two RCTs evaluated different methods of biofeedback. One compared biofeedback by palpation with EMG in women with stress UI. There were no significant differences between the biofeedback methods in urinary outcomes after 8 weeks' treatment (n = 50).[266][EL = 1+] The second study compared the use of a vaginal plus abdominal probe with a vaginal probe only, for 4 weeks. Greater improvement in QOL was seen using a vaginal probe only, with no differences reported in other outcomes (leakage, pelvic floor muscle strength or endurance) (n = 38).[267] [EL = 1+]

Two RCTs considered adverse effects. None were reported in one,[261] and another noted that two women (13%) found the vaginal probe uncomfortable, and that 17% from PFMT or biofeedback-assisted groups reported pain while training.[259,260]

5.3.4 Magnetic therapy

Magnetic therapy aims to stimulate the pelvic floor muscles and/or sacral roots by placing them within an electromagnetic field.

Two RCTs compared magnetic stimulation therapy with sham stimulation delivered via a portable device for the treatment of UI for 8 weeks. In the first study, in women with stress, mixed or urgency UI, significantly more women in the magnetic therapy group reported improvement in symptoms. No significant differences in improvements in other outcomes were seen (pad weight, PFM contraction, leakage episodes or nocturia). Two reports of a pulsating sensation in users of magnetic stimulation were noted.[295] [EL = 1+] The second study, in women with urgency-predominant mixed UI, reported a

significantly higher 'success' rate with magnetic stimulation; between-group comparisons for other outcomes were not reported (frequency, nocturia). No women experienced adverse effects (n = 39).[296][EL = 1−]

Two case series considered the effects of 6 or 8 weeks of magnetic therapy using a special chair (two 20 minute sessions a week). Women in one had stress UI (a minority having urgency-predominant mixed UI), and urgency or mixed UI in the other. Results for 74 patients have been reported, which showed significant improvement in all outcomes considered (leakage episodes, pad test results, frequency and satisfaction). Adverse effects were not considered in one study, while none were reported in the other.[297,298][EL = 3]

5.3.5 Economic evidence for physical therapies

There is a lack of good-quality evidence about the clinical and cost effectiveness of conservative therapies for UI. In the absence of evidence of a difference in efficacy between treatment options, cost minimisation analysis may be used to determine the most cost effective. Cost minimisation was undertaken for the physical therapies PFMT, cones, biofeedback and electrical stimulation. Estimates of the costs of the conservative therapies and an explanation of how these estimates were derived are given in Appendix S.

Additionally, because the other conservative treatment option for stress UI is duloxetine (see Section 5.4.4), a decision tree model was developed to compare the cost effectiveness of PFMT and duloxetine, as a first-line treatment for women with moderate to severe stress UI (assumed to be 14 or more leakage episodes per week). Treatment effects and costs were based on a 52 week time frame. This is described in detail in Appendix S. Under baseline assumptions, PFMT 'dominates' duloxetine. This means that it is both more effective and less costly. The sensitivity analyses undertaken (and detailed in Appendix S) did not change this conclusion.

Evidence statements for physical therapies

Daily PFMT is an effective treatment for stress or mixed UI compared with no treatment over the short term. Other than occasional cases of pain or discomfort, no other adverse effects were noted. [EL = 1+] Women's pelvic floor contraction was assessed at baseline in the majority of studies. Studies that did or did not assess pelvic floor muscle contraction prior to treatment both showed efficacy of active treatment compared with control. [EL = 3]

In studies of up to 1 year, higher intensity PFMT regimens confer greater subjective cure or Improvement than lower intensity regimens. Over the longer term, differences between these groups are not sustained. [EL = 1+] There is a lack of evidence for optimum training regimens for PFMT. [EL = 4]

There is no additional benefit from the use of PFMT in women undergoing treatment with tolterodine for OAB. [EL = 1++] In women with stress UI, vaginal cones are more effective than no treatment over the short term. There is no evidence of a difference in effectiveness between cones and PFMT. Compared with PFMT, cones are associated with more adherence problems. [EL = 1+] One study suggested that the training time for using vaginal cones is one-third of that for PFMT, which would make vaginal cones cheaper than PFMT. However, it is not clear what the appropriate training regimen should be for women using vaginal cones. Vaginal cones are not suitable for all women. Cones are inappropriate for use in some circumstances, such as when there is a moderate to severe prolapse, too narrow or too capacious a vagina causing difficulty with insertion or misplacement of the cone, untreated atrophic vaginitis, vaginal infection, or during menstruation or pregnancy. [EL = 4]

Evidence does not indicate additional benefit from biofeedback with PFMT in comparison with PFMT alone in treating UI. [EL = 1+] Biofeedback with PFMT is more costly than PFMT alone and therefore is not cost effective given a lack of additional benefit.

There is lack of consistency in the electrical stimulation protocols employed in available studies. There is limited evidence for the benefit of electrical stimulation versus sham electrical stimulation in the treatment of urgency UI. [EL = 1+] There is no evidence of additional benefit of electrical stimulation in combination with PFMT compared with PFMT alone. [EL = 1−]

There are limited data on the use of magnetic therapy for UI, and its role in the treatment of women with UI is unclear. [EL = 3]

An economic model constructed for the purposes of this guideline suggested that PFMT is more cost effective than duloxetine alone, as first-line treatment for stress UI. This result was generally not affected by making plausible changes to model parameters in favour of duloxetine. While the model was based on the best available clinical evidence, there is a lack of long-term effectiveness data for either treatment.

From evidence to recommendations

While there is no evidence of effectiveness for either biofeedback or electrical stimulation, the GDG considered that the information and support generated by biofeedback may assist motivation for some women, and that electrical stimulation may be of value for those who are unable to initiate a pelvic floor muscle contraction. [EL = 4]

In recommending the use of PFMT, the GDG considered that guidance should be given on the number of pelvic floor contractions to be undertaken within such a programme. Without clear evidence on optimal training regimens, the minimum number of daily pelvic floor muscle exercises advised across the studies was adopted by the GDG as the minimum number of contractions that women should be aiming for, that is 24 (eight contractions three times a day). Most studies evaluate 3 months' treatment and, in the view of the GDG, this is an appropriate period of time to recommend PFMT before assessing its effectiveness.

5.3.6 Therapeutic stimulation

A range of electrical stimulation methods and protocols were used in the RCTs, though the protocol used was poorly reported in some studies. Various types of current were used (interferential therapy, faradic stimulation, alternating pulse currents), with a range of current intensities. The setting (home or clinic), duration (15 to 30 minutes) and frequency (two to three times per week) of individual treatments also varied. Electrical stimulation parameters were generally tailored to the woman's tolerance.

Electrical stimulation versus sham stimulation

Eight RCTs compared electrical stimulation with sham stimulation. Treatment duration ranged from 4 to 15 weeks, with the number of women recruited in each study ranging from 24 to 121.[248,268–274] Four studies included women with stress UI,[248,268,270,271] two included women with stress, mixed or urgency UI,[272,273] and two included women or men and women (57% women) with urgency or urgency-predominant UI.[269,274] One study was of poor quality,[248] [EL = 1−] and the others were of good quality.[268–273] [EL = 1+]

The outcomes reported across these studies were leakage episodes, UI prevalence, pad tests, subjective cure or improvement, PFM strength, urodynamic parameters and QOL (SF-36, IIQ, UDI). The findings across these studies were inconsistent, with significant benefit with electrical stimulation versus sham stimulation reported for some but not all outcomes, and not across all studies. Not all studies reported between-group comparisons.

A further RCT compared electrical stimulation with 'lower urinary tract exercises' (PFMT and bladder training), and with both interventions combined, in women with DO (n = 68). At 9–11 weeks, no significant differences were found between groups in any outcome (detrusor activity index, leakage episodes, PFM strength).[275][EL = 1−]

PFMT versus electrical stimulation

Eight RCTs compared PFMT with electrical stimulation in women (six in women with stress UI,[226,228,248,276–278] one in those with stress, mixed or urgency UI,[279] and one in those with OAB with urgency UI[265]).

The RCTs involving women with stress UI recruited between 18 and 51 patients. Duration of treatment ranged from 6 weeks to 12 months. The PFMT group also used vaginal cones in one study.[248] The quality of two studies was poor,[248,278] [EL = 1−] while four were of good quality.[226,228,276,277] [EL = 1+] None of the studies reported significant differences between groups in subjective or objective cure rates. The subjective cure rates ranged from 10% to 56% with PFMT, and from 4% to 12% with electrical stimulation, and objective cure rates from 10% to 54% versus 4% to 40%. Several other outcomes were reported in one study, where improvements in PFM parameters, short pad test results, leakage and social activity indexes were significantly greater in the PFMT group compared with electrical stimulation.[226] No significant differences were reported between groups in leakage episodes or leakage

frequency (three studies),[226,248,277] or in 48 hour pad test results (one study).[226] One of the studies also compared propantheline with electrical stimulation, which reported no significant differences between groups in subjective or objective cure or improvement.[277]

The RCT involving women with stress or mixed or urgency UI (66% mixed) found no significant differences between PFMT and electrical stimulation groups in any outcome (subjective assessment, 48 hour pad test results, improvements in PFM strength orDOprevalence) after 8 weeks' treatment (n = 35).[279][EL = 1+]

The RCT in women with OAB and urgency UI reported significantly greater improvements in PFM parameters and QOL (KHQ) with PFMT compared with electrical stimulation, but no significant differences in self-reported cure or improvement after 12 weeks' treatment (n = 103).[265][EL = 1+]

Electrical stimulation in combination with PFMT

Four RCTs evaluated electrical stimulation in combination with PFMT versus PFMT alone in women with stress UI (stress or urgency in one RCT).[278,280–282] The duration of treatment ranged from 1 to six months, with the number of women enrolled ranging from 14 to 57. One RCT also compared the combination with electrical stimulation alone.[278] Three studies were of poor quality,[278,280,282][EL = 1−] and one of good quality.[281][EL = 1+]

Across these RCTs, electrical stimulation did not confer additional benefit to PFMT alone in the outcomes measured (self-reported cure or improvement, pad test, PFM parameters). No significant differences in self-reported cure or improvement were seen with electrical stimulation plus PFMT compared with electrical stimulation alone.

Adverse effects

Of all studies that considered the effectiveness of electrical stimulation, five considered adverse effects. None were reported in one study.[275] Across the others, adverse effects or complications noted were: vaginal irritation (12–22%), pain (6–9%), and cases of faecal incontinence, discomfort, and tenderness and bleeding.[226,268,269,277] One study reported difficulty in maintaining motivation in 32% of the electrical stimulation group.[226]

Recommendations

Number	Recommendation
33	Do not routinely use electrical stimulation in the treatment of women with OAB. **[2006]**
34	Do not routinely use electrical stimulation in combination with pelvic floor muscle training. **[2006]**
35	Electrical stimulation and/or biofeedback should be considered in women who cannot actively contract pelvic floor muscles in order to aid motivation and adherence to therapy. **[2006]**

Number	Research recommendation
RR7	Research into the optimal electrical stimulation of the pelvic floor parameters is required, to inform future clinical practice. Studies investigating the role of electrical stimulation in women who cannot contract the pelvic floor muscle are required.

5.4 Behavioural therapies

Behavioural therapy involves an individual learning new patterns of response or re-establishing previously learnt behaviour to fit in with what is considered usual. Women with OAB (wet or dry) usually void more frequently than usual due to urgency. Women with stress UI also often void more frequently

in the belief that they will pre-empt an involuntary urine loss associated with any increase in intra-abdominal pressure.

Various toileting programmes have been used. Bladder training (also described as bladder retraining, bladder drill, bladder re-education or bladder discipline) actively involves the individual, in attempting to increase the interval between the desire to void and the actual void.[299] This may occur by mandatory schedules in which the individual may not use the toilet between set times for voiding, or a self-scheduled regimen where the patient gradually increases their inter-voiding times, and may use the toilet between times if the urgency becomes unbearable.[300]

Studies considered for the behavioural therapies question

Evidence described in this section is derived from RCTs. Four systematic reviews of various toileting regimens have been published on the Cochrane library.[299,301–304] The RCTs within these systematic reviews were considered individually. Further RCTs identified are also included here. Several studies included both men and women, none of which reported data separately by gender.

5.4.1 Bladder training

Bladder training versus control

Two RCTs compared bladder training with control in women (n = 60, n = 123).[205,305] In the first study, supervised bladder training as inpatients towards a target voiding interval of 4 hours was compared with unsupervised training at home, in women with frequency, urgency and urgency UI (two-thirds of whom also had stress UI). At 6 months follow-up (duration of intervention unclear), more women in the supervised group were continent or symptom-free.[305][EL = 1+] The second RCT in women with UI (type unspecified) compared bladder training (target voiding interval of 2.5–3 hours) with an untreated control group. Urine loss, leakage episodes and QOL (IIQ) were improved in the bladder training group after 6 weeks' treatment.[205] [EL = 1+] Neither study considered adverse effects.

Bladder training versus drug treatment

Two RCTs compared bladder training with drug treatment in women with urgency or mixed UI (one oxybutynin,[306] one a combination of flavoxate and imipramine[307]).

In women with urgency UI, similar self-reported cure rates (about 73%) were seen with a 6 week bladder training programme (target voiding interval of 3–4 hours) and with oxybutynin (n = 81). Relapse occurred in 4% of the bladder training group, and in 44% of the oxybutynin group, at 6 months. About half of the oxybutynin group required dose reduction owing to adverse effects. No between-group comparisons were made for other outcomes.[306] [EL = 1+]

No details of the bladder training programme were provided for the comparison with flavoxate plus imipramine (n = 50). Significantly more women were subjectively or objectively cured after 4 weeks' bladder training than with drug therapy.[307] [EL = 1+]

Bladder training in combination with drug treatment

Three double-blind (DB) RCTs evaluated the addition of antimuscarinic drug treatment to bladder training (one oxybutynin[308], one terodiline[309] [no longer available in the UK], and one imipramine[310]). Bladder training aimed to reduce frequency by delaying voiding for as long as possible in two studies,[308,309] and aimed at a 4 hourly voiding target in one.[310] A further RCT compared tolterodine plus bladder training with tolterodine alone.[311] All studies included men and women; two included elderly people,[308,309] and two included a broader age group.[310,311]

In individuals with symptoms of urinary frequency, urgency and urgency UI, a significant reduction in daytime frequency was seen with oxybutynin plus bladder training compared with placebo plus bladder training, after 6 weeks' treatment (n = 60; 93% women). No significant differences were reported in other outcomes (daytime leakage episodes, nocturia, nocturnal enuresis, self-reported benefit, adverse effects).[308] [EL = 1+]

No significant differences in frequency, leakage episodes or self-reported improvement were seen between terodiline or placebo in addition to bladder training in individuals with urinary frequency and urgency UI, after 6 weeks' treatment (n = 37; 88% women). Two adverse effects were noted with terodiline (one oesophagitis, one dry mouth).[309][EL = 1+]

In individuals with incontinence and 'unstable bladders', no significant differences were seen between imipramine plus bladder training and bladder training alone, in cure or urodynamic parameters with follow-up to 11 months. Dry mouth and constipation were reported with imipramine, with no adverse effects reported with bladder training (n = 33).[310] [EL = 1−]

Bladder training in addition to tolterodine was compared with tolterodine alone in men and women (n = 501; 75% women) with urinary frequency, urgency, with or without urgency UI (61% with). The aim of bladder training was five to six voids per day while maintaining the same fluid intake. Combined treatment resulted in reduced frequency and increase in volume voided versus tolterodine alone, with no differences between groups in leakage or urgency episodes, patient's perception of change or adverse effects after 6 months' treatment.[311] [EL = 1++]

Bladder training versus PFMT

Two RCTs compared bladder training with biofeedback-assisted daily PFMT in women.[312,313] One did not report the type of UI or report between-group comparisons for bladder training, PFMT or no treatment (n = 50).[312][EL = 1−]

The other RCT compared bladder training, biofeedback-assisted PFMT and the interventions in combination in women with stress, urgency or mixed UI who had palpable pelvic floor contraction on vaginal examination.[313] After 3 months' treatment, a significantly greater reduction in leakage episodes was seen with combination treatment compared with monotherapy; this was not sustained after a further 3 months follow-up. No other significant differences were reported between groups (n = 204).[313][EL = 1+]

Recommendations

Number	Recommendation
36	Offer bladder training lasting for a minimum of 6 weeks as first-line treatment to women with urgency or mixed UI. **[2006]**

5.4.2 Multicomponent behavioural therapy

Eight RCTs evaluated the use of a multicomponent behavioural programme that included bladder training and PFMT.[199,231,314–324] The bladder training methods used were urge strategies in three studies,[314–319] bladder training in three studies (one also included fluid management),[199,231,320] education in one study,[321,322] and one study allocated PFMT or prompted voiding depending on the cognitive status of individuals.[323,324] In four of the RCTs, biofeedback-assisted PFMT was used.[199,314,315,317–319] PFMT involved daily exercises in six studies, and the programme was not described in two.[320–322] Six studies checked the ability of individuals to contract the pelvic floor muscle at baseline.[231,314–320,323,324] Seven RCTs enrolled women only, while one enrolled men and women.[323,324]

Compared with no active treatment or usual care

In four of the RCTs, the comparison group was no active treatment or usual care. Owing to the variety of behavioural methods used, each study is described individually. One RCT in women aged 55 years or above with stress, urgency or mixed UI compared a 6 month sequential programme of behavioural management (self-monitoring including fluid management, bladder training, EMGassisted PFMT) with no active treatment. The behavioural management group achieved significantly greater improvement in leakage episodes, 24 hour pad test, QOL (IIQ) and subjective severity assessment compared with control. Only 21% were followed up to 2 years, in whom improvements seemed to be maintained. No significant differences between groups were reported in voiding frequency or interval (n = 218).[199] [EL = 1++]

Another RCT compared 3 months of behavioural therapy with untreated control in women with any type of incontinence. The behavioural strategies used were PFMT for stress UI, bladder training for urgency UI and bladder training followed by PFMT for mixed UI. Overall, the results showed significant reduction in leakage episodes with behavioural therapy, and a higher proportion reporting improvement versus control (n = 110).[231][EL = 1+] Results for the 60% of women with stress UI were reported separately, which also showed significant reduction in leakage episodes.[232]

The third RCT, in women with any type of UI, reported significant reductions in leakage episodes with 6 weeks' behavioural therapy (bladder training and PFMT) compared with no active treatment. No significant differences were reported in frequency (n = 152).[320][EL = 1+]

The fourth RCT compared a 10 week behavioural therapy programme (education, PFMT), with usual care in women with stress or urgency UI. Significantly greater reductions in leakage episodes were reported with behavioural therapy, with no differences between groups in QOL (n = 145).[321,322] [EL = 1+]

Compared with other active interventions

Two RCTs in women with urgency or mixed UI compared a sequential 8 week programme of behavioural training (PFMT with anorectal biofeedback, urgency strategies, repeat PFMT if needed, review and reinforcement) with oxybutynin, or self-help.[314–318] Significant reductions in leakage episodes and in nocturia were seen with behavioural training versus oxybutynin, and oxybutynin versus placebo tablets, and significantly more reported satisfaction and improvement with behavioural training versus oxybutynin. Dry mouth and inability to void were significantly more frequent with oxybutynin than control groups (n = 197).[314,315,317][EL = 1+] In the study evaluating the same behavioural training programme with a group receiving biofeedback (vaginal palpation), and a self-help group receiving written instructions of the programme only, no significant differences were reported in satisfaction, improvement, QOL (IIQ, SF-36) or bladder capacity (n = 222).[318][EL = 1++]

After the initial 8 week period of one of these RCTs,[314] women initially treated with behavioural therapy or oxybutynin who were not cured or not completely satisfied were offered the other treatment option in addition to the initial therapy for a further 8 weeks. Significant additional improvement in leakage episodes was seen in those who took oxybutynin in addition to continued behavioural treatment (n = 8) and in those who continued with oxybutynin and, in addition, underwent behavioural treatment (n = 27).[325][EL = 2+]

A further RCT in women with predominant stress UI also compared an 8 week sequential programme of behavioural training (PFMT with anorectal biofeedback, the 'knack', managing urgencyncy, repeat PFMT if needed, review and reinforcement), with or without the addition of electrical stimulation, with a self-help group who received written instructions of the programme (n = 200). Leakage episodes were significantly reduced in both behavioural training groups versus self-help, and significantly more of the behavioural training (electrical stimulation) group reported 'much better' improvement (versus anorectal feedback) or satisfaction with treatment (versus self-help). No differences were reported in QOL (IIQ, SF-36), or bladder capacity. Vaginal irritation was reported in 6% of the electrical stimulation group.[319] [EL = 1++]

One RCT assigned homebound adults with UI (type unspecified) to different treatment strategies depending on cognitive status: biofeedback-assisted PFMT versus control for the cognitively intact (n = 93; 91% women), or prompted voiding versus control for the cognitively impaired (n = 19; 68% women). Although reported as one trial, this was effectively two separate 8 week trials.[323,324] PFMT was significantly more effective than control in reducing leakage episodes (the only outcome reported).[323][EL = 1+]

Recommendations

Number	Recommendation
37	If women do not achieve satisfactory benefit from bladder training programmes, the combination of an OAB drug with bladder training should be considered if frequency is a troublesome symptom. **[2006]**

Number	Research recommendation
RR8	A direct comparison of single-component and multicomponent behavioural therapy is required.

5.3.3 Prompted voiding

Prompted voiding and timed voiding are toileting programmes used in people who are not capable of independent toileting, such as the cognitively impaired. Prompted voiding teaches people to initiate their own toileting through requests for help and positive reinforcement from carers.[303] It has been used in institutionalised patients with cognitive and mobility problems. They are asked regularly if they wish to void and only assisted to the toilet when there is a positive response.[326]

Five RCTs compared 1 hourly prompted voiding (three studies[326–329]) or 2 hourly prompted voiding (two studies[324,330]) with usual care, or 'wet checks' only. Four studies were conducted in cognitively impaired elderly nursing home residents,[326–330] and one in homebound adults.[324] One study enrolled women only,[327] while the remainder enrolled both genders although predominantly women.

The findings of the RCTs of prompted voiding were as follows:

- significant benefit with 'functional incidental training', which included daytime 2 hour prompted voiding, in terms of leakage and urine toileting ratio compared with usual care in a 32 week study (n = 190; 84% women)[330][EL = 1+]
- significant reduction in wet episodes versus usual care after 13 weeks' intervention, which appeared to be sustained after a further 22 weeks follow-up; no differences were reported between groups in improvement or self-initiated requests (n = 143; all women)[327] [EL = 1+]
- reductions in leakage and an increase in requests for toileting assistance during the 3 week intervention period versus wet checks only (n = 21; 71% women)[328][EL = 1+]
- reductions in leakage and an increase in toileting into a receptacle over an intervention period of 10–20 days versus usual care (n = 126; 75% women)[326,329] [EL = 1+]
- No differences versus usual care in any outcome (leakage episodes, % wet, or self-initiated toileting) (n = 19; 68% women).[324] [EL = 1+]

None of the studies evaluating prompted voiding considered adverse effects.

A placebo-controlled RCT evaluated the effects of oxybutynin in non-responders to prompted voiding (n = 75; 78% women).[331] Significant improvement in leakage episodes was reported with oxybutynin after 20 days' treatment (40% versus 18% had one or fewer episodes per day). No other outcomes were significantly different (change in leakage episodes, continent voids, volume voided).[331][EL = 1+]

5.3.4 Timed voiding

Timed voiding (scheduled, routine or regular toileting) is a passive toileting assistance programme that is initiated and maintained by a caregiver, for example for patients who cannot participate in independent toileting. Toileting is fixed by time or event, on a regular schedule or on a schedule to match the patient's voiding pattern. The aim is to avoid incontinence episodes rather than restore bladder function.[302]

Three RCTs evaluated timed voiding in cognitively impaired elderly men and women (predominantly women) who were nursing home residents (two studies),[332,333] or had caregiver support at home (one study).[334] The comparator was no active treatment.

One 6 month RCT reported significant reduction in leakage episodes in the intervention group (scheduled toileting according to voiding pattern, mostly about 2 hours, and advice on fluid intake and environment; n = 118, 69% women).[334][EL = 1+] A cluster RCT of 36 weeks' duration reported limited results indicating greater reductions in leakage episodes, with scheduled toileting (toileting within 30

minutes prior to an individual's mean voiding time) but no differences between groups in volume voided (n = 113; 82% women).[332][EL = 1−]

The third RCT compared timed voiding (2 hourly) in combination with antimuscarinic drugs for urgency UI, or PFMT for stress UI, with no active intervention for 8 weeks (n = 278; 83% women). Significant improvements in night-time leakage episodes were reported in the active intervention group, but not in daytime leakage or pad test findings.[333] [EL = 1+]

None of the studies evaluating timed voiding considered adverse effects.

Evidence statements for behavioural therapies

Bladder training is more effective than no treatment in women with urgency or mixed UI, at 6 months follow-up. In women with urgency UI, bladder training had a similar subjective cure rate to oxybutynin after a 6 week programme but adverse effects and relapse rates were lower with bladder training. The combination of oxybutynin or tolterodine and bladder training programmes results in greater reduction in frequency of micturition but has not been shown to lead to further improvements in incontinence. Combination treatment of bladder training together with PFMT may confer a greater short-term benefit to women with stress, urgency or mixed UI, but in the long term combination and monotherapies are equally effective. [EL = 1+]

A wide range of behavioural therapies has been used within multicomponent treatment regimens in women with stress, mixed or urgency UI. All appear to show improvements in leakage episodes over comparators (no active treatment, drug therapy, written instructions, usual care) within a 6 week to 6 month time frame. [EL = 1+] No direct comparisons of single-component behavioural therapy with multicomponent behavioural therapies were identified.

Prompted voiding and timed voiding strategies lead to reduced leakage episodes in cognitively impaired men and women. [EL = 1+]

From evidence to recommendations

Bladder training is less costly than most antimuscarinic drug treatment and is not associated with adverse effects. [EL = 4]

5.5 Neurostimulation

5.5.1 Introduction

Neurostimulation is the alteration of neural pathways by the application of a stimulus (electrical or chemical) to a targeted site of the body. The exact mechanism of neurostimulation is unclear.

Neurostimulation of the sacral nerve roots may be achieved by direct conduction of electrical impulses from a lead implanted into the sacrum (percutaneous sacral neurostimulation [P-SNS]) by transcutaneous neurostimulation (T-SNS) delivered by surface electrodes applied directly over the sacrum in the region of the sacral nerve roots.

An alternative route for stimulation is through the retrograde stimulation of impulses through the posterior tibial nerve. Posterior tibial nerve stimulation may be delivered by surface electrodes (transcutaneous posterior nerve stimulation [T-PTNS]) or using a fine needle inserted close to the actual nerve (percutaneous posterior tibial nerve stimulation [P-PTNS]).

Intra-vaginal or intra-anal electrical stimulation with surface electrodes is another method of stimulating activity of the pelvic floor muscles via their nerve supply. This form of electrical stimulation may also have a neurostimulatory effect on bladder function; the evidence for this intervention can be found in section 3.5.6.

In the literature and in clinical practice, the terminologies for the various forms of neurostimulation are often confused. In the absence of an accredited and agreed naming system, this guideline will refer to each form of stimulation by the method of administration (either transcuteanous or percutaneous) followed by the point of stimulation (either at the sacral nerve or posterior tibial nerve). The four types of neurostimulation covered in this guideline are:

- Transcuteanous sacral nerve stimulation (T-SNS) – see Section 5.5.2

- Percutaneous sacral nerve stimulation (P-SNS) – see Section 8.4
- Transcuteanous posterior tibial nerve stimulation (T-PTNS) – see Section 5.5.3
- Percutaneous posterior tibial nerve stimulation (P-PTNS) – see Section 5.5.4

5.5.2 Transcutaneous sacral nerve stimulation (T-SNS)

Introduction

Transcutaneous sacral nerve stimulation (T-SNS) has historically been referred to as transcutaneous electrical nerve neurostimulation (TENS) in which skin surface electrodes are placed over the dermatomes of S2 to S4 for variable periods of time (estimated to be around 30 to 45 minutes) on a daily basis. A variation of this intervention has evolved where surface electrodes are placed over the posterior tibial nerve. This is covered in the Section 5.5.3.

Review question

In women with OAB (with or without detrusor overactivity) what is the effectiveness of transcutaneous sacral nerve stimulation (T-SNS) compared with no active treatment?

Description of included studies

No new evidence was identified on the efficacy of T-SNS for overactive bladder symptoms and overactive bladder caused by urodynamically proven detrusor overactivity (DO). The description of included studies relates to evidence published in the 2006 guideline only.

Transcutaneous electrical nerve stimulation

One 12 week crossover RCT compared T-SNS with oxybutynin in men and women (70% women) with idiopathic DO (n = 43). Significant improvements in functional capacity and frequency were reported with both treatments. No significant changes in SF-36 parameters were observed. Adverse effects reported were dry mouth, blurred vision and dry skin; these all had a lower incidence in the TENS group.[283] [EL= 1+]

Two case series reported findings of T-SNS over the short term (1–3 weeks) in men and women with OAB (total n = 103, with 84 analysed). These generally indicated improvements in frequency, nocturia and urgency,[284,285] and in urge UI.[285] [EL = 3]

Evidence to recommendations (2013)

The GDG found no new evidence since the 2006 review of T-SNS for the treatment of OAB.

The consensus view, based on the clinical experience and opinion of the GDG members, concluded that this form of transcutaneous electrical nerve stimulation had the least chance of being effective of the four forms of neurostimulation covered in this guideline. The positioning of the surface electrodes over the sacral nerve roots is not considered to be as effective as the stimulation of the posterior tibial nerve.

Furthermore, the clinical opinion of the GDG members was that this form of neurostimulation is unlikely to be effective in clinical practice. The GDG concluded that this type of electrical stimulation is likely to represent a poor use of NHS resources for women with OAB as other more effective treatments are available and should be offered in its place.

Therefore the GDG did not recommend the use of T-SNS for women with OAB but recognised the need for a more robust evaluation of T-SNS for the treatment of OAB.

Recommendations

Number	Recommendation
38	Do not offer transcutaneous sacral nerve stimulation* to treat OAB in women. **[new 2013]**

* This is often known as transcutaneous electrical nerve stimulation (TENS).

5.5.3 Transcutaneous posterior tibial nerve stimulation (T-PTNS)

Introduction

Transcutaneous posterior tibial nerve stimulation (T-PTNS) is carried out by placing surface electrodes over the posterior tibial nerve, normally at the ankle. Although this is the stimulation of the posterior tibial nerve, it should not be confused with the procedure using a needle, commonly known as P-PTNS, which is reviewed in Section 5.5.4.

Review question

In women with OAB symptoms (with or without detrusor overactivity) what is the effectiveness of transcutaneous electrical stimulation of the posterior tibial nerve (T-PTNS) compared with no active treatment?

Description of included studies

Two RCTs were included in this review. The studies compared transcutaneous posterior nerve tibial stimulation with either sham T-PTNS sessions (to control for participant bias) or no treatment (not controlling for participant bias). In one study (Svihra et al., 2002) a 30-minute session of T-PTNS was given once a week for 5 weeks and was compared to 5 mg oxybutynin three times a day or no treatment. In the second study, eight 30-minute sessions twice weekly were compared to sham T-PTNS (Bellette et al., 2009). All participants had overactive bladder symptoms. Neither study reported whether there was detrusor overactivity. Both studies included women only and neither study reported on previous management of OAB.

The mean (standard deviation [SD]) age of participants ranged from 47.73 to 54 years (SD 10.9 and not reported, respectively). Neither study reported on the mean number of incontinence episodes, mean number of urgency episodes or duration of OAB symptoms. The funding source was not reported for Bellette et al., 2009. The study by Svihra et al., 2002 was funded by a government ministry.

Evidence profile

The following GRADE profile shows the evidence for transcutaneous electrical stimulation of the posterior tibial nerve for overactive bladder symptoms compared to sham T-PTNS (no active treatment) or no treatment. One of the studies reported data on absolute rate of symptom reduction per day, psychological outcomes or clinical measures (post-void residual volume).

Table 5.1 GRADE findings for comparison of T-PTNS with no active treatment for overactive bladder

Number of studies	Number of women		Effect		Quality
	Comparator	Control	Relative (95% CI)	Absolute (95% CI)	
Patient satisfaction					
1 (Svihra et al., 2002)	5/9 (55.6%)	0/9 (0%)	RR 11 (0.7 to 173.66)	556 more per 1000 (from 140 more to 811 more)[5]	Low
Self reported rate of absolute symptom reduction: number of episodes of incontinence per day					
No evidence reported					
Self reported rate of absolute symptom reduction: number of episodes of urgency per day					
No evidence reported					
Continence status					
1 (Bellette et al., 2009)	12/21 (57.1%)	6/16 (37.5%)	RR 1.52 (0.73 to 3.17)	195 more per 1000 (from 101 fewer to 814 more)	Very low

Number of studies	Number of women		Effect		Quality
	Comparator	Control	Relative (95% CI)	Absolute (95% CI)	
Incontinence QOL (measured with: OAB-q total score; better indicated by higher values)					
1 (Bellette et al., 2009)	21	16	-	MD 16.02 higher (2.18 to 29.86 higher)	High
Adverse effects					
2 (Bellette et al., 2009); (Svihra et al., 2002)	0/30 (0%)	0/25 (0%)	not pooled	not pooled	High
Psychological outcomes					
No evidence reported					
Post-void residual volume					
No evidence reported					

CI confidence interval, GRA Global Response Assessment, MD minimal difference, QOL quality of life, OAB overactive bladder, T-PTNS transcutaneous posterior tibial nerve stimulation

Evidence statements

Patient satisfaction with treatment

A single RCT showed a clinical benefit in favour of T-PTNS. The evidence for this finding was of low quality.

Self reported rate of absolute symptom reduction: number of episodes of incontinence per day

No studies were identified for this outcome.

Self reported rate of absolute symptom reduction: number of episodes of urgency per day

No studies were identified for this outcome.

Continence status

A single study showed no clinical benefit between T-PTNS and no active treatment. The evidence was of very low quality.

Incontinence-specific quality of life

A single RCT showed a clinical benefit in favour of T-PTNS. The evidence was of high quality.

Adverse effects

A meta-analysis of two RCTs showed no adverse effects for T-PTNS and no adverse effects for no active treatment. The evidence was of high quality.

Psychological outcomes

No studies were identified for this outcome.

Post-void residual volume

No studies were identified for this outcome.

Evidence to recommendations

Relative value placed on the outcomes considered

The GDG considered patient satisfaction to be the primary outcome. However, because of the low sample size in the RCTs available, continence status was considered equally important.

Consideration of clinical benefits and harms

The RCT evidence available for T-PTNS was limited to two small RCT studies comparing T-PTNS with no active treatment. The evidence identified a small benefit in patient satisfaction and incontinence-specific quality of life but no improvement in the other self-reported or clinical outcomes. The wide error margins and small sample sizes meant that the GDG was not confident that the evidence showed an improvement in outcome using T-PTNS.

There were no reported adverse events reported in intervention or control groups of the two RCT studies. The GDG agreed this reflected current clinical practice.

Consideration of health benefits and resource uses

The GDG was of the opinion that the evidence of effectiveness suggests only a negligible improvement in health following treatment with T-PTNS in women with overactive bladder symptoms. Therefore, T-PTNS is very unlikely to be a cost-effective option, despite the low cost of the treatment.

The GDG suggested that T-PTNS use be restricted to a research setting due the lack of evidence of efficacy in the treatment of women with OAB from two small studies. Research is warranted because it is an inexpensive treatment with no reported adverse events that may provide some benefit to some women.

Despite not being recommended in the previous guideline, the GDG noted that in some treatment centres home units delivering T-PTNS continue to be offered on a short-term loan to patients. Since there are no adverse events associated with its use, the GDG's view was that women should be informed that there is no evidence of the clinically significant effectiveness of T-PTNS but that some women have found some satisfactory relief from symptoms using this intervention.

Quality of evidence

The quality of the evidence varied between outcomes and ranged from very low quality to high quality. The GDG judged the evidence to be insufficiently robust to overturn current practice, as recommended in the previous version of the guideline.

Recommendations

Number	Recommendation
39	Explain that there is insufficient evidence to recommend the use of transcutaneous posterior tibial nerve stimulation to treat OAB. **[new 2013]**
40	Do not offer transcutaneous posterior tibial nerve stimulation for OAB. **[new 2013]**

5.5.4 Percutaneous posterior tibial nerve stimulation (P-PTNS)

Introduction

Percutaneous posterior tibial nerve stimulation (P-PTNS) delivers neurostimulation to the S2-S4 roots of the sacral nerve plexus via the posterior tibial nerve. A fine needle is inserted close to the posterior tibial nerve slightly above the ankle and connected to a device delivering an electrical current to stimulate the nerve. Conventionally, a typical treatment would consist of 12 weeks of a single treatment every week lasting for approximately 30 minutes in a clinical setting. Symptoms may recur following withdrawal of treatment and top-up treatments may be required at varying intervals.

Review questions

In women with OAB, what is the effectiveness of percutaneous posterior tibial nerve stimulation (P-PTNS) compared with no active treatment?

In women with OAB, what is the effectiveness of P-PTNS compared with pharmacotherapy?

Description of included studies (evidence from 2006 onwards)

P-PTNS versus sham P-PTNS

Three RCTs were included in this review. They all compared P-PTNS sessions with sham P-PTNS sessions. In one study, a session of 30 minutes of P-PTNS or sham P-PTNS was performed once a week for 12 weeks (Peters et al., 2010). In two studies, a session of 30 minutes of P-PTNS or sham P-PTNS was performed 3 times a week for 4 weeks (Finazzi-Agro et al., 2009; Finazzi-Agro et al., 2010). All participants had OAB and had not responded to previous treatments, including behavioural and rehabilitation therapy and/or OAB drugs, although it was unclear how many women were resistent to each treatment. Detrusor overactivity was the cause of the overactive bladder symptoms in 100% of the population reported in one study (Finazzi-Agro et al., 2010). Detrusor overactivity was not reported in the remaining two studies (Finazzi-Agro et al., 2009; Peters et al., 2010). Two studies included women only (Finazzi-Agro et al., 2009; Finazzi-Agro et al., 2010). In the remaining study 79% of participants were women (Peters et al., 2010).

The mean age of participants ranged from 42 ± 7 to 62.5 years (SD not reported). The mean number of incontinence episodes per day at baseline in one study was 3.1 ± 3.5 to 3.4 ± 3.5 (Peters et al., 2010) and the mean number of incontinence episodes over 3 days in one study was 4.1 ± 1.8 to 4.2 ± 2.1. The mean number of urgency episodes per day at baseline in one study was 8.2 ± 4.5 to 8.5 ± 4.2 (Peters et al., 2010). The mean duration of symptoms reported in two studies ranged from 1.7 years (SD not reported) to 10.2 ± 11.5 years (Finazzi-Agro et al., 2009; Peters et al., 2010).

All three studies (Finazzi-Agro et al., 2009; Finazzi-Agro et al., 2010; Peters et al., 2010) were funded or supported by Uroplasty Inc.

P-PTNS versus OAB drugs

A single study (Peters et al., 2009) was included in this review. P-PTNS was performed once a week for 12 weeks and was compared with extended release tolterodine 4 mg. 94% of participants were women but the number with detrusor overactivity was not reported.

The mean age of participants ranged from 57.9 ± 23.3 years and the mean duration of symptoms was 9.6 ± 12.1 years. The mean number of incontinence episodes per day and mean number of urgency episodes per day were not reported.

The study was supported by Uroplasty Inc.

Evidence profiles

The following GRADE profiles show the evidence for P-PTNS for overactive bladder compared with sham P-PTNS (Table 5.2) and compared with drugs (Table 5.3) by outcome in order of GDG ranked importance.

Table 5.2 GRADE findings for comparison of P-PTNS with sham P-PTNS for overactive bladder

Number of studies	Number of women		Effect		Quality
	Comparator	Control	Relative (95% CI)	Absolute (95% CI)	
Patient satisfaction with treatment (follow-up 1 week[1]; assessed with: Global Response Assessment [GRA])					
1 (Peters et al., 2010)	60/110 (54.5%)	23/110 (20.9%)	RR 2.61 (1.75 to 3.9)	337 more women per 1000 (from 157 more to 606 more women)	High

Number of studies	Number of women		Effect		Quality
	Comparator	Control	Relative (95% CI)	Absolute (95% CI)	
Incontinence episodes (follow-up 1 week; measured with: 3-day voiding diary; better indicated by lower values)					
1 (Peters et al., 2010)	N = 103 (from a mean of 3.4 episodes at baseline to 1.4 episodes at endpoint)	N = 105 (from a mean of 3.1 episodes at baseline to 1.9 episodes at endpoint)	-	0.5 (MD) fewer episodes per day (range 1.18 fewer to 0.18 more episodes)	High
Urgency episodes (follow-up 1 week; measured with: 3-day voiding diary; Better indicated by lower values)					
1 (Peters et al., 2010)	N = 103 (change from 8.5 mean episodes at baseline to 4.6 mean episodes at endpoint)	N = 105 (change from 8.2 mean episodes at baseline to 6.1 mean episodes at endpoint)	-	1.5 (MD) fewer episodes per day (range 2.56 to 0.44 fewer episodes)	High
Continence status (after 12 sessions; assessed with: 3-day voiding diary)					
2 (Finazzi-Agro et al., 2009; Finazzi-Agro et al., 2010)	22/34 (64.7%)	0/25 (0%)	RR 16.15 (2.33 to 111.79)	667 more women per 1000 (444 to 802 more women)	Moderate
Incontinence QOL (follow-up 1 week; measured with: Overactive Bladder Questionnaire (OAB-q)[13]; Better indicated by lower values)					
1 (Peters et al., 2010)	N = 101 (change from baseline to endpoint = −36.7 points)	N = 102 (change from baseline to endpoint = −29.2 points)	-	7.5 points (MD) improvement on OAB-q scale (range 13.21 to 1.79 lower)	Moderate
Adverse effects					
2 (Finazzi-Agro et al., 2010; Peters et al., 2010)	6/128 (4.7%)	0/127 (0%)	RR 13 (0.74 to 228)	47 more women per 1000 (range 8 to 99 more women)	Low
Psychological outcomes					
No evidence reported					
Post-void residual volume					
No evidence reported					

[1] Outcome measurement was performed in week 13 after 12 weeks of P-PTNS or sham treatment

CI confidence interval, GRA Global Response Assessment, QOL quality of life, MD minimal difference, OAB overactive bladder, OAB-q overactive bladder questionnaire, P-PTNS percautaneous posterior tibial nerve stimulation, RR relative risk

Evidence statements – P-PTNS versus sham P-PTNS for OAB

Patient satisfaction with treatment

A single RCT showed a clinical benefit in favour of P-PTNS. The evidence for this finding was of high quality.

Self reported rate of absolute symptom reduction: number of episodes of incontinence per day

A single RCT showed no difference in clinical benefit between P-PTNS and sham P-PTNS. The evidence was of high quality.

Self reported rate of absolute symptom reduction: number of episodes of urgency per day

A single RCT showed no difference in clinical benefit between P-PTNS and sham P-PTNS. The evidence was of high quality.

Continence status (defined as more than 50% reduction in incontinence episodes)

A meta-analysis of two RCTs showed a clinical benefit in favour of P-PTNS. The evidence was of moderate quality.

Incontinence-specific quality of life

A single RCT showed a clinical benefit in favour of P-PTNS. The evidence was of moderate quality.

Adverse effects

A meta-analysis of two RCTs showed that fewer adverse effects were associated with sham P-PTNS. The evidence was of low quality.

Psychological outcomes

No studies were identified for this outcome.

Post-void residual volume

No studies were identified for this outcome.

Table 5.3 GRADE findings for comparison of P-PTNS with OAB drugs (extended-release tolterodine, 4 mg) for women with overactive bladder

Number of studies	Number of women		Effect		Quality
	Comparator	Control	Relative (95% CI)	Absolute (95% CI)	
Patient satisfaction with treatment					
No evidence reported					
Self reported rate of absolute symptom reduction: number of episodes of incontinence per day					
1 (Peters et al., 2009)	2/50 (4%)	2/50 (4%)	RR 1 (0.15 to 6.82)	0 fewer per 1000 (from 34 fewer to 233 more)	Moderate
Self reported rate of absolute symptom reduction: number of episodes of urgency per day					
No evidence reported					
Continence status (defined as cured)					
1 (Peters et al., 2009)	2/50 (4%)	2/50 (4%)	RR 1 (0.15 to 6.82)	0 fewer per 1000 (from 34 fewer to 233 more)	Moderate

Number of studies	Number of women		Effect		Quality
	Comparator	Control	Relative (95% CI)	Absolute (95% CI)	
Incontinence QOL (OAB-q scale used, better indicated by higher values)					
1 (Peters et al., 2009)	44	43	-	MD 3.2 higher (5.67 lower to 12.07 higher)	High
Adverse effects					
1 (Peters et al., 2009)	8/49 (16.3%)	7/49 (14.3%)	RR 1.14 (0.43 to 2.59)	20 more per 1000 (from 81 fewer to 227 more)	Low
Psychological outcomes					
No evidence reported					
Post-void residual volume					
No evidence reported					

CI confidence interval, QOL quality of life, OAB overactive bladder, OAB-q overactive bladder, P-PTNS percutaneous posterior tibial nerve stimulation, RR relative risk

Evidence statements – P-PTNS versus drugs for OAB

Patient satisfaction with treatment

No studies were identified for this outcome

Self reported rate of absolute symptom reduction: number of episodes of incontinence per day

A single study showed no clinical benefit for P-PTNS over extended release tolterodine. The evidence was of moderate quality.

Self reported rate of absolute symptom reduction: number of episodes of urgency per day

No studies were identified for this outcome

Continence status (defined as cured)

A single study showed no clinical benefit for P-PTNS over extended release tolterodine. The evidence was of moderate quality.

Incontinence-specific quality of life

A single study showed no clinical benefit for P-PTNS over extended release tolterodine. The evidence was of high quality.

Adverse effects

A single study showed no clinical benefit for P-PTNS over extended release tolterodine. The evidence was of low quality.

Psychological outcomes

No studies were identified for this outcome.

Post-void residual volume

No studies were identified for this outcome.

Percutaneous posterior tibial nerve stimulation versus OAB drug treatment

Percutaneous posterior tibial nerve stimulation was considered in one RCT.[286] The RCT evaluated the effects of oxybutynin 5 mg daily in addition to P-PTNS compared with P-PTNS alone in men and women (n = 43; 88% women). Improvements in frequency, urgency and urge UI episodes were reported for both treatments, with no significant difference between groups in response rates.[286][EL = 3]

Economic evidence

A health economic model was not prioritised for this intervention because the clinical evidence did show sufficient evidence of clinically significant benefit over sham treatment or extended release tolterodine. Health economic studies were identified that compared P-PTNS against other invasive treatments. However, the GDG did not consider P-PTNS to be a comparable to treatment to P-SNS or botulinum toxin A, thus the evidence from these health economic models was not included.

The GDG estimated that the cost of equipment is around £2,000 to 3,000 per unit, with an additional cost of £320 per patient for the percutaneous leads (12 per patient), usually paid in full before treatment begins. The time for a healthcare professional to carry out the procedure was estimated by GDG members to be 15 to 30 minutes for each treatment with monthly follow-up.

Evidence to recommendations

Relative value placed on the outcomes considered

The GDG considered patient satisfaction to be the primary outcome of a successful P-PTNS treatment. The GDG also noted that patient satisfaction is dependent on an individual's treatment goals, which can be influenced (raised or lowered) by the advice of healthcare professionals. For this outcome, it was especially relevant to consider the research context of published studies to ensure that it adequately reflected routine UK practice. Secondary outcomes were continence status and adverse effects, as these are often the most important outcomes to women with OAB and therefore influence their decisions about treatment.

Continence status and adverse events were reported in all studies considered in the review. However, the definition of continence status used in the studies (50% reduction of incontinence episodes) differed from the GDG defined outcome of continence status (zero episodes per day). The data on other outcomes came from only one study, which reported incontinence episodes per day, urgency episodes per day and incontinence-specific quality of life.

Consideration of clinical benefits and harms

Three RCTs were identified which reported a benefit for P-PTNS compared with sham treatment in patient satisfaction, continence status and quality of life. There was no difference reported in episodes of incontinence or urgency.

The reported incidence of adverse effects was low compared with other interventions for OAB. The GDG considered that the low rate of adverse events was an additional benefit, since the alternatives have higher rates of adverse effects that contribute to the high dropout rate at one year. Reported adverse events in Peters et al., 2010 were ankle bruising, discomfort at needle site and tingling in the leg. No adverse events were reported in either group in two of the studies (Finazzi-Agro et al., 2010; Finazzi-Agro et al., 2009).

One RCT (Peters et al., 2009) reported no difference in effectiveness between P-PTNS and the anti-muscarinic drug extended release tolterodine. In order for P-PTNS to be recommended as an alternative, more data is required comparing P-PTNS with a wider range of antimuscarinic drugs in more patients. Furthermore, the evidence was inadequate for inclusion in the network meta-analysis model reported in chapter 6, because the study participants were recruited at a different stage of the pathway. In the P-PTNS studies the majority of the patient population was recruited after failed OAB drug treatment.

The GDG concluded that although some evidence of clinical benefit of P-PTNS versus sham treatment was identified with a minimal adverse event profile, the evidence was equivocal (no evidence of benefit for incontinence or urgency episodes). Furthermore, the GDG noted that the data on continence status may overestimate the benefit because it did not report the proportion of women with zero episodes of incontinence per day ("absolutely dry"). There was also a lack of evidence comparing this with other treatments that could be offered at the same point on the clinical pathway and no evidence of duration of effect of P-PTNS.

Consideration of health benefits and resource uses

The effectiveness of P-PTNS compared with the alternative treatments (which could be OAB drugs, botulinum toxin A or sacral nerve stimulation) has not been evaluated. There was only one RCT

identified that compared P-PTNS with another treatment and that was against extended release tolterodine. This study showed that P-PTNS was no better than Tolterodine ER. The GDG did not prioritise P-PTNS for economic evaluation since it is likely to be a more expensive treatment option than drug therapy (involving more staff time and equipment costs) with little or no additional benefit.

In the absence of comparative evidence, the GDG view was that P-PTNS was very unlikely to be a clinically significant cost-effective alternative to the other treatment options available. However, in the event that a woman chooses not to proceed with invasive treatment following unsuccessful conservative treatment, the GDG considered that P-PTNS may be cost effective when compared with no active treatment.

Quality of evidence

The intervention and population of the included studies met the criteria specified in the systematic review protocol, although the timing of assessment in one study was unclear. The GDG noted that there was a lack of clarity in the studies regarding how many interventions women had failed before being offered P-PTNS. There were few drop-outs in the studies.

The continence status outcome was not reported in the way the GDG had prioritised (that is, the proportion of women who were absolutely dry at a given timepoint). This lowered the quality of evidence for continence status. Furthermore, the values in these studies could not be compared with other interventions, as the measurement of success differed. Finally, where data were pooled from two RCTs, there was a low level of heterogeneity in the outcome.

Given that the outcomes reported were not those prioritised by the GDG outcomes and the potential for bias in the studies included in the review, the GDG considered that the evidence was insufficient to support a positive recommendation for the use of P-PTNS. However, since P-PTNS is a safe intervention with unproven efficacy, it is appropriate for it to be offered in a research setting to improve the evidence base. Furthermore, it may be considered for the limited group of women who choose not to proceed with further treatment or are unable to have other interventions after unsuccessful antimuscarinic drug treatment.

Other considerations

Equalities

The GDG noted that the mean age of the populations studied was too low to be extrapolated to frail older women. The evidence did not reflect this population, which has a high risk of a range of co-morbidities. The GDG also noted that woman with cognitive dysfunction or a neurological disability may be unable to feel pain or translate discomfort into an emotional response. This type of feedback is an important component of treatment with P-PTNS. For this reason, the GDG considered that the recommendation to offer P-PTNS in a research setting should not routinely include this group of women.

NICE interventional procedure guidance 362

The GDG took into account the advice issued in the NICE interventional procedure guidance 362 (IPG362). The GDG members concurred with the decision that the procedure is safe. However, they chose not to recommend P-PTNS based on their assessment of treatment efficacy and cost effectiveness compared with other interventions that can be offered to women with OAB at same stage on the clinical pathway.

Long-term durability of P-PTNS

The GDG considered that a single course of treatment would not always be sufficient and many women may require repeat courses of treatment in the months or years following an initial course of P-PTNS. As the evidence for clinical benefit in the short term did not consistently favour P-PTNS, the longer term benefit of P-PTNS was prioritised for this guideline. Long-term follow-up (of up to 36 months) was reported in an extension of the STEP trial (Peters et al., 2012 and Peters at al., 2012a). This study reported a sustained benefit of P-PTNS when offered 3 times a week for 4 weeks and were continued after an initial 12-session course of treatment. However, a previous study by the same group reported no clear additional benefit beyond that achieved in the initial treatment (Peters et al., 2010).

Role in the care pathway for the treatment of OAB

The GDG concluded that the evidence was not adequate to compare P-PTNS with OAB drugs but that P-PTNS was unlikely to be a cost-effective alternative to OAB drugs after failure of conservative

treatment. Therefore P-PTNS should not be offered as an alternative to drugs for OAB at this stage of the treatment pathway.

The GDG discussed the appropriate comparators for P-PTNS and concluded that, in most NHS settings, these would be P-SNS or botulinum toxin A. After reviewing the evidence for these treatments, the GDG found that P-SNS and botulinum toxin A were both effective compared with placebo (or control) comparators. In contrast, P-PTNS was not found to be sufficiently effective compared with placebo (or control) comparators. In the absence of RCT data directly comparing the clinical effectiveness of P-PTNS with either botulinum toxin A or P-SNS, the GDG considered that P-PTNS should not recommended. However, the GDG did note that studies of P-PTNS indicated some limited evidence of effectiveness and that P-PTNS is also associated with minimal adverse events. Therefore the GDG view was that P-PTNS may be offered as an alternative to botulinum toxin A or P-SNS after unsuccessful OAB drug treatment, but only if botulinum toxin A and P-SNS were not acceptable to the woman for any reason.

The GDG concluded that the information offered to women following unsuccessful drug treatment should include all the options that are available to them. Women should be told that P-PTNS has limited evidence of benefit and is less likely to be effective than botulinum toxin A or P-SNS. P-PTNS should only be considered if a woman is unwilling or unable to undertake further invasive treatment. If P-PTNS is a woman's preferred option, it should only be initiated after multidisciplinary team (MDT) referral and urodynamic testing.

Since the GDG did not recommend the routine use of P-PTNS in any clinical setting, it does not form any part of the standard care pathway for the treatment of OAB.

Recommendations

Number	Recommendation
41	Do not offer percutaneous posterior tibial nerve stimulation for OAB unless: • there has been a multidisciplinary team (MDT) review, **and** • conservative management including OAB drug treatment has not worked adequately, **and** • the woman does not want botulinum toxin A* or percutaneous sacral nerve stimulation. **[new 2013]**
42	Explain that there is insufficient evidence to recommend the use of percutaneous posterior tibial nerve stimulation to routinely treat OAB. **[new 2013]**

Number	Research recommendations
RR9	What is the comparative effectiveness and cost-effectiveness of transcutaneous stimulation of the sacral nerve roots, and transcutaneous and percutaneous posterior tibial nerve stimulation for the treatment of OAB? Why this is important Transcutaneous neurostimulation can be applied either over the sacrum or over the posterior tibial nerve to modulate the sacral nerve supply to the bladder. The treatment uses surface electrodes and the woman can carry it out in her own home. Percutaneous posterior tibial nerve stimulation involves the introduction of a needle in the region of the posterior tibial nerve near the ankle, and at present is carried out in clinics in secondary care. Currently, it is offered widely as a conservative treatment for OAB without adequate evidence that it is effective. Although this is a

* At the time of publication (September 2013), most Botulinum toxin type A preparations did not have a UK marketing authorisation for this indication. Evidence was only available for the licensed Botulinum toxin A (BOTOX, Allergan) preparation

relatively low cost treatment, both the equipment and staff time have a cost implication, and because it has been widely used in conservative management this has large resource consequences for the NHS. Robust evidence is needed to establish whether it is a cost-effective option relative to other conservative therapies for all women or for a selected group of patients who are unsuitable for or have unsuccessful botulinum toxin A, percutaneous sacral nerve stimulation or OAB drug treatment.

5.6 Alternative conservative management options

This section covers the use of products that collect or contain leakage (e.g. absorbent products, urinals and toileting aids, catheters) and products used to prevent leakage (e.g. devices that support the bladder neck, intra- or extraurethral devices).

Studies considered for the non-therapeutic interventions section

Little primary research evidence was identified that addressed the guideline questions. No studies were identified that evaluated the effects of containment on maintenance of independent living, rates of institutionalism, or return to work, and only one study considered QOL (an evaluation of pessaries for UI, described below). Published consensus statements and narrative reviews that discussed issues relevant to the circumstances of use of containment products, or catheterisation, were used as a basis for the recommendations.[32,451–453][EL = 4]

5.6.1 Absorbent products, urinals and toileting aids

One RCT compared a conservative management strategy with the use of absorbent products (pads and pants) for 6 months (n = 90). Conservative management involved providing estriol (depending on oestrogen status), PFMT (six training sessions), bladder training (for urge or mixed UI), electrical stimulation, and pads and pants. Significantly greater reductions in UI severity and impact, and leakage episodes, were seen with conservative management compared with the control group. No significant differences were seen between groups in frequency. The pads and pants arm showed no change in incontinence impact at 6 months.[454] [EL = 1+]

Evidence statement for absorbent products, urinals and toileting aids

Pads and pants are ineffective in the treatment of UI. [EL = 1+] There is no evidence to support the use of hand-held urinals and toileting aids in the treatment of UI. There is a variety of such products available. There is a lack of evidence for their use in management. However, they are used by women in maintaining social continence. [EL = 4]

From evidence to recommendation

The GDG recognises that some women may not wish to pursue active interventions for UI and that absorbent products, urinals and toileting aids are an alternative management option in such circumstances. However, the GDG felt that women must be fully aware of all possible treatment options before adopting this course of action. In addition, the GDG agreed that the use of these products should be considered for women awaiting definitive treatment.

Recommendations

Number	Recommendation
43	Absorbent products, hand held urinals and toileting aids should not be considered as a treatment for UI. Use them only as: • a coping strategy pending definitive treatment • an adjunct to ongoing therapy • long-term management of UI only after treatment options have been explored. **[2006]**

5.6.2 Catheters

The care of patients with long-term urinary catheters is covered within the NICE clinical guideline Infection Control: Prevention of Healthcare-Associated Infection in Primary and Community Care.[22] Within that guideline, the recommendation that intermittent catheterisation is preferred to indwelling catheterisation was informed by a systematic review of risk factors for UTI, in adults with spinal cord dysfunction. The GDG's view is that the evidence relating to adults with spinal cord dysfunction is relevant to the use of catheters in women with idiopathic UI.[455] The systematic review found eight cohort studies that considered risk of infection according to type of catheter used by men and/or women with spinal cord injuries. In seven of eight studies, patients using intermittent catheters had fewer infections or lower prevalence of bacteriuria than those who used indwelling catheters (follow-up ranging from about 1 to 2.5 years). However, none of the primary studies adjusted for baseline differences between groups (total n = 1153). [EL = 2+]

Evidence statement for catheters

Intermittent catheterisation is associated with reduced risk of UTI compared with indwelling catheterisation. [EL = 2+]

From evidence to recommendations

In the absence of evidence on long-term catheterisation in women, but alongside the systematic review described, the GDG considered that suprapubic catheterisation is preferable to indwelling urethral catheterisation owing to reduced risk of urethral and other complications (symptomatic UTI, and 'bypassing'). Suprapubic catheterisation is not without risk, particularly at initial insertion, although the benefits and risks of this approach have not been fully established. Long-term medical management of suprapubic catheterisation may be problematic if healthcare providers lack knowledge and expertise in this area, and if the homebound patient lacks rapid access to medical care if a problem arises.

The population for whom catheterisation is recommended was also determined by GDG consensus.

The GDG feels that the use of an indwelling catheter in a woman with OAB may be associated with an increase in detrusor activity and therefore an increased tendency to 'bypassing' (urine leakage around the catheter). Assuming they empty their bladder completely, as most patients with idiopathic DO will, a catheter is unlikely to achieve continence.

Recommendations

Number	Recommendation
44	Bladder catheterisation (intermittent or indwelling urethral or suprapubic) should be considered for women in whom persistent urinary retention is causing incontinence, symptomatic infections, or renal dysfunction, and in whom this cannot otherwise be corrected. Healthcare professionals should be aware, and explain to women, that the use of indwelling catheters in urgency UI may not result in continence. **[2006]**
	Intermittent urethral catheters
45	Offer intermittent urethral catheterisation to women with urinary retention who can be taught to self-catheterise or who have a carer who can perform the technique. **[2006]**
	Indwelling urethral catheters
46	Give careful consideration to the impact of long-term indwelling urethral catheterisation. Discuss the practicalities, benefits and risks with the patient or, if appropriate, her carer. Indications for the use of long-term indwelling urethral catheters for women with UI include: • chronic urinary retention in women who are unable to manage intermittent self-catheterisation • skin wounds, pressure ulcers or irritations that are being contaminated by urine • distress or disruption caused by bed and clothing changes

- where a woman expresses a preference for this form of management. **[2006]**

Indwelling suprapubic catheters

47 Indwelling suprapubic catheters should be considered as an alternative to long-term urethral catheters. Be aware, and explain to women, that they may be associated with lower rates of symptomatic UTI, 'bypassing', and urethral complications than indwelling urethral catheters. **[2006]**

5.6.3 Products to prevent leakage

Studies reporting the use of the following products were identified:

- intravaginal devices: Continence Guard (also known as the ConveenContiguard),[456–462] Contrelle® continence tampon,[462] Contiform®,[463] bladder neck support prosthesis (Introl)[464]
- meatal devices: FemAssist®,[465,466] CapSure® shield,[467]Miniguard[468–470] (also called 'continence control pad'/Impress Softpatch[471])
- intraurethral devices: a urethral plug[472,473] (the ViVa Plug, also called Alive[474]), FemSoft® insert,[475] Reliance®[476,477] (one of the studies was a controlled trial versus NEAT).[478]

Two of these products are known to be available or could be obtained by women in the UK (Contrelle® Activgard [formerly known as Conveen Contiguard, or Continence Guard], and FemSoft®). Neither product can be provided on NHS prescription. The Rocket® incontinence device is also available, but no studies were found regarding its use. Many of the other products listed are known to have been withdrawn from the UK market for commercial reasons (FemAssist®, CapSure®,[479] Reliance®).

While there is no evidence to support the use of menstrual tampons in the management of UI, GDG members are aware that menstrual tampons are used by many women to support the bladder neck and to prevent leakage. Manufacturers of these products do not recommend this usage and state that they should be used only during menstruation.

Evidence relating to the use of the available products

A case series of women with stress or mixed UI who used FemSoft® (mean follow-up 15 months), reported that leakage episodes were fewer and more pad tests were negative with the device in place, compared with without the device. Symptomatic UTI was very common (47%), and the incidence of insertion trauma, haematuria, spotting, cystoscopic evidence of bladder or urethral irritation or trauma and device migration were common (n = 150).[480] [EL = 3]

Four case series[456–459,461] (patient numbers ranging from 15 to 38) and one crossover RCT[462] (n = 94; 62 completed and analysed) found that the majority of users of the Continence Guard reported cure or improvement (57–89%) after 3–5 weeks' treatment (up to 1 year in one study). Adverse effects reported were expulsion of the device (8–47%),[456,457,462] voiding difficulties (11– 14%),[456,457,462] UTI (11%)[458] and vaginal irritation (23%).[462] Three studies found no vaginal irritation or erosion on gynaecological examination.[456–459] No adverse effects were reported in two studies.[459,461]

Evidence statement for products to prevent leakage

There is limited evidence of efficacy for Contrelle®Activgard (formerly known as the Continence Guard or ConveenContiguard) and FemSoft® in the management of UI. Adverse effects, in particular UTI, are very common. [EL = 3]

From evidence to recommendation

In the GDG's view, some women find these products beneficial for occasional use in certain circumstances as a preventive strategy.

Recommendations

Number	Recommendation
48	Do not use intravaginal and intraurethral devices for the routine management of UI in women. Do not advise women to consider such devices other than for occasional use when necessary to prevent leakage, for example during physical exercise. **[2006]**

5.6.4 Pessaries

A small case series reported that QOL improved (IIQ) in women with stress or mixed UI and pelvic organ prolapse (POP) who used a ring pessary with diaphragm for 1 year (six of 38 women enrolled).[481][EL = 3]

Evidence statement for pessaries

The limited evidence available does not support the use of ring pessaries for the treatment of UI in women whether or not there is prolapse present. [EL = 3]

5.7 Complementary therapies

Women who do not find conventional treatments acceptable often explore the use of complementary therapies for UI, and as adjuncts to conventional treatments.

Studies considered for the complementary therapies section

Most of the articles identified reported the use of acupuncture or hypnotherapy for UI, or were narrative reviews regarding the use of complementary therapies for UI. Use of traditional Chinese medicines was also mentioned in a narrative review, but no further references to their use for UI were found.[482]

5.7.1 Acupuncture

Three RCTs[483–486] and three case series[487–490] evaluated the use of acupuncture for UI or OAB in women. Across these studies, the acupuncture points and duration of stimulation used varied. Duration of treatment ranged from 2 to 4 weeks. All were considered to be of poor quality because of lack of information or for only analysing results for women who completed treatment.

One RCT assessed the effects of daily acupuncture at acupoints Sp-6 and St-36 on nocturnal frequency in elderly people on long-stay hospital wards. The median reduction in frequency in the acupuncture group after 2 weeks' treatment (20 minutes per day) was −2.0 (95% CI −1.0 to −3.0). No significant change was seen in the placebo group, who received mock TENS. Two publications of this RCT were identified; one stated that 15 of the 20 studied were women, another stated that 17 were women.[483,484] [EL = 1−]

The acupuncture treatment given in the second RCT, to women with stress UI, depended on what the deficiency was considered to be. A total of 30 sessions were given every other day. Significantly more women treated with acupuncture than placebo were improved (assessed clinically and urodynamically) after treatment.[485] [EL = 1−]

An RCT in women with OAB with urgency UI reported significant improvements in frequency, urgency and QOL (UDI and IIQ) after 4 weeks' acupuncture treatment compared with placebo acupuncture (designed for relaxation). Changes in leakage episodes were not significantly different between groups. Adverse effects reported were bruising or bleeding from acupuncture sites (23%) and minor discomfort on needle placement (25%) (n = 85; 74 analysed).[486] [EL = 1−]

Case series

Three case series evaluated acupuncture for UI or OAB in a total of 87 patients (84 women).[487–489,491] The symptoms being treated were frequency, urgency and dysuria,[487] 'lower urinary tract symptoms'[489] and urgency or mixed UI.[491] Treatment consisted of a single session, or 6 or 12 weeks' regular treatment. The acupuncture points used also varied across studies.

Symptomatic improvement was reported in 53–60% of patients (assessed at 3 or 8 months).[487–489,491] No adverse effects were reported. Longer term follow-up (about 5 years) of 21 patients show that symptoms recur, and that repeated treatment may be necessary.[488] [EL = 3]

5.7.2 Hypnosis

The studies identified in relation to hypnotherapy in women with UI consisted of case series and case reports.

In the largest case series of women with incontinence due to DO, they underwent 12 sessions of hypnotherapy over 1 month, which involved symptom removal by direct suggestion and 'ego strengthening'. At the end of the 12 sessions, the majority of women were subjectively cured or improved, with the remainder unchanged (n = 50). Objective cure or improvement (on cystometry) was seen in the majority at 3 months (n = 44).[492] Limited follow-up data at 2 years for 30 of the women have been reported. Of the women who were subjectively or objectively cured at 3 months, fewer than half remained cured (n = 30).[493] [EL = 3]

In another publication, four cases (three women) of hypnotherapy for DO were reported. Hypnotherapy involved three 1 hour sessions, including anxiety control methods, ego strengthening, training in self-hypnosis, age progression, explanation of stable bladder function and 'handon-abdomen technique'. Two of the three women reported remission of symptoms at 6 months.[494] [EL = 3] A report of two women with UI who were 'successfully' treated with hypnotic techniques and waking counselling was also identified.[495] [EL = 3]

5.7.3 Herbal medicines

One report described the use of a tablet preparation containing crataeva (Crataevanurvala, a herb used in traditional Hindu science of medicine) and equisetum (horsetail) to treat women with symptoms of urgency and/or stress UI for 12 weeks (n = 8). Quality of life (UDI) showed significant positive change to perceptions of frequency, leakage related to urgency or activity and difficulty emptying the bladder. All parameters of the IIQ questionnaire except physical recreation and household chores improved significantly.[496] [EL = 3]

Evidence statements for complementary therapies

Poor-quality evidence shows that acupuncture may reduce nocturia and both stress and urgency incontinence in the short term (up to 4 weeks) but it is unclear whether any particular acupuncture treatment is more effective than others. [EL = 3]

There is limited evidence that hypnotherapy for women with UI secondary to detrusor overactivity offers some benefit over the short term (up to 6 months). About half of women relapsed over a 2 year period. [EL = 3] There is a lack of evidence on herbal medicines for UI or OAB.

The GDG recognises that, despite the limited and poor-quality evidence available, some women may wish to explore complementary therapies for their incontinence [EL = 4].

Recommendations

Number	Recommendation
49	Do not recommend complementary therapies for the treatment of UI or OAB. **[2006]**

5.8 Preventive use of conservative therapies

Studies considered for this section

Evidence described in this section is derived from RCTs. Two systematic reviews of the use of physical therapies for prevention of UI were identified.[497,498] The RCTs within these systematic reviews were considered individually if they addressed effectiveness. Any further RCTs identified are also included here.

No studies were identified that evaluated the use of lifestyle interventions for prevention of UI or OAB.

5.8.1 Behavioural therapy

One RCT evaluated a multicomponent behavioural modification programme comprising initial education, PFMT and bladder training in older women who had no UI (39%) or minimal UI (defined as one to five wet days in the previous year) (n = 480 randomised; 359 analysed). At 1 year follow-up, significantly more women maintained or improved their continence status compared with an untreated control group. Significantly greater improvements in frequency and voiding interval were also seen in the behavioural modification group versus control. Adverse effects were not considered.[499,500] [EL = -1]

5.8.2 Physical therapies

Preventive use during pregnancy

Four RCTs compared more structured PFMT with usual care during pregnancy (from weeks 18 or 20) in women in their first pregnancy.[501–504] One study enrolled women with increased bladder neck mobility,[501] which has been shown to be predictive of postnatal stress UI.[505] Women with UI were excluded from one study,[501] whereas in two studies between 25% and 32% had UI at baseline.[503,504] Between 72 and 1169 women were enrolled in these studies (total n = 1810); the proportion completing follow-up or responding to questionnaire follow-up was noted to be low in three studies (64–86%).

The PFMT programmes involved daily exercises with between 42 and 72 contractions.[501–504] The individual's ability to contract the pelvic floor muscle was checked at baseline. The comparison group was 'usual care' in each study, which comprised: 'usual' information from midwife or GP;[503] routine antenatal care (likely to have received verbal advice on pelvic floor exercises);[501] and routine care, no systematic PFMT programme.[502,504] Two of the studies reported that women in the control group also undertook PFMT regularly (20%[502] and 51%[501]).

In the first study, significantly fewer women who had been randomised to a 12 week PFMT programme reported UI at the end of treatment, and at 3 months postpartum, compared with those receiving usual care. Greater benefit was seen with PFMT in the number of leakage episodes and in pelvic floor muscle strength. No adverse effects were reported.[503][EL = 1++]

In a study of women with increased bladder neck mobility, significantly fewer reported stress UI or had a positive 1 hour pad test at 3 months postpartum, after a structured PFMT programme, compared with those receiving usual care. No significant differences were seen between groups in changes in bladder neck mobility, pelvic floor muscle strength or in QOL (KHQ). Women in the PFMT group had significantly higher scores in the general health domain of SF-36 compared with the usual care group.[501] [EL = 1+]

No numerical data were reported in the third RCT, although the authors noted that no significant differences were seen between groups in UI or pelvic floor muscle strength at 12 months postpartum (n = 46). Adverse effects were not considered.[502] [EL = 1−]

The largest study considered risk of urinary outcomes during the antenatal period and up to 6 months postpartum. At antenatal week 36, there was a trend towards reduced risk of any type of UI and of fewer leakage episodes in the PFMT group, although no difference between groups was statistically significant. At 6 months postpartum, differences between groups were less, again with none being significant (n = 1169).[504][EL = 1+]

Preventive use after pregnancy

Four controlled trials evaluated PFMT for the prevention of UI in postpartum women. UI was reported by 17–32% of women across all studies at baseline.[506–509] The intervention was started 24 or 48 hours after delivery in primi- or multiparous women in two RCTs.[506,507] A more structured 4 or 8 week PFMT programme was compared with usual care in both studies. At 3 months postpartum, the following results were seen:

- significantly lower prevalence of UI in the PFMT group following the 8 week treatment programme (n = 676); this difference was not sustained at 1 year (n = 569)[510][EL = 1+]
- no significant differences in UI prevalence between groups following the 4 week treatment programme (n = 1609; 89% of those randomised).[507] [EL = 1−]

A further two studies (one RCT,[509] one cohort[508]) recruited women 8 weeks postpartum. The RCT compared a 6 week programme of PFMT with biofeedback and electrical stimulation, with usual care in primiparous women (n = 107). Stress UI prevalence was not significantly different between groups at 10 months postpartum. However, the prevalence of stress UI differed between groups at baseline (31% PFMT versus 16% control), which was not accounted for in the analysis at 10 months.[509] [EL = 1−]

The cohort study reported a significantly lower stress UI prevalence in women (41% of whom had UI at baseline) who had undergone a structured 8 week PFMT programme compared with usual care, both at the end of the intervention (n = 198)[508] and at 1 year postpartum (n = 162).[511] No significant differences were found between groups in leakage index or social activity index. [EL = 2+]

Evidence statement for preventive use of physical therapies

There is evidence that PFMT used during a first pregnancy reduces the prevalence of UI at 3 months following delivery. [EL = 1+] The effects in the longer term are inconsistent and the impact of subsequent pregnancies unknown. [EL = 4]

Recommendations

Number	Recommendation
50	Offer pelvic floor muscle training to women in their first pregnancy as a preventive strategy for UI. **[2006]**

Number	Research recommendation
R10	Further studies need to be undertaken to evaluate the role and effectiveness of physical and behavioural therapies and lifestyle modifications in the prevention of UI in women. Long-term outcomes in particular should be evaluated.

5.9 Optimal sequence and timescales for conservative therapies

The GDG's view was that conservative management should be pursued prior to surgical procedures in the treatment of UI. The factors affecting the GDG's decisions regarding first-line conservative therapies are summarised below.

For stress UI, the GDG considered the cost effectiveness of PFMT and duloxetine as first-line treatment. The conclusion was that PFMT dominated and it was therefore recommended as the first-line intervention for stress UI.

For OAB (with or without urgency UI), cost minimisation was used to determine whether bladder training or antimuscarinic drug treatment should be offered as first-line treatment. Bladder training was recommended as the first-line intervention as it is less costly and not associated with adverse effects.

In the GDG's view, the management of mixed UI depends upon which symptom predominates (i.e. stress or urgency UI).

In the absence of evidence for optimal duration of treatment, the GDG considered that a 3 month trial period of PFMT is sufficient to determine whether treatment is effective and tolerated. A shorter trial period of 6 weeks would usually be appropriate for bladder training.

5.10 Progression of treatment

If a woman has had a period of unsuccessful conservative treatment then conventionally more invasive alternative interventions are considered. Over time, if optimal symptom management is not achieved, more aggressive procedures can be offered, some with a higher risk of adverse events, others requiring life-long care. No evidence was reviewed for the pathway of treatment; the GDG felt it was necessary to make recommendations for women who wish to continue their treatment and those who do not. The following text and recommendation, therefore, is based on the expert opinion and current clinical practice of the GDG members.

Throughout the guideline, and specifically following OAB drug treatment (see section 6.1), recommendations have addressed the needs of women who do not wish to continue treatment. The provisions are two-fold. First, the GDG recommended that if a woman did not wish to progress to more invasive treatment, the management of symptoms with conservative therapies should not cease as long as they continue to provide some benefit. The woman should remain within the healthcare system and provided with information about the options for continued management, recognising that women's needs and preferences will change over time.

The second point is that women who opt out of further treatment should have the option to recommence treatment should they wish to do so. Treatment should start without having to repeat earlier interventions if they were unsuccessful. The review should take place at the same point of care where treatment was last received, depending on local clinical pathways.

Recommendations

Number	Recommendation
51	If a woman chooses not to have further treatment for urinary incontinence: • offer her advice about managing urinary symptoms, **and** • explain that if she changes her mind at a later date she can book a review appointment to discuss past tests and interventions and reconsider her treatment options. **[new 2013]**

2013 Update

2013 Update

6 Pharmacological therapies

6.1 OAB drugs

6.1.1 Introduction

Drugs with antimuscarinic action are used to treat overactive bladder (OAB). They block muscarinic receptors in the bladder, which reduces the ability of the bladder muscle to contract and affects bladder sensation, reducing urinary urgency and the related symptoms of urgency incontinence, frequency and nocturia. The drugs differ in their selectivity for various muscarinic receptors, and some drugs have additional actions, such as direct smooth muscle effects.

Women who present with OAB may be categorised into one of two groups: 'OAB wet' and 'OAB dry'. OAB dry is diagnosed in women who experience urgency but remain continent. OAB wet is diagnosed when urgency is also present but the predominant symptom is the woman's incontinence. OAB wet and dry may be on a continuum of severity and the difference between the conditions is debateable. Most OAB drugs are designed to treat urgency as well incontinence. One of the aims of the review was to ascertain if specific recommendations should be made for each diagnosis and in order to facilitate this we considered two separate categories under continence status as follows; zero incontinence episodes per day and zero urgency episodes per day for this review.

Discussion of the interpretation of the evidence for treating OAB wet and OAB dry is presented in the evidence to recommendations section at the end of the chapter. .

The chapter includes the following reviews:

- The existing review from the 2006 guideline that compared OAB drugs with placebo in clinical trials. The review provided evidence that flavoxate, imipramine, other tricyclic antidepressants and propantheline offered little or no improvement and they were not recommended. That evidence has not been updated and is presented again in this chapter. All other OAB drugs reviewed in the 2006 guideline or introduced since 2006 have been included in an updated review in this chapter.
- A comparative review of OAB drugs incorporating reviews of conventional placebo controlled trials and head-to-head studies (direct evidence) and a network meta-analysis (indirect evidence). The network meta-analysis included placebo-controlled and head-to head trials.
- A health economic analysis incorporating the clinical data derived from the network meta-analysis.

6.1.2 Placebo-controlled trials of OAB drugs not recommended in original guideline

Flavoxate

Two double-blind (DB) placebo-controlled crossover randomised controlled trials (RCTs) evaluated 2 weeks of treatment with flavoxate for idiopathic detrusor overactivity (DO).[345,346] The first RCT in men and women (n = 41; only 25 analysed; 48% women) found no significant differences between flavoxate 200 mg three times a day and placebo in any urodynamic parameters. Complete results were not given for frequency, the only other outcome.[345] [EL = 1−] The second RCT, in women only, found no significant differences between flavoxate 200 mg taken for times a day and placebo in frequency (median per three days 25 versus 23), nocturia (medians 3 versus 0), or leakage episodes (medians 1

versus 0) after treatment (n = 20). The most common adverse effects reported across all treatment groups were dry mouth (5–7%), and nausea or heartburn (2–7%).[346] [EL = 1+]

A DB randomised study compared two different daily doses of flavoxate (600 or 1200 mg), given for 4 weeks to women with sensory and/or motor urge syndrome or incontinence (n = 27). Symptoms were scored on a scale of 0 to 2; no results were provided for individual symptoms although it was reported that total scores fell from baseline in both groups. Of the urodynamic variables evaluated, greater benefit was seen with the 1200 mg dose in volume at first desire to void and in bladder volume at capacity. Nausea was reported by about 22% of the women.[347] [EL = 1−]

A further RCT compared a combination of flavoxate and imipramine with bladder training. Significantly more women were subjectively or objectively cured after 4 weeks' bladder training than with drug therapy (n = 50).[307][EL = 1+]

Imipramine and other tricyclic antidepressants

No placebo-controlled RCTs evaluating the use of imipramine for urinary incontinence (UI) were identified. A DB placebo-controlled crossover RCT involving 3 week treatment periods evaluated doxepin (50–75 mg at night) in women with DO and frequency, urgency or urge UI, who had failed to respond to other drugs, mainly antimuscarinics (n = 19). Significantly greater reduction in night leakage episodes and frequency were seen with doxepin compared with placebo, and a greater increase in maximum cystometric capacity. No significant differences were reported between groups in day leakage episodes, frequency or the 1 hour pad test. More doxepin-treated women reported adverse effects than those treated with placebo (68% versus 16%).[348] [EL = 1+]

Propantheline

No placebo-controlled studies were identified for propantheline.

Evidence statements for OAB drugs not recommended in original guideline

There is limited evidence that doxepin reduces night-time leakage episodes and nocturia. [EL = 1+]

There is no evidence of efficacy for the use of flavoxate, propantheline or imipramine for the treatment of UI or OAB. [EL = 4]

Recommendations

Number	Recommendation
56	Do not use flavoxate, propantheline and imipramine for the treatment of UI or OAB in women. **[2006]**

6.1.3 Head-to-head comparison of OAB drugs

Introduction

A head-to-head review was undertaken to identify evidence for the seven outcomes prioritised by the guideline development group (GDG). Once this was completed it was apparent that there were too few studies to allow the GDG to draw conclusions about the superiority of any drug over another. A review of placebo-controlled trials was then undertaken so that all drugs could be compared with a common comparator (placebo). The review of placebo-controlled trials included a sufficient number of drugs for a network meta-analysis to be feasible. The network meta-analysis was considered for all seven of the GDG prioritised outcomes. However, sufficient data from published studies were only identified for a subset of outcomes. These outcomes were considered for inclusion in the health economic model. A sub-group analysis for women with OAB dry was considered where data were reported separately for OAB wet and OAB dry.

The review was restricted to RCT data.

Review question

In women with OAB, what is the comparative effectiveness of the following drugs:

- darifenacin
- fesoterodine
- oxybutynin (immediate release)
- oxybutynin (extended release)
- oxybutynin (transdermal)
- oxybutynin (topical gel)
- propiverine
- propiverine (extended release)
- solifenacin
- tolterodine (immediate release)
- tolterodine (extended release)
- trospium
- trospium (extended release).

Review introduction

In order to identify the most relevant data from the evidence and the correct studies for inclusion, the GDG members were asked to specify at the outset the length of time within which they would expect to see a benefit from OAB drug treatment. They were also asked to indicate the drug regimens that were relevant to the NHS so that papers that reported the effectiveness of regimens that were not used in clinical practice could be excluded. After consideration, the GDG agreed the following:

- A clinical benefit or harm would be obvious to the woman by 4 weeks and that this should therefore be the minimum time point for effectiveness reported in the review.
- Only studies that used the recommended starting dose reported in the British National Formulary (BNF) should be used in the review as a reflection of current best practice.

Methodology

Background

Conventionally, each intervention was analysed against its comparators in a series of head-to-head reviews and presented in GRADE profiles. The GRADE profiles showing GRADE findings for these comparisons can be found in appendix L.6:

- GRADE profile I.6.1 – oxybutynin immediate release compared with oxybutynin extended release for overactive bladder
- GRADE profile I.6.2 – oxybutynin immediate release compared with tolterodine immediate release for overactive bladder
- GRADE profile I.6.3 – oxybutynin immediate release compared with propiverine immediate release for overactive bladder
- GRADE profile I.6.4 – solifenacin compared with tolterodine immediate release for overactive bladder
- GRADE profile I.6.5 – solifenacin compared with tolterodine extended release for overactive bladder.
- GRADE profile I.6.6 – oxybutynin extended release compared with tolterodine immediate release for overactive bladder.
- GRADE profile I.6.7 – oxybutynin extended release compared with tolterodine extended release for overactive bladder.

- GRADE profile I.6.8 – tolterodine immediate release compared with tolterodine extended release for overactive bladder.
- GRADE profile I.6.9 – tolterodine extended release compared with fesoterodine for overactive bladder.
- GRADE profile I.6.10 – fesoterodine compared with placebo for overactive bladder
- GRADE profile I.6.11 – solifenacin compared with placebo for overactive bladder
- GRADE profile I.6.12 – darifenacin compared with placebo for overactive bladder
- GRADE profile I.6.13 – tolterodine immediate release compared with placebo for overactive bladder
- GRADE profile I.6.14 – tolterodine extended release compared with placebo for overactive bladder
- GRADE profile I.6.15 – oxybutynin immediate release compared with placebo for overactive bladder
- GRADE profile I.6.16 – transdermal oxybutynin compared with placebo for overactive bladder
- GRADE profile I.6.17 – oxybutynin topical gel compared with placebo for overactive bladder
- GRADE profile I.6.18 – propiverine immediate release compared with placebo for overactive bladder
- GRADE profile I.6.19 – propiverine extended release compared with placebo for overactive bladder
- GRADE profile I.6.20 – trospium with placebo compared for overactive bladder
- GRADE profile I.6.21 – trospium extended release compared with placebo for overactive bladder.

The findings of these reviews are summarised below for each outcome:

- Table 6.1 – patient satisfaction with treatment at 4 weeks (unshaded) and 12 weeks (shaded area)
- Table 6.2 – incontinence episodes per day at 4 weeks (unshaded area) and 12 weeks (shaded area)
- Table 6.3 – urgency episodes at 4 weeks (unshaded area) and 12 weeks (shaded area)
- Table 6.4 – zero incontinence episodes per day at 4 weeks (unshaded area) and 12 weeks (shaded area)
- Table 6.5 – zero urgency episodes per day at 4 weeks (unshaded area) and 12 weeks (shaded area)
- Table 6.6 – incontinence specific quality of life at 4 weeks (unshaded area) and 12 weeks (shaded area)
- Table 6.7 – discontinuation for any reason at 4 weeks (unshaded area) and 12 weeks (shaded area)
- Table 6.8 – discontinuation due to adverse effects at 4 weeks (unshaded area) and 12 weeks (shaded area)
- Table 6.9 – any adverse effect at 4 weeks (unshaded area) and 12 weeks (shaded area)
- Table 6.10 – dry mouth at 4 weeks (unshaded area) and 12 weeks (shaded area)
- Table 6.11 – psychological outcomes at 4 weeks (unshaded area) and 12 weeks (shaded area)

- Table 6.12 – post-void residual volume at 4 weeks (unshaded area) and 12 weeks (shaded area)

Description of included studies

A total of 48 RCTs were included in the review (Abrams et al., 1998; Appell et al., 2001; Cardozo et al., 2004; Cartwright et al., 2011; Chapple et al., 2004; Chapple et al., 2004a; Chapple et al., 2005; Chapple et al., 2007; Chapple et al., 2007b; Choo et al., 2008; Diokno et al., 2003; Dmochowski et al., 2002; Dmochowski et al., 2008; Dmochowski et al., 2010a; Dorschner et al., 2000; Drutz et al., 1999; Haab et al., 2004; Herschorn et al., 2010a; Hill et al., 2006; Ho et al., 2010; Homma et al., 2003; Huang et al., 2012; Jacquetin amd Wymdaele, 2001; Jonas et al., 1997; Junemann et al., 2006; Kaplan et al., 2011; Karram et al., 2009; Madersbacher et al., 1999; Malone-Lee & Al-Buheissi, 2009; Malone-Lee et al., 2001; Millard et al., 1999; Minassian et al., 2007; Nitti et al., 2007; Oreskovic et al., 2012; Rackley et al., 2006; Rogers et al., 2008; Rudy et al, 2006; Staskin et al., 2007; Staskin et al., 2009; Steers et al., 2005; Thuroff et al., 1991; VanKerrebroeck et al., 2001; Vardy et al., 2009; Weiss et al., 2012; Yamaguchi et al., 2007; Yamaguchi et al., 2011; Zat'ura et al., 2010; Zinner et al., 2004).

All studies included women with overactive bladder symptoms with either incontinence episodes or urgency episodes or both at baseline.

One study reported data separately for women with OAB wet and OAB dry.

The mean age of study participants ranged from 49 years (standard deviation [SD] ±12) to 75 years (SD ± 6). Where reported, the mean number of urgency episodes per day ranged from 2.7 (SD ± 1.8) to 11.4 (SD ± 4.0). As several studies included women who were continent at baseline, the range of number of incontinence episodes is not reported for the included studies. Where reported, the mean duration of OAB symptoms ranged from 4.2 years (SD ± 6.2) to 9.0 years (SD ± 11.2).

Table 6.1 Patient satisfaction with treatment at 4 weeks (unshaded) and 12 weeks (shaded area)

Relative risk and 95% confidence intervals at 12 weeks

Relative risk and 95% confidence intervals at 4 weeks

Oxybutynin IR		No data reported	0.98 (0.76,1.27)	No data reported									1.04 (0.75,1.44)
	Solifenacin		No data reported		1.05 (0.84,1.33)								1.41 (1.29,1.55)
No data reported		Oxybutynin ER	No data reported		No data reported								
No data reported	No data reported	No data reported	Tolterodine IR		0.92 (0.84,1.01)								1.34 (1.14,1.58)
0.95 (0.81,1.11)				Propiverine IR									No data reported
	No data reported	No data reported	No data reported		Tolterodine ER		0.90 (0.86,0.95)						1.30 (1.16,1.45)
						Propiverine ER							No data reported
					0.91 (0.85,0.99)		Fesoterodine						1.32 (1.22,1.42)
								Trospium					No data reported
									Oxybutynin TD				No data reported
										Darifenacin			No data reported
											Trospium ER		No data reported
												Oxybutynin TG	No data reported
1.11 (0.89,1.38)	No data reported		No data reported	1.17 (0.94,1.45)	1.21 (1.12,1.32)	1.45 (1.22,1.73)	1.32 (1.22,1.43)	No data reported	No data reported	No data reported	No data reported	No data reported	Placebo

Read table from left to right for direction of effect (for example the relative risk of oxybutynin IR compared with propiverine IR at 4 weeks is 0.95 [95% CI 0.81, 1.11])

Empty boxes indicate that no studies were identified for the comparison

No data reported indicates that studies were identified for the comparison but no data were provided for this outcome

The number of studies for each comparison was 1 except for: solifenacin versus placebo = 2 studies; tolterodine IR versus placebo = 3 studies; tolterodine ER versus fesoterodine = 2 studies (4 weeks) and 3 studies (12 weeks); tolterodine ER versus placebo = 2 studies (4 weeks) and 7 studies (12 weeks); fesoterodine versus placebo = 2 studies (4 weeks) and 5 studies (12 weeks).

Table 6.2 Incontinence episodes per day at 4 weeks (unshaded area) and 12 weeks (shaded area)

Mean difference and 95% confidence intervals at 12 weeks

Mean difference and 95% confidence intervals at 4 weeks

Oxybutynin IR		No data reported	-0.16 (-0.73,0.42)	No data reported									-0.77 (-1.26,-0.28)
	Solifenacin		-0.07 (-0.38,0.24)		1.88 (-1.48,5.24)								0.82 (-1.05,-0.60)
No data reported		Oxybutynin ER	-0.20 (-0.55,0.19)		No data reported								
No data reported	No data reported	No data reported	Tolterodine IR		0.30 (0.00,0.60)								-0.47 (-0.69,-0.26)
No data reported				Propiverine IR									No data reported
	No data reported	No data reported	No data reported		Tolterodine ER		0.17 (0.06,0.28)						-0.29 (-0.40,-0.18)
						Propiverine ER							No data reported
					0.14 (0.04,0.25)		Fesoterodine						-0.37 (-0.48,-0.26)
								Trospium					No data reported
									Oxybutynin TD				-0.40 (-1.08,0.28)
										Darifenacin			No data reported
											Trospium ER		-0.65 (-1.01,-0.30)
												Oxybutynin TG	-0.50 (-0.91,-0.09)
	-1.79		-0.90		-0.26	-0.81	-0.40				-0.66		Placebo

	No data reported	(-1.95,-1.63)		(-1.62,-0.18)	No data reported	(-0.39,-0.12)	(-1.25,-0.37)	(-0.52,-0.28)	No data reported	No data reported	No data reported	(-0.96,-0.36)	No data reported	

Read table from left to right for direction of effect (for example the mean difference of solifenacin compared with tolterodine IR at 12 weeks is -0.07 [95% CI -0.38, 0.24])

Empty boxes indicate that no studies were identified for the comparison

No data reported indicates that studies were identified for the comparison but no data were provided for this outcome

The number of studies for each comparison was 1 except for: oxybutynin IR versus tolterodine IR = 2 studies; oxybutynin versus placebo = 3 studies; solifenacin versus tolterodine IR = 2 studies; solifenacin versus placebo = 5 studies (12 weeks); tolterodine IR versus placebo = 5 studies (12 weeks); tolterodine ER versus fesoterodine = 2 studies (4 weeks), and 3 studies (12 weeks); tolterodine ER versus placebo = 2 studies (2 weeks) and 5 studies (12 weeks); fesoterodine versus placebo = 4 studies (4 weeks) and 7 studies (12 weeks); trospium ER = 2 studies (4 weeks) and 2 studies (12 weeks).

Table 6.3 Urgency episodes at 4 weeks (unshaded area) and 12 weeks (shaded area)

Mean difference and 95% confidence intervals at 12 weeks

Mean difference and 95% confidence intervals at 4 weeks

Oxybutynin IR		No data reported	No data reported	No data reported									-2.60 (-4.47,-0.73)
	Solifenacin		-0.39 (-1.26,0.48)		-0.55 (-1.94,0.84)								-1.21 (-1.50,-0.92)
No data reported		Oxybutynin ER	No data reported		No data reported								
No data reported	No data reported	No data reported	Tolterodine IR		No data reported								-0.64 (-1.28,0.00)
No data reported				Propiverine IR									No data reported
	No data reported	No data reported	No data reported		Tolterodine ER		0.18 (-0.33,0.69)						-0.89 (-1.54,-0.25)
						Propiverine ER							No data reported
					0.42 (0.01,0.83)		Fesoterodine						-0.93 (-1.16,-0.70)
								Trospium					No data reported
									Oxybutynin TD				No data reported
										Darifenacin			No data reported
											Trospium ER		No data reported

												Oxybutynin TG	No data reported
No data reported	-0.77 (-1.09,-0.45)		No data reported	No data reported	-0.90 (-1.49,-0.31)	-0.65 (-1.32,0.02)	-1.03 (-1.56,-0.51)	No data reported	No data reported	No data reported	No data reported	No data reported	Placebo

Read table from left to right for direction of effect (for example the mean difference of solifenacin compared with tolterodine IR at 12 weeks is -0.39 [95% CI -1.26, 0.48])

Empty boxes indicate that no studies were identified for the comparison

No data reported indicates that studies were identified for the comparison but no data were provided for this outcome

The number of studies for each comparison was 1 except for: solifenacin versus tolterodine IR = 2 studies; solifenacin versus placebo = 3 studies (12 weeks); tolterodine versus fesoterodine = 2 studies (4 weeks) and 3 studies (12 weeks); tolterodine ER versus placebo = 2 studies (4 weeks) and 3 studies (12 weeks); fesoterdoine versus placebo = 4 studies (4 weeks) and 7 studies (12 weeks).

Table 6.4 Zero incontinence episodes per day at 4 week (unshaded area) and 12 weeks (shaded area)

Relative risk and 95% confidence intervals at 12 weeks

Relative risk and 95% confidence intervals at 4 weeks

Oxybutynin IR		No data reported	0.00 (0.55,1.62)	No data reported									2.00 (1.23,3.26)
	Solifenacin		No data reported		1.19 (1.07,1.32)								1.46 (1.31,1.64)
No data reported		Oxybutynin ER	No data reported		1.33 (0.98,1.80)								
No data reported	No data reported	No data reported	Tolterodine IR		No data reported								1.74 (0.75,4.04)
No data reported				Propiverine IR									No data reported
	1.13 (0.97,1.31)	No data reported	No data reported		Tolterodine ER		0.91 (0.86,0.96)						1.20 (1.07,1.34)
						Propiverine ER							No data reported
					0.93 (0.86,1.00)		Fesoterodine						1.33 (1.15,1.55)
								Trospium					1.91 (1.20,3.03)
									Oxybutynin TD				1.69 (0.80,3.58)

											Darifenacin			1.92 (1.24,2.96)
												Trospium ER		1.70 (1.34,2.14)
													Oxybutynin TG	1.61 (1.23,2.10)
No data reported	No data reported		No data reported	1.45 (0.81,2.58)	1.31 (1.08,1.59)	1.35 (1.10,1.66)	1.40 (1.18,1.66)	No data reported	No data reported	No data reported	1.65 (1.20,2.27)	No data reported	Placebo	

Read table from left to right for direction of effect (for example the mean difference of solifenacin compared with tolterodine ER at 4 weeks is 1.13 [95% CI 0.97, 1.31])

Empty boxes indicate that no studies were identified for the comparison

No data reported indicates that studies were identified for the comparison but no data were provided for this outcome

The number of studies for each comparison was 1 except for: solifenacin versus placeo = 3 studies; tolterodine ER versus fesoterodine = 2 studies (4 weeks) and 2 studies (12 weeks); tolterodine ER versus placebo = 2 studies (4 weeks) and 4 studies (12 weeks); fesoterodine versus placebo = 2 studies (4 weeks) and 4 studies (12 weeks); trospium ER versus placebo = 2 studies (12 weeks).

Table 6.5 Zero urgency episodes per day at 4 weeks (unshaded area) and 12 weeks (shaded area)

Relative risk and 95% confidence intervals at 12 weeks

Relative risk and 95% confidence intervals at 4 weeks

Oxybutynin IR		No data reported	No data reported	No data reported									No data reported
	Solifenacin		No data reported		No data reported								1.82 (1.32,2.51)
No data reported		Oxybutynin ER	No data reported		No data reported								
No data reported	No data reported	No data reported	Tolterodine IR		No data reported								No data reported
No data reported				Propiverine IR									No data reported
	No data reported	No data reported	No data reported		Tolterodine ER		No data reported						No data reported
						Propiverine ER							No data reported
					No data reported		Fesoterodine						No data reported
								Trospium					No data reported

									Oxybutynin TD					No data reported
										Darifenacin				No data reported
											Trospium ER			No data reported
												Oxybutynin TG		No data reported
No data reported	No data reported		No data reported	3.00 (1.18, 7.61)	No data reported	No data reported	No data reported	No data reported	No data reported	No data reported	No data reported	No data reported	Placebo	

Read table from left to right for direction of effect (for example the relative risk of propiverine IR compared with placebo at 4 weeks is 3.88 [95% CI 1.28, 11.74])

Empty boxes indicate that no studies were identified for the comparison

No data reported indicates that studies were identified for the comparison but no data were provided for this outcome

The number of studies for each comparison was 1

Table 6.6 Incontinence specific quality of life at 4 weeks (unshaded area) and 12 weeks (shaded area)

Mean difference or standard mean difference and 95% confidence intervals at 12 weeks

Mean difference or standard mean difference and 95% confidence intervals at 4 weeks

Oxybutynin IR		-0.40 (-0.89,0.09)	No data reported	No data reported									No data reported
	Solifenacin		No data reported		-0.18 (-0.35,-0.01)								No data reported
No data reported		Oxybutynin ER	No data reported		No data reported								
No data reported	2.30 (-6.12,10.72)	No data reported	Tolterodine IR		No data reported								No data reported
No data reported				Propiverine IR									No data reported
	No data reported	No data reported	No data reported		Tolterodine ER		-0.12 (-0.19,-0.05)						0.05 (-0.11,0.22)
						Propiverine ER							No data reported
					No data reported		Fesoterodine						0.14 (-0.02,0.31)
													-18.00

								Trospium					(-33.52,-2.48)
									Oxybutynin TD				No data reported
										Darifenacin			No data reported
											Trospium ER		-0.32 (-0.48,-0.16)
												Oxybutynin TG	No data reported
No data reported	-10.51 (-13.14, -7.88)		-0.35 (-0.84,0.14)	No data reported	No data reported	-3.65 (-7.44,0.14)	No data reported	No data reported	No data reported	No data reported	-0.34 (-0.50, -0.18)	No data reported	Placebo

Read table from left to right for direction of effect (for example the mean difference of solifenacin compared with tolterodine IR at 4 weeks is 2.30 [95% CI -6.12, 10.72])

Empty boxes indicate that no studies were identified for the comparison

No data reported indicates that studies were identified for the comparison but no data were provided for this outcome

The number of studies for each comparison was 1 except for: solifenacin versus placebo = 2 studies; tolterodine versus fesoterodine = 2 studies; tolterodine ER versus placebo = 3 studies; fesoterodine versus placebo = 5 studies

Table 6.7 Discontinuation for any reason at 4 weeks (unshaded area) and 12 weeks (shaded area)

Relative risk and 95% confidence intervals at 12 weeks

Relative risk and 95% confidence intervals at 4 weeks

Oxybutynin IR		1.45 (0.83,2.56)	2.84 (1.56,5.17)	No data reported									2.15 (1.14,4.07)
	Solifenacin		1.03 (0.71,1.50)		0.82 (0.55,1.24)								0.83 (0.69,1.00)
No data reported		Oxybutynin ER	1.19 (0.69,2.03)		1.26 (0.86,1.85)								
No data reported	0.60 (0.15,2.33)	No data reported	Tolterodine IR		1.11 (0.79,1.56)								0.95 (0.75,1.20)
0.87 (0.46,1.62)				Propiverine IR									No data reported
	No data reported	No data reported	No data reported		Tolterodine ER		0.77 (0.65,0.90)						0.89 (0.77,1.02)
						Propiverine ER							No data reported
					No data reported		Fesoterodine						1.18 (1.05,1.33)

								Trospium					1.13 (0.84,1.50)
									Oxybutynin TD				No data reported
										Darifenacin			0.80 (0.56,1.15)
											Trospium ER		1.11 (0.81,1.51)
												Oxybutynin TG	0.98 (0.66,1.46)
1.20 (0.62,2.33)	0.64 (0.36,1.14)		1.06 (0.49,2.32)	1.21 (0.58,2.98)	No data reported	1.08 (0.54,2.17)	1.38 (0.97,1.98)	No data reported	1.57 (0.67,3.71)	No data reported	No data reported	No data reported	Placebo

Read table from left to right for direction of effect (for example the relative risk of oxybutynin IR compared with propiverine IR at 4 weeks is 0.87 [95% CI 0.46, 1.62])

Empty boxes indicate that no studies were identified for the comparison

No data reported indicates that studies were identified for the comparison but no data were provided for this outcome

The number of studies for each comparison was 1 except for: oxybutynin IR versus placebo = 2 studies (4 weeks) and 2 studies (12 weeks); solifenacin versus tolterodine IR = 2 studies (12 weeks); solifenacin versus tolterodine ER = 2 studies; Solifenacin versus placebo = 2 studies (4 weeks) and 6 studies (12 weeks); tolterodine IR versus placebo = 2 studies (4 weeks) and 6 studies(12 weeks); tolterodine ER versus fesoterodine = 3 studies; tolterodine ER versus placebo = 8 studies; fesoterodine versus placebo = 8 studies (12 weeks); trospium versus placebo = 2 studies; darifenacin versus placebo = 4 studies; trospium ER versus placebo = 2 studies

Table 6.8 Discontinuation due to adverse effects at 4 weeks (unshaded area) and 12 weeks (shaded area)

Relative risk and 95% confidence intervals at 12 weeks

Relative risk and 95% confidence intervals at 4 weeks

Oxybutynin IR		1.28 (0.68,2.41)	2.46 (1.44,4.20)	No data reported									2.06 (0.99,4.26)
	Solifenacin		1.92 (0.78,4.71)		1.13 (0.61,2.07)								1.17 (0.83,1.66)
No data reported		Oxybutynin ER	0.97 (0.48,1.96)		1.07 (0.58,1.98)								
No data reported	1.00 (0.06,15.40)	No data reported	Tolterodine IR		1.02 (0.61,1.71)								1.48 (0.54,4.08)
No data reported				Propiverine IR									No data reported
	1.08 (0.56,2.08)	No data reported	No data reported		Tolterodine ER		0.60 (0.46,0.78)						1.77 (0.92,3.43)

						Propiverine ER								No data reported
					No data reported		Fesoterodine							1.88 (1.50,2.37)
								Trospium						1.55 (1.00,2.39)
									Oxybutynin TD					No data reported
										Darifenacin				1.01 (0.55,1.84)
											Trospium ER			1.58 (0.78,3.21)
												Oxybutynin TG		1.50 (0.75,3.00)
4.14 (0.20,84.38)	3.08 (0.13,73.25)		1.18 (0.38,3.66)	No data reported	No data reported	5.68 (0.74,43.71)	1.50 (0.71,3.14)	No data reported	2.00 (0.38,10.41)	No data reported	No data reported	No data reported	Placebo	

Read table from left to right for direction of effect (for example the relative risk of oxybutynin IR compared with placebo at 4 weeks is 4.14 [95% CI 0.20, 84.38])

Empty boxes indicate that no studies were identified for the comparison

No data reported indicates that studies were identified for the comparison but no data were provided for this outcome

The number of studies for each comparison was 1 except for: oxybutynin IR versus tolterodine IR = 2 studies; oxybutynin IR versus placebo = 3 studies (12 weeks); solifenacin versus toilterodine IR = 2 studies (12 weeks); solifenacin versus tolterodine ER = 2 studies (12 weeks); solifenacin verus placebo = 6 studies (12 weeks); tolterodine versus placebo = 4 studies (4 weeks) and = 6 studies (12 weeks); tolterodine ER versus fesoterodine = 3 studies; tolterodine versus placebo = 8 studies; fesoterodine versus placebo = 8 studies (12 weeks); trospium versus placebo = 2 studies; darifenacin verus pacebo = 4 studies, trospium ER versus placebo = 2 studies.

Table 6.9 Any adverse effect at 4 weeks (unshaded area) and 12 weeks (shaded area)

Relative risk and 95% confidence intervals at 12 weeks

Relative risk and 95% confidence intervals at 4 weeks

Oxybutynin IR		1.00 (0.62,1.60)	1.10 (1.04,1.17)	No data reported									1.23 (1.03,1.47)
	Solifenacin		No data reported		1.54 (0.77,3.07)								1.86 (1.56,2.21)
No data reported		Oxybutynin ER	No data reported		No data reported								
	1.00												1.05

	No data reported	(0.52,1.93)	No data reported	Tolterodine IR		No data reported								(0.95,1.17)
	1.14 (0.97,1.33)				Propiverine IR									No data reported
		No data reported	No data reported	No data reported		Tolterodine ER		0.72 (0.49, 1.05)						1.28 (1.13,1.45)
							Propiverine ER							No data reported
						No data reported		Fesoterodine						1.50 (1.24,1.82)
									Trospium					1.28 (1.11,1.48)
										Oxybutynin TD				No data reported
											Darifenacin			1.41 (1.06,1.88)
												Trospium ER		1.31 (1.04,1.66)
													Oxybutynin TG	1.18 (1.03,1.35)
	1.80 (1.41,2.29)	2.05 (0.86,4.90)		1.26 (0.90,1.76)	1.53 (1.13,2.06)	No data reported	1.69 (1.24,2.29)	1.11 (0.96,1.28)	No data reported	No data reported	No data reported	No data reported	No data reported	Placebo

Read table from left to right for direction of effect (for example the relative risk of oxybutynin IR compared with propiverine IR at 4 weeks is 1.14 [95% CI 0.87, 1.33])

Empty boxes indicate that no studies were identified for the comparison

No data reported indicates that studies were identified for the comparison but no data were provided for this outcome

The number of studies for each comparison was 1 except for: oxybutynin IR versus tolterodine IR = 2 studies; oxybutynin IR versus placebo = 2 studies (4 weeks) and 3 studies (12 weeks); solifenacin versus placebo = 3 studies (12 weeks); tolterodine IR versus placebo = 4 studies (4 weeks) and 5 studies (12 weeks); tolterodine ER versus placebo = 6 studies; fesoterodine versus placebo = 7 studies (12 weeks); darifenacin versus placebo = 3 studies; trospium ER versus placebo = 2 studies.

Table 6.10 Dry mouth at 4 weeks (unshaded area) and 12 weeks (shaded area)

Relative risk and 95% confidence intervals at 12 weeks

Relative risk and														
	Oxybutynin IR		0.00 (0.78,2.33)	1.93 (1.47,2.53)	No data reported									4.50 (3.02,6.69)

	Solifenacin		0.60 (0.33,1.09)		1.25 (1.04,1.51)								3.15 (2.50,3.98)
No data reported		Oxybutynin ER	0.85 (0.62,1.15)		1.33 (1.05,1.69)								
No data reported	0.56 (0.21,1.50)	No data reported	Tolterodine IR		1.30 (1.06,1.60)								3.35 (2.62,4.28)
No data reported				Propiverine IR									No data reported
	1.21 (0.94,1.57)	No data reported	No data reported		Tolterodine ER		0.72 (0.49,1.05)						2.67 (2.14,3.33)
						Propiverine ER							No data reported
					No data reported		Fesoterodine						3.62 (2.88,4.57)
								Trospium					3.57 (2.49,5.14)
									Oxybutynin TD				1.15 (0.53,2.51)
										Darifenacin			1.93 (0.52,7.19)
											Trospium ER		2.95 (1.84,4.72)
												Oxybutynin TG	2.52 (1.27,5.02)
4.13 (1.86,9.15)	11.29 (0.65,197.21)		5.69 (2.91,11.12)	No data reported	No data reported	3.38 (1.93,5.90)	0.45 (0.33,0.61)	No data reported	No data reported	No data reported	No data reported	No data reported	Placebo

Read table from left to right for direction of effect (for example the relative risk of oxybutynin IR compared with placebo at 4 weeks is 4.13 [95% CI 1.86, 9.15])

Empty boxes indicate that no studies were identified for the comparison

No data reported indicates that studies were identified for the comparison but no data were provided for this outcome

The number of studies for each comparison was 1 except for: oxybutynin IR versus tolterodine IR = 2 studies; oxybutynin IR versus placebo = 3 studies (12 weeks); solifenacin versus tolterodine IR = 2 studies (12 weeks); solifenacin versus tolterodine ER = 2 studies (12 weeks); solifenacin versus placebo = 3 studies (12 weeks); tolterodine IR versus placebo = 4 studies (4 weeks) and 7 studies (12 weeks); tolterodine ER versus

fesoterodine = 3 studies; tolterodine ER versus placebo = 7 studies; fesoterodine versus placebo = 7 studies (12 weeks); trospium versus placebo = 2 studies; darifenacin versus placebo = 4 studies; trospium ER versus placebo = 2 studies.

Table 6.11 Psychological outcomes at 4 weeks (unshaded area) and 12 weeks (shaded area)

Mean differencxe and 95% confidence intervals at 12 weeks

Mean difference and 95% confidence intervals at 4 weeks

Oxybutynin IR		No data reported	No data reported	No data reported									No data reported
	Solifenacin		No data reported		No data reported								No data reported
No data reported		Oxybutynin ER	No data reported		No data reported								
No data reported	No data reported	No data reported	Tolterodine IR		No data reported								No data reported
No data reported				Propiverine IR									No data reported
	No data reported	No data reported	No data reported		Tolterodine ER		No data reported						No data reported
						Propiverine ER							No data reported
					No data reported		Fesoterodine						No data reported
								Trospium					No data reported
									Oxybutynin TD				No data reported
										Darifenacin			No data reported
											Trospium ER		No data reported
												Oxybutynin TG	No data reported
No data reported	No data reported		No data reported	No data reported	No data reported	No data reported	No data reported	No data reported	No data reported	No data reported	No data reported	No data reported	Placebo

Read table from left to right for direction of effect

Empty boxes indicate that no studies were identified for the comparison

No data reported indicates that studies were identified for the comparison but no data were provided for this outcome

Table 6.12 Post-void residual volume at 4 weeks (unshaded area) and 12 weeks (shaded area)

Mean difference and 95% confidence intervals at 12 weeks

Mean difference and 95% confidence intervals at 4 weeks

Oxybutynin IR		No data reported	No data reported	No data reported									No data reported
	Solifenacin		No data reported		-2.91 (-17.92,12.10)								No data reported
No data reported		Oxybutynin ER	No data reported		No data reported								
No data reported	3.60 (-6.06,13.26)	No data reported	Tolterodine IR		No data reported								No data reported
-1.70 (-6.09,2.69)				Propiverine IR									No data reported
	No data reported	No data reported	No data reported		Tolterodine ER		No data reported						No data reported
						Propiverine ER							No data reported
					No data reported		Fesoterodine						7.90 (0.93,14.87)
								Trospium					No data reported
									Oxybutynin TD				No data reported
										Darifenacin			-5.40 (-42.29,31.49)
											Trospium ER		No data reported
												Oxybutynin TG	No data reported
28.90 (25.90,31.90)	No data reported		15.00 (-5.25,35.25)	1.30 (-2.83,5.43)	No data reported	No data reported	No data reported	No data reported	No data reported	No data reported	No data reported	No data reported	Placebo

Read table from left to right for direction of effect (for example the relative risk of oxybutynin IR compared with propiverine IR at 4 weeks is -1.70 [95% CI -6.09, 2.69])

Empty boxes indicate that no studies were identified for the comparison

No data reported indicates that studies were identified for the comparison but no data were provided for this outcome

The number of studies for each comparison was 1

Evidence statements

As the described in the Methodology (see Chapter 3), for dichotomous outcomes clinical benefit is defined as a relative risk where the confidence intervals do not cross the threshold of 1.25 or 0.75, depending to whether it is superior or inferior to its comparator. Where continuous outcomes are reported, clinical benefit is defined by the minimum important difference agreed by the GDG.

Patient satisfaction with treatment (Table 6.1)

No evidence was identified for this outcome for the following drugs:

- darifenacin
- oxybutynin ER
- oxybutynin, transdermal
- oxybutynin topical gel
- trospium
- trospium ER.

The head-to-head and placebo-controlled reviews demonstrated that there was evidence of a clinical benefit for the following:

- solifenacin over placebo at 12 weeks (high quality evidence from 2 studies).

Incontinence episodes per day (Table 6.2)

No evidence was identified for this outcome for the following drugs:

- darienacin
- propiverine IR
- trospium.

The head-to-head and placebo-controlled reviews demonstrated that there was evidence of a benefit for the following:

- solifenacin over placebo at 4 weeks (high quality evidence from 1 study).

Urgency episodes per day (Table 6.3)

No evidence was identified for this outcome for the following drugs:

- oxybutynin ER
- propiverine IR
- trospium
- oxybutynin transdermal
- darifenacin
- trospium ER
- oxybutynin topical gel

The head-to-head and placebo-controlled reviews demonstrated that there was no evidence of a clinical benefit for any of the comparisons.

Zero incontinence episodes per day (Table 6.4)

The head-to-head and placebo-controlled comparisons demonstrated that there was evidence of a benefit for the following:

- oxybutynin IR over placebo at 12 weeks (moderate quality evidence from 1 study)
- solifenacin over placebo at 12 weeks (moderate quality evidence from 3 studies)

- trospium ER over placebo at 12 weeks (high quality evidence from 1 study).

Zero urgency episodes per day

No evidence was identified for this outcome for the following drugs:

- oxybutynin IR
- oxybutynin ER
- tolterodine IR
- tolterodine ER
- propiverine ER
- fesoterodine
- trospium
- oxybutynin transdermal
- darifenacin
- trospium ER
- oxybutynin topical gel.

The head-to-head and placebo-controlled comparisons demonstrated that there was evidence of a benefit for the following

- solifenacin over placebo at 12 weeks (high quality evidence from 1 study).

Incontinence specific quality of life (Table 6.6)

No evidence was identified for this outcome for the following drugs:

- oxybutynin ER
- propiverine IR
- oxybutynin transdermal
- darifenacin
- oxybutynin topical gel

The head-to-head and placebo-controlled comparisons demonstrated that there was evidence of a benefit for the following:

- solifenacin over placebo at 4 weeks (low quality evidence from 2 studies).

Discontinuation for any reason (Table 6.7)

The head-to-head and placebo-controlled comparisons demonstrated that there was evidence of clinical benefit for the following:

- tolterodine IR over oxybutynin IR at 12 weeks (high quality evidence from 1 study).

Discontinuation for adverse effects (Table 6.8)

No evidence was identified for this outcome for the following drug:

- propiverine IR.

The head-to-head and placebo-controlled comparisons demonstrated that there was evidence of a benefit for the following:

- tolterodine IR over oxybutynin IR at 4 weeks (high quality evidence from 2 studies)
- placebo over fesoterodine at 12 weeks (high quality evidence from 8 studies).

Any adverse effect (Table 6.9)

No evidence was identified for this outcome for the following drugs:

- oxybutynin ER
- oxybutynin transdermal.

The head-to-head and placebo-controlled comparisons demonstrated that there was evidence of a benefit for the following:

- placebo over oxybutynin IR at 4 weeks (high quality evidence from 2 studies)
- placebo over solifenacin at 12 weeks (high quality evidence from 3 studies).

Dry mouth (Table 6.10)

No evidence was identified for this outcome for the following:

- propiverine IR.

The head-to-head and placebo-controlled comparisons demonstrated that there was evidence of a benefit for the following:

- tolterodine IR over oxybutynin IR at 12 weeks (moderate quality evidence from 2 studies)
- placebo over oxybutynin IR at 4 weeks (high quality evidence from 1 study) and at 12 weeks (high quality evidence from 3 studies)
- placebo over solifenacin at 12 weeks (high quality evidence from 6 studies)
- placebo over tolterodine IR at 4 weeks (high quality evidence from 4 studies) and at 12 weeks (high quality evidence from 7 studies)
- placebo over tolterodine at 12 weeks (high quality evidence from 7 studies)
- placebo over propiverine ER at 4 weeks (high quality evidence from 1 study)
- fesoterodine over placebo at 4 weeks (high quality evidence from 1 study)
- placebo over fesoterodine at 12 weeks (moderate quality evidence from 7 studies)
- placebo over trospium at 12 weeks (high quality evidence from 2 studies)
- placebo over trospium ER at 12 weeks (high quality evidence from 2 studies)
- placebo over oxybutynin topical gel at 12 weeks (high quality evidence from 1 study).

Psychological outcomes (Table 6.11)

No evidence was identified for this outcome for the following drugs:

- oxybutynin IR
- solifenacin
- oxybutynin ER
- tolterodine IR
- propiverine IR
- tolterodine ER
- propiverine ER
- fesoterodine
- trospium
- oxybutynin transdermal
- darifenacin

- trospium ER
- oxybutynin topical gel.

Post-void residual volume (Table 6.12)

No evidence was identified for this outcome for the following drugs:

- oxybutynin ER
- tolterodine ER
- propiverine ER
- trospium
- oxybutynin transdermal
- trospium ER
- oxybutynin topical gel.

The head-to-head and placebo-controlled reviews demonstrated that there was no evidence of a clinical benefit for any of the comparisons.

6.1.4 Network meta-analysis (NMA) for OAB wet

Introduction

A robust NMA has the potential to provide both direct and indirect comparisons between all drugs in a methodologically sound way. The NMA presented here includes all studies comparing OAB drugs, including those that were reviewed in 2006. However, evidence from the head-to-head studies did not complete the network of 13 drug comparisons (that is, some drugs were not evaluated with a comparator that was also a comparator in another study allowing indirect comparison to be made). Therefore it was decided to include all published placebo-controlled studies to complete the network (see Appendix M). With the inclusion of placebo-controlled trials, the network was complete because the placebo acted as the common comparator across the included RCT studies.

The inclusion of placebo-controlled studies was undertaken with the sole purpose of completing the NMA and not to inform recommendations. Placebo values were not used as the comparator in the analysis on which baseline probabilities of continence or discontinuation were estimated. Instead, the NMA adopted baseline probabilities derived from studies of oxybutynin (immediate release) as it was the primary recommendation for first-line drug treatment in the previous guideline. Given the methodological superiority of NMA it was decided that:

- The NMA replaced the review of head-to-head studies that was undertaken prior to the NMA. That review can be found in Appendix M.
- The recommendations developed by the GDG would be based on the NMA and not on individual trials or the head-to-head reviews.

Data inputs and outcomes

To ensure a robust comparison of similar studies and retain a level of heterogeneity to ensure confidence in the NMA, the following studies were excluded:

- studies where outcomes of interest were not reported at either 4 weeks or 12 weeks
- studies that used a starting dose lower than that recommended in the BNF for that population (in one instance we included studies which used a starting dose greater than that recommended in the BNF as no other data were available).

Data were not imputed to compensate for missing data in the study reports.

Assumptions and data used in the network meta-analysis

Table 6.13 outlines the assumptions that were agreed with the GDG prior to undertaking the meta-analysis.

Table 6.13 Assumptions and data used in the network meta-analysis.

Description	Source
That the relative treatment effects at 4 and 12 weeks were the same, although the baseline probability of continence and discontinuation at 4 and 12 weeks were allowed to be different.	GDG discussion and validated by the analysis of model fit and lack of evidence of heterogeneity between different study results at different time-points
Baseline probability of discontinuation at 4 weeks on oxybutynin (Immediate release)	Published data from 1 study (Madersbacher et al., 1999) The data used were 16 events out of 145 patients (estimated probability = 0.110) Based on previous guideline recommendation for first-line treatment
Baseline probability of discontinuation at 12 weeks on oxybutynin (Immediate release)	Published data from 1 study (Drutz et al., 1999) The data used were 35 events out of 112 patients (estimated probability = 0.313)
Baseline probability of continence at 4 weeks on oxybutynin (Immediate release)	Published data from 1 study (Anderson et al., 1999)* The data used were 9 events out of 32 patients (estimated probability = 0.281)
Baseline probability of continence at 12 weeks on oxybutynin (Immediate release)	Published data from 1 study (Drutz et al., 1999) The data used were 22 events out of 103 patients (estimated probability = 0.214)

*Data from this study were not used in the network meta-analysis as the study duration was 6 weeks not 4 weeks

NMA methods

Clinical opinion is that most trials have a timescale for follow-up that reflects the time at which most discontinuations and continence will occur. Therefore, the number of discontinuations and people achieving continence at 4 and 12 weeks were modelled as probabilities rather than rates.

The probabilities of continence and discontinuation were modelled separately. A model to check the correlation between the two outcomes was considered; this model could not be fitted as there were too much missing data.

A binomial/logit model within a generalised linear model framework was used to model each of the two outcomes – discontinuation and continence – at 4 and 12 weeks, as this model is appropriate for probability outcomes. The use of a generalised linear model framework is a unified approach for comparing the models; it reports the deviance information criterion (DIC) and goodness-of-fit using the residual deviance.

Due to lack of data and in acknowledgment of the fact that some of the studies were very small, it was assumed that relative treatment effects were equal at 4 and 12 weeks. Few trials reported at both time points, making it difficult to check this assumption. However, the assumption is clinically plausible and the evaluation of model fit seems to confirm that the chosen models fit the data well.

The trial data formed four treatment networks: discontinuation at 4 weeks and 12 weeks and continence at 4 and 12 weeks. There are several treatments that were not connected to the main network at each of the time points.

For continence, a network meta-analysis was carried out assuming binomial likelihood with a logit link, and assuming that the log-odds ratios of continence were the same at 4 and 12 weeks for trials reporting at both time points. Since there were 4 trials reporting continence status at both 4 and 12 weeks, a further network meta-analysis model was considered for continence, where the log-odd ratios of continence at 4 and 12 weeks within a trial reporting at both time points were allowed to differ, but were assumed similar (exchangeable) with a common mean and variance.

For discontinuation, a network meta-analysis was carried out assuming binomial likelihood with a logit link, and assuming that the long odds ratios of discontinuation were the same at 4 and 12 weeks for trials reporting at both time points. Since only one trial reported at both 4 and 12 weeks, a model where the treatment effects are considered similar instead of equal could not be fitted.

The posterior distribution of the log-odds of discontinuation at 4 weeks on oxybutynin IR was approximately normal with posterior mean −2.114 and standard deviation 0.27, which translates into a baseline probability of discontinuation on oxybutynin IR of 11% with 95% credible interval (CrI) from 7% to 17%. The posterior distribution of the log-odds of discontinuation at 12 weeks on oxybutynin IR was approximately normal with posterior mean −0.7959 and standard deviation 0.52, which translates into a baseline probability of discontinuation on oxybutynin IR of 31% with 95% CrI from 23% to 40%.

The probabilities of achieving continence in the oxybutynin IR arm of trial *i* (*i* = 1 for both 4 weeks and 12 weeks) were modelled in the same way as the probabilities of discontinuation. The posterior distribution of the log-odds of continence at 4 weeks on oxybutynin (immediate release) was approximately normal with posterior mean −0.9714 and standard deviation 0.4, which translates into a baseline probability of continence on oxybutynin IR of 28% with 95% CrI from 14% to 45%. The posterior distribution of the log-odds of continence at 12 weeks on oxybutynin (immediate release) was approximately normal with posterior mean −1.321 and standard deviation 0.24, which translates into a baseline probability of continence on oxybutynin IR of 21% with 95% CrI from 14% to 30%.

The residual deviance and DIC were used to check model fit for the identical and exchangeable within-trial log odds ratios at different time points and to compare fixed and random effects models.

Model fit

Convergence was assessed using the Brooks-Gelman-Rubin plots and by examination of the history plots, and was satisfactory by at least 50,000 iterations in all cases. Models were then run for a further 20,000 iterations on three separate chains, and all results are based on this further sample.

Comparing the posterior mean of the residual deviance for the fixed effect model with equal relative effects at 4 and 12 weeks – 76.67 – to 94 data points for discontinuation, we can say that the model is a good fit to the data. Comparing the DIC for the fixed and random effects models with equal relative effects (589.9 and 591.8, respectively) we conclude that there is no reason to choose the more complex random effect model. We will therefore report all results for the fixed effect model only for discontinuation.

Similarly, for continence, the posterior mean of the residual deviance for the fixed effect model with equal effects at 4 and 12 weeks is 53.5, which means the model is a good fit to the data, when compared to 56 data points. Comparing the DIC for the fixed and random effects models with equal relative effects (415.3 and 416.2, respectively,) the fixed effect model was preferred as it is simpler.

A model that relaxed the assumption of equal relative effects at 4 and 12 weeks within a trial reporting at both time points was also fitted to the continence data with fixed treatment effects. The DIC for this model was 575.4 with posterior mean of the residual deviance of 76.0. This is not a substantial improvement in fit over the fixed effect model with equal relative effects. This supports the assumption of equal treatment effects at 4 and 12 weeks, and we therefore do not consider the model that relaxes this assumption any further.

We report all results for the fixed effect model assuming equal relative effects at 4 and 12 weeks for continence and discontinuation.

Consistency

Consistency was checked for both the continence and discontinuation networks, by fitting an inconsistency model (Dias & Welton, 2011) and comparing the model fit to the fixed effect model. The values of the posterior mean of the residual deviances and the effective number of parameters (pD) are comparable, indicating no evidence of inconsistency in this network.

Description of included studies

A total of 44 RCTs with 25,147 participants were included in the NMA (Appell et al., 2001; Cardozo et al., 2004; Cartwright et al., 2011; Chapple et al., 2004; Chapple et al., 2004a; Chapple et al., 2005; Chapple et al., 2007; Chapple et al., 2007b; Choo et al., 2008; Diokno et al., 2003; Dmochowski et al., 2002; Dmochowski et al., 2008; Dmochowski et al., 2010a; Dorschner et al., 2000; Drutz et al., 1999;

Haab et al., 2004; Herschorn et al., 2010a; Hill et al., 2006; Ho et al., 2010; Homma et al., 2003; Huang et al., 2012; Junemann et al., 2006; Kaplan et al., 2011; Karram et al., 2009; Madersbacher et al., 1999; Malone-Lee & Al-Buheissi, 2009; Malone-Lee et al., 2001; Millard et al., 1999; Minassian et al., 2007; Nitti et al., 2007; Rackley et al., 2006; Rogers et al., 2008; Rudy et al, 2006; Staskin et al., 2007; Staskin et al., 2009; Steers et al., 2005; Thuroff et al., 1991; VanKerrebroeck et al., 2001; Vardy et al., 2009; Weiss et al., 2012; Yamaguchi et al., 2007; Yamaguchi et al., 2011; Zat'ura et al., 2010; Zinner et al., 2004). In total, 12 RCTs provided data at 4 weeks (6 for continence status and 7 RCTs for discontinuation for any reason, with a single study providing for both outcomes). For the 12 week analysis, 36 RCTs provided data (20 for continence status and 36 for discontinuation for any reason) with 18 studies providing data at both time points. Four studies reported on continence status at both time points, and a single study reported on discontinuation for any reason at both time points.

All studies included women with overactive bladder symptoms but seven studies also included women who were dry at baseline. In these studies, only those who were incontinent at baseline were included in the continence status analysis.

The mean age of the study participants ranged from 49 years (SD ± 12) to 75 years (SD ± 6). Where reported the mean number of urgency episodes per day ranged from 2.7 (SD ± 1.8) to 11.4 (SD ± 4.0). As several studies included women who were continent at baseline, the range of number of incontinence episodes is not reported for the included studies. Where reported, the mean duration of OAB symptoms ranged from 4.2 years (SD ± 6.2) to 9.0 years (SD ± 11.2).

Review findings (Evidence profile)

Table 6.14 presents the median odds ratios and associated credible intervals for each pair-wise comparison of drugs used in the network meta-analysis. Tables 6.15 and 6.16 report the absolute probability of continence and discontinuation for each drug at both time points.

Table 6.14 Posterior median (and credible intervals) for the odds ratios.

Discontinuation: posterior median and CrI

Continence: posterior median and CrI

Oxybutynin IR	0.38 (0.24,0.60)	0.54 (0.33,0.89)	0.44 (0.28,0.68)	1.01 (0.52,1.95)	0.42 (0.27,0.65)	0.53 (0.23,1.29)	0.55 (0.35,0.86)	0.55 (0.32,0.95)	0.85 (0.27,2.81)	0.38 (0.21,0.68)	0.54 (0.31,0.94)	0.47 (0.25,0.87)	0.48 (0.31,0.73)
0.66 (0.29,1.42)	Solifenacin	1.41 (0.96,2.09)	1.15 (0.89,1.48)	2.64 (1.24,5.61)	1.10 (0.89,1.35)	1.38 (0.65,3.11)	1.44 (1.15,1.79)	1.44 (0.99,2.11)	2.23 (0.77,6.87)	0.98 (0.64,1.52)	1.40 (0.94,2.10)	1.23 (0.75,1.97)	1.25 (1.05,1.49)
0.69 (0.29,1.62)	1.06 (0.71,1.57)	Oxybutynin ER	0.81 (0.56,1.17)	1.86 (0.85,4.09)	0.78 (0.55,1.10)	0.98 (0.43,2.31)	1.01 (0.70,1.48)	1.02 (0.62,1.67)	1.57 (0.52,5.03)	0.70 (0.41,1.19)	0.99 (0.60,1.65)	0.86 (0.49,1.54)	0.88 (0.62,1.26)
0.83 (0.45,1.55)	1.26 (0.59,2.90)	1.19 (0.51,2.97)	Tolterodine IR	2.31 (1.09,4.85)	0.96 (0.76,1.21)	1.21 (0.56,2.74)	1.25 (0.97,1.61)	1.26 (0.84,1.88)	1.94 (0.66,6.06)	0.86 (0.55,1.35)	1.22 (0.81,1.86)	1.07 (0.65,1.76)	1.09 (0.88,1.36)
0.60 (0.18,1.95)	0.91 (0.37,2.29)	0.87 (0.33,2.33)	0.72 (0.22,2.36)	Propiverine IR	0.42 (0.20,0.87)	0.53 (0.19,1.54)	0.54 (0.26,1.15)	0.55 (0.24,1.23)	0.84 (0.16,0.86)	0.37 (0.24,1.21)	0.53 (0.20,1.10)	0.46 (0.23,0.99)	0.47 (0.60,2.81)
0.49 (0.22,1.05)	0.75 (0.65,0.86)	0.71 (0.49,1.03)	0.59 (0.26,1.28)	0.82 (0.33,2.02)	Tolterodine ER	1.26 (0.60,2.81)	1.31 (1.11,1.54)	1.31 (0.91,1.90)	2.03 (0.70,6.23)	0.90 (0.59,1.36)	1.28 (0.87,1.89)	1.11 (0.70,1.77)	1.14 (0.99,1.31)
0.57 (0.24,1.32)	0.87 (0.60,1.28)	0.83 (0.49,1.40)	0.69 (0.29,1.60)	0.96 (0.36,2.50)	1.17 (0.82,1.69)	Propiverine ER	1.04 (0.47,2.18)	1.04 (0.44,2.32)	1.60 (0.43,6.08)	0.71 (0.29,1.64)	1.02 (0.43,2.29)	0.88 (0.36,2.09)	0.91 (0.41,1.88)
0.59 (0.27,1.26)	0.90 (0.77,1.04)	0.85 (0.58,1.24)	0.71 (0.31,1.53)	0.98 (0.39,2.42)	1.20 (1.09,1.32)	1.03 (0.71,1.47)	Fesoterodine	1.01 (0.70,1.45)	1.55 (0.54,4.76)	0.69 (0.45,1.04)	0.98 (0.67,1.44)	0.85 (0.53,1.36)	0.87 (0.76,1.00)
0.70 (0.28,1.77)	1.07 (0.63,1.88)	1.02 (0.53,1.98)	0.85 (0.32,2.18)	1.18 (0.41,3.34)	1.43 (0.85,2.49)	1.23 (0.65,2.34)	1.20 (0.71,2.09)	Trospium	1.54 (0.51,4.93)	0.68 (0.41,1.15)	0.97 (0.60,1.59)	0.85 (0.49,1.48)	0.87 (0.62,1.21)
0.60 (0.19,1.91)	0.92 (0.40,2.20)	0.87 (0.35,2.22)	0.73 (0.23,2.33)	1.01 (0.29,3.48)	1.23 (0.54,2.93)	1.06 (0.43,2.67)	1.03 (0.45,2.45)	0.85 (0.32,2.35)	Oxybutynin TD	0.44 (0.14,1.37)	0.63 (0.20,1.92)	0.55 (0.17,1.73)	0.56 (0.18,1.61)
0.78 (0.30,2.00)	1.19 (0.69,2.10)	1.13 (0.59,2.21)	0.94 (0.36,2.42)	1.31 (0.46,3.70)	1.59 (0.94,2.79)	1.36 (0.72,2.60)	1.33 (0.78,2.34)	1.11 (0.52,2.37)	1.30 (0.47,3.49)	Darifenacin	1.42 (0.84,2.42)	1.24 (0.68,2.25)	1.27 (0.86,1.87)
0.78 (0.30,2.00)	0.99 (0.75,1.31)	0.94 (0.59,1.47)	0.79 (0.33,1.75)	1.08 (0.43,2.74)	1.32 (1.02,1.72)	1.13 (0.74,1.73)	1.11 (0.85,1.44)	0.92 (0.51,1.63)	1.08 (0.44,2.54)	0.83 (0.46,1.47)	Trospium ER	0.87 (0.49,1.54)	0.89 (0.62,1.27)
0.61 (0.26,1.42)	0.94 (0.65,1.36)	0.89 (0.53,1.49)	0.74 (0.31,1.73)	1.02 (0.39,2.68)	1.25 (0.88,1.80)	1.07 (0.66,1.75)	1.05 (0.73,1.50)	0.87 (0.46,1.62)	1.02 (0.40,2.49)	0.79 (0.41,1.47)	0.95 (0.62,1.44)	Oxybutynin TG	1.02 (0.65,1.60)

	0.33 (0.15,0.71)	0.51 (0.44,0.58)	0.48 (0.33,0.70)	0.40 (0.18,0.86)	0.56 (0.22,1.36)	0.68 (0.61,0.75)	0.58 (0.41,0.82)	0.57 (0.51,0.63)	0.47 (0.27,0.79)	0.55 (0.23,1.26)	0.43 (0.25,0.72)	0.51 (0.40,0.65)	0.54 (0.38,0.76)	Placebo

For continence (unshaded area), odds ratios (OR) lower than 1.0 favour the column defining treatment and ORs greater than 1.0 favour the row defining treatment
For discontinuation (shaded area), odds ratios (OR) higher than 1.0 favour the row defining treatment and ORs lower than 1.0 favour the column defining treatment

Table 6.15 Posterior median odds ratios (and credible intervals) for the absolute probability at 4 weeks.

Drug	Continence	Discontinuation
Oxybutynin (immediate release)	0.27 (0.15 to 0.46)	0.11 (0.07 to 0.17)
Solifenacin	0.20 (0.07 to 0.43)	0.04 (0.02 to 0.09)
Oxybutynin (extended release)	0.21 (0.07 to 0.46)	0.06 (0.03 to 0.12)
Tolterodine (immediate release)	0.24 (0.10 to 0.46)	0.05 (0.03 to 0.09)
Propiverine (immediate release)	0.18 (0.05 to 0.48)	0.11 (0.05 to 0.22)
Tolterodine (extended release)	0.16 (0.06 to 0.36)	0.05 (0.03 to 0.09)
Propiverine (extended release)	0.18 (0.06 to 0.41)	0.06 (0.02 to 0.15)
Fesoterodine	0.18 (0.07 to 0.40)	0.06 (0.03 to 0.12)
Trospium	0.21 (0.07 to 0.48)	0.06 (0.03 to 0.12)
Oxybutynin (transdermal)	0.19 (0.05 to 0.48)	0.09 (0.03 to 0.27)
Darifenacin	0.23 (0.08 to 0.50)	0.04 (0.02 to 0.09)
Trospium (extended release)	0.20 (0.07 to 0.43)	0.06 (0.03 to 0.12)
Oxybutynin (topical gel)	0.19 (0.07 to 0.42)	0.05 (0.02 to 0.11)

Table 6.16 Posterior median odds ratios (and credible intervals) for the absolute probability at 12 weeks.

Drug	Continence	Discontinuation
Oxybutynin (immediate release)	0.21 (0.14 to 0.30)	0.31 (0.23 to 0.40)
Solifenacin	0.15 (0.06 to 0.30)	0.15 (0.09 to 0.24)
Oxybutynin (extended release)	0.16 (0.06 to 0.33)	0.20 (0.11 to 0.32)
Tolterodine (immediate release)	0.18 (0.9 to 0.33)	0.17 (0.10 to 0.26)
Propiverine (immediate release)	0.14 (0.04 to 0.36)	0.31 (0.17 to 0.50)
Tolterodine (extended release)	0.12 (0.05 to 0.24)	0.16 (0.09 to 0.26)
Propiverine (extended release)	0.13 (0.05 to 0.29)	0.19 (0.09 to 0.39)
Fesoterodine	0.14 (0.06 to 0.28)	0.20 (0.12 to 0.31)
Trospium	0.16 (0.06 to 0.35)	0.20 (0.11 to 0.33)
Oxybutynin (transdermal)	0.14 (0.04 to 0.36)	0.28 (0.10 to 0.57)
Darifenacin	0.17 (0.07 to 0.37)	0.15 (0.08 to 0.26)
Trospium (extended release)	0.15 (0.06 to 0.30)	0.20 (0.11 to 0.33)
Oxybutynin (topical gel)	0.14 (0.06 to 0.30)	0.17 (0.09 to 0.31)

Evidence statements – odds ratios and credible intervals

The network meta-analysis demonstrated that there was no difference in clinical benefit in terms of continence at 4 or 12 weeks between any of the active drugs compared with the exception of solifenacin, fesoterodine and trospium ER over tolterodine (extended release). The evidence for the whole network meta-analysis was high quality.

The network meta-analysis also demonstrated no difference in clinical benefit in terms of discontinuation at 4 or 12 weeks between the drugs with the exception of the following comparisons:

- solifenacin over oxybutynin (immediate release), propiverine (immediate release) and fesoterodine,
- oxybutynin (extended release) over oxybutynin (immediate release)
- tolterodine (immediate release) over oxybutynin (immediate release) and propiverine (immediate release)
- tolterodine (extended release) over oxybutynin (immediate release) and propiverine (immediate release)
- fesoterodine over oxybutynin (immediate release)
- trospium over oxybutynin (immediate release)
- oxubutynin (transdermal) over propiverine (immediate release)
- darifenacin over oxybutynin (immediate release)
- trospium ER over oxybutynin (immediate release)
- oxybutynin (topical gel) over oxybutynin (immediate release).

The evidence for the whole network meta-analysis was high quality.

Evidence statements – absolute probabilities

The absolute probability of being continent at 4 weeks ranged from 16% for tolterodine (extended release) to 27% for oxybutynin (immediate release). The evidence was of high quality.

The absolute probability of being continent at 12 weeks ranged from 12% for tolterodine (extended release) to 21% for oxybutynin (immediate release). The evidence was of high quality.

The absolute probability of discontinuing from treatment at 4 weeks range from 4% for solifenacin and darifenacin to 11% for oxybutynin (immediate release) and propiverine (immediate release). The evidence was of high quality.

The absolute probability of discontinuing from treatment at 12 weeks range from 15% for solifenacin and darifenacin to 31% for oxybutynin (immediate release) and propiverine (immediate release). The evidence was of high quality.

6.1.5 Economic evidence for OAB wet

Economic evidence

Introduction

Health economic analyses of alternative OAB drugs have been published recently but none of these studies include all the drugs included in the clinical review undertaken for this guideline. This was a clinical topic that was prioritised for health economic analysis in the guideline. Updated evidence on comparative clinical efficacy and discontinuation rates were available for the health economic model from the network meta-analysis. The main results are reported here; details of the methods and further sensitivity analyses are presented in the technical appendix (see Appendix N).

Economic evaluation question

What is the cost effectiveness of OAB drugs compared with no treatment and with each other as first-line treatment for women with overactive bladder induced incontinence?

Background health economic literature

Details of the approach taken and methods used in published studies are only reported here as background information to inform the health economic modelling and not as evidence to support recommendations. Evidence tables reporting methods and results can be found in the guideline appendices. None of the published health economic studies were presented as evidence to the GDG to inform recommendations.

Six new economic evaluations of drug therapies were identified in the literature since the previous guideline was published.

Table 6.17. Summary of the health economics evaluations on drug treatment for women with OAB

Author and year	Country	Study type	Drugs evaluated
(Arlandis-Guzman et al., 2011)	Spain	Cost-utility analysis (decision analytic model)	Fesoterodine vs solifenacin and tolterodine
(Cardozo et al., 2010)	UK	Cost-utility analysis (one year decision-model)	Solifenacin vs fesoterodine, oxybutynin IR, propiverine, tolterodine ER, tolterodine IR
(Hakkaart et al., 2009)	The Netherlands	Cost-utility analysis (Markov)	Solifenacin vs placebo
(Speakman et al., 2008)	UK	Cost-utility analysis (Markov)	Solifenacin vs tolterodine
(Herschorn et al., 2010b)	Canada	Cost-utility analysis (Markov)	Solifenacin vs oxybutynin plus tolterodine (as 2nd line)
(Ko et al., 2006)	USA	Cost-effectiveness analysis	Solifenacin vs oxybutynin, tolterodine, darifenacin and trospium

Five of the studies were cost-utility analyses (Speakman et al., 2008), (Hakkaart et al., 2009), (Herschorn et al., 2010b), (Arlandis-Guzman et al., 2011) and one was a cost-effectiveness analysis (Ko et al., 2006).

All six studies adopted a modelling approach. Five studies were models of 1 year duration using clinical trials data for the first 3 months and assuming efficacy status did not change in the follow-up period up to 1 year. No study considered costs and effects beyond 1 year. Two studies (Herschorn et al., 2010b; Cardozo et al., 2010) were based on efficacy data reported in the clinical review for this guideline. Two studies (Ko et al., 2006; Herschorn et al., 2010b) incorporated published data on discontinuation rates at 1 year in their analysis.

Four cost-utility analyses were undertaken alongside RCTs. Patient-level data were available for the health economic analysis. These studies were designed as Markov models with cycles of 1 month and finishing 1 year after the start of treatment (Cardozo et al., 2010; Speakman et al., 2008; Hakkaart et al., 2009; Herschorn et al., 2010b). This is an efficient way of modelling chronic conditions where an individual may move between several health states over time. All three studies used the same model structure as that developed in a previous study published in 1998 as this study reported quality adjusted life year (QALY) values for five health states based on severity of symptoms of OAB (Kobet et al., 1998). This study had derived QALY values from a willingness-to-pay study of women with OAB.

In the Markov models (where women could move between health states over time), women with OAB were assigned to a health state depending on the level of severity of their condition at the start of treatment (none were in the mild state). Every month an individual either moved health state or stayed in the same state. If an individual discontinued treatment they moved to a discontinuation state for the duration. Specific costs and health-related quality of life values were assigned to each health state depending on the level of severity of OAB and associated comorbidities. Each drug regimen was associated with different probabilities of moving between health states, depending on treatment efficacy and likelihood of discontinuation. The total number of patients in each health state in each cycle was summed to arrive at total cost and number of QALYs associated with each drug alternative for that cohort. The studies all used estimates of QALY values for each health state from a Markov model for OAB developed in Sweden (Kobet et al., 1998), which was based on a willingness-to-pay analysis undertaken by the same study team (Johannesson et al., 1997). The three subsequent economic evaluations used the same QALY values but used patient-level data from clinical trials to map the health

state of every individual in the trial at each time point. None of these studies reported the transition probabilities of moving between health states, and patient level data was not reported.

Another recent study also adopted a decision-analytic approach rather than a Markov model structure (Arlandis et al., 2011). The study included men and women in the analysis. It did not use the same QALY values reported in the Swedish study as the previous three studies had done. The authors obtained data from a more recent economic study that derived QALYs from the King's Health Questionnaire. Much higher QALY values were reported for all women with UI. No subgroup analyses were reported by severity of OAB.

Only two economic studies were based in the NHS (Cardozo et al., 2010 Speakman et al., 2008). The clinical efficacy data on which the earlier study is based was published prior to the 2006 cut-off date for this guideline update (Speakman et al., 2008). The study was based on a single head-to-head trial of solifenacin and tolterodine. The later study used data published in 2008 and compared six treatment scenarios and included switching to a higher dose formulation if a lower dose was not effective. Cycle length was 3 months. Outputs were measured as symptom resolution, and differentiated between symptoms of urgency and frequency. The model assumed clinical effectiveness was constant over time for women who continued with drug therapy.

The most recent study is from Spain. Clinical efficacy data were obtained from placebo-controlled trials not included in the clinical review for this guideline (Arlandis-Guzman et al., 2011). The studies from the Netherlands and the USA are both based on efficacy data published before 2006 (Hakkaart et al., 2009; Ko et al., 2006).

Only one study from Canada was based on efficacy data reported in this guideline (Herschorn et al., 2010b). The efficacy study on which it is based evaluated solifenacin versus oxybutynin plus tolterodine as second line treatment. The STAR trial on which this study is based was published in 2010.

None of these studies provided sufficient data on their own to inform recommendations in this guideline. The outcomes in the Markov model studies do not correspond to the outcomes reported in this guideline. Combining micturition and leakage was not considered a clinically useful outcome by the GDG. Micturition is a normal physiological function for which there is a normal range that is considered to be healthy. Leakage, on the other hand, is an involuntary voiding that requires treatment. Studies that report a combination of micturition and leakage do not distinguish between the two health states. A combined micturition and leakage rate of 7–9 hours out of 24 hours may be healthy or may be unhealthy, depending on whether the leakage was voluntary or involuntary. Therefore a utility cannot be assigned to this outcome. This is a common outcome reported in trials. However, studies that report this outcome may introduce bias as they report voluntary and involuntary micturition together, which may make a drug appear to be more effective than it is. A less biased study would report these outcomes separately.

In addition, transition probabilities used in the studies based on single RCTs were not reported, which meant it was not possible to repeat any of these analyses with updated UK-based cost data. Also, clinical efficacy data from placebo-based trials is included in the studies that use data from meta-analysis (not a single trial). Data from single placebo-based trials was not considered by the GDG to be sufficiently unbiased evidence of efficacy for head-to-head comparison of OAB drugs. The more recent models assumed constant effectiveness over time for women on treatment.

Finally, none of the studies included all the OAB drugs that have shown clinical benefit in the head-to-head trials included in the systematic review for this guideline, and none of the studies were sufficiently similar in model structure to incorporate more than one published model into a new analysis evaluating all the relevant drug comparisons.

Structure of the health economic model

The health economic evaluation of drugs for women with OAB wet is presented as a cost-utility analysis with QALYs as the outcome of interest. It is a model-based evaluation in a UK clinical setting over a 12-month period. It was the GDG expert opinion that, in reality, very few women remain on OAB drug treatment for more than 12 months. By that time, all women who do not achieve acceptable improvement or have unacceptable side-effects have discontinued treatment and those left on treatment will continue to have benefit from the treatment. Therefore, increasing the length of time of

the model would not change the order of cost effectiveness. Estimates of clinical effectiveness and other model parameters are derived from the systematic review undertaken for this guideline.

Since there are 13 drug options in the NMA and two alternative surgical interventions (anaboltulinum and sacral nerve stimulation), a health economic model did not consider the full clinical pathway with all options after conservative management had failed. The GDG considered that the level of complexity, the number of assumptions required and the associated uncertainty would not aid its decision making.

Two model structures were developed after stakeholder feedback. This was because the network meta-analysis only calculated the probability of being continent from 4-week trial data due to lack of evidence. The probability of achieving absolute continence at 12 weeks was calculated from the relative probabilities at 4 weeks, anchored to the actual 12-week probability of continence for oxybutynin immediate release only. This may have biased the results. Therefore, results of the analysis using the second model structure are presented in the technical appendix along with the other sensitivity analyses undertaken (see Appendix N). In the base case model structure, a woman could be in a treatment state and a continence state independently. This is because clinical review for this guideline reported data from RCTs on the probability of a woman being continent separately from the probability of a woman being on treatment. A woman could be on treatment and continent or on treatment and incontinent (achieving some or no relief of symptoms without full continence) or could be on treatment and incontinent. The model assumed that all women who discontinued treatment would be incontinent (that is, with no chance of spontaneous recovery without treatment). The base case model structure is illustrated in the technical appendix (Appendix N).

Table 6.18 illustrates the costs and outcomes used in the health economic model for treatment states (on treatment or discontinued) and health states (continent or incontinent).

Table 6.18 Cost and QALY data included in the evaluation of OAB drug treatment for women with OAB wet

Model state	Cost	QALY
Treatment state		
On treatment	Drug cost only	None
Discontinued treatment	No additional cost	None
Continence state		
Incontinent	Pads only	Treatment failure
Continent	No additional cost	Treatment success

Model validation

Two models were developed independently by two health economists at NCC-WCH, using the same data but without reference to the other model. Discrepancies were discussed and Excel® cell reference errors were corrected in earlier drafts.

Values used in the model

Estimates of effectiveness and discontinuation rates

The efficacy data used in the economic evaluation comes from the network meta-analysis of all OAB drugs on which there is published evidence from RCTs. Data were not reported separately for women with OAB wet and OAB dry. Therefore, the health economic analysis did not distinguish between interventions for women with the different forms of OAB. Two outcomes were identified which were relevant to women with OAB wet for which there was sufficient evidence to include an analysis in the NMA: these were continence status and discontinuation rate. Therefore, the health economic model considers the cost effectiveness of antimuscarinic drugs for women with OAB wet. This limitation is discussed in the 'Linking evidence to recommendations' section at the end of this chapter.

The advantage of using levels of severity in a model is that it can capture improvements in symptoms that do not lead to complete recovery. However, the GDG had two concerns about this approach. First, the GDG view was that for women with incontinence, the most important outcome (but not the only important outcome) is to be completely dry. A reduction in symptoms can bring relief, but in terms of

activities of daily living (such as working, socialising, travelling), any symptoms of incontinence can be extremely debilitating and an improvement, while welcome, may not make those activities any easier to manage. This view was strongly supported by the lay members of the GDG.

Second, there is a complete lack of evidence on the impact on quality of life for women who experience an improvement in continence status without achieving full continence, whereas there is published data on the mean change in quality of life associated with "diseased" or "not diseased" health states. Assumptions have been made in other models about the relationship between severity of symptoms and quality of life but with insufficient justification or empirical basis. Therefore, the GDG chose to focus on continence status as the primary outcome in the health economic modelling, which is a clearly understood outcome and for which QALY values have been reported (see appendix N). The GDG's view was that drugs that lead to the most improved continence status ("absolutely dry") would also be the drugs leading to the most improved symptoms without achieving continence. The GDG recognised that this approach restricted the analysis to women with OAB wet.

The GDG further recognised that continence status is only one outcome, which serves as a proxy for the effectiveness of OAB drug treatment overall. It is recognised by the GDG that it is a conservative estimate of benefit and that more women will experience some benefit from drug treatment without achieving complete continence. But the analysis does provide a less biased approach than a head-to-head review of drugs for treating the same condition. The GDG took into account the limitations of the NMA and HE analysis in reaching its conclusions.

The network meta-analysis produced 20,000 simulated probabilities of continence and discontinuation of treatment for 13 OAB drugs. A probabilistic sensitivity analysis was constructed in an Excel® model. Details of the structure, equations for transition probabilities and output of the NMA from which the state transitions were derived are presented in Appendix N.

Table 6.19 Mean discontinuation and continence status probabilities derived from 20,000 random simulations in the network meta-analysis

Antimuscarinic treatment	Discontinuation		Continence status ('absolutely dry')	
	Week 4	Week 12	Week 4	Week 12
Oxybutynin IR	11.0%	31.3%	28.2%	21.3%
Solifenacin	4.7%	15.2%	21.3%	15.8%
Oxybutynin ER	6.5%	20.2%	22.3%	16.7%
Tolterodine IR	5.3%	17.0%	25.1%	18.8%
Propiverine IR	11.6%	31.9%	20.8%	15.5%
Tolterodine ER	5.1%	16.4%	17.1%	12.4%
Propiverine ER	6.7%	20.4%	19.4%	14.3%
Fesoterodine	6.6%	20.3%	19.6%	14.4%
Trospium	6.7%	20.6%	22.8%	17.1%
Oxybutynin TD	10.8%	29.4%	20.8%	15.5%
Darifenacin	4.7%	15.1%	24.6%	18.5%
Trospium ER	6.5%	20.1%	21.2%	15.8%
Oxybutynin TG	5.8%	18.2%	20.4%	15.1%

Estimates of costs

The costs used in the base case model were the cost over 4 weeks of drugs for women on antimuscarinic treatment and incontinence pad use for women who were incontinent (regardless of whether they were on treatment or not). Health service cost was assumed to be equal.

Additional GP visits were included in the sensitivity analysis for women who discontinue treatment. An additional cost for women on oxybutynin (immediate release) was included in a sensitivity analysis. It was suggested that hospitalisation rates might be higher for this group due to the increased risk of delirium.

Model inputs

The model inputs are describeded below. In accordance with the NICE guidelines manual (2012), drug costs were obtained from the NHS drug tariff where available and calculated for a four-week cycle (see Appendix N for the detailed calculations). NHS drug tariff prices were correct as of June 2013. For one drug (trospium extended release), no NHS drug tariff was published, so the BNF price was used. No price for oxybutynin topical gel was published in the NHS drug tariff or the BNF, so the price for oxybutynin transdermal was assumed. On occasions, the NHS Commercial Medicines Unit may obtain price reductions for drugs procured through secondary care and it publishes prices of some generic drugs through its Electronic Marketing Information Tool (eMIT). However, as the population covered by this model will largely be treated in primary care and eMIT costs were not used. Health service costs were derived from Health Resource Group (HRG) codes for 2012/13 and staff costs from NHS Unit Costs of Health and Social Care (PSSRU 2012).

The estimates of continence and discontinuation at 4 weeks and 12 weeks were derived from the network meta-analysis (see Table 6.19). No published data on continence rates at 1 year was identified in the literature. The continence rate at 52 weeks was 20% for all drugs, which was an assumption based on GDG opinion. At the start of development, data on discontinuation rates at 52 weeks were not available. During development, a study was published (Wagg et al., 2012) and these data were input into the base case model. For drugs in the model where 52 week discontinuation rates were not reported, the median value in the range was used. This assumption was tested in one-way sensitivity analysis. Results for both modelling assumptions for 52 week discontinuation rates are reported in this chapter. Further sensitivity analyses are reported in the technical appendix.

A review of quality of life data was undertaken in a Health Technology Appraisal (Imamura, 2010). This review presented what was known at the time about the evidence on quality of life and utility estimates for incontinence. No new studies were identified that have been published since 2010 on utility estimates for incontinence. The study from which the utility estimates were derived did include an estimate of the distribution and so could be included in the PSA. Table 6.20 reports the 4-week drug cost used in the model. Further details about how these costs were calculated are reported in the appendix N.

The appendix N gives more details about how values were calculated and their distributions.

Table 6.20 Parameters and values included in the base case model and sensitivity analyses (for a full table of all parameters and modelling assumptions, see Appendix N)

Parameter	Value	Notes	Included in PSA or one-way SA*
Effectiveness parameters			
Continence status at 4 and 12 weeks	See table 6.19		PSA
Continence status at 52 weeks	20%, or same as 12 week rate if that is the lower value		No
Discontinuation rate at 52 weeks:	80% for all drugs **and**	First assumption by GDG before Wagg study data were available	
Solifenacin	65%	From Wagg et al 2012. Values for drugs with missing data assumed to be midpoint value in the range	One-way SA
Tolterodine ER	72%		
Propiverine	73%		
Oxybutynin ER	74%		

Parameter	Value	Notes	Included in PSA or one-way SA*
Trospium	74%		
Tolterodine IR	76%		
Oxybutynin IR	78%		
Darifenacin	83%		
Utility			
Continence	0.85	• Derived from Haywood et al 2008, reported in Imamura et al 2010.	PSA
Incontinence	0.74		PSA
Health service costs			
GP visits	£40	Based on PSSRU 2012 for GP patient contact lasting £11.7 minutes excluding staff costs, and with qualification costs. Model assumed one consultation every 2 months for women who discontinue treatment or who are not treated	One-way SA
Hospitalisation	£2,029	Hospitalisation episode for delirium based on HRG code WD11Z. Risk = 1/5,000 based on GDG expert opinion	One-way SA
Incontinence pads	£8	GDG opinion based on NHS costs for a continence service in England, with additional costs added for overheads (see Appendix N for details)	One-way SA

*sensitivity analysis

Table 6.21 Four-week cost of OAB drugs included in the PSA, NHS Drug Tariff and BNF, June 2013.

Cost parameters	Dose	Daily frequency	4-week cost	Notes
Oxybutynin IR	5 mg	3	£4.71	Non-proprietary formulation price
Solifenacin 5 mg and 10 mg	5 mg & 10 mg	1	£29.39	Weighted average price (see Table 7 in Appendix N for calculation)
Oxybutynin ER	10 mg	1	£25.70	-
Tolterodine IR	2 mg	2	£4.36	Non-proprietary formulation price
Propiverine IR	15 mg	3	£27.00	BNF starting dose is 1–3 times daily. Studies included in the clinical review report 3 times daily.
Tolterodine ER	4 mg	1	£25.78	Non-proprietary formulation price
Propiverine ER	30 mg	1	£24.45	-

Cost parameters	Dose	Daily frequency	4-week cost	Notes
Fesoterodine	4 mg & 8 mg	1	£25.78	Same price for 4 mg and 8 mg
	20 mg	2	£24.27	Non-proprietary formulation price
Oxybutynin TD	patch	twice weekly	£27.20	-
Darifenacin	7.5 mg	1	£20.90	-
Trospium ER	60 mg	1	£23.05	-
Oxybutynin TG	60 mg			Not in NHS tariff or the BNF; assumed to be the same as price as oxybutynin (transdermal patch)

Model assumptions

All health economic models are simplifications of reality. They balance requirements from decision-makers that the outputs reflect the complexity of clinical reality against the need to retain integrity by keeping to a minimum the number of assumptions that are required to drive the model. The GDG requested that all model assumptions and the description of those assumptions be clearly reported to maximise transparency of reporting. Table 6.22 presents the assumptions in the model alongside the GDG's view of the rationality of each assumption, and whether the assumption was tested in further sensitivity analysis.

Table 6.22 Assumptions used in the health economic model of OAB drugs for OAB wet

Assumption	Basis of the assumption
1. Women who discontinue treatment with an OAB drug stay off treatment for the remainder of the year. Switching treatment is not included in this model.	This model does not focus on the treatment pathway. Therefore it does not reflect clinical reality but compares the cost effectiveness of all the OAB drugs considered for first-line treatment.
2. Continence status should be measured as 'completely dry' rather than an improvement in episodes of incontinence.	The GDG view was 'improvement' was a more subjective measure of health gain than 'completely dry'. Depending on severity at the start of treatment, a change in the number of episodes could have great, little or no impact on quality of life.
3. OAB drugs that lead to the most improved continence status (complete dryness) would also be the drugs leading to the most improved symptoms without complete dryness.	The assumption is that OAB drugs that are the most effective in making women with OAB wet completely dry are also more effective at improving symptoms. Additional benefit is associated with some improvement in symptoms so the cost effectiveness of drugs is likely to be underestimated in the model.
4. Women who are off treatment are incontinent for the remainder of the model (up to 1 year).	This may represent an overestimate of the number of women who are incontinent in 1 year as some women will resume continence without treatment.
5. Weekly continence rates are linear throughout the model, and are determined by 12-week continence rates reported in RCTs and continence rates at 1 year.	This was a simplifying assumption given the lack of data for discontinuation rates.

Assumption	Basis of the assumption
6. All women with continued incontinence are offered the same package of care to manage their incontinence.	The baseline weekly cost of managing continence was based on pad use only. Other costs were assumed to vary little between drugs. Personal and NHS costs were included because including NHS costs only was likely to skew the analysis.
7. Adverse events stop when OAB drug treatment stops; also, there are no prolonged adverse effects.	The GDG accepted that this was a reasonable assumption reflecting clinical practice (see assumptions 8 and 11).
8. The cost of adverse events is not included in the analysis.	Adverse events with long-term health consequences are rare and were considered to be equally likely with all the drugs being compared. The majority of adverse events are experienced only while on treatment and will stop when treatment is discontinued.
9. All women in the hypothetical cohort can be offered drug therapy.	In reality some antimuscarinics are not suitable for all women, such as oxybutynin IR in the frail elderly. This is reflected in the recommendations.
10. No additional primary care or nursing support is required by women who are incontinent; that is, they would require the same amount of support as women on successful treatment.	The GDG acknowledged that women who have successful treatment may continue to have problems with urgency or have side effects that may require additional health care. Women who continued to be incontinent are likely to have healthcare needs requiring support from primary care or a specialist team.
11. The discontinuation rate at 1 year is the same for all OAB drugs – 80%.	It is widely reported that discontinuation is high for all OAB drugs at 1 year. No data were identified to allow the model to discriminate between drugs on the basis of discontinuation. This assumption was tested in sensitivity analysis by using recently published data for 12 month discontinuation.
12. The model ends after 1 year due to the fact that the majority of women have discontinued treatment at that stage.	The GDG view was that this assumption mirrored clinical experience. This was explored in one-way sensitivity analysis by extending the model to 2 and 5 years.

Probabilistic sensitivity analysis and one-way sensitivity analyses

Probabilistic sensitivity analysis (PSA) was undertaken on effectiveness and discontinuation rates using probabilities derived from the network meta-analysis. For further explanation of how values were obtained to run the PSA, see Appendix N. Utility estimates were also included in the PSA using the standard deviations reported to calculate the distribution of parameter values. See tables 6.19 and 6.20 for all the inputs into the PSA model and Appendix N for further details of the distributions used in the PSA.

A second model was constructed where continence and continuation rates were no longer independent after 4 weeks because of uncertainty of the assumption that continence and discontinuation could be modelled independently. In the second model, for cycles beyond 4 weeks, the probability of being continent was derived from the discontinuation rate only. For a description of model structure and the equations used to calculate health state transitions, see Appendix N.

Assumptions explored in the probabilistic sensitivity analysis model were:

- option 1 – inputting recently published UK data on discontinuation rates at 1 year (Wagg et al., 2012) assuming highest discontinuation rates for drugs with missing data

- option 2 – inputting recently published UK data on discontinuation rates at one year (Wagg et al., 2012) assuming lowest discontinuation rates for drugs with missing data.

Assumptions explored in one-way sensitivity analyses in the base case model were:

- increasing health service costs for women who are incontinent who seek further medical advice in primary care
- increasing hospital admissions costs associated with adverse events associated with oxybutynin IR
- lower and higher cost of incontinence pads
- extending the time horizon to 2 and 5 years, assuming no change after 12 months (all women who are continent/incontinent and on/off drug treatment remain in the same health state and treatment state for the remainder of the model term).

Results

Analysis with initial (base case) values, model structure 1

Deterministic and probabilistic sensitivity analysis results:

Table 6.23 shows the incremental cost-effective ratios and net benefits for all the OAB drugs included in the health economic analysis. This model assumed a constant rate of discontinuation at 52 weeks of 80%.

A granulated breadown of the total costs is presented in Appendix N.

Table 6.23. Base case cost per QALY per woman for first-line treatment with OAB drugs for OAB wet assuming 80% discontinuation at 52 weeks. One year analysis, PSA based on 20,000 simulations

Treatment	Cost	QALY	ICER	Net benefit	Probability of being cost effective at £20,000 per QALY
Oxybutynin IR	£363.82	0.7623	dominates	£14,883	64%
Tolterodine IR	£374.09	0.7598	dominated	£14,822	24%
No treatment	£416.00	0.7400	dominated	£14,384	0%
Darifenacin	£503.84	0.7592	dominated	£14,679	5%
Trospium ER	£523.56	0.7568	dominated	£14,613	0
Trospium	£527.99	0.7579	dominated	£14,630	1%
Propiverine IR	£538.82	0.7563	dominated	£14,586	3%
Propiverine ER	£539.01	0.7554	dominated	£14,568	0%
Oxybutinin ER	£540.27	0.7576	dominated	£14,612	0
Oxybutynin TD	£543.21	0.7563	dominated	£14,582	2%
Fesoterodine	£548.32	0.7556	dominated	£14,563	0
Oxybutinin TG	£559.44	0.7562	dominated	£14,564	0
Tolterodine ER	£561.03	0.7535	dominated	£14,510	0
Solifenacin	£577.50	0.7569	dominated	£14,561	0

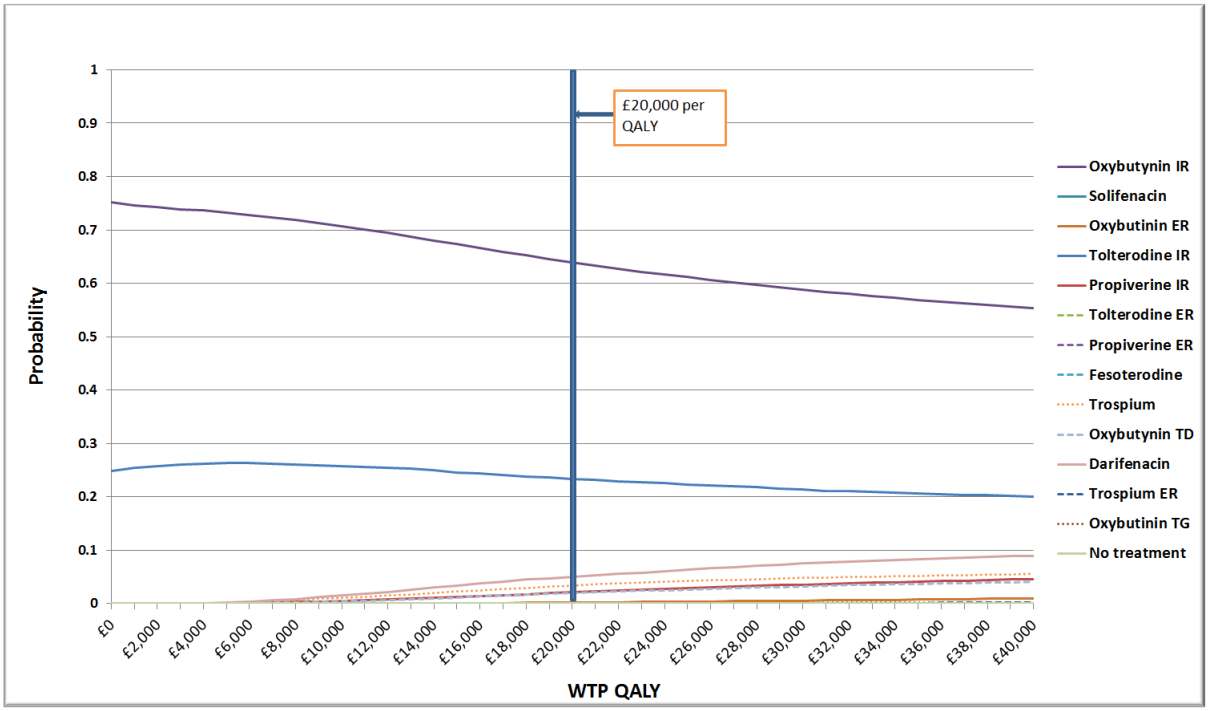
*net benefit is calculated as (QALYs x £20,000) - cost of treatment)

The cost per year of OAB drugs ranged from £364 to £578. The difference in effectiveness was very small – a difference less than of 0.01 QALY between the most effective and least effective drug over a year (oxybutynin immediate release and tolterodine extended release, respectively). The weekly cost of oxybutynin (immediate release), and tolterodine (immediate release) were below the cost of no treatment since the latter included £8 per week for incontinence pads in the base case model. Oxybutynin (immediate release) was the most cost-effective first-line antimuscarinic therapy. All other drugs were more expensive and less effective than oxybutynin (immediate release).

The probability of any drug being the most cost effective at £20,000 per QALY is shown in the final column of Table 6.23. The probability was highest for oxybutynin (immediate release) and tolterodine (immediate release). All other drugs had no more than a 5% chance of being cost effective at that threshold.

The cost effectiveness acceptability curve illustrates the same data in graphic form.

Figure 6.1 Cost effectiveness acceptability curve for first-line antimuscarinic treatments, base case with a constant 80% discontinuation rate at 52 weeks



Results of the base case model using published data on long-term discontinuation rates for OAB drugs

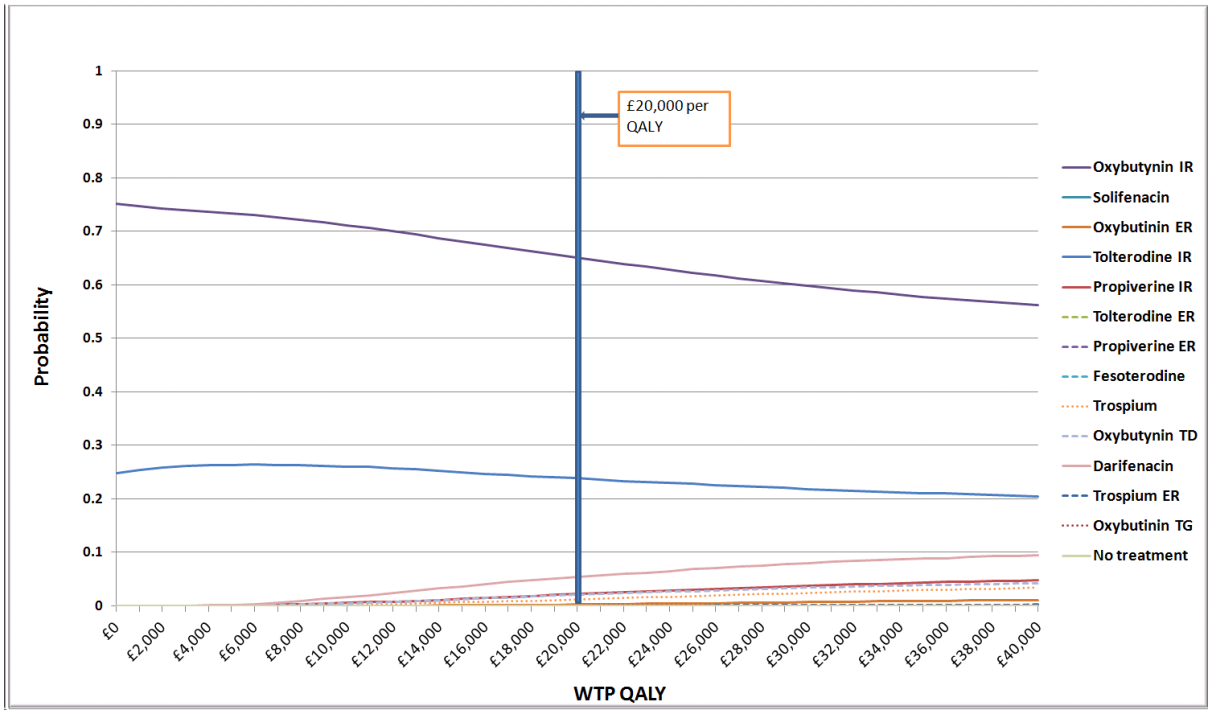
The model was re-presented to the GDG with newly published data on the long-term discontinuation rates. However, these data did not alter the ranking of the most cost-effective drugs and drugs with lower continuation rates still had a very low (no more than 5%) probability of being cost effective at £20,000 per QALY.

Table 6.24. Base case cost per QALY per woman for first-line treatment with OAB drugs for OAB wet assuming differential discontinuation rates at 52 weeks. One year analysis, PSA based on 20,000 simulations

Treatment	Cost	QALY	ICER	Net benefit	Probability of being cost effective at £20,000 per QALY
Oxybutynin IR	£364.50	0.7623	dominates	£14,882	65%
Tolterodine IR	£375.43	0.7598	dominated	£14,821	24%
No treatment	£416.00	0.7399	dominated	£14,382	0
Darifenacin	£498.60	0.7592	dominated	£14,685	5%
Trospium ER	£533.80	0.7568	dominated	£14,603	0
Trospium	£538.74	0.7579	dominated	£14,619	1%
Propiverine ER	£549.84	0.7554	dominated	£14,558	0%
Oxybutynin ER	£551.68	0.7576	dominated	£14,601	0
Propiverine IR	£551.77	0.7563	dominated	£14,573	2%
Oxybutynin TD	£554.63	0.7562	dominated	£14,571	2%
Fesoterodine	£559.76	0.7556	dominated	£14,552	0
Oxybutynin TG	£571.65	0.7562	dominated	£14,552	0
Tolterodine ER	£576.34	0.7535	dominated	£14,494	0
Solifenacin	£608.73	0.7569	dominated	£14,529	0

*Net benefit is calculated as (QALYs x £20,000) - cost of treatment

Figure 6.2. Cost effectiveness acceptability curve for first-line antimuscarinic treatments, base case with differential discontinuation dates at 52 weeks.



Using the published data on longer term discontinuation did not change the result, in that the most cost-effective drugs were still oxybutynin (immediate release) and tolterodine (immediate release) despite higher discontinuation rates at 1 year. All other drugs had no more than a 5% probability of being cost effective at the £20,000 per QALY threshold.

Summary of the results of the sensitivity analyses

The tables of results and cost effectiveness acceptability curves for all sensitivity analyses are presented in Appendix N. A summary of the findings is presented below.

Impact of changing inputs into the PSA

Changing the model structure to include only the probability of discontinuation after four weeks (as a proxy for incontinence) did not change the options that were most cost-effective, which were oxybutynin (immediate release) and tolterodine (immediate release). The order of cost effectiveness changed for the drugs that were dominated by oxybutynin in the model (more expensive and less effective). Both oxybutynin immediate release and tolterodine (immediate release) were more effective and less costly than no active treatment (incontinence pads only).

Changing the discontinuation rate at 1 year did not change the order of the most cost-effective options but it changed the order of cost effectiveness of the other drugs that were not cost effective. Inputting the highest, lowest and midpoint value for drugs with missing data did not make any other drug more cost effective than oxybutynin IR or tolterodine IR.

Impact of changing a specific variable in a one-way sensitivity analysis

The inclusion of GP costs for women who discontinue treatment did not change the drugs that were most cost-effective in the base case model. The analysis changed the cost ranking of some of the drugs that were dominated by oxybutynin IR.

Increase in health service costs for women who take oxybutynin (immediate release)

Oxybutynin IR remained the most cost-effective option with the inclusion of higher hospitalisation costs.

Change in cost of pads

Changing the costs of incontinence pads to £2 per week did not change the options that were most cost effective in the model, although oxybutynin (immediate release) and tolterodine (immediate release)

were no longer less expensive than no active treatment. Oxybutynin IR had an ICER of £471 compared with no treatment.

Change in time horizon to 2 and 5 years

Oxybutynin (immediate release) and tolterodine (immediate release) remained the most cost-effective options using longer time horizons in both model structure 1 and model structure 2, assuming no further change in health states or treatment status after 12 months. Darifenacin remained the most cost-effective once-daily alternative drug treatment option.

Economic summary

Oxybutynin (immediate release) was the most cost-effective antimuscarinic therapy as first-line drug treatment for OAB wet. In the base case model it was both less expensive and more effective than no treatment and was the most cost-effective option for first-line treatment in 65% of simulations in the probabilistic sensitivity analysis. With differential long-term discontinuation rates considered, the cost per woman per year was £364.50 (see Table 6.24) for the most cost-effective drug (oxybutynin immediate release) and £608.73 for the least cost-effective drug (solifenacin). There was a very small difference in effectiveness (0.01 QALY per year). Therefore the opportunity cost of choosing a more expensive OAB drug was around £244 per woman per year.

The probabilities reported in the NMA for continence status were based on 4 week data only for continence status. Twelve-week data were calculated assuming the same relative effects as that for 4 weeks, relative to oxybutynin (immediate release). Given the limitations of the continence data and the correlation between continence and discontinuation, a second model was developed that assumed that discontinuation was determined by continence status. Discontinuation probabilities only were used to calculate health state transition. Using this model, oxybutynin (immediate release) and tolterodine (immediate release) remained the most cost-effective drugs.

There was a lack of evidence about longer term (12 months and longer) discontinuation and how this differed between OAB drugs. The first base case model assumed that all drugs had a discontinuation rate of 80% at 12 months, reflecting the evidence at the time about all drug treatments for OAB wet. A sensitivity analysis was undertaken when a new study was published that reported discontinuation rates for specific OAB drugs. The results did not change the overall conclusion of the analysis. Oxybutynin (immediate release) remained the most cost-effective drug for first-line treatment where best and worst case scenarios were explored for drugs where discontinuation rates were not reported.

The effect of increasing the cost associated with OAB drug treatment was also explored in sensitivity analysis. The base case analysis assumed no additional costs associated with discontinuation and treatment of adverse effects. An additional analysis was undertaken which included costs of GP care after discontinuation (as a proxy for any additional primary or community care contact associated with stopping antimuscarinic therapy). It was assumed that women who discontinued antimuscarinic treatment would require an additional GP surgery visit every 8 weeks for the remainder of the year of the model. Oxybutynin immediate release remained the most cost-effective treatment but the ranking changed for other OAB drugs that were less cost effective than oxybutynin IR.

The cost of managing rare and acute events requiring hospitalisation that have been associated with oxybutynin (immediate release) was also included in this analysis. Assuming a hospitalisation rate of 1/5000 for oxybutynin (immediate release) only, it remained the most cost-effective option at an acceptable cost per QALY (under £20,000 per QALY).

Altering the cost of incontinence pads from £2 to £10 a week did not have an impact on the order of cost effectiveness in the model. This was predictable, given the fact that the difference in efficacy (and therefore the demand for incontinence pads) was very small between OAB drugs.

Limitations of the analysis

The assumptions in the model are set out in Table 6.22, which was requested by the GDG in order to explain the key decisions that were made in the evaluation and to make the GDG's assumptions fully transparent. The discussion of the GDG's view of the clinical reality of these assumptions is also reported in the translation of the evidence to recommendations.

The choice of outcome in the health economic model limits its applicability to women with OAB wet who have symptoms of incontinence (as opposed to urge incontinence or OAB dry). Further discussion of

the GDG's principles on choosing the outcome for the model is presented in the evidence to recommendations.

Adverse events were assumed not to incur additional costs or to continue beyond treatment. Women on treatment were assumed to have few or no adverse effects in the base case analysis (sufficient to change the relative cost effectiveness of OAB drugs) and women no longer on antimuscarinic treatment were assumed to have no lasting side-effects. The GDG was aware that treatment of OAB drugs is associated with rare but acute side-effects, but that these tend to be associated with an older class of drugs that have been found not to be cost effective. However, since oxybutynin (immediate release) is an older drug and concerns have been raised about its side-effect profile, a sensitivity analysis was undertaken that took into account the cost of hospitalisation associated with acute side-effects.

The longer term effectiveness of OAB drug therapy could not be determined with the available data. It is well documented that the discontinuation rates for all OAB drugs is high, and there is recent data that shows there may be a difference between OAB drugs in discontinuation at 1 year but this has not been shown definitively in long-term head-to-head studies. In the first (base case) analysis, the health economic model assumed a common 1 year discontinuation rate for all drugs in the baseline analysis. The value was set an approximate level of 80% by the GDG. Since continence is associated with continuation of treatment, OAB drugs with higher rates of continence would also have higher continuation rates. The effect would be to make drugs that have higher rates of long-term use more cost effective than the alternatives. This assumption was tested in sensitivity analysis using other assumptions and these changes to the model did not change the results.

The effectiveness data on which the model is based came from trials of first-line treatment only. It did not include data on the effectiveness of a second antimuscarinic once a first drug had failed. In an earlier draft of the guideline, the cost effectiveness of second-line antimuscarinic therapy was presented assuming the same probability of effectiveness. This approach may overestimate the cost effectiveness of second-line OAB drugs without robust evidence to support it. The second-line analysis was therefore removed as there was a danger that it could give false credibility to analysis that was not evidence-based.

The analysis did not include the cost of treating adverse events, the need for hospitalisation or long-term care as a result of serious adverse events. The range and incidence of adverse events by drug were not included in all the individual studies in the systematic review and were not reported to the GDG as they were not the outcomes prioritised by the group. The GDG's view was that a large proportion of adverse events associated with OAB drugs only continued as long as the patient was on drug therapy and resolved quickly after discontinuation. The cost to the NHS of managing rare adverse events, such as psychosis, could be very high but there is a lack of evidence about whether the rates of these conditions differ by type of OAB drugs used.

Evidence to recommendations

Relative value placed on the outcomes considered

In the head-to-head review that was undertaken prior to the network meta-analysis (NMA), all seven prioritised outcomes were reported. Before considering whether an NMA was feasible for each outcome, the GDG prioritised continence episodes and continence status for women with OAB wet and urgency episodes for women with symptoms of OAB dry only. For the NMA and health economic model undertaken after the head-to-head review, a single measure of effectiveness was required against which all the drugs could be compared on a 'level playing field'. The GDG's consensus opinion was that an unambiguous, dichotomous measure of effectiveness should be prioritised; that is, one that reports absolute health status, not a change in health status. After considerable discussion, the GDG agreed that the outcome of interest should be zero episodes of incontinence per day ('absolutely dry'). Once the NMA results were presented to the GDG, it was clear that continence status was the only outcome that had sufficient data to develop an NMA. However, the decision to prioritise continence status was taken prior to the GDG seeing the results of the NMA.

The GDG's view was that for women with incontinence, the most important outcome (but not the only important outcome) is to be completely dry. A reduction in symptoms can bring relief, but in terms of activities of daily living (such as leaving the house, participating in work or leisure, travelling, socialising), any symptoms of incontinence can be extremely debilitating and an improvement, while welcome, may

not make those activities any easier to manage. This view was strongly supported by the lay members of the group. However, it was acknowledged that this choice limited the analysis to women with OAB wet since incontinence is not a symptom of OAB dry.

The choice of outcomes was restricted by the data reported in the studies. Zero episodes per day was the effectiveness outcome most consistently reported across all the RCTs, allowing a network of drugs to be connected (as shown in the head-to-head review, see Table 6.3). Other effectiveness outcomes, such as zero episode of urgency, were not reported in enough studies to be included in a NMA (see Table 6.4).

The GDG acknowledged that zero episodes per day was a conservative estimate of the effectiveness of an OAB drug since some women will have improvement without cure. However, there is a biological plausibility that the drugs that lead to the highest rates of continence will also be associated with higher chance of improvement in symptoms of incontinence (although not necessarily urgency). Therefore the GDG chose continence status as a conservative proxy for effectiveness across a range of outcomes.

The impact of adverse events was also prioritised by the GDG and reported in the head-to-head review. For the NMA, a single measure of negative impact of treatment was required to allow the GDG to consider the trade-off between treatment effect and adverse events for all the drugs being compared. The adverse events reported with antimuscarinic treatment are common, especially dry mouth, which leads to high numbers of women dropping out of treatment. Discontinuation for any reason was chosen as the outcome for the NMA and health economic model, as the GDG was mindful of the fact that some women may tolerate adverse effects if they are satisfied with the improvement in symptoms. If a woman remained on treatment, then it can be assumed that the benefits of treatment outweigh the harms. If she discontinued, then the harms outweigh the benefits. Furthermore, in order to calculate the cost of treatment in the health economic model, the rate of discontinuation across all drugs included in the model was required

Consideration of clinical benefits and harms

Head-to-head review

The head-to-head review of RCTs was presented first to the GDG. No conclusions could be drawn from this direct evidence without making possibly erroneous assumptions about comparative effectiveness of drugs that had not been directly evaluated in trials.

Data on incontinence episodes and continence status were reported more widely that other outcomes in the head-to-head trials. With the inclusion of placebo-controlled trials, data on continence status and discontinuation was reported across a sufficient number of enough trials to develop an NMA. Therefore a review of trials of OAB drugs against placebo was undertaken for the purpose of developing the NMA.

Once the review of the placebo controlled trials had been completed, a network meta-analysis was undertaken that included all drugs included in the head-to-head reviiew.

Network meta-analysis

The evidence profile for continence status showed that there was no statistically significant difference in effectiveness between the 13 OAB drug preparations included in the review, except superiority of solifenacin, fesoterodine and trospium (extended release) over tolterodine (extended release). The GDG noted positive and negative trends in the data; for continence status, the odds ratios favoured oxybutynin (immediate release) compared with all other drugs and favoured tolterodine (immediate release) except when compared with oxybutynin (immediate release). However, none of these results were statistically significant.

The network analysis outputs for discontinuation rates were more conclusive. It showed that oxybutynin (immediate release), propiverine (immediate release) and fesoterodine all had clinically significantly higher discontinuation rates than other OAB drugs.

The probabilities shown in the posterior medians calculations show the absolute effect of each of the drugs. This absolute effect is as useful as the relative difference between drugs, and is given as odds ratios. The GDG noted that the difference between the drugs for both outcomes was small; there was no difference in continence status at 4 or 12 weeks and all OAB drugs were effective for the majority of women.

The GDG concluded that no drug should be removed or recommended based solely on the clinical data presented. Instead, these data were used in a health economic model to take into account the different costs of OAB drugs currently on the market.

Consideration of health benefits and resource use

The health economic model showed that despite its higher discontinuation rate compared with other OAB drugs, oxybutynin (immediate release) was the most cost-effective option due to its lower price and higher rates of effectiveness than all other drugs except tolterodine (immediate release).

The probabilistic sensitivity analysis showed that oxybutynin (immediate release) was the most cost-effective option for first-line treatment in 65% of model simulations, with tolterodine (immediate release) the most cost effective in 24% of simulations.

The GDG acknowledged that there is a perception that oxybutynin (immediate release) is not well tolerated by women with OAB and that it is perceived as an inferior treatment option by many clinicians. There was a concern that women who do not get optimal efficacy with their first OAB drug could be discouraged by their experience from trying another OAB drug. Also, clinicians' low expectations of the likelihood of success with oxybutynin (immediate release) might adversely affect a woman's willingness to tolerate the side-effects that indicate the drug is working effectively. Therefore, the GDG decided to recommend another immediate release OAB drug (tolterodine immediate release) which the health economic analysis showed was less costly overall than no treatment since no treatment incurs a cost of managing the symptoms of urinary incontinence.

There was a cost associated with having a choice of first-line OAB drugs of around £11 per woman per year (which is the difference in cost per woman per year of choosing tolterodine versus oxybutynin immediate release). The GDG considered that this additional cost to the NHS was acceptable.

The GDG was aware that some women will prefer a drug that only has to be taken once a day. For this reason, they included darifenacin in the list of options for first-line treatment as this was the once-a-day drug with the highest probability of being cost effective.

Trospium (extended release), oxybutynin (extended release), fesoterodine, oxybutynin topical gel, tolterodine (extended release) and solifenacin had a zero per cent chance of being cost effective as first-line drugs. Sensitivity analyses incorporating other health care costs and changing the long-term effectiveness of OAB treatment did not change which two drugs were the most cost effective for OAB.

The choice of second-line treatment was not considered in the health economic analysis because of the lack of data on the efficacy of OAB drug treatment after a first drug has failed. After consultation, the GDG's view was that it was not reasonable to use the same effectiveness rates as for first-line treatment; if a woman does not achieve satisfactory improvement with one OAB drug that may suggest that she will not have a successful outcome with any OAB drug.

There was a lack of evidence of a difference in effectiveness between OAB drugs, and few women achieve adequate long-term outcomes to continue treatment beyond 1 year. In this context, the GDG's view was that if a woman wished to try another OAB drug before considering other treatment options, she should be offered a drug that could be obtained at the least cost locally since this would free up resources that could be used for more effective treatments further on in the treatment pathway. Given the lack of difference in effectiveness between drugs, the relative cost effectiveness was determined mostly by the difference in cost between OAB drugs. The GDG wished to highlight that the more expensive drugs do not confer sufficient additional benefit (in terms of either continuation or continence) to justify their current higher cost. The GDG considered that the arguments for recommending the most expensive OAB drugs as second–line treatment on the basis of improved side-effects profile were inadequate since these drugs had not been widely compared with other OAB drugs in head-to-head trials.

Quality of evidence

The network meta-analysis was undertaken because there was sufficient data to complete a network for all 13 drugs when placebo trials were included. The odds ratios from the head-to-head studies were used to validate the findings from the NMA. Some RCTs used in the head-to-head review were removed from the NMA because they included doses that were above the recommend level.

The NMA used high quality RCT evidence. For one drug (darifenacin) there were no head-to head studies reporting continence status, so evidence of effectiveness is based on placebo-controlled trials only. This is a legitimate methodological approach but it is acknowledged that the evidence driving the cost effectiveness model would be stronger if it had been possible to include only head-to-head trials in the analysis.

Other considerations

Recommendations for women with OAB dry

The head-to-head review of OAB drugs concluded that there was insufficient evidence to draw conclusions based on reported data of urgency episodes, which was the prioritised outcome for women with OAB dry. Therefore the GDG did not make specific recommendations for women with OAB dry based on the evidence for urgency episodes.

However, the GDG decided the effectiveness evidence based on continence status could be extrapolated to the OAB dry group. The GDG noted that OAB dry and OAB wet have similar mechanisms of action and that the action of the OAB drugs would be similar for both conditions. Furthermore, the distinction between OAB dry and OAB wet may be unhelpful (commonly women are diagnosed as having OAB dry because they are able to reach the bathroom in time whereas a woman with OAB wet cannot). It was the GDG's expert opinion that many women with OAB dry eventually develop OAB wet as their condition deteriorates. Therefore, due to the similarities between OAB dry and OAB wet, it was the GDG's consensus view that the OAB drugs recommended for OAB wet would be equally effective for women with OAB dry.

Starting treatment with antimuscarinic therapy

OAB drug treatment for women with OAB wet or OAB dry should be considered for women who have not achieved success with conservative management alone. OAB drugs can also be considered as an adjunct to conservative management in some circumstances (see Conservative management, Chapter 4).

The GDG noted that OAB drug therapy can be offered before establishing whether the cause of the OAB symptoms is detrusor overactivity. The evidence in the review included populations in whom detrusor overactivity had been proven, as well as populations in whom urodynamics had not been performed. Therefore, the recommendations are applicable to both groups.

Treatment should be initiated on the lowest dose to reduce the likelihood of side-effects. Because of the risk of high anticholinergic load, the GDG recommended that the initial dose of a new medication should be at the BNF quoted minimum effective amount. It was reasoned that this would allow enough scope to increase the dose to optimise effectiveness until the time of medication review.

The GDG's view was that women should be given all the information about treatment effects and side-effects, including information about the lack of evidence of long-term effectiveness. The GDG's view was that if a woman receives information reporting adverse effects and the time it takes for effective treatment to be noticeable there is greater chance that she will continue treatment. This increases the likelihood that treatment will be effective and mild adverse effects will be tolerated.

When deciding on which drug should be offered or whether these drugs are appropriate for any individual woman, the decision should take into account: the frequency and route of administration; co-existing conditions (for example stress urinary incontinence [SUI]); and the continuing use of other medications (related and unrelated to OAB).

The GDG noted that some women might not get optimal outcomes with oral medication (for example those who have difficulty swallowing). Therefore, a transdermal alternative may be offered for these women. The topical gel formulation for oxybutynin should not be used as it not currently licensed in the UK for this condition. No recommendation has been made for this preparation.

Switching to another OAB drug

The GDG was mindful of the potential loss of dignity and embarrassment surrounding incontinence care and considered that treatments and incontinence care should be focussed on what has been shown to be effective and cost effective. Current practice in the NHS is to prescribe up to four or five drugs, one after the other, for a woman with OAB. The GDG wished to restrict this practice, given the lack of evidence of long-term efficacy for OAB drug therapy. If a drug is not providing optimal benefit then

another low cost, effective OAB drug should be offered as an alternative. If that drug also fails to improve symptoms then other treatment options should be considered.

The GDG acknowledged that, while most women will be willing to try a different drug, others will be reluctant for various reasons. For some women, the idea of long-term medication is difficult to accept or they may have had significant side-effects from the first drug and so are less keen to try another one. Therefore women should be offered alternative treatments if they are unwilling to try another OAB drug.

Frail older women

Antimuscarinic drugs may work differently in particular patient groups, for example frail older women and women with multiple co-morbidities of any age. These drugs have differing affinities for antimuscarinic receptors within the brain and a variable ability to cross the blood brain barrier. This has the potential for adverse effects on cognitive function, both in the short term, with a risk of acute confusional states, and in the longer term. This is particularly important in the context of absolute anticholinergic load; that is, the number of other medications the women is taking that have anticholinergic activity. These patient groups should still be offered treatment with these drugs for overactive bladder symptoms, but only after a full medication review.

The GDG defined a frail older woman as one with multiple comorbidities, functional impairments related to age, such as walking or dressing difficulties, and any degree of cognitive impairment. Although all women at risk of high anticholinergic load should be prescribed drugs for overactive bladder with caution, the GDG felt an explicit recommendation should be made to prohibit the use of oxybutynin because of the risk of impairment of daily functioning, which is common, as well as the less common risk of chronic confusion. In very rare cases, women can experience acute delirium, which is a serious adverse event that may require hospitalisation.

Medication reviews

The GDG noted that the evidence suggests high rates of discontinuation with all OAB drugs due to adverse effects and that there is a lack of data on long-term efficacy. Women should be told explicitly about the likelihood of success and failure with a specific drug before they start treatment. They should also be told about the known side-effects of each drug, such as dry mouth and constipation, and that side-effects may indicate that the treatment is working. They should also be made aware that they may not experience a positive effect on their condition before 4 weeks of treatment and should be encouraged to persevere for at least this period of time if possible. Realistic expectations of treatment are likely to improve continuation with OAB drugs and increase the likelihood of successful treatment in the short and medium term.

Some women on OAB drugs may stop taking the treatment soon after starting due to intolerable side-effects. If they do not notify their healthcare professional that they have withdrawn from treatment they may continue to have untreated symptoms. A prescribed medication review has been recommended to allow efficient management of a woman's drug regime and provide support for women who may not request it for themselves. The evidence suggested that 4 weeks is a minimum time for the optimal effect to become apparent with antimuscarinic treatment. A review at this stage would be the earliest point in most women's treatment to measure effect. However, an earlier review may be required and access to advice should be available. If a woman shows limited improvement, no improvement or reported intolerable adverse effects, then treatment should be revised. This amendment could be either a change in dosage, a change in drug or switching to another type of treatment.

The 4-week review should be arranged for women on new treatment and after any change in treatment in order to check progress. This meeting can happen in clinic or remotely (via telephone).

The GDG's view was that once a woman continues treatment beyond 12 weeks a further review should be offered to assess continuing effectiveness. At this point, if the outcomes of the treatment remain satisfactory to the woman, treatment should continue as long as it remains effective. If the outcomes are unsatisfactory, a change in treatment or dose should be considered and reviewed again 4 weeks after the change is made.

Long-term follow-up of continuing treatments should take place alongside medication reviews. These medication reviews usually take place annually, or every 6 months if the woman is 75 years or older. The annual/6-monthly reviews can take place in primary care.

If OAB drug treatment is not successful, the options for further management (both non-therapeutic interventions and invasive therapy) should be reviewed with the woman. Not all women will opt for further invasive treatment. Their health care needs will still require review as they (and, where appropriate, their carers) continue to manage the physical and emotional demands of their condition, which will change over time.

For women who wish to consider invasive treatment a referral to a multidisciplinary team (MDT) should be arranged. Urodynamic testing should also be offered in conjunction with the referral to the MDT.

Recommendations

Number	Recommendation
	General principles when using OAB drugs
52	When offering antimuscarinic drugs to treat OAB always take account of: • the woman's coexisting conditions (for example, poor bladder emptying) • use of other existing medication affecting the total anticholinergic load • risk of adverse effects. **[new 2013]**
53	Before OAB drug treatment starts, discuss with women: • the likelihood of success and associated common adverse effects, **and** • the frequency and route of administration, **and** • that some adverse effects such as dry mouth and constipation may indicate that treatment is starting to have an effect, **and** • that they may not see the full benefits until they have been taking the treatment for 4 weeks. **[new 2013]**
54	Prescribe the lowest recommended dose when starting a new OAB drug treatment. **[new 2013]**
55	If a woman's OAB drug treatment is effective and well-tolerated, do not change the dose or drug. **[new 2013]**
	Choosing OAB drugs
56	Do not use flavoxate, propantheline and imipramine for the treatment of UI or OAB in women. **[2006]**
57	Do not offer oxybutynin (immediate release) to frail older women.* **[new 2013]**
58	Offer one of the following choices first to women with OAB or mixed UI: • oxybutynin (immediate release), **or** • tolterodine (immediate release), **or** • darifenacin (once daily preparation). **[new 2013]**
59	If the first treatment for OAB or mixed UI is not effective or well-tolerated, offer another drug with the lowest acquisition cost.† **[new 2013]**
60	Offer a transdermal OAB drug to women unable to tolerate oral medication. **[new 2013]**
61	For guidance on mirabegron for treating symptoms of overactive bladder, refer to Mirabegron for treating symptoms of overactive bladder (NICE technology appraisal guidance 290). **[new 2013]**

* The Guideline Development Group defined 'frail older women' as those with multiple comorbidities, functional impairments such as walking or dressing difficulties and any degree of cognitive impairment.
† This could be any drug with the lowest acquisition cost from any of the drugs reviewed, including an untried drug from recommendation 58. The evidence review considered the following drugs: darifenacin, fesoterodine, oxybutynin (immediate release), oxybutynin (extended release), oxybutynin (transdermal), oxybutynin (topical gel), propiverine, propiverine (extended release), solifenacin, tolterodine (immediate release), tolterodine (extended release), trospium and trospium (extended release). See chapter 6.

Reviewing OAB drug treatment

62 Offer a face-to-face or telephone review 4 weeks after the start of each new OAB drug treatment. Ask the woman if she is satisfied with the therapy:

- If improvement is optimal, continue treatment.
- If there is no or suboptimal improvement or intolerable adverse effects change the dose, or try an alternative OAB drug (see recommendations 59–60), and review again 4 weeks later. **[new 2013]**

63 Offer review before 4 weeks if the adverse events of OAB drug treatment are intolerable. **[new 2013]**

64 Offer referral to secondary care if the woman does not want to try another drug, but would like to consider further treatment. **[new 2013]**

65 Offer a further face-to-face or telephone review if a woman's condition stops responding optimally to treatment after an initial successful 4-week review. **[new 2013]**

66 Review women who remain on long-term drug treatment for UI or OAB annually in primary care (or every 6 months for women over 75). **[new 2013]**

67 Offer referral to secondary care if OAB drug treatment is not successful. **[new 2013]**

68 If the woman wishes to discuss the options for further management (non-therapeutic interventions and invasive therapy) refer to the MDT and arrange urodynamic investigation to determine whether detrusor overactivity is present and responsible for her OAB symptoms:

- If detrusor overactivity is present and responsible for the OAB symptoms offer invasive therapy (see recommendations in chapter 8).
- If detrusor overactivity is present but the woman does not wish to have invasive therapy, offer advice as described in recommendation 51.
- If detrusor overactivity is not present refer back to the MDT for further discussion concerning future management. **[new 2013]**

6.2 Desmopressin

Desmopressin (also known as DDAVP) is a synthetic analogue of vasopressin or antidiuretic hormone, which acts by inhibiting diuresis while avoiding vasopressive effects. Used at night, it decreases nocturnal urine production.

Nocturia

Three DB placebo-controlled RCTs evaluated the use of desmopressin for nocturia. One evaluated 3 weeks' treatment in women (n = 144),[413] who were then offered continued desmopressin treatment for up to 1 year.[414] The two other RCTs were smaller crossover studies that evaluated 2 weeks' treatment (n = 17, n = 25),[415,416] one of which enrolled men and women.[415] An oral formulation of desmopressin was used in two studies (dose ranging from 100 to 400 μg),[413–415] and an intranasal formulation in the third (dose 20 micro grams).[416]

In the 3 week RCT in women, significantly greater improvements were seen with desmopressin in all nocturia-related outcomes (nocturia episodes, volume of nocturnal voids, duration of sleep to first nocturnal void, diuresis, ratio of day/night to 24 hour urine volume), and a reduction in the 'bothersome factor' of nocturia (assessed using BFLUTS).[413] [EL = 1+] Follow-up of women who took desmopressin for up to 1 year indicated sustained benefit in the outcomes measured (50% or greater reduction in nocturia, duration of sleep to first nocturnal void, 'bothersome factor').[414] [EL = 3]

In the crossover study in men and women, nocturia episodes and nocturnal diuresis were significantly lower with desmopressin compared with placebo, with no significant change in either group in 24 hour diuresis.[415] [EL = 1+] Nocturnal frequency and urine output were significantly reduced with

desmopressin (from baseline and compared with placebo) in the crossover study in women only, with no significant change in diurnal outcomes.[416] [EL = 1+]

Urinary incontinence

A placebo-controlled 'pilot' RCT evaluated the use of desmopressin in the treatment of women with daytime UI. Four sequences of desmopressin 40 micro grams (seven doses) or placebo (three doses) were evaluated, with treatment administered intranasally when required. At both 4 and 24 hours after dose administration, the number of periods with no leakage was greater with desmopressin compared with placebo, and the volume voided or leaked during a UI episode lower with active treatment, although the confidence intervals for all mean values overlapped, indicating that differences were not statistically significant.[417] [EL = 1+]

Adverse effects

Adverse effects reported across the short-term studies included headache, nausea, hyponatraemia, abdominal pain, frequency, dry mouth, dizziness, fatigue, peripheral oedema and earache.[415–417] In the longer term study (up to 1 year), the most frequent adverse effects related to treatment in women were: hyponatraemia 12% (none required treatment, none with sodium below 125 mmol/l); headache 7%; frequency, peripheral oedema and UTI (each 3%); and nausea and dizziness (each 2%).[414]

Evidence statements for desmopressin

The use of desmopressin significantly reduces nocturia. There is insufficient evidence that desmopressin reduces incontinence in adult women. A reduction in serum sodium is very common (more than 10%). [EL = 1+]

Symptomatic hyponatraemia due to therapy with desmopressin may be more common in elderly women, and is more likely to occur soon after treatment initiation. Pretreatment and early posttreatment (72 hours) serum sodium monitoring is recommended. Where there are new symptoms or a change in medication, further measurement of serum sodium is recommended. [EL = 4]

Evidence to recommendation 2013

The GDG chose to update the recommendation for desmopressin in light of the cautions outlined within the BNF.

Recommendations

Number	Recommendation
69	The use of desmopressin may be considered specifically to reduce nocturia* in women with UI or OAB who find it a troublesome symptom. Use particular caution in women with cystic fibrosis and avoid in those over 65 years with cardiovascular disease or hypertension. **[2006, amended 2013]**

2013 Update

6.3 Diuretics

Only one RCT involving women was identified. This was a small DB placebo-controlled crossover study that evaluated bumetanide 1 mg for the treatment of nocturia in men and women (n = 33; 28 completed; 13 women). Treatment was given 4–6 hours before bedtime for 2 weeks. Weekly nocturia episodes were significantly fewer after bumetanide treatment compared with placebo (10 versus 14).[418][EL = 1−] No studies evaluating furosemide in women were identified.

Evidence statement for diuretics

There is insufficient evidence to support the use of diuretics for the treatment of nocturia in women with UI. [EL = 1−]

* At the time of publication (September 2013), desmopressin did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

6.4 Duloxetine

Duloxetine is a serotonin and noradrenaline reuptake inhibitor that acts chiefly in the sacral spinal cord. It is thought that the resultant increase in pudendal nerve activity increases urethral sphincter contraction and closure pressure. It is licensed for use in moderate to severe stress UI.

A systematic review has considered the effectiveness of serotonin and noradrenaline reuptake inhibitors (duloxetine) for the treatment of stress UI.[419] Because some of the studies included in the review were only published as abstracts, and because some relevant studies were not included in the review, all relevant studies are considered individually.

Six DB placebo-controlled RCTs evaluated the effectiveness of duloxetine for the treatment of predominant stress UI in women, five of which were considered to be of good quality.[420–424] [EL = 1+] A further RCT compared duloxetine (with or without pelvic floor muscle training [PFMT]) with PFMT alone or no active treatment (placebo drug and sham PFMT) in women with stress UI, 11% of whom had had prior continence surgery (n = 201).[229]

Of the six placebo-controlled RCTs, one was a 12 week dose-ranging study, comparing 20, 40 and 80 mg daily doses of duloxetine in women with at least four leakage episodes per week (n = 553).[420] Three other 12 week studies, identical in design, evaluated duloxetine 80 mg in women with at least seven (mean about 17) leakage episodes per week (total n = 1635).[421–423] The fifth study considered the impact of duloxetine 80 mg on QOL after 9 months' treatment (n = 451).[424] [EL = 1+] One study evaluated duloxetine use in women awaiting surgery for stress UI (n = 92).[425] [EL = 1−] Across the six studies, between 8% and 18% had had prior continence surgery. Up to 35% of women across four studies performed PFMT.[420–423]

The outcomes evaluated across the 12 week studies were leakage episodes, voiding interval, QOL (I-QOL) and patient global impression of improvement (PGI-I). The findings for duloxetine 80 mg per day (40 mg twice a day) compared with placebo were as follows:

- leakage episodes: significantly greater median reductions with duloxetine in each study (range of median reductions 50–64% versus 28–41% placebo)[420–423]
- voiding interval: significantly greater increases with duloxetine in each study (range of mean increases 15–24 minutes versus 4–9 minutes)[420–423]
- QOL: significantly greater improvement (I-QOL) with duloxetine in three studies;[420–422] no significant difference between groups in one[423]
- PGI-I: significantly more women reported improvement with duloxetine in three studies;[420−422] no significant difference between groups in one.[423][EL = 1+]

The lower daily duloxetine dose of 20 mg twice a day. (40 mg daily) was associated with significantly greater reductions in leakage episodes and in frequency compared with placebo, but not in QOL or PGI-I.[420][EL = 1+]

The RCT that focused on QOL as an outcome after 9 months' treatment found no significant differences between duloxetine 80 mg and placebo in increases in I-QOL scores or in PGI-I at 3 or 9 months. About one-quarter of the women had dropped out of the study at the endpoint.[424] [EL = 1+]

In the study of women awaiting surgery, significantly greater improvements in leakage episodes, I-QOL and PGI-I scores were seen with duloxetine compared with placebo. A 'willingness to consider surgery' questionnaire indicated that a greater proportion of women treated with duloxetine versus placebo would change their mind about having surgery, although seven women (one duloxetine, six placebo) were excluded from this analysis.[425][EL = 1−]

In the comparison of duloxetine 80 mg (with or without PFMT) with PFMT alone or no active treatment (sham PFMT and placebo drug), PFMT involved a target of 200 contractions a week (over 4 days), and the 'knack'. Sham PFMT involved contracting hip abductor muscles. Significantly greater reductions in leakage episodes were reported with duloxetine (with or without PFMT) compared with PFMT alone after 12 weeks' treatment. Global improvement and I-QOL scores indicated greater improvement in the duloxetine plus PFMT group compared with no active treatment.[229] No significant differences were

reported between the PFMT and placebo groups in any outcome (leakage episodes, global improvement, I-QOL scores) after 12 weeks' treatment.[229] [EL = 1+]

Adverse effects

Across all studies, significantly more women in all duloxetine dosage groups discontinued treatment owing to adverse effects compared with placebo (range 15–33% versus 0–6%). Nausea was significantly more common with all daily dosages of duloxetine (range 13–46% versus 2–13% placebo), and accounted for a significant proportion of withdrawals compared with placebo in one study.[422] Other adverse effects that occurred significantly more commonly with duloxetine in two or more studies were dry mouth, constipation, fatigue, insomnia, dizziness, increased sweating, vomiting and somnolence.[229,421–423,425] Adverse effects occurring in the PFMT and no active treatment arms of the duloxetine study were pooled, and thus a distinction between duloxetine and PFMT or no active treatment is not possible.[229]

Cost effectiveness of duloxetine

Duloxetine is the only drug therapy currently available for stress UI. As part of this guideline, we considered the cost effectiveness of duloxetine in order to inform recommendations about the sequencing of conservative therapies, something that could potentially have a large impact on clinical practice.

One published article considered the cost effectiveness of duloxetine.[426] This described a state transition (Markov) model to evaluate the cost effectiveness of duloxetine alone or in combination with PFMT against 'standard' treatment (PFMT and surgery), either as a first-line treatment or as second line to PFMT for stress UI, over 2 years. The Markov approach was adopted so as to capture the effect of waiting times on access to services, with a concomitant effect on deferred costs and benefits. The results of the model suggested that, using a willingness to pay threshold of £30,000 per QALY, duloxetine was a cost effective treatment for stress UI. Using baseline assumptions, the authors reported that the ICER of duloxetine alone when used first-line was £8,730 per QALY and £5,854 per QALY when used first-line in combination with PFMT.[426] When used second-line to PFMT, duloxetine dominates standard treatment.

The health economics model of the use of duloxetine as a first-line treatment for stress UI in women used in this study factored in delays for access to services.[426] Clinical trials would normally try to eliminate differential timings of treatment, to ensure a like-for-like comparison. Similarly, it could be argued that economic evaluation should be neutral with respect to treatment timing so that the results are not contingent on a particular service configuration. Indeed, it seems that service delivery should be configured to produce cost effective health care rather than be a driver of what is deemed cost effective. Therefore, two additional health economics models, which did not consider access times to health services, were developed for this guideline. The first sought to compare the cost effectiveness of PFMT versus duloxetine as a first-line treatment for women with moderate to severe stress UI, which is assumed to be 14 or more leakage episodes per week. In this model, treatment effects and costs were based on a 52 week time frame. A second model, based on a 2 year follow-up, assessed the cost effectiveness of duloxetine versus surgery as a second-line treatment for women with moderate to severe stress UI in whom first-line treatment with PFMT had been unsuccessful. These models are described in detail in Appendix T.

Under baseline assumptions, PFMT 'dominates' duloxetine as a first-line treatment. This means that it is both more effective and less costly. The sensitivity analyses undertaken (and detailed in Appendix T) did not change this conclusion. The second-line treatment model suggests that surgery is more cost effective than duloxetine. Surgery is more costly but the ICER, in the baseline analysis, falls below the £20,000 per QALY threshold used by NICE as a willingness to pay benchmark for cost effectiveness.

Evidence statements for duloxetine

Short-term studies (up to 12 weeks) suggest that the use of duloxetine is associated with a reduction in leakage episodes, an increased voiding interval and improved quality of life in women with stress UI or mixed UI where stress-related leakage is the predominant symptom. Between-group differences are clinically small. Adverse effects, particularly nausea, and discontinuation rates are very common (more than 10%). There is a lack of long-term safety data. The combination of duloxetine and PFMT is more effective than no treatment. It remains unclear whether the combination is better than either treatment alone. [EL = 1+]

An economic model constructed for the purposes of this guideline suggested that PFMT is more cost effective than duloxetine alone as first-line treatment for stress UI. This result was generally not affected by making plausible changes to model parameters in favour of duloxetine. While the model was based on the best available clinical evidence, there is a lack of long-term effectiveness data for either treatment. A second model suggested that surgery was cost effective relative to duloxetine as a second-line treatment to PFMT. However, duloxetine was the lower cost treatment option and therefore its use does not necessarily impose opportunity costs on the NHS relative to surgery.

Recommendations

Number	Recommendation
70	Do not use duloxetine as a first-line treatment for women with predominant stress UI. Do not routinely offer duloxetine as a second-line treatment for women with stress UI, although it may be offered as second-line therapy if women prefer pharmacological to surgical treatment or are not suitable for surgical treatment. If duloxetine is prescribed, counsel women about its adverse effects. **[2006]**

6.5 Oestrogens

Oestrogens help to maintain health of the tissues that are essential for normal pressure transmission in the urethra. This includes the sphincter muscles, urothelium and vascular tissues, as well as the urethral secretions that may help to create a 'seal'. Oestrogen replacement has been promoted as a solution to UI in postmenopausal women, although its chief mode of action is unclear.

Four systematic reviews of oestrogens for the treatment of UI and/or OAB were identified, which were completed at different times and which considered different questions.[427–430] Therefore, studies included in these reviews were considered individually, together with other relevant RCTs.

Ten RCTs evaluated the use of oestrogens for the treatment of postmenopausal women with stress UI[228,431–434] or other types of UI or OAB.[435–439] Four further RCTs that primarily evaluated the effects of oestrogen on symptoms of vaginal atrophy reported some data for urological symptoms.[440–443] Additionally, secondary analyses of data from three RCTs that were designed to evaluate the benefits and risks of hormone replacement therapy (HRT) provide data on UI and/or OAB.[444–449]

The comparator group was placebo in all except two studies. One of these two studies is also considered in the physical therapies section and involved a comparison of PFMT with oestrogen, electrical stimulation and no treatment.[228] The second study compared two oestrogen preparations.[436]

Intravaginal oestrogens

Five RCTs evaluated the use of intravaginal oestrogens for UI and/or other urological symptoms. Two RCTs enrolled women with stress UI (n = 100). One reported significantly greater subjective improvement of incontinence with intravaginalestriol compared with placebo at 6 months (68% versus 16%, n = 88).[431] [EL = 1+] No comparisons were made between the conjugated oestrogen cream and control groups in the 3 month RCT; cure rates were 12% versus 0.[228] [EL = 1+]

One RCT compared two intravaginal oestrogen preparations (the estradiol vaginal ring with estriolpessaries) in women with urgency, frequency, stress or urge UI. No significant differences were seen between groups in any outcome after 6 months' treatment (subjective improvement; responder or cure rates for urgency, frequency, nocturia, urge or stress UI). Responder rates across all outcomes ranged from 51% to 61%, and cure rates from 27% to 44% (n = 251).[436] [EL = 1+]

Two placebo-controlled RCTs, in which an intravaginal oestrogen preparation was used to treaturogenital symptoms, reported the following:[439,443] [EL = 1+]

- The prevalence of UI and frequency/nocturia fell to a greater extent with an intravaginalestradiol tablet than with placebo at 1 year (UI prevalence 18% versus 10%; frequency/nocturia 38% versus 10%) but no between-group analyses were reported. At baseline, 28% of women had UI and 43% frequency or nocturia (n = 1612).[439]

- Significantly more women who had urological symptoms (41–53%) reported improvement in symptoms (frequency, dysuria, urge or stress UI) with intravaginal 17β-estradiol versus placebo after 3 months' treatment (63% versus 32%, n = 164).[443]

Systemic oestrogens

Systemic oestrogens for UI or OAB

Three RCTs evaluated oral oestrogens for the treatment of stress UI for 3 or 6 months.[432–434] The oestrogens evaluated were conjugated equine oestrogen (CEE) with medroxyprogesterone acetate (MPA), given for 10 days a cycle;[432] estradiol;[433] and estrone.[434] No significant differences were seen between oestrogen and placebo groups in any outcome across the studies (leakage episodes, pad tests, frequency, QOL, perception of improvement, objective cure).[432–434][EL = 1+]

Two RCTs evaluated systemic oestrogens for the treatment of stress or urge UI.[435,438] One reported no differences between a subcutaneous estradiol or placebo implant in subjective outcomes (selfreported cure, leakage episodes, frequency) after 6 months' treatment (n = 40).[438] [EL = 1+] In the second RCT, improvements in leakage episodes, frequency and urgency were seen after 3 months' treatment with oral estriol and placebo, but no between-group differences were reported (n = 56).[435] [EL = 1−]

A further RCT evaluated CEE+MPA in female nursing home residents who were incontinent. No significant differences were found between CEE+MPA and placebo groups in any outcome (leakage, bladder capacity), although only data from 21 of the 32 women randomised, who completed 6 months' treatment, were analysed.[437] [EL = 1−]

Systemic oestrogens for urogenital symptoms

Three RCTs that primarily evaluated the effects of systemic oestrogen on symptoms of vaginal atrophy reported some continence data.[440–442] One of these studies compared oral estradiol and estriol with placebo in women with stress or mixed UI. At 4 months, a higher cure rate was reported for women on active treatment compared with placebo, although no baseline data were given (n = 29).[440] [EL = 1−] A second RCT comparing oral estriol with placebo in women with stress, urge or mixed UI was of unclear duration (3 or 6 months) and only reported that symptoms were alleviated in the majority of women with urge or mixed UI (n = 34).[441] [EL = 1−] No significant changes in frequency were reported with oral estriol or placebo in a 10 week RCT investigating the effects of oestrogen on vaginal flora, cytology and urogenital symptoms (n = 35).[442] [EL = 1+]

Studies evaluating HRT for other indications

Data from two RCTs that were designed to evaluate the benefits and risks of HRT have been analysed with respect to continence outcomes. In the 'HERS' RCT,[445] which compared CEE+MPA with placebo, 55% of women had UI (stress, mixed or urge) at baseline (n = 1525).[444] After 4 years' treatment, significantly fewer women in the HRT group reported improvement and significantly more reported worsening of UI symptoms, compared with the placebo group. Leakage episodes were increased in the HRT group compared with placebo.[444] In women who did not have UI at baseline, the risk of reporting any type of UI at study end was also significantly higher in the HRT group.[450] [EL = 1++]

In women enrolled in the Women's Health Initiative (WHI) RCTs (CEE+MPA versus placebo[447] or CEE versus placebo[448]), 85% had continence data at baseline and at 1 year (n = 23 296). In women who were continent at the beginning of the study (35%), the relative risk of incident UI of any type at 1 year was significantly higher in the CEE+MPA and CEE groups compared with placebo. When the relative risk of each type of UI was considered separately, all results remained significant except for the risk of urge UI in the CEE+MPA versus placebo study. The relative risk of worsening prevalent UI (leakage quantity and episodes, limitations of daily activities, bother factor) was also significantly higher with HRT compared with placebo.[446] [EL = 1++]

A further placebo-controlled RCT, which evaluated both CEE and raloxifene for the prevention of osteoporosis in postmenopausal women, reported a significantly higher incidence of UI with CEE compared with other treatment groups at 3 years. Fewer women treated with oestrogen reported improvement of pre-existing UI (n = 619).[449] [EL = 1+]

Adverse effects

Adverse effects reported across the studies of intravaginal oestrogens (mostly uncommon) included vaginal irritation or discomfort, burning and itching,[431,436] breast pain,[436] and vaginal spotting or discharge.[439] One study reported that no systemic adverse effects occurred.[431]

Adverse effects reported with systemic oestrogens included breast tenderness,[437,438] vaginal spotting[437] and increased vaginal discharge.[439] No adverse effects were reported in two RCTs.[435,440] Adverse effects were not considered in four RCTs.[432,433,441,442] In the HERS study, the risk of venous thromboembolism was significantly higher with CEE+MPA compared with placebo.[445] In the WHI studies, the risk of stroke was significantly higher with CEE+MPA (mean follow-up 5.2 years) and with CEE (mean follow-up 6.8 years), compared with placebo.[447,448] The risk of coronary heart disease, venous thromboembolism and invasive breast cancer was also significantly higher with CEE+MPA compared with placebo.[447]

Evidence statements for oestrogens

Short-term studies (up to 6 months) of intravaginal oestrogens suggest some improvement in symptoms of incontinence and frequency in postmenopausal women who have urogenital symptoms secondary to vaginal atrophy. There is a lack of evidence to support the use of intravaginal oestrogens for the treatment of UI. [EL = 1+]

Systemic oestrogen does not confer any benefit in women with UI and there is evidence that it may increase the likelihood of developing incontinence in postmenopausal women. Systemic oestrogens are associated with increased risk of systemic adverse effects such as thromboembolism. [EL = 1+]

Recommendations

Number	Recommendation
71	Do not offer systemic hormone replacement therapy for the treatment of UI. **[2006]**
72	Offer intravaginal oestrogens for the treatment of OAB symptoms in postmenopausal women with vaginal atrophy. **[2006]**

7 Multidisciplinary team

8 Invasive procedures for overactive bladder

8.1 Introduction

When conservative treatment of overactive bladder (OAB) symptoms has failed it is usual to consider surgical therapy. The objective of all surgery for OAB symptoms should be to restore the woman's lower urinary tract function as closely as possible to normal, with minimum short- and long-term morbidity, and for this improvement to be durable; indeed, this is the expectation of most patients. Yet such ideal outcomes are often unrealistic in women with OAB symptoms. There is a lack of relevant information for women to help them to arrive at realistic expectations about the likely outcomes of surgical treatment. This includes the chance of potential perioperative complications and long-term adverse effects.

The range of procedures is wide, but in principle all surgical procedures for OAB due to detrusor overactivity aim to reduce involuntary detrusor contractions and thereby improve OAB symptoms. The best chance of long-term success lies with the primary procedure. Therefore this chapter should be read in conjunction with the section in the guideline on surgical competence (see chapter 10). Many procedures have been described to treat OAB symptoms over the last century but this guideline addresses only those procedures that are currently in common clinical practice.

8.2 Botulinum toxin

Introduction

Botulinum toxin is a potent neurotoxin derived from the bacterium *Clostridium botulinum*. Two strains are available for clinical use, type A and type B. One of the actions of botulinum toxin is to block the release of acetylcholine and it will temporarily paralyse any muscle into which it is injected. However, the precise mechanism of action when injected into the detrusor muscle is not known. It is injected directly into the bladder wall, usually as a day case procedure using a flexible or rigid cystoscope. This can be carried out under a local or general anaesthetic according to the wishes of the patient and local service provision.

There are currently two preparations of botulinum toxin A available in the UK for the treatment of OAB – BOTOX® (Allergan Ltd) and Dysport® (Ipsen Ltd). These have different formulations and molecular structures. Safety and efficacy may not be the same for both products and therefore each formulation was reviewed separately.

Review question

In women with idiopathic overactive bladder, what is the effectiveness of botulinum toxin A when compared with placebo?

Review introduction

In order to identify the most useful information in the evidence the guideline development group (GDG) was asked specific questions relating to the length of time to see improvement in symptoms, and the most appropriate doses of botulinum toxin A. The GDG consensus was:

- Under normal circumstances botulinum toxin A would be expected to last approximately 6 months and therefore the injection would be repeated about every 6–12 months.
- 200U (units) is the commonly used dose.

- If 200U is better or worse than placebo then it would be useful to know whether different doses are equally or more effective.

Description of included studies

No studies were identified for Dysport® (Ipsen Ltd) but a number of studies were identified for BOTOX® (Allergan Ltd) botulinum toxin A. The evidence was reviewed as follows:

- botulinum toxin A 200U versus placebo
- botulinum toxin A 200U versus 100U
- botulinum toxin A versus placebo.

Botulinum toxin A 200U versus placebo

Five randomised controlled trials (RCTs) were included in this review (Brubaker et al., 2008; Dmochowski et al., 2010; Flynn et al., 2009; Sahai et al., 2007; Tincello et al., 2012). All participants had OAB symptoms and had not responded to previous treatments including bladder training, pelvic floor exercise and antimuscarinic drugs. Detrusor overactivity was the cause of the overactive bladder symptoms in 79.2% to 100% of the populations reported in four studies. This information was not recorded in the remaining study (Flynn et al., 2009). Three studies included women only (Brubaker et al., 2008; Flynn et al., 2009; Tincello et al., 2012). The other two studies included men and women; in one 55.9% of participants were female (Sahai et al., 2007) and in the other 92.0% were female (Dmochowski et al., 2010).

The mean (standard deviation [SD]) age of participants in four studies ranged from 50.3 to 75.4 years (SD ± 10.5) but was not reported in one (Tincello et al., 2012). The mean (SD) number of incontinence episodes per day was 3.98 (SD ± 2.7) to 6.86 (SD ± 6.29) in four studies but was not reported in one study (Flynn et al., 2009). The mean (SD) number of urgency episodes was 8.15 (SD ± 3.6) to 9.5 (SD ± 2.22) per day in three studies but was not reported in two studies (Tincello et al., 2012; Flynn et al., 2009). The mean (SD) duration of symptoms was only reported in one study and was 117.9 months (SD ± 109.8) (Dmochowski et al., 2010).

Two studies (Dmochowski et al., 2010; Sahai et al., 2007) were funded or supported by Allergan Ltd and two by the US National Institutes of Health (NIH) (Flynn et al., 2009; Brubaker et al., 2008) and the fifth study (Tincello et al., 2012) was funded by charities.

Botulinum toxin A 200U versus 100U

Two RCTs were included in this review (Altaweel et al., 2011; Dmochowski et al., 2010). All participants had OAB symptoms and had not responded to previous treatments, including antimuscarinic drugs. Detrusor overactivity was the cause of OAB symptoms in 80.4% of participants in one study (Dmochowski et al., 2010) but it was not reported in the second study (Altaweel et al., 2011).

In one study 89.7% were female (Dmochowski et al., 2010) but the percentage of women in the second study was not reported (Altaweel et al., 2011).

The mean (SD) age of participants was 58.3 years (SD ± 14.1) in one study (Dmochowski et al., 2010) but was not reported in other (Altaweel et al., 2011). The mean (SD) number of urge incontinence episodes was 3.65 (SD ± 2.9) and 4.0 (no SD) in the two studies. The mean number of urgency episodes was 9.3 (SD ± 4.0) and 10.4 (no SD) in the two studies. The mean (SD) duration of symptoms was only reported in one study (Dmochowski et al., 2010) and was 103.2 (SD ± 92.9) months.

One study (Dmochowski et al., 2010) was funded by Allergan. There was no funding source reported for the second study (Altaweel et al., 2011).

Botulinum toxin A 100U versus placebo

Four RCTs were included in this review (Denys et al., 2012; Dmochowski et al., 2010; Dowson et al., 2011; Jabs et al., 2010). All participants had OAB symptoms and had not responded to previous treatments including antimuscarinic drugs. Detrusor overactivity was the cause of OAB symptoms in 80.4% of participants in one study (Dmochowski et al., 2010) and all participants in a second (Denys et al., 2012) but it was not reported in the remaining two studies (Dowson et al., 2011; Jabs et al., 2010).

Jabs et al., 2010 only included women. Of the study populations in the other three studies (Dowson et al.,2011; Denys et al., 2012; Dmochowski et al., 2010) between 71.4% and 91.8% were female. The mean (SD) age of participants ranged from 48.1 years (SD 16.6) to 64.5 (no SD). The mean (SD) number of urge incontinence episodes ranged from 1.6 (no SD) to 5.9 (SD 5.3). The mean number of urgency episodes was 8.2 (SD 4.8) and 11.6 (no SD) in two studies and was not reported in the other two studies (Jabs et al., 2010; Dmochowski et al., 2010).

Two studies (Dowson et al., 2011; Dmochowski et al., 2010) were funded by Allergan, one of which (Dmochowski et al., 2010) was a regulatory approval required dose ranging phase 2 study. A third study was funded by a charity and a government department (Denys et al., 2012). There was no funding source reported for the fourth study (Jabs et al., 2010).

Evidence profiles

The following GRADE profiles show the evidence for botulinum toxin A 200U versus placebo (Table 8.1), botulinum toxin A 200U versus botulinum toxin A 100U (Table 8.2) and botulinum toxin A 100U versus placebo (Table 8.3) by outcome in order of GDG ranked importance.

Table 8.1 GRADE findings for comparison of botulinum toxin A 200U with placebo

Number of studies	Number of women		Effect		Quality
	Botulinum toxin A 200U	Placebo	Relative (95% CI)	Absolute (95% CI)	
Patient satisfaction with treatment (assessed with: self-report as 'improved' or 'not improved')					
No evidence reported					
Incontinence episodes (better indicated by lower values)					
4 (Sahai et al., 2007; Flynn et al., 2009; Tincello et al., 2012; Dmochowski et al., 2010)	196	180	-	MD 1.3 lower (2.58 to 0.02 lower)	Low
Urgency episodes (better indicated by lower values)					
3 (Sahai et al., 2007; Tincello et al., 2012; Dmochowski et al., 2010)	185	173	-	MD 2.05 lower (2.87 to 1.22 lower)	High
Continence status (zero episodes per day) (assessed with: self-rated as 'continent' or 'incontinent')					
3 (Sahai et al., 2007; Tincello et al., 2012; Dmochowski et al., 2010)	68/185 (36.8%)	18/174 (10.3%)	RR 3.32 (1.81 to 6.07)	240 more per 1000 (from 84 more to 524 more)	High
Incontinence QOL (better indicated by lower values)					
3 (Tincello et al., 2012; Sahai et al., 2007; Brubaker et al., 2008)	160	144	-	SMD 0.71 lower (0.94 to 0.48 lower)	High

Number of studies	Number of women		Effect		Quality
	Botulinum toxin A 200U	Placebo	Relative (95% CI)	Absolute (95% CI)	
Adverse effects (assessed with: need to self-catheterise)					
5 (Flynn et al., 2009; Sahai et al., 2007; Tincello et al., 2012; Dmochowski et al., 2010; Brubaker et al., 2008)	48/232 (20.7%)	4/202 (2%)	RR 5.79 (2.48 to 13.5)	95 more per 1000 (from 29 more to 248 more)	High
Psychological outcomes					
No evidence reported					
Post-void residual volume					
No evidence reported					

CI confidence interval, MD minimal difference, QOL quality of life, RR relative risk, SMD standardised minimal difference, U units

Evidence statements

Patient satisfaction with treatment

No studies were identified for this outcome.

Self reported rate of absolute symptom reduction: number of episodes of incontinence per day

A meta-analysis of four RCTs showed no difference in clinical benefit between botulinum toxin A and placebo. The evidence was of high quality.

Self reported rate of absolute symptom reduction: number of episodes of urgency per day

A meta-analysis of three RCTs showed no difference in clinical benefit between botulinum toxin A and placebo. The evidence was of high quality.

Continence status

A meta-analysis of three RCTs showed a clinical benefit in favour of botulinum toxin A 200U over placebo. The evidence was of high quality.

Incontinence-specific quality of life

A meta-analysis of three studies showed a clinical benefit in favour of botulinum toxin A 200U over placebo. The studies also reported that women who received botulinum toxin A 200U had improved incontinence-specific QOL compared with those women who received placebo, which was equivalent to an improvement of 34 (95% CI 45 to 23) points on the Incontinence Quality-of-Life scale. The evidence was of high quality.

Adverse effects

A meta-analysis of five RCTs showed a clinical benefit in favour of placebo over botulinum toxin A 200U. Women who received botulinum toxin A 200U were more likely to need to self-catheterise than those who received placebo. The evidence was of high quality.

Psychological outcomes

No studies were identified for this outcome.

Post-void residual volume

No studies were identified for this outcome.

Evidence profile

The following GRADE profile shows the evidence for botulinum toxin A 200U for OAB caused by detrusor overactivity compared to botulinum toxin A 100U by outcome in order of GDG ranked importance. None of the studies reported patient satisfaction with treatment, number of incontinence episodes per day, urgency episodes per day, incontinence-specific quality of life or psychological outcomes.

Table 8.2 GRADE findings for comparison of botulinum toxin A 200U with 100U

Number of studies	Number of women		Effect		Quality
	Botulinum toxin A 200U	Botulinum toxin A 100U	Relative (95% CI)	Absolute (95% CI)	
Patient satisfaction with treatment					
No evidence reported					
Incontinence episodes (better indicated by lower values)					
1 (Dmochowski et al., 2010)	53	54	-	MD 0.13 lower (1.04 lower to 0.78 higher)	Moderate
Urgency episodes (better indicated by lower values)					
1 (Dmochowski et al., 2010)	53	54	-	MD 0.12 higher (1.26 lower to 1.5 higher)	Very low
Continence status					
2 (Altaweel et al., 2011; Dmochowski et al., 2010)	32/64 (50%)	16/65 (24.6%)	RR 2.01 (1.24 to 3.26)	249 more per 1000 (from 59 more to 556 more)	Low
Incontinence QOL (better indicated by lower values)					
No evidence reported					
Adverse effects					
2 (Dmochowski et al., 2010; Altaweel et al., 2011)	13/64 (20.3%)	1/65 (1.5%)	RR 6.05 (0.43 to 84.89)	78 more per 1000 (from 9 fewer to 1000 more)	Low
Psychological outcomes					
No evidence reported					
Post void residual volume (better indicated by lower values)					
1 (Altaweel et al., 2011)	11	11	-	MD 16 higher (19.24 lower to 51.24 higher)	Moderate

CI confidence interval, MD minimal difference, QOL quality of life, RR relative risk, U units

Evidence statements

Patient satisfaction with treatment

No studies were identified for this outcome.

Self reported rate of absolute symptom reduction: number of episodes of incontinence per day

A single RCT showed no difference in clinical benefit between botulinum toxin A 200U and 100U. The evidence was of moderate quality.

Self reported rate of absolute symptom reduction: number of episodes of urgency per day

A single RCT showed no difference in clinical benefit between botulinum toxin A 200U and 100U. The evidence was of very low quality.

Continence status

A meta-analysis of two RCTs showed a clinical benefit in favour of botulinum toxin A 200U over 100U. The evidence was of low quality.

Incontinence-specific quality of life

No studies were identified for this outcome.

Adverse effects

A meta-analysis of two RCTs showed no clinical benefit for either botulinum toxin A 200U or 100U. The evidence was of very low quality.

Psychological outcomes

No studies were identified for this outcome.

Post-void residual volume

A single RCT showed no clinical benefit for either botulinum toxin A 200U or 100U. The evidence was of low quality.

Evidence profile

Table 8.3 GRADE findings for comparison of botulinum toxin A 100U with placebo

Number of studies	Number of women		Effect		Quality
	Comparator	Control	Relative (95% CI)	Absolute (95% CI)	
Patient satisfaction					
1 (Dowson et al., 2011)	2/10 (20%)	0/13 (0%)	RR 6.36 (0.34 to 119.4)	-	Low
Incontinence episodes (better indicated by lower values)					
3 (Dmochowski et al., 2010; Dowson et al., 2011; Jabs et al., 2010)	75	64	-	MD 1.2 lower (2.71 lower to 0.32 higher)	Low
Urgency episodes (better indicated by lower values)					
2 (Dmochowski et al., 2010; Dowson et al., 2011)	63	55	-	MD 1.68 lower (3.2 to 0.17 lower)	Moderate
Continence status					
2 (Dmochowski	25/77 (32.5%)	8/75 (10.7%)	RR 3.23 (1.02 to 10.21)	238 more per 1000 (from 2	Low

Number of studies	Number of women		Effect		Quality
	Comparator	Control	Relative (95% CI)	Absolute (95% CI)	
et al., 2010; Denys et al., 2012)				more to 982 more)	
Incontinence QOL (measured with: OAB-q total score; better indicated by higher values)					
No evidence reported					
Adverse effects					
3 (Dmochowski et al., 2010; Denys et al., 2012; Dowson et al., 2011)	10/87 (11.5%)	1/88 (1.1%)	RR 4.83 (0.95 to 24.38)	44 more per 1000 (from 1 fewer to 266 more)	Moderate
Psychological outcomes					
No evidence reported					
Post-void residual volume					
No evidence reported					

CI confidence interval, MD minimal difference, OAB-q overactive bladder questionairie, QOL quality of life, RR relative risk, U units

Evidence statements

Patient satisfaction with treatment

A single study showed a clinical benefit in favour of botulinum toxin A 100U over placebo. The evidence was of low quality.

Self reported rate of absolute symptom reduction: number of episodes of incontinence per day

A meta-analysis of three RCTs showed no difference in clinical benefit between botulinum toxin A 100U and placebo. The evidence was of low quality.

Self reported rate of absolute symptom reduction: number of episodes of urgency per day

A meta-analysis of two RCTs showed a clinical benefit in favour of botulinum toxin A 100U over placebo. The evidence was of moderate quality.

Continence status

A meta-analysis of two RCTs showed a clinical benefit in favour of botulinum toxin A 100U over placebo. The evidence was of low quality.

Incontinence-specific quality of life

No studies were identified for this outcome.

Adverse effects

A meta-analysis of three RCTs showed a clinical benefit in favour of placebo over botulinum toxin A 100U. The evidence was of high quality.

Psychological outcomes

No studies were identified for this outcome.

Post-void residual volume

No studies were identified for this outcome.

Health economics profile

The heath economic evaluation (found in Section 8.9) suggests that botulinum toxin A (BoNT-A) is a cost-effective intervention with an estimated incremental cost effectiveness ratio (ICER) of £12,247 per QALY compared with no active treatment. If BoNT-A fails, BoNT-A with percutaneous sacral nerve stimulation (P-SNS) is not a cost-effective option (£30,235 per QALY). However, if the improvement in quality of life associated with moving from a state of incontinence to continent was assumed to be 6 percentage points higher, then if BoNT-A failed BoNT-A with P-SNS was a cost-effective option (£19,976 per QALY).

Other one-way sensitivity analysis on key model parameters did not change the conclusion. Effectiveness and cost data reflecting 100U dose of botulinum did not change the conclusions of the analysis.

Evidence to recommendations

Relative value placed on the outcomes considered

The GDG prioritised self-reported patient satisfaction, clinical improvement and adverse effects reported in the evidence for this intervention. The need for clean intermittent catheterisation (CIC) was specified as the most important adverse effect because women (with or without the assistance of a carer) who are unable to catheterise should not be offered botulinum toxin A.

Consideration of clinical benefits and harms

The evidence of benefit for women with proven detrusor overactivity was uncertain for botulinum toxin A compared with placebo. High quality RCTs reported no reduction in episodes of urgency or incontinence and no improvement in patient satisfaction. However, the evidence did indicate an improvement in continence status (the number of women who were absolutely dry) and in quality of life for women who were given botulinum toxin A injections for OAB.

The studies also identified higher levels of self-catheterisation reported as an adverse outcome in women treated with botulinum toxin A compared with placebo.

Three outcomes (continence status, incontinence-specific quality of life and adverse effects) showed a greater difference in effectiveness for botulinum toxin A versus placebo than the minimum differences specified by the GDG for these outcomes at the outset. This means that the difference in effect was clinically meaningful for these outcomes. The remaining outcomes (patient satisfaction with treatment, self-reported rate of absolute symptom reduction) did not show a clinically meaningful difference between Bbulinum toxin A and placebo.

The GDG considered the trade-off between improvements in quality of life associated with botulinum toxin A and the risk of harm associated with CIC. Women's preferences and levels of tolerance of adverse events are not the same. The GDG noted that current practice dictates that around 20–25% of women would be required to catheterise after treatment with botulinum toxin A. However, this may be an overestimation of normal clinical practice.

The GDG also noted that treatment for OAB with botulinum toxin A is a relatively new procedure that is outside the current UK license for this drug. As a consequence, there is no UK or international data on the longer term effects of the use of botulinum toxin A for this condition.

The physiological action of botulinum toxin A is probably only effective in women where detrusor overactivity is the cause of their OAB. It is believed that when it is injected into the walls of the bladder, it paralyses the detrusor muscle so that it is no longer contracts involuntarily. If this is the case, then it is probably not effective for women for whom detrusor overactivity is not the cause of their symptoms, although this has not been analysed by scientific study.

The GDG concluded that there was sufficient evidence of efficacy to support the use of botulinum toxin A provided it was a cost-effective option compared with the alternatives. However, only women who had proven detrusor overactivity identified by urodynamic investigation should be considered for treatment.

Quality of evidence

The population, intervention and outcome of the included studies were as specified in the review protocol for this question with the exception of the timing of follow-up assessment. The protocol specified that follow-up should be 6 months as this was the time lapse that the GDG considered would show some benefit from botulinum toxin A. However, in one study women were assessed after 12 weeks, and in a second study they were only assessed after 9 months. There were few drop-outs in the studies included in the review.

Where data were pooled for meta-analysis there was a low level of heterogeneity, indicating that the effect of botulinum toxin A versus placebo was similar in the included studies. This increases the confidence in synthesising the results of different studies using a meta-analysis

There was no imprecision in the review findings for any outcome. This increases the confidence that the true effect of botulinum toxin A versus placebo was observed in the included studies.

Consideration of health benefits and resource use

The health economics suggests that botulinum toxin A was a cost-effective intervention both as in comparison with no active treatment and also in comparison P-SNS. On the basis of a favourable clinical efficacy and the health economic profile, the GDG felt that, on balance, the evidence justified the recommendation to offer botulinum toxin A as the first intervention to be routinely offered to women who have had unsuccessful conservative treatment (including antimuscarinic drugs) and have proven detrusor overactivity.

Other considerations

Type of botulinum toxin

There are currently two types of botulinum toxin A available for the treatment of OAB, BOTOX® (Allergan Ltd) and Dysport® (Ipsen Ltd). The evidence reported outcomes using only doses of the BOTOX® preparation; no studies were identified that used Dysport® for the treatment of OAB in women. The GDG acknowledged that the two types of botulinum toxin A are not biologically identical and as such the efficacy of one type cannot be extrapolated to the other. Therefore, all the recommendations made for botulinum toxin A refer solely to the use of BOTOX® preparation.

Sequencing of treatment

The GDG considered the sequence of treatments for OAB, when botulinum toxin A should be offered and to whom. All the published studies identified for the clinical review considered the effectiveness of botulinum toxin A in populations in which conservative treatment (including at least one antimuscarinic drug) had failed, albeit over different time periods and for different doses of botulinum toxin A. The evidence reflected clinical practice in the NHS where botulinum toxin A is usually offered after conservative treatments (lifestyle advice and antimuscarinic drugs) have failed. Botulinum toxin A is a more invasive treatment than drug therapy requiring specialist input usually in a secondary care setting, whereas treatment with antimuscarinic drugs can be offered in a primary care setting without delay. For these reasons, the GDG view was that the evidence supported the use of botulinum toxin A after conservative management for women who are willing and able, or assisted by their carers, to catheterise.

Need for catheterisation

For some women, botulinum toxin A will not be an option because they are unable to catheterise, normally because of co-existing conditions preventing the woman or her carer (with her consent) from carrying out the procedure. It requires physical dexterity, it may be emotionally demanding, and it may be required over variable lengths of time. Furthermore, there are women who have a cultural or ethical objection to catheterisation. It may therefore not be practical to implement botulinum toxin A as a long-term strategy in some women. These women should be offered sacral nerve stimulation instead (see Section 7.4).

Ensuring that women and their carers understand what is involved in CIC prior to starting treatment (including the continuing risk of urinary tract infection and urinary retention if they do not catheterise) is central to effective management, along with follow-up support. In order to ensure that a woman (and her carer, if applicable) understands the implications of catheterisation and can tolerate continuing CIC without assistance from healthcare professionals, it is necessary that training and demonstration of the

technique is undertaken before botulinum toxin A is offered. The demonstration of successful clean intermittent self-catheterisation (CISC) is important to show the woman the extent of what may be expected should retention occur during botulinum toxin A treatment. Furthermore, if demonstrations are not commonly undertaken then there is little reassurance that the procedure will be done properly when un-aided. The GDG noted that the procedure is complex and failure to be carried out properly can increase discomfort with retention and lead to more serious adverse events. The woman, and where appropriate her carer, should feel satisfied that they are able to catheterise confidently prior to the start of treatment with botulinum toxin A. The discussion should also explain the known risks and benefits of treatment as well as the absence of evidence on duration of effect between treatments and the long-term efficacy and risks

Multi-disciplinary team (MDT)

The GDG's view was that botulinum toxin A should only be offered after an MDT review to ensure that the review of the woman's health care needs is carried out and an appropriate professional is available who is competent in teaching CIC and capable of fully discussing with the woman the physical and emotional demands of treatment with botulinum toxin A. The MDT should make sure that botulinum toxin A is only offered after urodynamic testing has been undertaken.

Access to repeat treatment

The effect of botulinum toxin A on bladder function reduces over time so that the treatment needs to be repeated. Effects can diminish fairly rapidly, so access to repeat botulinum toxin A injections needs to be fairly rapid. The duration of effect following injections is thought to be variable between women and dose; however, most of the evidence suggests that the effect begins to diminish after about 24 weeks. Therefore, women who have had a previous injection require routine follow-up after 6 months to monitor their symptoms and provide additional support if required. Women also need to be able to refer themselves back quickly within that timeframe for repeat botulinum toxin A injections to prevent a rapid return of symptoms should they reoccur before the fixed repeat appointment. The time-limited effectiveness of therapy requires women to have confidence that they can access prompt specialist review and, where appropriate, repeat botulinum toxin A injections when they require them. Services that offer botulinum toxin A injections have to be set up for this to be possible.

Treatment dose

The meta-analysis of a 100 unit dose compared with 200 units showed that there was a significant benefit in continence status when using the higher dose and no evidence of a significant increase in adverse events that would offset the presumed increase in efficacy.

The GDG noted the relative paucity of evidence that reported adverse events, specifically rates of catheterisation. It was the GDG's expert opinion that an increased dose would be associated with a higher risk of catheterisation. The GDG also acknowledged that, although no statistically significant difference in the risk of adverse events was identified in the evidence, the difference in adverse events between doses was clinically significant in the experience of the GDG. Furthermore, it is expected that when phase III studies in development at the time of writing this guideline are published, the association between dose and catheterisation will be more comprehensively documented.

The GDG concluded that, for the majority of women, catheterisation was an accepted part of botulinum toxin A treatment and therefore many women would have already acknowledged this risk prior to the discussion of the risks and benefits of the more effective higher dose. There is, however, a minority of women who would prefer to have a reduced risk of catheterisation but who do not wish to have P-SNS. In these women a lower 100 unit initial dose should be made available along with an explanation that the expected effect of such a dose would be reduced compared to the higher dose.

Botulinum toxin B

A crossover placebo-controlled RCT evaluated botulinum toxin B in men and women with refractory detrusor overactivity (DO), most of idiopathic origin. After treatment periods of 6 weeks, a statistically significant increase in mean voided volume, and reductions in leakage episodes and frequency, were seen, together with improvements in five of nine domains of the King's Health Questionnaire (KHQ). Transient adverse effects were urinary retention, constipation and dry mouth (n = 20; 17 women).[548] [EL = 1+]

A case series evaluated several doses of botulinum toxin B (between 2500 and 15,000 units) in women with OAB. Women were followed for the duration of response. Except for one woman, significant reduction from baseline in frequency was reported with all doses in all women, with duration of response significantly related to dose (19–25 days at lower dose, 80–98 days at the higher dose). Adverse effects were reported to be mild, which were transient injection site discomfort, and mild general malaise and dry mouth (n = 15).[549] [EL = 3]

Recommendations

Number	Recommendations
79	After an MDT review, offer bladder wall injection with botulinum toxin A* to women with OAB caused by proven detrusor overactivity that has not responded to conservative management (including OAB drug therapy). **[new 2013]**
80	Discuss the risks and benefits of treatment with botulinum toxin A§§§§§ with women before seeking informed consent, covering: • the likelihood of being symptom free or having a large reduction in symptoms • the risk of clean intermittent catheterisation and the potential for it to be needed for variable lengths of time after the effect of the injections has worn off • the absence of evidence on duration of effect between treatments and the long-term efficacy and risks • the risk of adverse effects, including an increased risk of urinary tract infection. **[new 2013]**
81	Start treatment with botulinum toxin A§§§§§ only if women: • have been trained in clean intermittent catheterisation and have performed the technique successfully, **and** • are able and willing to perform clean intermittent catheterisation on a regular basis for as long as needed. **[new 2013]**
82	Use 200 units when offering botulinum toxin A.**Error! Bookmark not defined. [new 2013]**
83	Consider 100 units of botulinum toxin A† for women who would prefer a dose with a lower chance of catheterisation and accept a reduced chance of success. **[new 2013]**
84	If the first botulinum toxin A****** treatment has no effect discuss with the MDT. **[new 2013]**
85	If botulinum toxin A****** treatment is effective, offer follow-up at 6 months or sooner if symptoms return for repeat treatment without an MDT referral. **[new 2013]**
86	Tell women how to self-refer for prompt specialist review if symptoms return following a botulinum toxin A****** procedure. Offer repeat treatment as necessary. **[new 2013]**
87	Do not offer botulinum toxin B to women with proven detrusor overactivity. **[2006]**

2013 Update

* At the time of publication (September 2013), most Botulinum toxin type A preparations did not have a UK marketing authorisation for this indication. Evidence was only available for the licensed Botulinum toxin A (BOTOX, Allergan) preparation
† At the time of publication (September 2013), most Botulinum toxin type A preparations did not have a UK marketing authorisation for this indication. Evidence was only available for the licensed Botulinum toxin A (BOTOX, Allergan) preparation

Number	Research recommendations
RR11	What is the long-term effectiveness, optimal dose and optimal frequency of repeat therapy of botulinum toxin A in women with OAB based on detrusor overactivity including risk of adverse events such as urinary infection and intermittent catheterisation? Why this is important There are currently no trials looking at long-term outcomes, quality of life, satisfaction, optimal dose, optimal frequency and long-term adverse effects of botulinum toxin A for women with OAB. Further research into these outcomes will have an impact on future updates of key recommendations within the guideline and would impact on how resources are used within urinary incontinence services. Effective treatment with botulinum toxin A may need repeated injections to remain effective but the frequency of these is not reported in the current evidence. Botulinum toxin A has the potential to cause incomplete bladder emptying resulting in the need for women to perform catheterisation indefinitely. This not only has financial implications but catheterisation and the morbidity associated with it will not always be acceptable to women. Additionally, there are currently no data on whether repeated botulinum toxin A injections alter bladder function.
RR12	What is the comparative effectiveness of all formulations of botulinum toxin A preparations for the treatment of OAB symptoms in women?

8.3 Percutaneous sacral nerve stimulation

Introduction

The principle of neurostimulation is that electrical stimulation of the sacral reflex pathway will inhibit the reflex behaviour of the bladder and reduce detrusor overactivity. Permanently implantable sacral nerve root stimulators have been developed to provide chronic stimulation directly to the S3 nerve roots. Patients first undergo test stimulation before treatment using either percutaneous nerve evaluation (PNE) or tined leads in which a needle is inserted through the sacral foramina under local anaesthetic. This is connected to an external stimulation source and left in place for a few days. Those who show satisfactory response (normally a 50% improvement of symptoms) to the test stimulation may then proceed to a permanent implant.

NICE interventional procedure guidance

Guidance on percutaneous sacral nerve stimulation (P-SNS) for OAB symptoms was issued by the Interventional Procedures Programme of NICE in 2004.[26] It states that:

> 'Current evidence on the safety and efficacy of sacral nerve stimulation for overactive bladder symptoms appears adequate to support the use of this procedure, provided that the normal arrangements are in place for consent, audit and clinical governance.'

The systematic review conducted to inform the NICE interventional procedures (IP) guidance aimed to evaluate the efficacy and safety of P-SNS for urgency UI and urgency–frequency of any aetiology (OAB dry) in men and women.[512] In considering the effectiveness of P-SNS within this guideline, studies of any design that were conducted in women with idiopathic OAB wet or OAB dry are of relevance. Studies that only reported results for PNE ('test stimulation') were not considered, as these do not address effectiveness of the implanted device. One additional case series to those considered by NICE IP was identified.[513]

All studies considered P-SNS in the S3 foramen via an implanted device. Most studies included men and women. The majority also included patients with urinary retention as well as OAB wet or OAB dry; only a few reported data separately for those with urge urinary incontinence (UUI) or OAB dry. Overall, the proportions of people who responded to PNE, in studies that reported this, ranged from 28% to 63% (median 42%).

Review questions

- In women with OAB symptoms, what is the effectiveness of sacral nerve stimulation (SNS) compared with no active treatment?
- In women with OAB symptoms caused by detrusor overactivity, what is the effectiveness of percutaneous sacral nerve stimulation (P-SNS) compared with no active treatment?

Description of included studies

No new evidence was identified on the efficacy of P-SNS for OAB symptoms and OAB caused by urodynamically proven detrusor overactivity. The description of included studies relates to evidence published in the 2006 guideline.

Randomised controlled trials

Three RCTs evaluated P-SNS in men and women (mostly women) who had failed prior conservative and/or surgical treatment for UUI[514,515] or urgency–frequency (OAB dry).[516] Two of the three RCTs were conducted by the Sacral Nerve Stimulation Group.[515,516]

The RCTs had a 6 month controlled phase, after which patients in the control groups were offered the implant. The quality of the RCTs was considered to be poor: of the OAB studies, some only analysed data from patients who completed treatment; and others did not state whether intention-to-treat analysis was undertaken. None of the RCTs provided sufficient data to determine whether groups were similar at baseline, other than in the intervention given. [EL = 1−]

After 6 months of treatment in patients with UUI, leakage episodes, leakage severity and pad usage were significantly lower with P-SNS compared with control (continued prior treatment).[514,515] Scores on the SF-36 physical health status domain were significantly higher in the P-SNS group.[515] Following crossover of patients in the control groups to receive sacral nerve stimulation, these results were reported:

- treatment failure in 21% of patients (median 18 months, range 6–36 months); very common adverse effects were pain at implant site, lead migration and leg pain; common effects were leg stimulation, disturbed bowel function, urinary retention, vaginal cramps, anal pain and skin irritation at implant site (n = 44; 91% women)[514] [EL = 3]
- 52% of patients were dry at 18 months and a further 24% reported at least 50% reduction in leakage episodes (n = 58); at 3 years, 46% were dry and 13% improved (n = 41, of 98 originally randomised).[515,517]

In the RCT of patients with urgency–frequency (OAB dry), after 6 months of treatment, frequency was significantly reduced, mean voided volume and bladder volume at first sensation to void were significantly increased in the P-SNS group compared with control, with improvements in several SF-36 domains in the active treatment group (n = 51; 90% women).[516] [EL = 1−] At 2 years follow-up of 21 patients, 43% had at least 50% reduction in frequency and 62% had at least 50% increase in voided volume.[517] [EL = 3]

Of 157 patients enrolled across the Sacral Nerve Stimulation Group studies, 33% had adverse events that required surgical revision. Pain at stimulator or implant sites was very common, and lead migration, infection or skin irritation requiring removal of the implant were common.[515,516][EL = 3]

Case series

The Italian National Register[518] and 12 case series[513,519–529] reported the outcomes of sacral neuromodulation in patients with UUI or OAB dry resistant to conservative treatment. All except one study[527] included men and women and did not report results separately for women. The majority of studies included people with urinary retention or voiding difficulty, as well as OAB and/or UUI.[518–521,523,525,526,529] Four studies reported results of patients with idiopathic UUI or OAB dry separately.[518,520,521,523] Some studies included a minority of patients with neurogenic bladder.

The number of patients included in each study ranged from 12 to 113 (total 550), with eight studying fewer than 50 patients. The mean duration of follow-up ranged from 8 months to 5 years; reasons for withdrawal or missing data were not generally given. The Italian National Register included both retrospective and prospective data, which were considered separately (total n = 196). The outcomes

considered were bladder diary variables, continence status, satisfaction, QOL, urodynamic variables and adverse effects and complications.

Evidence statement

No new evidence was identified on the efficacy of P-SNS for OAB and OAB caused by detrusor overactivity. The description of included studies relates to evidence published in the 2006 guideline.

Bladder diary

These outcomes were considered in nine studies, with significant reduction in leakage episodes and frequency reported in five studies with up to 5 years follow-up.[513,521,522,524,529] Another two studies found variable reductions in leakage episodes and frequency at various time points.[518,523] No significant change was seen in these outcomes in one study (n = 12),[527] and a significant change in frequency only in one other (n = 15).[525]

Continence status

Subjective or objective cure or improvement was considered in eight studies, with varying definitions of cure, success or improvement used.[518–522,524,528,529] Across the studies, at least some improvement was reported in 39–77% of patients (median 63%). In a study with follow-up to 41 months, cure rates fell to 39% from 59% at 12 months.[518]

Satisfaction and quality of life

A satisfaction rate of 68% was reported at mean follow-up of 2 years in one study.[519] Three studies found significant improvement in QOL (IIQ at mean 8 months[527] or I-QOL at 18 months[518,523]).

Adverse effects and complications

Complications relating to the device were reported across 11 studies.[513,518–522,525–527,529] These were:

- pain or discomfort – median 11% (range 2–34%)
- technical device problems, such as current-related problems, device malfunction – median 11% (3–42%)
- lead problems – median 6% (3–11%).

Surgical intervention for these complications was reported in between 7% and 66% (median 22%) of patients, across seven studies.[513,518,520–522,528,529] Removal of the implant was required in 4–11% (median 7%) in three studies.[518,524,528]

Other adverse effects were cases of seroma formation,[521,528] disturbed bowel function (1–7%),[519,524,525,528] wound dehiscence or infection (3–15%),[513,521,526] infection (2–9%),[519–521] toe flexion (8%)[519] and pain (abdominal, leg, pelvis and gluteal incision; 2–20%).[513,525]

A cost–consequence analysis was undertaken for sacral nerve stimulation; see Appendix U for further details.

Up to two-thirds of patients achieve continence or substantial improvement in symptoms after P-SNS, and the available data show that beneficial effects appear to persist for up to 3–5 years after implantation. Around one-third of patients may require re-operation, most often owing to pain at the implant site, infection or the need for adjustment and modification of the lead system. Permanent removal of the electrodes may be required in one in ten patients. [EL = 3] Developments in the devices and leads have resulted in reduced rates of complications since introduction of the technique. [EL = 4]

Health economics profile

Two cost-effective analyses were undertaken for two populations; one for women who are unable to catheterise and one for women are able to catheterise (see Section 7.9).

For the first population (women who are unable to catheterise), P-SNS was only compared with no active treatment as botulinum toxin A was not an option for these women. The analysis suggested that the ICER was £28,723 per QALY. This would indicate that it is not cost effective to routinely offer P-SNS since it is above the £20,000 per QALY threshold. However, the sensitivity analysis showed that a small change (6 percentage points) in the improvement of health related QALY lead to the ICER for

P-SNS falling to below the £20,000 per QALY threshold (£19,976 per QALY). A high success rate for P-SNS was assumed in the model, which was not based on robust evidence. Lowering that estimate increased the ICER above the reduced cost-effective threshold.

In the second population (women who are able to catheterise) P-SNS was compared with botulinum toxin A and no active treatment to consider which treatment should be offered first, and which alternative option should be offered if first-line treatment is not successful.

The model suggested that P-SNS was not a cost-effective option compared with BoNT-A at £97,000 per QALY. If very high failure rates for BoNT-A were assumed (0.80 every three month cycle) then P-SNS was more favourable at £27,288 per QALY.

The sensitivity analysis also showed that a change (6 percentage points) in the improvement of health-related quality of life associated with continence reduced the ICER to £19,976.

Consideration of health benefits and resource use

The model was designed to compare botulinum toxin A or P-SNS as the first-line treatment after conservative management and also whether to offer the other intervention after first-line treatment had failed. The cost effectiveness analysis suggested that P-SNS is unlikely to be cost effective in women who are unable to catheterise as the ICER is outside the £20,000 per QALY threshold for cost effectiveness. P-SNS is also unlikely to be cost effective as first or second-line treatment in women who are able to catheterise (and therefore can have botulinum toxin A treatment). However, the GDG acknowledged that the model was sensitive to key parameters and reported different results with different model assumptions, making it a less robust basis on which to base recommendations than the ideal model with high quality data for the 10-year follow-up. Also, the GDG acknowledged that that there were other considerations about the choice of intervention that were not captured in the economic analysis.

First, although the model compared P-SNS and botulinum toxin A, the model did not include all the possible interventions that could be considered as a second-line treatment. The GDG noted that while botulinum toxin A was included as a comparator, augmentation cystoplasty and urinary diversion were not as they would not be considered as a first-line treatment option.

The GDG acknowledged that to not recommend P-SNS on the grounds of poor cost effectiveness would mean that augmentation cystoplasty and urinary diversion would be the only viable alternatives in this scenario. The clinical opinion of the GDG was that both of these interventions would involve a more serious surgical procedure and would have far greater lifelong implications. The GDG concluded that these were more costly and less effective, and less acceptable to patients than P-SNS. The complications and severity of these two interventions are explained in more detail in Chapter 8. The GDG did not consider that the implementation of a recommendation to remove P-SNS as a treatment choice was a feasible or reasonable option within current practice when, for most women, urinary diversion and augmentation cystoplasty would be unacceptable.

Second, the GDG agreed that the QALY gain reported in the base case model did not reflect the population with OAB symptoms who would be considered for P-SNS. The GDG noted that the QALY values came from a recent review in a health technology assessment (HTA) paper on stress incontinence that reported the QALY gain associated with all successful treatments for incontinence (Imamura et al., 2010). The GDG argued that while this value may be an accurate reflection of women's experience early in the clinical pathway, it did not reflect the QALY benefit that women at this point in the pathway would experience following successful treatment. The GDG suggested that for women to get to this point they will have had numerous unsuccessful interventions and therefore would have a more serious symptom profile. The sensitivity analysis showed that an increased improvement in QALY would make P-SNS cost effective. This was considered reasonable by the GDG as a realistic reflection of this population.

Evidence to recommendations

The usual sub-sections are not included here, since the GDG did not have any new clinical evidence to review for this question. Instead, the rest of this section explains changes to the recommendations on how to use P-SNS and who should be involved in the decision to offer treatment. Recommendations are based on GDG consensus of best clinical practice when offering P-SNS.

Multidisciplinary teams (MDT)

The GDG noted that there has been a significant increase in the use of sacral nerve stimulation since publication of the previous guideline although it is not available in all centres across the NHS. The decision to offer P-SNS should be made by an MDT including the nurse or physiotherapist who has been involved in the care of the woman with UI up to this point, as well as the surgeon responsible for carrying out the procedure. This is the minimum membership of an MDT taking this decision and the team may include other healthcare professionals depending on local treatment centre policy.

Urodynamic investigation

The GDG acknowledged that the recommendation to use P-SNS in the previous version of the guideline implied that this treatment could only be offered after urodynamic investigation and a positive diagnostic test for detrusor overactivity, but this was not explicit. The GDG decided that more emphasis was required on the importance of proving that the woman's symptoms are caused by detrusor overactivity and this was added to the previous first recommendation.

Sequence of treatment

The GDG"s view was that P-SNS should only be offered after a negative or poor response to lifestyle and behavioural interventions and antimuscarinic treatment (see Section 5.2). The evidence only included populations who had already received conservative treatments (including antimuscarinic treatment). Furthermore, the cost for the implantation of a device is considerable compared with conservative treatments that can be offered earlier. Therefore, the GDG determined that there is no clinical or cost effectiveness justification to consider offering P-SNS before conservative management.

The health economic model (see Section 8.9) considered the order of treatment following unsuccessful conservative treatment. In summary, the cost effectiveness analysis showed that P-SNS had a lower probability of being cost effective than botulinum toxin A at a £20,000 per QALY threshold. Therefore botulinum toxin A should be offered first to women who are able to catheterise. For women who are unable to catheterise, P-SNS was a cost-effective option compared with no treatment.

Test stimulation

The GDG consensus was that the implantation of an InterStim device should only be carried out after the woman has responded positively to either a percutaneous nerve evaluation or tined lead test stimulation. This is normally demonstrated by an improvement in symptoms of more than 50%. Therefore, when P-SNS is considered for an individual woman, it should be assumed that treatment includes the test stimulation (or stage one) phase.

Specialist long-term follow-up

The GDG consensus was that, due to the lack of long-term data on treatment efficacy and side-effects, specialist long-term follow-up is required for women who are treated with P-SNS. Furthermore, because of the length of time between battery replacements (estimated by the GDG to be required every 7 years on average), if symptoms return the patient should be able to access prompt specialist referral and consultation

Recommendations

Number	Recommendation
88	Offer percutaneous sacral nerve stimulation to women after MDT review if: • their OAB has not responded to conservative management including drugs, **and** • they are unable to perform clean intermittent catheterisation. **[new 2013]**
89	Consider percutaneous sacral nerve stimulation after MDT review if a woman's OAB has not responded to conservative management (including drugs) and botulinum toxin A*. **[new 2013]**

* At the time of publication (September 2013), most Botulinum toxin type A preparations did not have a UK marketing authorisation for this indication. Evidence was only available for the licensed Botulinum toxin A (BOTOX, Allergan) preparation

90	Discuss the long-term implications of percutaneous sacral nerve stimulation with women including: • the need for test stimulation and probability of the test's success • the risk of failure • the long-term commitment • the need for surgical revision • the adverse effects. **[new 2013]**
91	Tell women how to self-refer for prompt specialist review if symptoms return following a percutaneous sacral nerve stimulation procedure. **[new 2013]**

Number	Research recommendations
RR13	Further RCT evidence is required for drugs, botulinum toxin A and P-SNS in women with OAB due to idiopathic detrusor overactivity
RR14	Further research is required to evaluate P-SNS test stimulation techniques, placement of leads on S3 and S4 root and the benefit of continuous nerve stimulation in comparison with an intermittent stimulation.
RR15	What is the effectiveness and optimum sequence of treatment with botulinum toxin A and percutaneous sacral nerve stimulation for the treatment of OAB after failed conservative (including drug) management? Why this is important It is not currently known which treatment option, either botulinum toxin A or percutaneous sacral nerve stimulation, is the most effective in the medium- and long-term for women with OAB in whom initial treatment, including OAB drugs, has failed. The initial outlay for percutaneous sacral nerve stimulation is high but when successful it appears to be effective. Botulinum toxin A also has a high failure rate but a lower outlay and it is not yet understood the cost threshold (in terms of treatment cycles or length of follow-up) at which botulinum toxin A is likely to be the less cost-effective option compared with percutaneous sacral nerve stimulation. Currently, funding for percutaneous sacral nerve stimulation is on an individual basis because of its high cost, leading to geographical inequalities in access. A head-to-head longitudinal study of these 2 treatments would determine both which should be offered first and at what point in the treatment pathway. Such studies have not been done. This evidence could reduce inequalities in access to treatment. In subsequent NICE guidance, evidence would be available to inform recommendations on the treatment pathway and at which point in the treatment pathway for OAB each of these options should be offered. It would also provide more robust information to patients about the risk of adverse events and support women's choice about whether to proceed with treatment.

2013 Update

8.4 Augmentation cystoplasty

Augmentation cystoplasty aims to increase functional bladder capacity by bivalving the bladder wall and incorporating a segment of bowel into the resultant defect. Most commonly, this has been a segment of ileum but ileocaecal and sigmoid segments are occasionally used. Other vascularised bowel segments have been used, with and without their surface epithelium, but these techniques have been largely experimental or applied to children.

No prospective controlled trials were identified that evaluated augmentation cystoplasty for the treatment of UUI or OAB in women. One case series reported outcomes of the intervention in women with idiopathic UUI who had not responded to prior treatment (conservative and surgical). About half

the women also had evidence of interstitial cystitis on cystoscopy. Additionally, about half underwent Burch colposuspension for stress UI. At mean follow-up of about 5 years, 53% were continent, 53% were satisfied with treatment, 25% had occasional leaks and 18% were incontinent. One-quarter required treatment with antimuscarinics, and about one-quarter patch revision or further surgery. Very common adverse effects were recurrent UTI (49%), mucus retention requiring intermittent catheterisation (20%) and chronic diarrhoea (12%). Other adverse effects were partial bowel obstruction (8%) and cases of incisional hernia, bladder calculus and augmentation necrosis (n = 51).[530] [EL = 3]

Another five case series reported outcomes of augmentation cystoplasty in men and women with neurogenic or idiopathic DO.[531–535] Concomitant surgery was performed in 15–33% of patients in three studies.[531,532,535] One study reviewed patients who had either cystoplasty or detrusor myectomy, but did not report the time point of the outcomes considered and it is thus not considered further.[534] One only reported satisfaction with surgery, which was noted in 78%.[535] The other three studies reported the following effects on urinary symptoms:

- significant reduction in urgency and UUI; 53% cured or much improved at mean follow-up 20 months (n = 45)[533]
- about 90% of patients had improved frequency; significant reduction in urinary symptom scores at 12 months (n = 48)[531]
- 90% cured at 12 months mean follow-up (n = 40).[532]

Two of the studies also considered urodynamic outcomes: one reported no significant change in the parameters measured,[533] while the other reported significant increase in total bladder capacity.[531] Across these studies, adverse effects or complications reported were:

- recurrent UTI (median 37%, range 5–58%)[531–533,535]
- voiding dysfunction (18–39%),[532,533,535] problems with CISC 11%[531]
- disturbed bowel habit: increased bowel frequency (22–25%),[531,535] faecal incontinence (17%), diarrhoea (11%), constipation (4%).[531]

Other complications included mucus plug retention (3%),[532] anastomotic leak (2%),[531] persistent urine leak (3%),[532] incisional hernia (4–6%),[531,533] calculus formation (2%)[531] and urethral stricture (2–4%).[531,533]

A narrative review on augmentation cystoplasty included complications of the procedure in a series of 267 patients at 5–17 years follow-up. However, the indications for the procedure were not clear. Short-term complications were small intestine obstruction (2%), infection (1.5%), thromboembolism (1%), bleeding (0.75%) and fistula (0.4%). Long-term complications were CISC (38%), UTI (20% symptomatic), stones (13%), metabolic disturbance (16%), deterioration in renal function (2%) and bladder perforation (0.75%).[536] [EL = 3]

Evidence statements for augmentation cystoplasty

Data on augmentation cystoplasty in women with OAB are limited to case series. Cure or improvement has been reported in at least half of patients with idiopathic DO. Postoperative complications, such as bowel disturbance, metabolic acidosis, mucus production and/or retention in the bladder, UTI and urinary retention, are common or very common. There is a high incidence of recurrent UTI postoperatively, and many patients will need to self-catheterise. [EL = 3] Malignant transformation in the bowel segment or urothelium has been reported in a small number of cases. [EL = 4]

Evidence to recommendations (2013)

Although augmentation cystoplasty was not reviewed within the 2013 guideline update, to improve the implementation of the recommendation the GDG has included a note of clarification on the indications of its use.

The GDG noted that following augmentation cystoplasty there has been a reported long-term risk of bladder cancer. Therefore women should have annual cystometry appointments as a precautionary measure immediately following the procedure.

2013 Update

Recommendations

Number	Recommendation
92	Restrict augmentation cystoplasty for the management of idiopathic detrusor overactivity to women whose condition has not responded to conservative management and who are willing and able to self-catheterise. Preoperative counselling for the woman or her carer should include common and serious complications: bowel disturbance, metabolic acidosis, mucus production and/or retention in the bladder, UTI and urinary retention. Discuss the small risk of malignancy occurring in the augmented bladder. Provide life-long follow-up. **[2006, amended 2013]**

8.5 Urinary diversion

Urinary diversion implies that urine drainage has been rerouted away from the urethra. This is most commonly achieved by means of transposing the ureters to an isolated segment of ileum, which is used to create a permanent cutaneous stoma (ileal conduit). Urine, which drains continuously, is collected in a stoma bag, which is attached to the skin of the abdominal wall. Other bowel segments can be used including jejunum and colonic segments but these are unusual. Continent urinary diversion may be achieved by creation of a catheterisable abdominal stoma, or by formation of a rectal bladder. These techniques are largely employed in children and patients with neurogenic bladder dysfunction and rarely in adult women with UUI.

Little information on the outcomes of urinary diversion in women with idiopathic UUI/OAB was identified. Some data on the complications of urinary diversion, for benign conditions, are provided in a case series of men and women with neurogenic disease (76%), or intractable UI or interstitial cystitis (24%). After a minimum of 2 years follow-up, very common complications were vesical infection (52%), stoma problems including parastomal hernia, and upper tract dilatation (n = 93; 63% women).[537] [EL = 3]

Stress UI

A retrospective study of women with stress UI who underwent ileal loop diversion also reported complications relating to the procedure (n = 18; minimum 1 year follow-up). Overall, eight women required surgical revisions of the loops/stomas and eight required formation of a vesicovaginal fistula arising from complications related to the defunctioned bladder.[538]

Evidence statement for urinary diversion

There are limited data on the outcomes of urinary diversion in women with UUI/OAB. Where the procedure has been used in men and women with benign conditions, vesical infection, stoma related problems and the need for surgical revisions occur very commonly. [EL = 3]

Recommendations

Number	Recommendation
93	Urinary diversion should be considered for a woman with OAB only when conservative management has failed, and if botulinum toxin A*, percutaneous sacral nerve stimulation and augmentation cystoplasty are not appropriate or are unacceptable to her. Provide life-long follow-up. **[2006, amended 2013]**

At the time of publication (September 2013), most Botulinum toxin type A preparations did not have a UK marketing authorisation for this indication. Evidence was only available for the licensed Botulinum toxin A (BOTOX, Allergan) preparation

8.6 Detrusor myectomy

Detrusor myectomy aims to improve the functional bladder capacity by excising bladder muscle from the fundus of the bladder while leaving the mucosa intact, thus creating a permanent wide-necked diverticulum. The defect is usually covered with a segment of mobilised omentum. Theoretically, this should avoid the complications associated with bowel interposition.

No prospective controlled trials were identified that evaluated detrusor myectomy for the treatment of UUI/OAB in women. One case series reported the outcomes of detrusor myectomy in men and women with idiopathic or neurogenic DO, resistant to antimuscarinic drug treatment (n = 30; 20 women). Improvement was reported in 19 of 24 patients with idiopathic DO, with minimum follow-up of 2 years (median 6.5 years, maximum ~12). Three patients underwent further treatment (two ileal conduit, one colposuspension for stress UI). Other outcomes were not reported separately for patients with idiopathic DO. There was one case of bowel perforation. Overall, one-third of patients required intermittent self-catheterisation (ISC).[539,540] [EL = 3]

Evidence statement for detrusor myectomy

All case series on detrusor myectomy include patients with both neurogenic bladder dysfunction and those with idiopathic detrusor overactivity. While urodynamic parameters may improve in some patients, the clinical outcomes are unclear; hence the role of detrusor myectomy in the treatment of detrusor overactivity is not yet established. [EL = 3]

8.7 Vanilloid receptor agonists

Resiniferatoxin, originating from cactus, has a similar action to capsaicin (chilli pepper). Intravesical instillation of resiniferatoxin was considered in two case series of patients with OAB, one in women (n = 30)[550] and another in men and women (n = 41; 20 women).[551] The duration of follow-up is unclear in one study, making interpretation of the results difficult.[551] In the other study, in women refractory to antimuscarinic treatment, urgency and urge UI were significantly reduced 1 month after resiniferatoxin treatment. Adverse effects were not considered.[550] [EL = 3]

No relevant studies of sufficient quality regarding the use of capsaicin were identified.

Reduction in OAB and urgency in women has been reported in one case series, 1 month after intravesical instillation of resiniferatoxin. [EL = 3]

8.8 Sequence of surgical procedures for overactive bladder – economic evaluation

Introduction

The economic evaluation considered the cost effectiveness of P-SNS alone for women unable to catheterise, and single and combination treatment strategies for women for whom both P-SNS and botulinum toxin A are treatment options. Where the evidence was reported, data from the systematic review for this guideline was used to inform the model. Evidence of the effectiveness of combined treatment options was not searched for in the systematic review for this guideline, therefore an assumption was made that the effectiveness of botulinum toxin A and P-SNS used one after the other is independent of each other. This assumption was made in order to develop a model that reflected real decisions for the NHS. The explicit assumptions used in this economic evaluation are presented below alongside the GDG's consideration of their validity.

Background health economic literature

The health economic studies identified the literature search that did not form part of the evidence base for the recommendations on treatments for overactive bladder are only reported here as background information to inform the health economic modelling. None of the published health economic studies were presented as evidence to the GDG. However, clinical data from published health economic evaluations were incorporated into the model where specific model parameters were not included in the

review. The evidence from published health economic models that informed the health economic analysis for this guideline is presented as background information below. Evidence tables reporting methods and results can be found in the guideline appendix O.

The health economic review considered studies published since 2006 that had compared botulinum toxin A and neuromodulation in a cost effectiveness analysis that could inform the structure and model parameters for the model developed for this guideline.

Three new health economic analyses were identified with relevant comparisons; one from the USA (Siddiqui et al., 2009), one from the Netherlands (Wu et al., 2010) and one from Spain (Arlandis et al., 2011). All three developed Markov decision models and all studies identified the study population as women with OAB symptoms who had failed conservative management including treatment with an anticholinergic drug.

Siddiqui et al. compared botulinum toxin A and neuromodulation for the treatment of refractory UUI. A Markov decision model was developed with 3-month cycles. This model provided additional data for the health economic model developed for this guideline as it included variables that were not part of the guideline clinical review. The population included in Siddiqui's analysis was women with refractory idiopathic detrusor overactivity. The additional variables were:

- the probability of retention of urine after treatment with botulinum toxin A requiring additional health care
- the probability of contracting a urinary tract infection (UTI) in a treatment cycle of botulinum toxin A
- the probability of retention together with UTI.

Leong and colleagues compared P-SNS and botulinum toxin A and included in each arm the possibility of switching to the other treatment if the first failed. If a patient failed both, then no other treatment options were offered. This clinical pathway was adopted for the health economic model for this guideline. Effectiveness data was identified in non-randomised trials with additional parameter estimates derived from an expert clinical panel

Arlandis compared P-SNS, P-PTNS, optimal medical management and botulinum toxin A. The analysis was conducted over a 10 year period. This was the timeframe adopted for the economic model for this guideline because the GDG considered that sacral nerve stimulation, when successful, would provide health benefits for at least this period. The treatment cycles were 1 year so trial data could not be used as they did not report this length of follow-up. Effectiveness data was identified in non-randomised trials with additional parameter estimates derived from an expert clinical panel.

None of these studies provided sufficient data on their own to inform recommendations in this guideline. Although all three studies included the relevant comparators for the cost effectiveness analysis for this guideline, none of these studies were undertaken in the NHS. They were not based on the outcome that the GDG considered to be the most relevant for this analysis (see 'Outcomes' below) and used estimates of effectiveness that are superseded by the clinical review for this guideline. This review was based on randomised controlled trial evidence and, for longer term data, on the expert opinion of the GDG members.

None of the published health economic studies were presented as evidence to the GDG to inform recommendations and hence no quality assessment of these studies is presented in the guideline.

New health economic analysis

Choice of interventions

The model considers treatment following antimuscarinic therapy that has not achieved optimal success. Continuing medical management was not considered an option since at this stage of the treatment pathway it was assumed that women have already failed to respond adequately to at least one antimuscarinic drug recommended in this guideline.

A second antimuscarinic drug was not included as a treatment alternative in any analysis. The GDG view was that in the time that was needed to be referred to secondary care, there is the opportunity to try an alternative antimuscarinic drug after referral to secondary care. The option of continuing medical

management after the failure of at least two antimuscarinic drugs was not seen as a viable treatment alternative in the NHS.

P-PTNS was not included as a treatment option because the GDG did not consider there to be sufficient evidence to recommend its use on effectiveness grounds (see Chapter 5).

Structure of the health economic model

A model was developed that compared five treatment strategies.

- treatment with botulinum A toxin alone, or
- treatment with sacral nerve stimulation (P-SNS) alone, or
- treatment starting with botulinum toxin A and then offering P-SNS if botulinum toxin A is ineffective, or
- treatment starting with P-SNS and then offering botulinum toxin A if P-SNS (or percutaneous nerve evaluation) is ineffective
- no treatment.

Two separate and independent analyses were undertaken based on this model. The first analysis considered the cost effectiveness of P-SNS for women who cannot tolerate clean intermittent catheterisation (CIC), for example because of a co-existing condition. For this group, the only treatment options were strategy 2 or strategy 5 because any strategy that included botulinum toxin A could require CIC.

The second analysis considered treatment for women who are able to tolerate CIC, for whom both P-SNS and botulinum toxin A are viable treatment options. For this group, the cost effectiveness of all treatment strategies was included in the analysis.

The health economic models followed a hypothetical cohort of women with OAB caused by detrusor overactivity over a 10-year treatment period. This was the timeframe adopted for the economic model for this guideline because it was used in a recent health economic model (Arlandis et al., 2011) although there was a lack of long-term data on efficacy. The GDG considered that, given that both P-SNS and botulinum toxin A are relatively new technologies and data on longer term effects have not yet been collected, the timeframe reflected current clinical experience of these interventions.

Each treatment cycle lasted 3 months. In each cycle, there was a probability that a woman was either on successful treatment (continent) or on unsuccessful treatment (incontinent). Depending on the treatment strategies, a women on unsuccessful treatment could be offered an alternative in the next 3-month cycle or revert to no active treatment. No active treatment was an ‘absorbing state’ meaning that women could move to another state from this one for the rest of the model term.

This highly structured pathway does not exactly reflect clinical practice in the NHS but allows the model to estimate the costs and outcomes for each treatment pathway without the added complications of other treatment options. It is a simplification of reality and not all decisions and health states are represented. For example, mortality is not factored into the model for simplification purposes because it was thought that differences in mortality between treatment arms would not affect the relative cost effectiveness of treatment options. Since the analysis did not include death, it was assumed that all women would be alive at the end of the model term.

At the beginning (time zero), all the women were in an incontinent state. The first and second strategies – treatment with either botulinum toxin A or P-SNS alone – are straightforward. For both strategies, women can be either in a continent state and continue treatment or in an incontinent state and stop treatment.

In strategy 1 (P-SNS alone) the implant remains in place until either there are complications or the battery in the device needs replacing in the seventh year of use. The probability of complications arising from the use of P-SNS is included in the model. Complications can lead to revision and continuation with P-SNS or removal of the implanted device. If a woman stopped treatment with P-SNS she reverts to no active treatment (management with pads only) for the remainder of the model term.

In strategy 2 (botulinum toxin A alone) the woman is assumed to require another course of treatment every 9 months on average. During a cycle, a woman can be either continent or incontinent, and have complications or no complications. The complications included in the model are urinary tract infection and retention. These complications do not lead directly to discontinuation of treatment but the cost of additional treatment for UTI is included in the model. If a woman stops treatment with botulinum toxin A, no additional service associated with botulinum toxin A is required.

For the third and fourth strategies (one treatment, then switching to the other if that fails) the pathway is more complex. In strategy 3, women could be offered botulinum toxin A first and if is initially unsuccessful they go straight to the P-SNS test stimulation (percutaneous nerve evaluation) within the first 3 months of treatment. If that succeeds they proceed to an implant and if it fails they remain off treatment (management with pads only) for the remainder of the model term having exhausted both treatment options available in the model. If botulinum toxin A treatment is successful, they continue to be treated this way until either the end of the model term or until the treatment is no longer successful where they are offered P-SNS test stimulation in the next cycle. A proportion of women are assumed to have complications (UTI with or without retention) in each botulinum toxin A cycle. Complications are assumed not to have a direct effect on treatment efficacy but do incur treatment costs. If P-SNS is successful, they continue with P-SNS until the end of the model term with a battery change after 7 years, or until it is no longer effective. Complications associated with P-SNS may require surgical revision or removal, which incurs additional costs. If P-SNS is also unsuccessful, they stop treatment. They revert to no active treatment (management with pads only) for the rest of the model term.

In strategy 4, women may be offered test stimulation with P-SNS in the first 3-month cycle. If this is successful, they will go on to have a permanent P-SNS implant in the following 3-month cycle. They remain on P-SNS until either the end of the model term with a battery change at 7 years, or until P-SNS fails. In the latter case they switch to botulinum toxin A in the next treatment cycle. If botulinum toxin A is effective they remain on botulinum toxin A until the end of the model term or until it is no longer effective. If botulinum toxin A is not effective, they stop treatment. They revert to no active treatment (management with pads only) for the rest of the model term.

The model uses the effectiveness probabilities published in this guideline where possible (Table 7.3) to determine the proportion of women in a successful treatment state (either P-SNS or botulinum toxin A) or in a persistent OAB state (with no active treatment) at every time point. The costs and outcomes associated with each strategy are calculated for each time point. The definition of successful treatment used in this model is zero episodes of continence per day or ‘completely dry’. There was considerable discussion about these assumptions with the GDG during development, as other health economic models have measured success as a proportion of women with improved symptoms. However, the benefit to women of improved symptoms is more uncertain than symptom-free days. (See ‘Outcomes’ below for further discussion).

At the end of the 10-year timeframe, the costs and outcomes (measured in quality adjusted life years [QALYs]) were calculated for each strategy. Where one strategy was both more expensive and more effective the additional cost per QALY was calculated. Since the data points used in the model are uncertain, the model can be made probabilistic to estimate the likelihood that any strategy is cost effective. This approach can help quantify the uncertainty in the model results. Costs were discounted at 3.5% per year and QALYs at 3.5% per year. An NHS perspective for costs was adopted, which assumed that all costs (including incontinence pads) were born by the NHS.

Data used in the model

Effectiveness

Tables 8.4 to 8.6 below present the values that were used in the model and model assumptions agreed with the GDG. The effectiveness of P-SNS was not updated in the 2013 guideline due to lack of robust data. However, for health economic analysis, less robust data can be used and included in sensitivity analysis to assess how important the value is to the final result. A review of the evidence published in 2010 by Leong and colleagues provided evidence of the effectiveness of P-SNS. A high value for effectiveness reported in the review was used in the base case model as it was anticipated that P-SNS would not be cost effective compared with botulinum toxin A which is a cheaper intervention.

There was a paucity of long-term data on the effectiveness of any of the treatment options. Data for the first 6 months, although derived from high quality evidence, comes from small trials.

Table 8.4 Effectiveness parameters used in the health economic model comparing botulinum toxin A and sacral nerve stimulation treatment strategies.

Description	Value	Included in PSA	Notes
Botulinum toxin A			
1. Failure rate after 3 months of botulinum toxin A	0.40	Yes	From the clinical review in this guideline. This is calculated from the NCC review of the cumulative 6-month failure rate (64%). The rate was assumed to be the same at 3 and 6 months. N = 191 women. This was varied from 0.2 to 0.8 in sensitivity analysis.
2. Failure rate after 6 months of botulinum toxin A	0.40	Yes	See parameter 1 above
3. Failure rate at 9 months	0.01	No	This is based on the assumption that Botulinum toxin A is a successful treatment for women for whom it is successful at 6 months, with a failure rate of only 1%. Data were not identified for time periods above 6 months.
4. Failure rate at 12 months of botulinum toxin A	0.01	No	See parameter 3.
5. Failure rate in every cycle after twelve months	0.01	No	See parameter 3.
6. Rate of retention with botulinum toxin A	0.33	No	Not from the clinical review in this guideline but published in a health economic model (Siddiqui et al., 2009)
7. Rate of UTI with retention	0.75	No	See parameter 6.
8. Rate of UTI with no retention	0.19	No	See parameter 6.
9. Rate of repeat injections in women who are successful on botulinum toxin A	1.00	No	From the clinical review for this guideline. N = 68 women.
P-SNS			
Failure rate of P-SNS test stimulation	0.56	Yes	Based on UI guideline update clinical review. N = 329 women
Rate of complications	0.31	Yes	From the clinical review for this guideline, the cumulative complication rate of 0.56 in 6 months
Rate of surgical revision	0.32	Yes	From the clinical review for this guideline. N = 157
Rate of consent to surgical revision	0.95	No	Published in a health economic model (Siddiqui et al., 2009)
Rate of effectiveness of P-SNS per 3-month cycle	0.88	Yes	Not from UI guideline update clinical review. From a review by Leong et al (2010) that reported effectiveness ("good clinical response") of between 64% and 88% for P-SNS. Upper value was used in the base case and included in one-way sensitivity analysis.

PSA probabilistic sensitivity analysis (see below), P-SNS percutaneous sacral nerve stimulation, UI urinary incontinence, UTI urinary tract infection

Costs

Table 8.5 is a summary of the total costs. Where possible, data supplied from manufacturers was checked with NHS sources. The cost for P-SNS used in the model assumed that all women had a percutaneous nerve evaluation. An alternative procedure is the two-stage tined lead requiring only one lead implantation. The cost of this process is not included in the table of costs because it is currently a less widespread procedure. Data on pad and catheter use was supplied by expert members of the GDG. All women who fail PNE incur a cost of removal and all women who get no benefit from P-SNS have to have the lead removed. These are additional costs to the NHS. The cost of adverse events was also included as reported in previous health economic models.

It was assumed that women who are treated with botulinum toxin A receive a dose of 200 units in the base case analysis with follow-up injections every 9 months. This was a GDG assumption based on the members' clinical experience. This is a longer interval between injections than assumed in previous health economic models. The dose of botulinum toxin A was varied to 100 units in a one-way sensitivity analsyis.

Appendix O reports all the data and sources in more detail.

Table 8.5 Treatment and adverse event cost for botulinum toxin A, P-SNS and 'no active treatment' used in the model

Procedure	Cost	Notes
P-SNS		
Percutaneous nerve evaluation	£1,485	Bottom-up costing, see Appendix O
Permanent implant of tined lead	£8,641	Bottom-up costing, see Appendix O
Removal of permanent implant	£923	Bottom-up costing, see Appendix O
Change of battery every 7 years	£6,623	Bottom-up costing, see Appendix O
Botulinum toxin A		
Botulinum toxin A initial injection	£852	Bottom-up costing, see Appendix O (£713 per injection using the lower 100 unit dose which was included in one-way sensitivity analysis)
Repeat injection	£352	1/3 cost first procedure as model assumes a repeat injection every 9 months is required, plus catheters. See Appendix O
Adverse events		
Treatment for UTI	£36	From an RCT of management strategies for urinary tract infections in the UK NHS (Turner et al., 2010), uplifted to 2012 prices
Cost to the NHS of incontinence (pads)	£8 per week	GDG opinion based on data from a continence service in an English county in 2012. No other additional healthcare resources were assumed in the base case model
Cost of urinary retention	£59	Consultant-led non-admitted face-to-face attendance (gynaecology) (NHS reference costs 2012)
P-SNS management of complications	£112	Consultant-led non-admitted non face-to-face attendance (gynaecology) (NHS reference costs 2012)

GDG guideline development group, P-SNS Percutaneous sacral nerve stimulation, RCT randomised controlled trial, UTI urinary tract infection

Quality of life

The GDG chose to use the outcome continent (absolutely dry) in the health economic analysis. Incontinence was chosen for methodological and clinical reasons. It was the view of the lay members that achieving complete continence was the most meaningful effectiveness outcome to women with OAB symptoms and the reason they seek treatment in the first place. It is a conservative estimate of efficacy since women may also gain some benefit from treatment without achieving full continence. However, it is a reasonable clinical assumption that interventions that achieve the highest rates of continence will also achieve the highest rates of improvement in symptoms. A QALY value for 'symptoms of incontinence' and 'no symptoms' was identified in a systematic review of the literature of all the studies that have published QALY values for stress incontinence, which included studies for all types of incontinence (Imamura 2010) and this was used for the health states 'continence' and 'incontinent' (see below).

It was the GDG's view that published studies based on improvements in incontinence may have led to an overestimation of effectiveness of treatments for OAB symptoms by combining micturition (both voluntary and involuntary) and leakage per day. This approach was based on an economic study by (Kobelt et al., 1998). Kobelt's study defined the best possible health state as less than nine episodes of micturition or leakage per day rather than zero episodes of incontinence, which the GDG considered was the most important outcome for patients. The utility values published in the Kobelt study became the standard values used in economic evaluation of urinary incontinence treatments published subsequently (and reviewed in the previous guideline). The GDG did not consider this a useful outcome in measuring incontinence because there was no definition of what the micturition rate per day would be for a woman who did not have incontinence. Therefore, a less ambiguous outcome was chosen by the GDG, which was continence (completely dry) or incontinence (one or more episodes of leakage). The GDG's view was that treatment strategies that led to the highest probability of being completely dry would also be the strategies with the highest number of women who were continent by other measures of success (for example ≥50% improvement in symptoms). Therefore, an economic analysis based on a narrower, less ambiguous definition of continence would be very likely to underestimate the cost effectiveness of the more effective treatment strategies compared with the alternatives.

A range of values for health state quality of life (utility) values are published in health economic models. A recent HTA included a comprehensive review of health state utilities associated with urinary incontinence. The review was published as part of a cost effectiveness model for treatments for stress urinary incontinence (Imamura et al., 2010). It included a study by Haywood et al. (2008) that reported generic quality of life scores (EQ-5D) obtained by questionnaires from women with successful and unsuccessful treatment. EQ-5D scores can be converted into the health related quality of life weightings to drive QALYs. Haywood reported a median EQ-5D score of 0.85 (SD ± 0.23) for women with successful treatment (no episodes of incontinence). At 5 months, the mean score for women who said they had no benefit from treatment for their condition (remained in an incontinent state) was reported as 0.74 (SD ± 0.38). The HTA cost effectiveness analysis used these utility values to define treatment success and treatment failure of treatments for SUI. Using the 'treatment failure' utility value to represent incontinence may not capture the variability of continence states and improvements in women's continence status who do not reach a fully continent state. The GDG felt that it was a plausible assumption that treatments which increase the proportion of women who are fully continent also improve the proportion of women who have some benefit but without achieving full continence. Therefore the analysis is likely to underestimate the effectiveness of the more effective treatments and the treatments identified as cost effective are likely to be even more cost effective than reported. The base case values used in the model are those reported in the HTA report, converted into 3-month cycle values. These values were varied in the one-way sensitivity analysis.

Table 8.6 Health-related quality of life values for urinary incontinence used in the health economic model Imamura et al., 2010 (from Haywood et al., 2008)

Health state	EQ-5D value per year	EQ-5D value per 3 month cycle
Continent (completely dry)	0.85	0.2125
Incontinent	0.74	0.185

Probabilistic sensitivity analysis

There was sufficient data to derive probabilistic distributions for five model parameters in the PSA. All other model parameters were fixed. Complication rates for botulinum toxin A included retention and urinary tract infection only. Data for these adverse events were not included in the systematic review and were taken from data published in previous health economic models (see Table 8.6).

Table 8.7 Parameters for the distributions applied in the probabilistic sensitivity analysis

Item	Alpha	Beta	Distribution
Failure rate botulinum toxin A at 6 months	123	68	Beta
P-SNS test stimulation failure rate	184	145	Beta
P-SNS complication rate at 6 months	83	74	Beta
Surgical revision rate following complications	51	106	Beta
Maintenance of efficacy after test simulation in first 3 months	64.31	44.69	Beta

P-SNS percutaneous sacral nerve stimulation

Assumptions in the model

Table 8.8 summarises the assumptions that the GDG has agreed in order to develop this model. The GDG was keen that the assumptions in this model were transparent so that readers could understand the decisions that were made and the consequences, where possible. The GDG also wanted the model to reflect clinical experience and NHS practice.

Table 8.8 Assumptions used to construct the health economic model comparing botulinum toxin A and P-SNS treatment strategies

Assumption	Further explanation and consideration by the GDG
All women in each strategy are able to have that treatment. Women who cannot tolerate clean intermittent catheterisation (CIC) are not offered botulinum toxin A.	This assumption only holds for the health economic analysis for women who are able to catheterise. The other economic analysis assumes that women who cannot tolerate CIC and are only offered P-SNS or no active treatment.
The effectiveness of botulinum toxin A and P-SNS are independent of each other so that the likelihood of success with P-SNS is not affected by treatment failure using botulinum toxin A and vice versa.	The GDG considered this to be a strong simplifying assumption but noted that making any other assumptions (that these populations are different) would require estimations for the efficacy of treatment for different populations, which the GDG did not feel able to do without evidence.
Treatment efficacy and the risk of failure is the same every cycle, independent of how long a woman has been on treatment.	This is a strong assumption, but no data was identified to inform this parameter. The GDG recognised that it is a simplification of reality. However, using values based on expert opinion would add to complexity without any guarantee that these would be a more robust estimate.
All women who fail P-SNS test stimulation proceed to treatment with botulinum toxin A in the next cycle with no second attempt. None refuse botulinum toxin A as an alternative treatment at that stage.	This model was developed to compare P-SNS and botulinum toxin A as alternative strategies. Women who cannot tolerate botulinum toxin A were not included in the analysis of treatment strategies that included botulinum toxin A .

Assumption	Further explanation and consideration by the GDG
All women who succeed with a test stimulation of P-SNS proceed with P-SNS.	The GDG's view was that once women have agreed to P-SNS, nearly all would continue with a permanent implant. The small numbers of women that refuse would not change the overall conclusion of the analysis.
All women who fail their first treatment with botulinum toxin A proceed directly to P-SNS.	The model does not include the cost/outcome associated with a second treatment with botulinum toxin A at the same or a higher dose as there was no clinical data on the effectiveness of this strategy.
There is no additional loss of health-related quality of life associated with complications resulting from P-SNS or botulinum toxin A.	Evidence was not identified on health-related quality of life associated with complications as co-morbidities of incontinence. This is recognised as a limitation of the analysis.
Women who require a surgical revision are incontinent during that cycle.	The GDG recognised that some women may have some benefit from P-SNS while requiring a revision, but that it was far more likely that women would seek medical attention due to device failure.
All women who require a surgical revision following P-SNS consent to having a revision.	This was an assumption in other health economic models and seen as reasonable by the GDG
Women who are successfully treated with botulinum toxin A require additional injections with botulinum toxin A every 9 months on average	This was an estimate by clinical experts within the GDG.
Women who fail treatment with BoNT are not offered a second treatment.	The GDG considered that it is usual practice in the NHS not to repeat a course of botulinum toxin A injections if a woman had not had any benefit from the first course. This was common across study protocols in the RCT evidence included in the systematic review.
The complications associated with botulinum toxin A are UTI and retention only and these events have no impact on treatment efficacy.	This is a simplification of the model that reflects other health economic analyses. Some models (Arlandis et al., 2011) included a more extensive range of adverse events, which increased the complexity of the model. These adverse outcomes were not prioritised by the GDG for the UI update guideline systematic review given the rarity of these events. It was not considered to affect the overall results of the analysis.
The long-term cost of P-SNS includes the cost of managing complications and undertaking revisions only.	Evidence for long-term complications was not prioritised by the GDG for the UI update systematic review. The GDG acknowledged the lack of evidence in this area as a weakness in the evidence for all treatment for OAB. Medical review may be more frequent for women on P-SNS, or alternatively women on no treatment and who are incontinent may require more (and different) long-term health care support. The cost of this support was not known but not considered sufficient to change the results of the analysis.
Women who fail P-SNS and BoNT have persistent UI for the remainder of the model term.	This is a simplification of the model that may not reflect NHS practice as women are likely to be reviewed and offered additional support, which is a cost to the NHS

Assumption	Further explanation and consideration by the GDG
	that has not been included. It was not considered that this would change the result of the model. Given that they have not had any benefit from medical or surgical intervention, it is unlikely that they will experience full continence for the remainder of the model term.
All women who are incontinent require incontinence pads to manage their incontinence.	This reflects the experiences of GDG members who care for women who are not on active treatment
Women who are continent incur no additional costs apart from their treatment .	This does not reflect reality but the exact cost is not known and the additional cost of management was not deemed to be sufficiently different from that of women who remain incontinent (usually a regular clinical review in primary care) to change the magnitude of cost effectiveness in this model.
Longer term effectiveness data are assumed to be the same as at 3 years.	No long-term data for botulinum toxin A were identified, and health economic models published data were based on clinical opinion. Further analysis could be done if the GDG agreed values based on clinical opinion.
All women are alive at the end of the model term.	The GDG considered that mortality would not be affected by treatment for OAB.

CIC clean intermittent catheterisation, GDG guideline development group, OAB overactive bladder, P-SNS percutaneous sacral nerve stimulation, RCT randomised controlled trial, UI urinary incontinence, UTI urinary tract infection

Approach to sensitivity analysis

Table 8.4 indicates the effectiveness parameters that were included in the model and Table 8.6 shows the sub-group of parameters that could be included in the PSA. The PSA ran 1000 random simulations derived from the data identified in clinical trials. The smaller the trials on which data inputs are based, the more variation would be expected in the simulation, indicating more uncertainty in the results. Long-term effectiveness assumptions were not included in the probabilistic sensitivity analysis.

One-way sensitivity analysis was also undertaken on the key model parameters not included in the PSA. The purpose was to understand the importance of a specific estimate used in the model in driving the cost effectiveness results. However, changing a model parameter within a reasonable range (decided by the GDG) could change the order of cost effectiveness, making a different strategy the most cost effective relative to the others. If a suggested change in a variable changes the conclusion of the analysis, then the GDG may have less confidence in that conclusion. The GDG may decide that the results of the model are not conclusive and therefore do not support any specific guideline recommendation. Model parameters were therefore varied within realistic ranges derived from by other sources of published data or GDG opinion. For the sensitivity analysis altering the dose of botulinum toxin A to 100U, two effectiveness studies provided data for the model (Dmochowski et al., 2010, Denys et al., 2012). Drug costs were taken from the BNF in July 2013 and included in the calculation of 3-month health service costs (see Appendix O).

Model validation

A second health economist reviewed the methods, model structure, data inputs and results of the model, and changes were made to earlier drafts.

Results

Model 1 – Treatment strategy for women who cannot tolerate CIC

In the first analysis, treatment with P-SNS for women who cannot tolerate catheterisation was compared with no active treatment.

Table 8.9 Cost effectiveness of P-SNS versus no active treatment (NAT) for women with OAB

Treatment option	10-year discounted cost	10-year discounted QALYs	ICER
NAT	£3,581	6.37	
P-SNS only	£13,398	6.71	£28,723

NAT no active treatment, P-SNS percutaneous sacral nerve stimulation

Table 8.9 shows that P-SNS costs around £13,400 over 10 years but is more effective than no active treatment which costs around £3,400 over the same time period. Nearly all the additional cost of P-SNS occurred in the first year with no additional costs until year 7 when the P-SNS battery required replacement. The cost of no active treatment was the cost of daily pads over 10 years as the cost of medical review was assumed to be the same.

The difference in total QALYs over 10 years assumed that women who are incontinent had a decrement in quality of life from 0.85 to 0.74 (see Table 8.6). The analysis shows that P-SNS was only cost effective if the willingness-to-pay per QALY threshold is £30,000 per QALY.

Model 2 – Treatment strategy for women who are able to tolerate CIC

In the second analysis, women who can tolerate clean intermittent catheterisation can be offered either no active treatment, botulinum toxin A alone, botulinum toxin A followed by P-SNS if the first treatment fails, or P-SNS followed by botulinum toxin A if the first treatment fails.

Table 8.10 presents the treatment alternatives in ranked order of cost (lowest to highest). The notes in the table explain which strategies are being compared in each row.

On average, 'botulinum toxin A only' was cost effective compared with no active treatment as the mean ICER was well below the £20,000 per QALY threshold. 'P-SNS only' was not cost effective compared with the 'botulinum toxin A only'. The ICER for botulinum toxin A first strategy was just outside £30,000 per QALY threshold. The 'P-SNS first' was dominated by the 'botulinum toxin A first' strategy as it cost more with no additional QALY benefits.

In the base case analysis, 56% of women who were offered P-SNS failed the test stimulation before a permanent implant could be inserted. These women did not have any benefit from P-SNS treatment in the 10-year period although they incur some costs (of the test stimulation). The 'P-SNS first' treatment strategy was a more expensive and marginally more effective than 'botulinum toxin A first'.

Table 8.10 Mean estimates of the cost effectiveness of treatment strategies for women with OAB, in order of cost, 1000 simulations

Treatment option	10-year discounted cost	10-year discounted QALYs	ICER	Notes on the cost effectiveness comparisons
No active treatment	£3,581	6.37		
Botulinum toxin A only	£7,018	6.65	£12,427	This shows the additional cost and effectiveness of botulinum toxin A only compared with no active treatment
P-SNS only	£13,398	6.71	£97,912	This shows the additional cost and effectiveness of 'P-SNS only' compared with 'botulinum toxin A only'. This is a different ICER than that reported in table 8.9 which compared 'P-SNS only' with no active treatment

Treatment option	10-year discounted cost	10-year discounted QALYs	ICER	Notes on the cost effectiveness comparisons
Botulinum toxin A first then P-SNS	£14,417	6.89	£30,235	This shows the additional cost and effectiveness of 'botulinum toxin A first' compared with 'botulinum toxin A only' (that is, the cost-effectiveness of adding P-SNS to the botulinum toxin A treatment strategy)
P-SNS first then botulinum toxin A	£15,756	6.89	Dominated*	This shows the additional cost and effectiveness of 'P-SNS first' compared with 'botulinum toxin A first'

* There are other cheaper strategies associated with the same or higher QALY benefit

ICER incremental cost-effectiveness ratio, P-SNS percutaneous sacral nerve stimulation, QALY quality adjusted life year

Figure 8.1 shows all four active treatment strategies and the likelihood that any of them are cost effective at different thresholds of willingness-to-pay for a quality adjusted life year for women for whom botulinum toxin A is an option.

The graph shows that at a cut-off of £20,000 per QALY, botulinum toxin A alone was most likely to be the cost-effective option for women who are able to catheterise (with a probability of 99.5%). However, at a higher willingness-to-pay threshold (£30,000 per QALY) botulinum toxin A followed by P-SNS ('botulinum toxin A first') was cost effective in some of the simulations (44% of the simulations at £30,000). However, botulinum toxin A only was still the most likely to be cost effective (55% probability). The graph below illustrates the lower level of certainty that any strategy is cost effective at higher thresholds of willingness-to-pay for a QALY.

Figure 8.1. Cost effectiveness acceptability curves for P-SNS and botulinum toxin A strategies for women with OAB

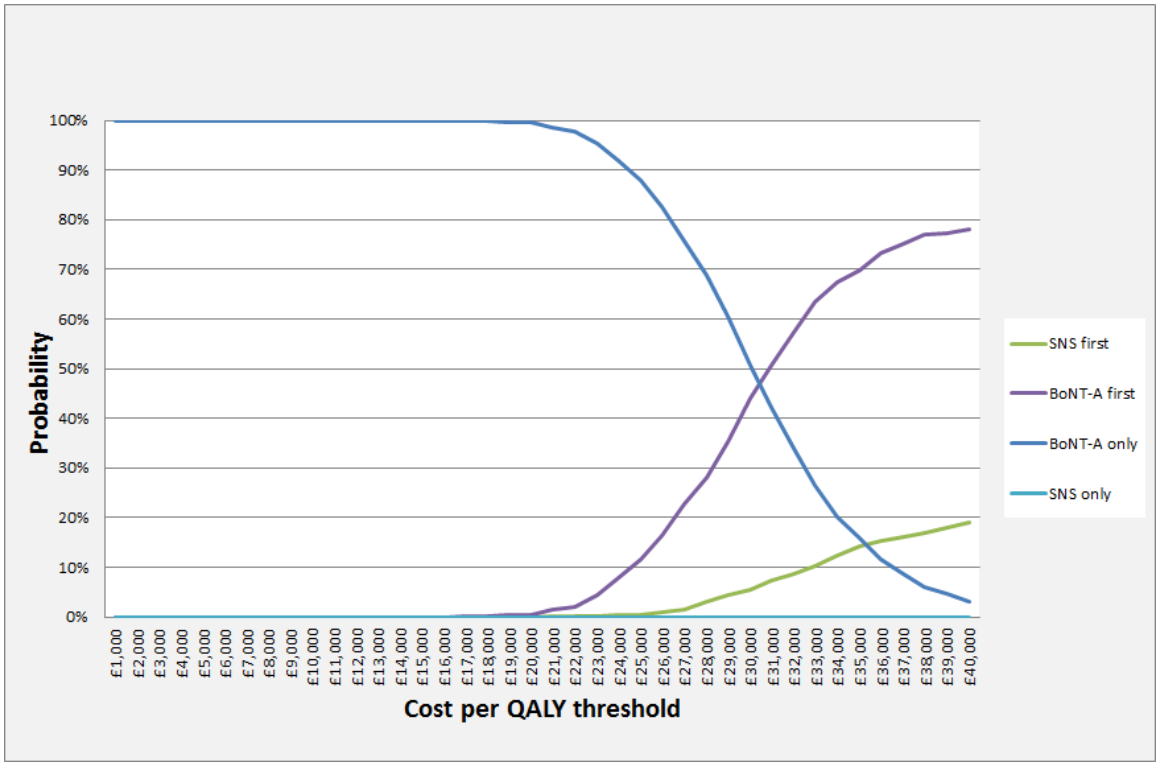


Table 8.11 shows the net benefit for the four active treatments. Net benefit is the calculated as the QALY value multiplied by £20,000, subtracted by the cost of the strategy. The table shows the ranking of the strategies in terms of their cost effectiveness. 'Botulinum toxin A only' had the highest net benefit. The confidence intervals were narrow but the lower confidence interval does not cross the upper confidence interval of the 'botulinum toxin A first' strategy, indicating the high level of certainty of this result. The net benefit for 'botulinum toxin A first', 'P-SNS only' and 'P-SNS first' cross each other. This indicates that there is a lower level of certainty of a true difference between these strategies.

Table 8.11 Net benefit and confidence of surgical treatments for OAB at £20,000 per QALY, 1000 simulations

Net benefit at £20,000 per QALY	**Net benefit**	**Confidence intervals**	
Treatment		**CI min**	**CI max**
Botulinum toxin A only	£125,908	£124,700	£127,116
Botulinum toxin A first	£123,403	£122,131	£124,675
P-SNS first	£122,112	£120,634	£123,591
P-SNS only	£120,832	£119,270	£122,394
P-SNS only	£120,832	£119,270	£122,394

CI confidence interval, QALY quality adjusted life year, P-SNS percutaneous sacral nerve stimulation

One-way sensitivity analysis

The next section explores the results using a one-way sensitivity analysis which takes into account parameter uncertainty in specific model inputs which were not included in the problastic senstiviey analysis

The table below shows the impact of changes in specific variables on the model outputs. The fourth column indicates whether the order of cost effectiveness changed as a result of changing a specific parameter in the model.

Table 8.12 One-way sensitivity analysis varying key parameters in the model for women able to catheterise

Variable	**Base case value**	**Variation range**	**Result**	**Notes and interpretation of the results**
Botulinum toxin A variables				
Failure rate for Botulinum toxin A at 3 and 6 months	0.40	0.40–0.80	Sensitive	At a 0.80 failure rate of botulinum toxin A at 3 and 6 months, 'botulinum toxin A only' was no longer a cost-effective option and 'P-SNS only' was cost effective at the upper willingness to pay for a QALY (£30,000). See Table 8.13 for results.
Failure rate for Botulinum toxin A after 6 months	0.01	0.01–0.20	Insensitive	At 0.20, only the 'botulinum toxin A only' strategy was below the NICE lower WTP threshold of £20,000 per QALY. 'P-SNS only' was only cost effective at the upper WTP threshold for women who could not catheterise.
Dose of Botulinum toxin A per injection	200u	100u	Insensitive	'Botulinum toxin A only' remained the most cost-effective option at £20,000 per QALY (99% probability of being cost-effective. At £30,000 per QALY, 'Botulinum toxin A first' had a 43% probability of being the most cost-effectiv ('Botulinum toxin A only' 45%).

Variable	Base case value	Variation range	Result	Notes and interpretation of the results
P-SNS variables				
PNE (test) failure	0.56	0.2–0.8	Insensitive	At a PNE failure rate of 0.2, 'botulinum toxin A first' remained highly cost effective. 'Botulinum toxin A first' was only cost effective at the upper WTP threshold (£30,000 per QALY). 'Botulinum toxin A first' was only cost effective at the upper WTP threshold. 'P-SNS only 'was dominated by 'botulinum toxin A first' and 'P-SNS first' remained cost-ineffective. 'P-SNS first' versus no treatment remained cost effective only at the upper WTP threshold. At a PNE failure rate of 0.8, the 'P-SNS only' strategy and the 'P-SNS first' strategy were both dominated by the 'botulinum toxin A first' strategy. 'Botulinum toxin A only' was not cost effective even at the higher WTP threshold. 'P-SNS first' versus no treatment was not cost effective at the upper WTP threshold.
P-SNS implant efficacy	0.88	0.88–1.0	Insensitive	At 100% efficacy of P-SNS: 'P-SNS only' was only cost effective compared to no treatment for women who cannot catheterise at the upper WTP threshold (at £27,000 per QALY. The 'botulinum toxin A only' strategy remained highly cost-effective. 'Botulinum toxin A first' was only cost-effective at the upper WTP threshold (at £28,000 per QALY relative to 'botulinum toxin A only'). P-SNS only remained dominated by the 'Botulinum toxin A -first' strategy and P-SNS first was highly cost ineffective.
Cost P-SNS implant	£8,641	£2,000 - £8,641	Sensitive	At a cost of the permanent P-SNS implant of £2,000, the ICER for 'P-SNS only' for women who cannot tolerate botulinum toxin A dropped to the £20,000 per QALY threshold (see Table 8.14). At a cost of P-SNS implant of £5,000, 'botulinum toxin A first' at the £25,000/QALY threshold was cost effective based on extended dominance. The 'P-SNS only' and 'P-SNS first' strategies were not cost effective. (See Table 8.15)

Variable	Base case value	Variation range	Result	Notes and interpretation of the results
Utility values				
Continent Incontinent	0.85 0.74	Threshold analysis	Sensitive	By increasing the utility value of continence to 0.91 (6 percentage points), the ICER for 'botulinum toxin A first' relative to 'botulinum toxin A only' was just below the £20,000 per QALY threshold for cost effectiveness. For women who are unable to catheterise, P-SNS was cost effective (under £20,000/QALY) when the utility value for continence was 0.91 (see Table 8.16)
Discount rates				
Costs QALYs	3.5% 3.5%	Zero discount rates for both	insensitive	Order of cost effectiveness did not change but magnitude of net benefit for all strategies was increased and the difference between P-SNS and botulinum toxin A strategies (the single treatment and double treatment strategies) increased.

ICER Incremental cost-effectiveness ratio, PNE percutaneous nerve evaluation, P-SNS Percutaneous sacral nerve stimulation, QALY quality adjusted life year, WTP willing to pay

The conclusions were insensitive to many of the parameter changes explored. However, the conclusions changed when a high rate of failure for botulinum toxin A was assumed (80% failure per 3 month cycle). With a high failure rate, 'botulinum toxin A only' conferred very little benefit compared with no active treatment and therefore was not cost effective. 'P-SNS only' was a cost-effective strategy at an upper willingness to pay threshold of £30,000 per QALY.

Tables 8.13 to 8.16 show results of one-way sensitivity analysis for parameters that changes the results of the analysis.

Table 8.13 Mean estimates of the cost effectiveness of treatment strategies for women with OAB, in order of cost assuming an 80% failure rate for botulinum toxin A, 1000 simulations

Treatment option	10-year discounted cost	10-year discounted QALYs	ICER	Probability of being cost effective at £20,000/QALY
No active treatment	£3,581	6.37		0
Botulinum toxin A only	£4,733	6.39	£57,600	99%
P-SNS only	£13,446	6.71	£27,228	0
P-SNS first then Botulinum toxin A	£14,232	6.73	£39,300	0.5%
Botulinum toxin A first then P-SNS	£14,332	6.73	dominated	0.5%

ICER incremental cost-effectiveness ratio, P-SNS percutaneous sacral nerve stimulation, QALY quality adjusted life year

Table 8.14 Mean estimates of the cost effectiveness of treatment strategies for women with OAB, assuming P-SNS implant cost of £2,000, 1000 simulations

Treatment option	10-year discounted cost	10-year discounted QALYs	ICER	Extended dominance	Probability of being cost-effective at £20,000/QALY
No active treatment	£3,581	6.37			0
Botulinum toxin A only	£7,028	6.65	£12,413		57
P-SNS only	£10,491	6.71	£54,816		0
P-SNS first then botulinum toxin A	£12,223	6.89	£9,533	£21,215	10
Botulinum toxin A first then P-SNS	£12,814	6.89	dominated		33
For women unable to catheterise					
P-SNS only			£20,121		

ICER incremental cost-effectiveness ratio, P-SNS percutaneous sacral nerve stimulation, QALY quality adjusted life year

Table 8.15 Mean estimates of the cost effectiveness of treatment strategies for women with OAB, assuming P-SNS implant cost of £5,000, 1000 simulations

Treatment option	10-year discounted cost	10-year discounted QALYs	ICER	Extended dominance	Probability of being cost effective at £20,000/QALY
No active treatment	£3,581	6.37			0
Botulinum toxin A only	£7,028	6.64	£12,506		93
P-SNS only	£11,816	6.71	£71,612		0
Botulinum toxin A first then P-SNS	£13,197	6.89	£7,716	£25,122	0
P-SNS first then Botulinum toxin A	£14,145	6.89	dominated		7

ICER incremental cost-effectiveness ratio, P-SNS percutaneous sacral nerve stimulation, QALY quality adjusted life year

The results were also sensitive to the health-related quality of life values assumed in the model.

For women who are not able to catheterise, increasing the health benefit of experiencing continence up six percentage points from 0.85 to 0.91 QALYs made the 'botulinum toxin A first' strategy cost effective (under £20,000 per QALY threshold) relative to no active treatment.

For women who are able to catheterise, increasing the health status continence from 0.84 to 0.91, made the ICER for 'botulinum toxin A first' cost effective relative to 'botulinum toxin A only' due to extended dominance*.

* Extended dominance refers to a scenario where a more expensive option has a lower cost-per QALY when compared to an even cheaper option than the next cheapest alternative, in this case, when 'Botulinum toxin A first' was compared with 'Botulinum toxin A only.'

Table 8.16 Mean estimates of the cost effectiveness of treatment strategies for women with OAB, assuming a higher benefit associated with achieving continence (0.91 QALY), 1000 simulations

Treatment option	10-year discounted cost	10-year discounted QALYs	ICER	Extended dominance	Probability of being cost effective at £20,000/QALY
No active treatment	£3,581	6.37			0
Botulinum toxin A only	£7,019	6.81	£7,834		43
P-SNS only	£13,441	6.90	£71,100		0
Botulinum toxin A first then P-SNS	£14,419	7.18	£3,542	£19,976	50
P-SNS first then botulinum toxin A	£15,795	7.18	dominated		7
For women unable to catheterise					
P-SNS only			£18,639		

ICER incremental cost-effectiveness ratio, P-SNS percutaneous sacral nerve stimulation, QALY quality adjusted life year

The results for the sensitivity analysis using botulinum A with 100U dose per injection is shown in table 8.17.

Table 8.17 Mean estimates of the cost effectiveness of treatment strategies for women with OAB, assuming 100 units of botulinum toxin A per injection (based on 6 month failure rate in 2 included studies)

Treatment option	10-year discounted cost	10-year discounted QALYs	ICER	Extended dominance	Probability of being cost effective at £20,000/QALY
No active treatment	£3,581	6.37			0
Botulinum toxin A only	£6654	6.62	£12,358		99%
P-SNS only	£13,444	6.71	£72,933		0
Botulinum toxin A first then P-SNS	£14288	6.87	£5,211	29,913	1%
P-SNS first then botulinum toxin A	£15,522	6.88	£301,928		0
For women unable to catheterise					
P-SNS only			£28,856		

ICER incremental cost-effectiveness ratio, P-SNS percutaneous sacral nerve stimulation, QALY quality adjusted life year

Conclusion

Treatment options for women who cannot catheterise

For women who are unable to intermittently catheterise, the model suggests that P-SNS is a cost-effective option compared with no active treatment, but only if an upper threshold for cost effectiveness is adopted (£30,000 per QALY). The analysis was sensitive to changes in the health-related quality of life values used. If P-SNS led to a greater improvement in quality of life than assumed in the model, then P-SNS would be more cost effective to offer as a treatment option for women who cannot be offered botulinum toxin A. There is considerable uncertainty around the quality of life increment associated with moving from a health state of incontinence to a health state of continence. A small increase in quality of life associated with continence made P-SNS cost effective relative to no active treatment for women unable to catheterise. For P-SNS to be recommended for this population, the GDG would need to be convinced that the health benefit of treatment is greater for than that reported in published studies (Imamura et al., 2010).

Treatment options for women who are able to catheterise

In the base case analysis (Table 8.10), the additional cost per QALY of offering botulinum toxin A only was lower than the NICE willingness-to-pay (WTP) threshold for cost effectiveness (£12,247 per QALY). If a woman was able to tolerate botulinum toxin A, the analysis suggested that it was not cost effective to offer P-SNS as a second-line treatment as the ICER was outside the upper WTP threshold for cost effectiveness (£30,235). However, the results were sensitive to the failure rate of botulinum toxin A. Higher rates of failure made the intervention relatively less cost effective. 'Botulinum toxin A only' remained the most cost-effective option in comparison with the other alternatives, although the ICER was higher than the £20,000 per QALY threshold for cost effectiveness. The dose of botulinum toxin (100U or 200U) did not alter this conclusion.

P-SNS first was borderline cost effective at a low cost for P-SNS implants (£2,000) with an ICER of £21,215. However the 'botulinum toxin A only' strategy remained the most likely strategy to be cost effective in the probabilistic sensitivity analysis. At £5,000 for P-SNS, the ICER for the P-SNS first strategy was higher (£25,122 per QALY) and the 'botulinum toxin A only' strategy remained the most cost effective.

The results were also sensitive to the quality of life estimates used in the model. Small increases in the additional quality of life a woman following successful treatment (or reduction in quality of life at the start of treatment) changed the order of cost effectiveness of the four active therapies: P-SNS became increasingly cost effective as the increment in quality of life associated with continence compared with incontinence widened. When the quality of life estimate for continence was 0.91 (compared with 0.74 for incontinence), the 'botulinum toxin A first' (followed by P-SNS if it failed) strategy was cost effective (££19,976). At higher estimates of quality of life for successful treatment, P-SNS was also a cost-effective treatment (£18,639 per QALY) for women who could not tolerate catheterisation.

Limitations of the analysis

Although the model captured some of the complexity in treatment options available in the NHS, like all models it is a simplification of reality and does not reflect all of the range of clinical experiences of women with OAB in this phase of treatment. Nevertheless the GDG members discussed all the values and assumptions that were used in the model throughout the development process and were satisfied that the assumptions reflected their own clinical experience and NHS practice.

The choice of outcome (continence status, defined as zero episodes of incontinence) was defined early on in the stakeholder consultation on the draft scope. The GDG supported the use of this outcome as it was the most important outcome to women with OAB, which is correlated to all other quality of life outcomes. The health states associated with moving from incontinence to continence can be defined unambiguously whereas the state of moving from a higher to lower number of episodes of urgency or incontinence cannot. The GDG considered that studies that define improvement as a proportional change in episodes of incontinence were more open to interpretation than an absolute change in health state.

The model assumed that women who are offered P-SNS before botulinum toxin A are the same population that could be offered botulinum toxin A first. There were no head-to-head comparisons of P-SNS and botulinum toxin A, so the assumption is that the studies were on sufficiently similar

populations. The GDG was satisfied that this was an acceptable assumption based on the descriptions of population in the studies included in the analysis.

The model also assumed that, for the two-treatment strategies, the populations are the same for treatment one and treatment two. Women for whom botulinum toxin A fails have the same chance of success with P-SNS as all women with OAB and the same assumption is made for those for whom P-SNS fails first. This assumes that women for whom botulinum toxin A fails do not have a higher probability of failure with P-SNS than women who begin invasive treatment with P-SNS. There is no data to support or refute this assumption, but the GDG accepted this limitation of the model.

This model was based on clinical data identified in the systematic review undertaken for this guideline update but not all parameters in the model were updated for the clinical guideline. There was a lack of long-term data to populate the model and a lack of direct evidence comparing botulinum toxin A and P-SNS in the same study.

No robust data were identified on the effectiveness of P-SNS. A high value was used which was reported in a recent review which included non-trial evidence. Even using this high value, P-SNS was not a cost-effective option under most assumptions due to its high cost.

The GDG was aware that other models include a wider range of adverse events associated with each treatment option and have made other assumptions about longer term effectiveness and discontinuation rates. Data from previous models described in the literature review were included where data were not available. This included adverse events such as urinary retention and urinary tract infection. The GDG did not consider that these data were critical to the model and including updated data would not be likely to change the overall results.

The GDG was keen for the simplifying assumptions in the model to be explicit for transparency and also to show the limitations in the data available for this type of analysis. The GDG considered that adding more complexity to a model where baseline data on effectiveness and longer term continuation rates were not robust would not be a good use of additional analytical resources.

The health economic model incorporated the GDG's understanding of how decision-making works in the NHS for women with OAB symptoms who have failed medical management. The GDG did not believe that further medical management, after first and second line drug treatment had failed, was a viable alternative to surgical intervention and therefore this is not included in the model. The model captures the two treatment options the GDG considered viable for women with OAB who are able to catheterise. It also reflects the GDG's expertise in making assumptions about effectiveness of care where data is lacking, as well as the members' expertise in understanding the costs of these treatments for the NHS. Therefore it represents the GDG's 'best guess' as to the relative cost effectiveness of P-SNS and botulinum toxin A, acknowledging that there are important gaps in the data which have to be filled with clinical knowledge and understanding of how these treatments are offered across the NHS.

The GDG's consideration of the economic evidence and the recommendations relating to sequencing of treatments for women with OAB can be found in the separate sections for each specific intervention.

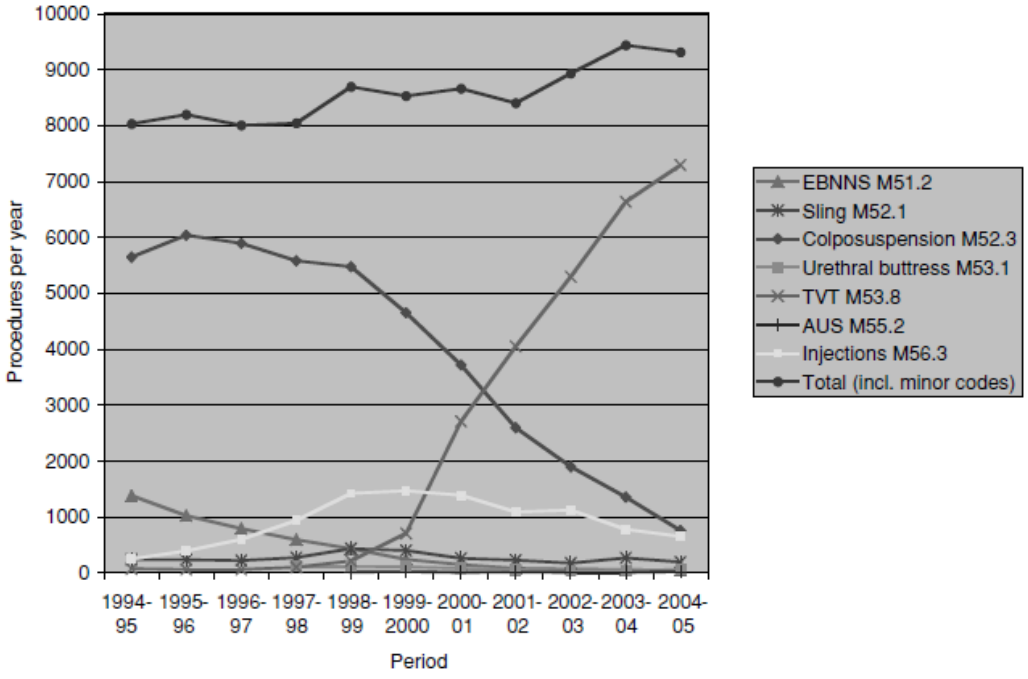
9 Surgical procedures for stress urinary incontinence

9.1 Introduction

The large number of different procedures described for the surgical management of stress urinary incontinence (UI) reflects the numerous theories proposed to explain the pathophysiology of the condition and the continuing search for a procedure that can successfully deal with all cases. Although the range of procedures described can be confusing, a proposal for a new surgical classification simplifies them into a) those that aim to augment urethral closure, and b) those that aim to support or stabilise the bladder neck or urethra.[552]

Over a 12 month period in 1997–98 approximately 8000 operations for stress UI were carried out in England. By 2004–05 the annual number had increased by 16%, despite an approximately 90% reduction in the numbers of colposuspension and needle suspension procedures, and a 30–50% reduction in bladder neck buttress, sling and periurethral injection procedures. The increase was entirely made up of operations using tension-free vaginal tape and similar mid-urethral tape procedures which had been introduced rapidly (see Figure 9.1).[553]

Figure 9.1 Hospital episode statistics for England, 1994–95 to 2004–05, illustrating trends in surgery for stress UI



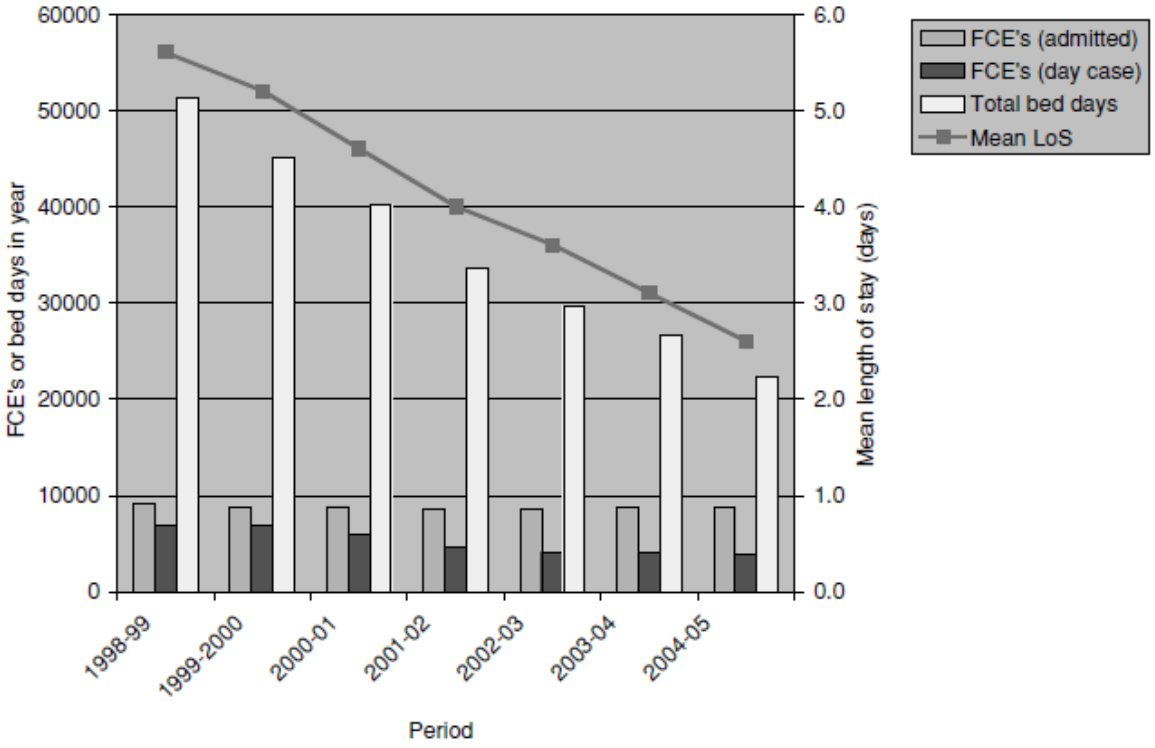
AUS artificial urinary sphincter, EBNNS endoscopic bladder neck needle suspension, retropubic 'bottom-up' tapes (TVT) tension-free vaginal tape, injections = periurethral bulking agents

These trends in surgical techniques applied in the treatment of stress UI appear to be having a substantial impact on resource utilisation within acute hospital trusts. The average length of hospital stay for women undergoing surgical treatment has reduced by over 50% since the introduction of mid-urethral tapes in 1998. As a result, the number of hospital bed days used in the treatment of stress UI has reduced by a similar amount (see Figure 9.2).[553]

The reduction in peri-and-post-operative morbidity associated with mid-urethral tapes has resulted in a dramatic increase in their use in the treatment of stress incontinence of urine. Less than 10% of women will have one of the previous generation of procedures (such as colposuspension or fascial sling) as a primary or secondary procedure. The transobturator route has gained popularity over the retropubic route.

The majority of procedures in the UK are performed under general anaesthesia and most patients will be discharged home on the day of surgery. This has resulted in a reduction in use of hospital beds for this type of surgery.

Figure 9.2 Hospital episode statistics for England, 1998–99 to 2004–5, illustrating trends in bed utilisation for women with a diagnosis of stress UI



FCEs finished consultant episodes, LoS length of stay

9.2 Procedures to suspend the vaginal wall

9.2.1 Introduction

Many procedures have been devised that share the common objective of preventing the downward displacement of the urethra which plays a part in the pathogenesis of stress UI. These include retropubic suspension procedures such as the Burch colposuspension, Marshall–Marchetti–Krantz (MMK) and vagino-obturator shelf procedure, each of which secures the paraurethral or vaginal tissues to a fixed structure by means of sutures.

A separate group of procedures was devised to be minimally invasive and suspend the paraurethral tissues by means of a suspensory suture, usually inserted under endoscopic control and secured to the rectus sheath to provide support. These include the Raz, Pereyra, Stamey and Gittes procedures.

Sling operations aim to stabilise the urethra by placing a strip of material around the underside of the urethra and securing the ends to a fixed structure above. These differ in numerous ways but could be classified according to the following framework:

- the tissues to which they are fixed (pubic arch or rectus sheath)
- the route by which they are inserted:
    - traditional open surgery:
        - abdominal
        - combined abdomino-vaginal
    - minimally invasive:
        - retropubic space (from bottom upwards or from top downwards)
        - obturator foramen (from outside inwards or from inside outwards)
- the materials used:
    - synthetic – the following classification of various materials used in hernia repair[615] has been adopted to describe materials used in surgery for UI and pelvic organ prolapse (POP):
        - type I – macroporous with pore size greater than 75 microns (allowing macrophages, fibroblasts, blood vessels, collagen fibres to penetrate pores), for example Prolene® ,Marlex® , Trelex Natural®
        - type II – microporous with pore size less than 10 microns, for example Gore-Tex® , DualMesh®
        - type III – macroporous, but with multifilamentous or microporous components, for example PTFE mesh (Teflon®), braided Dacron® mesh (Mersilene®), braided polypropylene mesh (Surgipro®)
        - type IV – submicron pore size, for example Silastic, Cellgard, Preclude® Pericardial Membrane, Preclude® Dura-substitute
    - moulded
    - woven tapes
    - biological:
        - autograft, for example autologous rectus fascia, vaginal wall
        - allograft, for example cadaveric dura mater
        - xenograft, for example porcine dermis, porcine small bowel submucosa.

The emphasis on recent innovations in sling surgery has been for slings to be placed with ‘no tension’ under the urethra. This may not have been the case with early sling techniques.

Other procedures such as anterior colporrhaphy and abdominal paravaginal repair are aimed primarily at treating POP but may have a secondary effect in preventing associated stress UI.

Studies considered for the 2006 review of procedures to suspend the vaginal wall

Evidence on relative effectiveness of procedures described in this section is derived from randomised controlled trials (RCTs). Due to the relatively short duration of follow-up in RCTs of surgical interventions, studies of other designs, notably cohort studies or case series, were considered if they provided information on outcomes over the longer term. Four systematic reviews of relevance have

Review question

What is the comparative effectiveness (in both the short- and long-term) of surgical approaches for mid-urethral procedures in women undergoing a primary surgical tape procedure?

- retropubic 'bottom-up'
- retropubic 'top-down'
- transobturator 'outside-in'
- transobturator 'inside-out'
- single incision.

Methodological approach for short-term outcomes review

Only RCTs reporting data at follow-up at 12 months were included in the review of short-term outcomes.

The included studies reported a variety of adverse effects. The GDG chose to focus on those adverse events or complications that are most important from a woman's perspective to allow her to make an informed decision about treatment on the basis of the risks and benefits of each procedure. These include tissue injury (bladder, urethra or vaginal wall perforation), tape erosion, urinary retention rate, rate of voiding dysfunction and new overactive bladder symptoms after surgery.

Overview of the evidence

The following comparisons were identified in the evidence. Evidence identified in the 2006 guideline review was also included in the GRADE because of the limited evidence for these interventions.

- retropubic 'bottom-up' versus retropubic 'top-down'– three RCTs
- retropubic 'bottom-up' versus transobturator 'outside-in' – 11 RCTs
- retropubic 'bottom-up' versus transobturator 'inside-out' – 13 RCTs
- retropubic 'bottom-up' versus single incision – five RCTs
- transobturator 'outside-in' versus retropubic 'top-down' – one RCT
- transobturator 'outside-in' versus transobturator 'inside-out' – three RCTs
- transobturator 'inside-out' versus single incision – five RCTs.

Retropubic 'bottom-up' versus retropubic 'top-down'

Description of included studies

Two RCTs were included in the 2006 guideline (Andonian et al., 2005; Tseng et al., 2005) that compared retropubic 'top-down' with retropubic 'bottom-up'. One new study was included in the guideline update (Lord et al., 2006).

The mean age of participants ranged from 50.4 (SD +/-11.5) to 62.6 (SD +/-10.6) years. The mean number of incontinence episodes and the duration of symptoms was not reported in any study.

Two studies included women with mixed urinary incontinence (Andonian et al., 2005; Lord et al., 2006). Concomitant surgery was performed in two studies (Andonian et al., 2005; Tseng et al., 2005).

The 'top-down' device in the two studies was SPARC (American Medical Systems Inc, Minnetonka, MN, USA). The 'bottom-up' device in both studies was Gynecare (Ethicon, Johnson & Johnson, Somerville, NJ, USA) (Andonian et al., 2005; Tseng et al., 2005). The manufacturer of the devices used in Lord et al., 2006 was unclear.


Updated 2019


Updated 2019


Updated 2019

Number of studies	Number of women		Effect		Quality
	Retropubic 'bottom-up'	Transobturator 'outside-in'	Relative (95% CI)	Absolute (95% CI)	
Incontinence-specific quality of life (better indicated by lower values)					

Number of studies	Number of women		Effect		Quality
	Retropubic 'bottom-up'	Transobturator 'outside-in'	Relative (95% CI)	Absolute (95% CI)	
Scheiner et al., 2012)					

Tissue injury

A meta-analysis of ten RCTs showed no difference in clinical benefit between retropubic 'bottom-up'

Number of studies	Number of women		Effect		Quality
	Retropubic 'bottom-up'	Transobturator 'inside-out'	Relative (95% CI)	Absolute (95% CI)	
al., 2010; Liapis et al., 2006; Scheiner et al.,					

Number of studies	Number of women		Effect		Quality
	Retropubic 'bottom-up'	Transobturator 'inside-out'	Relative (95% CI)	Absolute (95% CI)	

Number of studies	Number of women		Effect		Quality
	Retropubic 'bottom-up'	Transobturator 'inside-out'	Relative (95% CI)	Absolute (95% CI)	
al., 2009; Zullo et al., 2007)					
Voiding dysfunction					
1 (Karateke et al., 2009)	8/81 (9.9%)	6/83 (7.2%)	RR 1.37 (0.5 to 3.76)	27 more per 1000 (from 36	Low

approach. The mean age of participants ranged from 39.2 ± 9 years to 57.3 ± 9.5 years. In two studies the mean duration of symptoms ranged from 4.4 ± 3.6 years to 9 years (no SD reported) (Andrada et al., 2011; Wang et al., 2011). The mean number of incontinence episodes per day was 3 (range 0 to 16) in one study (Andrada et al., 2011). Two studies included women with mixed urinary incontinence (Barber et al., 2012; Basu & Duckett, 2010). Concomitant surgery was not performed in any of the

Wang et al., 2011)					
Erosion rate					
1 (Barber et al., 2012)	1/127 (0.79%)	0/136 (0%)	RR 3.21 (0.13 to 78.11)	-	Very low

The transobturator 'outside-in' device was MONARC and the retropubic 'top-down' device was SPARC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Number of studies	Number of women		Effect		Quality
	Transobturator 'outside-in'	Transobturator 'inside-out'	Relative	Absolute	

Incontinence-specific quality of life

One RCT showed no difference in clinical benefit between transobturator 'inside-out' and transobturator

Number of	Number of women	Effect	Quality

The percentage of women with mixed urinary incontinence in the included studies ranged from 19% to

The retropubic 'bottom-up' device in four studies (Deffieux et al., 2010; Koops et al., 2006; Lleberia-Juanos et al., 2011; Nwabineli et al., 2012;) was TVT Gynecare (Ethicon, Johnson & Johnson, Somerville, NJ, USA). In the remaining studies the manufacturer was not stated.

Evidence profile

Table 9.8 GRADE profile for long-term outcomes of retropubic 'bottom-up'

No of studies	Relative effects (range of events)	Quality
Patient satisfaction		
2 years		
2 (Nwabineli et al., 2012; Serati et al., 2012)	72.6% to 92.1%	Low
3 years		
2 (Palva et al., 2010; Serati et al., 2012)	86.8% to 87.3%	Low
5 years		
2 (Doo et al., 2006; Serati et al., 2012)	76.8% to 85.7%	Low
7 years		
1 (Serati et al., 2012	85.7%	Low
10 years		
1 (Serati et al., 2012)	82.5%	Low
Continence status		
2 years		
7 studies (Castillo-Pino et al., 2010; Deffieux et al., 2010; Koops et al., 2006; Lleberia-Juanos et al., 2011; Meschia et al., 2006; Nwabineli et al., 2012; Serati et al., 2012)	74.1% to 95.0%	Low
3 years		
5 studies (Koops et al., 2006; Lleberia-Juanos et al., 2011; Palva et al., 2010; Serati et al., 2012; Viereck et al., 2006)	81.9% to 92.6%	Low
5 years		
4 studies (Chene et al., 2007; Doo et al., 2006; Liapis et al., 2008a; Serati et al., 2012)	69.2% to 85.7*	Low

No of studies	Relative effects (range of events)	Quality
Adverse effects – Tape erosion		
2 years		
4 studies (Castillo-Pino et al., 2010; Lleberia-Juanos et al., 2011; Meschia et al., 2006; Serati et al., 2012)	0% to 4.1%	Low
3 years		
2 studies (Palva et al., 2010; Serati et al., 2012)	0%	Low
5 years		
4 studies (Chene et al., 2007; Doo et al., 2006; Liapis et al., 2008a; Serati et al., 2012)	0% to 1.4%	Low
7 years		
2 studies (Liapis et al., 2008a; Serati et al., 2012)	0% to 1.4%	Low
10 years		
No evidence reported		
Adverse effects – Urinary retention		
2 years		
4 studies (Lleberia-Juanos et al., 2011; Meschia et al., 2006)	9.5% to 13.2%	Low
3 years		
1 study (Palva et al., 2010)	0%	Low
5 years		
2 studies (Chene et al., 2007; Doo et al., 2006)	2.1% to 5.3%	Low
7 years		
No evidence reported		
10 years		
No evidence reported		
Adverse effects – Voiding dysfunction		
2 years		
1 study (Castillo-Pino et al., 2010)	18.2%	Low
3 years		
No evidence reported		
5 years		
1 study (Chene et al., 2007)	0.7%	Low
7 years		
No evidence reported		


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Adverse effects – Voiding dysfunction

This review found that up to 18% (1 study) of women suffered from voiding dysfunction 2 years after the surgery and 1% (1 study) at 5 years. The evidence was low quality.

No evidence on urinary retention at 3, 7 or 10 years after surgery was identified.

Adverse effects – De novo overactive bowel (OAB) symptoms

This review found that up to 24% (4 studies) of women developed *de novo* OAB symptoms 2 years after the surgery, 23% (2 studies) at 3 years, 18% (3 studies) at 5 years, 17% (1 study) at 7 years and 17% (1 study) at 10 years. The evidence was low quality.

Transobturator 'inside-out'

Description of included studies

Three prospective cohort studies and data from the transobturator 'inside-out' arms of two RCTs were included in the review of long-term outcomes. One RCT (Deffieux et al., 2010) reported outcomes at 2 years and the second (Palva et al., 2010) reported outcomes at 3 years. Data from the three cohort studies (Cheng & Liu, 2012; Groutz et al., 2011; Neuman et al., 2011) provided data at either 3 years or 5 years.

Between 27% and 72.1% of women had mixed urinary incontinence but this was not reported in one study (Palva et al., 2010).

Concomitant surgery was not reported in any of the included studies.

The mean age of participants ranged from 52.4 years (SD 11.1) to 56.6 years (SD 10.2) but mean age was not reported in Palva et al., 2010. The mean number of incontinence episodes and the mean duration of symptoms were not reported in any of the included studies.

The transobturator 'inside-out' device in two studies (Deffieux et al., 2010; Groutz et al., 2011) was Gynecare (Ethicon, Johnson & Johnson, Somerville, NJ, USA). The device manufacturer was not stated in the remaining studies.

Evidence profile

Table 9.9 GRADE profile for long-term outcomes of transobturator 'inside-out'

No of studies	Relative effects (range of events)	Quality
Patient satisfaction		
2 years		
No evidence reported		
3 years		
1 study (Palva et al., 2010)	87.1%	Low
5 years		
1 study (Cheng & Liu, 2012)	87.4%	Low
Continence status		
2 years		
1 study (Deffieux et al., 2010)	87.8%	Low
3 years		
2 studies (Neuman et al., 2011; Palva et al., 2010)	75.0% to 84.9%	Low
5 years		
2 studies (Cheng & Liu, 2012; Groutz et al., 2011)	69.2% to 89.3*	Low


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This review found that up to 18% (1 study) of women suffered from voiding dysfunction 2 years after the surgery. The evidence was low quality.

No evidence on voiding dysfunction at 3 and 5 years after surgery was identified.

Adverse effects – De novo OAB symptoms

This review found no instances of *de novo* OAB symptoms (1 study) 5 years after the surgery. The evidence was low quality.

No evidence on voiding dysfunction at 2 and 3 years after surgery was identified.

Transobturator 'outside-in'

Description of included studies

A single prospective cohort study (Taweel & Rabah, 2010) was included in the review of long-term outcomes of transobturator 'outside-in': this study reported on outcomes at 2 years. The mean age of women in this study was 50 years (range 37 to 72) but the number with mixed incontinence, mean number of incontinence episodes and the mean duration of symptoms was not reported.

The transobturator 'outside-in' device manufacturer was not stated.

Evidence profile

Table 9.10 GRADE profile for long-term outcomes of transobturator 'outside-in'

No of studies	Relative effects (range of events)	Quality
Patient satisfaction		
2 years		
1 study (Taweel & Rabah, 2010)	71.2%	Low
Continence status		
2 years		
1 study (Taweel & Rabah, 2010)	80.8%	Low
Adverse effects – Tape erosion		
2 years		
1 study (Taweel & Rabah, 2010)	0%	Low
Adverse effects – Urinary retention		
2 years		
1 study (Taweel & Rabah, 2010)	4.3%	Low
Adverse effects – De novo overactive bladder symptoms		
2 years		
1 study (Taweel & Rabah, 2010)	7.7%	Low

Evidence statements

No studies were identified which reported the following outcomes:

- number of episodes of incontinence per day
- incontinence-specific quality of life
- psychological outcomes

Patient satisfaction

This review found that up to 71% (1 study) of women were satisfied with treatment 2 years after the surgery. The evidence was low quality.

Continence status

This review found that up to 80% (1 study) of women were continent 2 years after the surgery. The evidence was low quality.

Adverse effects – Tape erosion

This review found that no instances of tape erosion 2 years after the surgery. The evidence was low quality.

Adverse effects – Urinary retention

This review found that up to 4% (1 study) of women suffered from urinary retention 2 years after the surgery. The evidence was low quality.

Adverse effects – De novo OAB symptoms

This review found up to 7% (1 study) of women developed *de novo* OAB symptoms 2 years after the surgery. The evidence was low quality.

Single-incision

Description of included studies

Four cohort studies were included in the review of long-term outcomes. Three studies (Bernasconi et al., 2012; Kennelly et al., 2012; Shin et al., 2011) reported on outcomes at 2 years and the fourth study (Neuman et al., 2011) reported on outcomes at 3 years.

Between 10.8% and 67.6% of women had mixed urinary incontinence.

In Kennelly et al., 2012, 19.7 % of women received concomitant surgery but this was not reported in any of the other included studies.

The mean age of participants ranged from 51.1 years (SD 10.6) to 59.5 years (SD 9.66). The mean number of incontinence episodes and the mean duration of symptoms was not reported in any of the included studies.

The transobturator 'inside-out' device in three studies (Bernasconi et al., 2012; Neuman et al., 2011; Shin et al., 2011) was TVT-Secur Gynecare (Ethicon, Johnson & Johnson, Somerville, NJ, USA) and in Kennelly et al., 2012 it was MIniArc (American Medical Systems, Minnetonka, MN. USA).

Evidence profile

Table 9.11 GRADE profile for long-term outcomes of single incision

No of studies	Relative effects (range of events)	Quality
Continence status		
2 years		
3 studies (Bernasconi et al., 2012; Kennelly et al., 2012; Shin et al., 2011)	63.8% to 83.1%	Low
3 years		
1 study (Neuman et al., 2011)	85.4%	Low
Adverse effects – Tape erosion		
2 years		
3 studies (Bernasconi et al., 2012; Kennelly et al., 2012; Shin et al., 2011)	0% to 2.1%	Low


Updated 2019


Updated 2019

Health economics profile 2013

One recent study was published after the 2006 guideline comparing the cost effectiveness of surgical procedures was identified in the literature. The literature search also identified several other cost effectiveness studies published since the 2006 guideline, but either the cost data was out of date by ten years or more (Valpas et al., 2006; Ankardal et al., 2007, Dumbille et al 2006), or did not include the relevant comparators (Jacklin et al., 2010).

The included study was from Canada and compared transobturator tape with tension-free vaginal tape. It was published in 2011 alongside a randomised controlled study and reported cost data from 2007 (Lier et al 2011). It concluded that there was no difference in health outcome (measured in QALYs) between procedures and reported the cost of transobturator 'outside-in' to be lower than retropubic 'bottom-up'.

One recent cost effectiveness study using UK cost data was identified but this compared retropubic 'bottom-up' with drug treatment (Duloxetine) (Jacklin et al., 2010). The cost of retropubic 'bottom-up'

In the 2012 NHS Tariff, the equivalent HRG codes are for Lower Genital Tract Major Procedures with complications (£2,271) and without complications (£1,986). No distinction is made between the types of surgical procedure in the NHS Tariff. In order to undertake a health economic analysis, detailed costs that differentiated between surgical procedures on resource use would be required. This level of detail on resource use was not identified in the published evidence for the NHS.

Health economic evidence statements

No recent UK-based cost effectiveness analyses were identified in the literature. There is evidence from a Canadian study that the costs are lower for transobturator 'outside-in' procedures compared with retropubic 'bottom-up' procedures but one study from Canada is not sufficient evidence to make inferences about the relative cost effectiveness of surgical procedures in the NHS.

There is a lack of detailed data on the differences in resource use between procedures in the NHS, which is the focus of this clinical question. A new health economic model was not prioritised for this guideline as only one procedure had sufficient clinical evidence on which to make a comparison.

Evidence to recommendations

Relative value placed on the outcomes considered

Initially patient satisfaction was the primary outcome for measuring the success of the reviewed mid-urethral tapes approach. As with other reviews, the GDG was concerned about how patient satisfaction was measured across studies. Therefore, continence status was additionally selected as an equally appropriate measure of treatment success.

A mid-urethral tapes procedure has two adverse effect profiles; one related to the device being used and other associated with the surgical approach.

The adverse effects reported were prioritised by the GDG as the key complications that the women should be informed of prior to surgery.

Consideration of clinical benefits and harms

'Bottom-up' retropubic, 'inside-out' transobturator and 'outside-in' transobturator

The evidence profile for the short-term (less than 1 year) effectiveness of mid-urethral tapes showed that there was no significant difference in continence status between the following three approaches: 'bottom-up' retropubic, 'inside-out' transobturator and 'outside-in' transobturator.

The long-term data (more than 2 years) showed that continence status remained relatively consistent for up to 10 years after tape insertion for both the retropubic 'bottom-up' and transobturator 'inside-out' approaches. There were fewer equivalent long-term data for 'outside-in' transobturator tape. Based on the evidence of short-term outcomes and clinical experience, the GDG consensus was that long-term effectiveness would be equivalent to the other two approaches.

The GDG acknowledged that the retropubic 'bottom-up' was the first of the mid-uretheral procedures to be introduced. Therefore it was expected that it would have more comprehensive data on long-term outcomes in comparison with the more recent alternative transobturator approaches ('inside-out' and 'outside-in'). While the short-term data for the transobturator approaches were adequate, the procedures have not been used for a sufficiently long period for an extensive long-term follow-up to be completed. The GDG concluded was that the data on short-term effectiveness and more limited data on the longer term showed a strong enough benefit to recommend their use, on the condition that women are informed of the current lack of long-term data on the transobturator approach. Based on the evidence found for treatment success, the GDG recommended retropubic 'bottom-up', transobturator 'inside-out' and transboturator 'outside-in' approaches.

Furthermore, the GDG noted that the effectiveness of the three mid-urethral tape procedures was similar to the effectiveness of open colposuspension and autologous rectus fascial slings published in the 2006 guideline. Therefore the GDG agreed to retain these interventions as alternative treatment options to mid-urethral tapes.

There were ten RCTs that investigated the single incision approach, all of which were compared with either retropubic 'bottom-up' or transobturator 'inside-out' approaches. None of the trials demonstrated a clinical benefit of the single incision approach over the comparator procedures. These reviews suggested that a single incision procedure had lower cure rates (measured as 'absolutely dry' continence status) compared with the other two procedures. Furthermore, the GDG noted that the single incision approach required more specialist training than required for the other procedures. There is also a higher risk of more difficult revision in cases of failure with single incision approaches. The GDG noted that single incision tapes were introduced to clinical practice as alternative to more conventional approaches that could be undertaken as an outpatient procedure. The rationale for its development was to assess whether it would be associated with less risk of injury and faster recovery, but the evidence does not support this.

Retropubic 'top-down' approach

Three RCTs comparing retropubic 'top-down' with retropubic 'bottom-up' showed no significant difference between procedures. Another study comparing retropubic 'top-down' with transobturator 'outside-in' found no difference in immediate peri-operative outcomes and no evidence of improved long-term effectiveness using the retropubic 'top-down' approach.

The GDG concluded that more evidence was required before recommending the use of retropubic 'top-down' approaches to demonstrate its effectiveness compared with other mid-urethral approaches and its long-term efficacy and safety. By contrast, the long-term effectiveness of the 'bottom-up' retropubic approach is supported by a large body of evidence. Therefore the GDG felt that retropubic approaches should also demonstrate equal or superior long-term efficacy in order to be recommended.

Peri-operative adverse effects

The difference in the angle of surgical incision used in the retropubic and transobturator approach means that the risk of iatrogenic damage caused by the surgery will vary. For example, the insertion of transobturator tapes presents a greater risk of vaginal wall injury than the retropubic approach, whereas there is a lower chance of bladder perforation. The classification of the severity of an adverse effect is often misinterpreted: for example, bladder perforation would be reported as a minor adverse event when seen in the short term but if it goes unnoticed the longer-term implications are more serious with mesh erosion into the bladder.

The GDG concluded that while one approach will show a reduction in risk for one specific adverse event, this is offset by another increased risk in another. Therefore the GDG could not recommend a specific approach based upon differences in adverse events. The risks will be interconnected with the surgeon's skill in a given procedure. It is therefore important that a choice is available, taking into account the expected chance of adverse events. The procedure with which a surgeon is most familiar and has most experience is likely to be safer.

Consideration of health benefits and resource uses

The GDG members discussed the differences in the implementation costs between the different types of mid-urethral tapes reviewed. Using their clinical experience, they acknowledged that the surgeon's time and the cost of the tape did not vary significantly from one type of tape to another.

There were, however, some subtle differences that the GDG highlighted for consideration. Firstly, when using a retropubic approach there is a higher risk of bladder perforation. Therefore, in order to check for and rectify any damage, a cystoscope is routinely used at the end of the procedure. This extra cost is not incurred using the other techniques because of the substantially lower likelihood of bladder perforation.

Detailed cost information that classifies surgical intervention by the type of procedure is not routinely available for the NHS. The consensus view was that time in the operating theatre, the surgeon's time, hospital stay or follow-up would differ significantly between mid-urethral tape procedures. Surgical skill and familiarity with a procedure would have an effect on the rate of adverse events and the need for revision or removal of a tape, and consequently on long-term resource use. Consequently, the GDG did not choose to recommend the least expensive surgical intervention on the basis of its procurement cost alone.

was likely to be marginal and would not therefore affect the decision to offer a particular surgical tape procedure.

Quality of evidence

The GDG noted that the populations were not consistent in all RCTs included in the review and the GDG was concerned that some studies included women with a diagnosis of mixed UI or who had concomitant prolapse surgery. Including such patients would lead to a lower reported efficacy due to unrelated symptoms, which would not be resolved by successful stress urinary incontinence (SUI) treatment. In addition, some studies included women who had had previous surgery for SUI. There is evidence that secondary surgery will have differing success rates to the initial procedure (see Section 9.6). The GDG also noted that the reason for secondary surgery could have an impact on the outcome, although this could not be concluded from the evidence.

The measures used to calculate continence status varied across the trials. Objective and subjective tests were used and the reporting of these meant that the potential for outcome reporting bias could not be determined.

Finally, the GDG noted that the long-term data was largely derived from observational studies whereas the short-term data was taken from RCTs only, removing this risk of bias.

Other considerations

Burch colposuspension and autologous rectus fascial sling

The GDG noted that open colposuspension is more complex and resource intensive procedure than using a mid-urethral tape; it is done under general anaesthetic with a longer recuperation period (around 8 weeks).

The GDG noted that the evidence for benefit had not changed since 2006 and chose to retain the recommendation for colposuspension and autologous rectus fascial sling. Based on clinical experience, the GDG concluded that Burch colposuspension and autologous rectus fascial sling should continue to be recommended because synthetic tapes are unacceptable for some women. Women should be advised of the risks and prognosis for both procedures so that an informed decision can be made.

Selection of intervention

The population in each study included women for whom conservative treatments for SUI or mixed urinary incontinence had not been successful. As outlined elsewhere in the guideline, the GDG sought to reinforce that surgical treatments for SUI should only be offered once conservative treatments have failed for an individual woman.

The range of interventions that should be considered for each individual woman should be based on their outcome goals and clinical history. Five procedures were recommended, including bulking agents, following a period of unsuccessful conservative treatment. Consultation between the multidisciplinary team (MDT) and woman should be integral to the decision of what to offer and that choice should be made based on the woman's clinical history and a discussion with the woman of the risks and benefits for each procedure. The GDG acknowledged that in some cases women may not opt for an invasive surgical procedure following failure of conservative treatments for SUI. In these circumstances women should be referred to the conservative management chapter (chapter 5).

Other factors may influence the choice of intervention. The primary considerations before surgery should be a woman's co-morbidities, particularly those that increase the anaesthetic or surgical risk, or make access more difficult. A list of the more common examples to be considered is presented in Table 9.13, based on the expert opinion of the GDG. Patients with additional co-morbidities or complicating factors should always be referred for discussion to a local MDT as other colleagues may have helpful ideas or have different operations in their repertoire.

Anaesthetic risks	Surgical risks
COPD, chronic cough	Obesity
Diabetes	Previous abdominal surgery or mesh hernia repair
Neurological disease	Warfarin, clopidgrel etc
Spinal injury or damage, arthritis	Fractured pelvis or RTA
Liver or renal disease	Problems with hip abduction
Heart disease	Previous retropubic surgery
Allergy to agents	
Difficult intubation	

COPD chronic obstructive pulmonary disease, RTA road traffic accident, SUI stress urinary incontinence

Surgeon experience

The choice of intervention is subjective and dependant on discussions between patient and consultant, culminating in the clinical judgements described above. It is therefore important that all types of recommended mid-uretheral tape approaches and colposuspension are made available. If a surgeon cannot offer one or more procedures, then the MDT should refer to an alternative surgeon.

As described in Chapter 10 the ability of the surgeon and their experience for each procedure correlates with the success of the procedure. Therefore to ensure the best outcome the recommendations in Chapter 10 should also be followed.

Type of device

There is currently no stringent regulation of the type of tape devices that can be used. According to the Medicines and Healthcare products Regulatory Agency (MHRA) these devices are ‘class 2’ products and therefore do not need to demonstrate RCT-based evidence of efficacy.

The market for new tape devices is dynamic; NHS procurement is presented with numerous options with no clear recommendation of which product should be used. Without guidance, the choice of device can be pragmatic. The GDG is aware that cheaper tape alternatives have been purchased on the assumption that all devices have equal efficacy, which has not been examined in clinical trials. The GDG strongly believed that the regulation and evaluation of these devices is important both for patient safety and to evaluate the short- and long-term efficacy of different tapes. In order to guarantee that patients are offered the safest and most effective devices, the GDG has only recommended tapes with proven efficacy (continence status at 12 months) based on robust RCT evidence. This meant that some devices, for example, I-STOP, cannot be recommended at this stage. The GDG did, however, acknowledge that technological advances are frequent and that recommendations should not be used to restrict the development of new devices. Moreover, if new evidence emerges that is based on robust RCTs which demonstrate that a device is not inferior to devices currently recommended, then the device should be considered for use, depending on procurement cost and clinical judgement. Recommendation 96 includes a footnote to explain which devices meet these criteria and are available in the UK at the time of publication of this guideline.

Understanding adverse events

The risks of adverse events associated with surgical interventions for the treatment of SUI vary. Some women may be reluctant for their treatment to include specific types of surgery. In order to alleviate their concerns, information leaflets should be provided to assist the discussion between a clinician and the woman about choosing treatment. To ensure consistency of information, a table is presented (Table 9.12) indicating the long-term and short-term adverse events, as well the predicted success rates of the

the tape is visualised through separated vaginal epithelium) or 'extrusion' (where the tape protrudes into the vaginal cavity). However, the GDG considered 'erosion' to be suitable until an agreed terminology has been implemented.

Tape failure

Concerns have been raised, particularly in the USA, about the safety of the polypropylene Type 1 mesh used in tape procedures for incontinence and for pelvic organ prolapse. The amount of polypropylene mesh used in a tape procedure is much smaller than that for a prolapse operation. However, there are still recognised risks, including tape erosion through the vaginal mucosa and failure of the vagina to heal over the mesh. In some cases, severe life-threatening infection has been reported. These types of tapes and meshes were introduced in the belief that they were the same as abdominal mesh procedures for hernias, but it is now recognised that the vagina is a very different environment in which to place a foreign body. For these reasons and others, some manufacturers have withdrawn their devices from the UK.

Type 1 macroporous monofilament meshes are extremely inert in tests (Sangster et al., 2010) and patients can be reassured that the incidence of severe problems in tape procedures is around 5%. If erosion does occur at any stage (reports include new erosions up to 10 years post-operatively), it is usually a simple procedure to remove the area of eroded mesh and oversew the vaginal mucosa. The same rationale applies to pelvic organ prolapse meshes, which have an overall incidence of erosion of about 15%.

The main complication of removing parts of an incontinence tape is the loss of function of the tape, leading to recurrent incontinence. A removal procedure would benefit from the use of a coloured tape in the initial procedure for ease of identification. Occasionally, major surgery may be required for removal of tape from the bladder or urethra (less than 1%) although success rates for tapes remains high.

Other materials for synthetic tapes

Slings made of silicone

No controlled trials evaluating the used of a silicone sling were identified. Three case series reported outcomes relating to this sling (reinforced with polyethylene) in women with stress UI. Two included 30 and 54 women,[858,859] while the third described the complication of sinus formation in 18% of 40 women who underwent the procedure.[860]

The majority of women in one series had undergone prior continence surgery;[859] in another, the decision to use the sling was made intra-operatively when colposuspension was seen not to be technically feasible.[858] Both included a proportion of women with mixed UI (17% and 60%).

Subjective cure rates were 79% at mean follow-up of 15 months,[858] and both subjective and objective (pad test) cure rates were 83% in the series with complete follow-up at 3 months.[859] Intra-operative complications were haemorrhage requiring blood transfusion (6%),[858] and vaginal perforation, and bladder or urethral perforation (7% each; one case of urethrovaginal fistula needing sling removal).[859] *De novo* detrusor overactivity *(*DO) and voiding difficulty was very common (more than 10%) in both; voiding difficulty required sling release in four of seven cases in one study.[859] Pulmonary embolism, enterocele, and sinus formation (which required removal or trimming of the sling) occurred in 4% of women in one study.[858] The third report described sinus formation in 18% of cases treated, with sling removal in each case at 3–16 months, following the procedure.[860]

Slings made of polytetrafluoroethylene

Three controlled trials evaluated a polytetrafluoroethylene (PTFE) sling, each of which was small with maximum follow-up of about 2 years. Compared with open colposuspension in women with stress UI, and urethral hypermobility, cure rates with PTFE were not significantly different at 2.5 years (objective 85% versus 100%; subjective 93% versus 84%). At baseline, the proportion of women with DO was significantly lower in the PTFE group (41% versus 95%). *De novo* DO was reported in 24% versus 5%. Complications over the longer term in the sling group were erosion (12%) and urethrolysis for retention (6%) (n = 36).[668,669] [EL = 1+]

One RCT compared PTFE and rectus fascial slings in women with stress UI (n = 48; 92% of whom had had prior continence surgery). Combined objective and subjective cure rates were 88% and 81%,

respectively, at 6 months. Urethral erosion, recurrent UTI and *de novo* DO were very common with PTFE, whereas no complications were reported in the fascial sling group.[861] [EL = 1−]

A quasi-RCT compared PTFE with a vaginal wall sling in women with stress or mixed (approximately 60%) UI. Cure and satisfaction rates were high across both groups at mean follow-up of 22 months (75–100%), but no statistical analysis was reported. Complications reported were wound infection, UTI, bleeding, vaginitis and transient *de novo* urge UI (n = 40).[862] [EL = 1−]

Seven case series evaluated slings or a soft tissue patch made of PTFE in women with stress UI (total n = 453; range 24–115).[863–871] Some women in three studies had mixed UI (36–90%).[863–865,871] Between 26% and 100% of women across five studies (median 56%) had had prior continence surgery.[863–866,868,869,871] Concomitant surgery was undertaken in 26% and 78% of women in two studies.[868,869,871]

Duration of follow-up ranged from about 1 to 5 years. All except one study considered continence,[870] all considered complications and two reported satisfaction.[864,865,867] The median subjective cure rate was 83% (range 72–89%). The objective cure rates, reported in two studies, were 61% and 89%. Satisfaction was reported by 81–82% of women.[864,865,867]

Complications were:

- sling removal (all studies): median 8% (range 3–31%) for varying reasons (rejection, reactions to sling [sinus formation, granulation tissue, abdominal wound abscess, erosions of vaginal mucosa], urethral obstruction, urethral erosion, non-healing of vaginal incision, urinary retention, persistent pain, sling infections)
- wound complications or infections (three studies): median 15% (range 6–40%)[863–865,868,869]
- *de novo* urge UI or DO (four studies): median 9% (range 0–12%)[863–866,871]
- voiding difficulties (two studies): 22% and 37%[867–869]
- intermittent self-catheterisation (two studies): 3% and 8%[863,868,869]
- surgery for retention (two studies): 4% and 9%.86[3–865]

Other complications noted were irritative symptoms and recurrent UTI (21%),[866] and pelvic pain (16%).[867] No cases of sling intolerance[863] or of bladder or urethral erosion were seen in two studies.[864,865]

Tapes made of polyester

No controlled trials were identified for slings made of polyester. Four case series evaluated the use of a polyester graft mesh (Mersilene®), two with very limited baseline data for the women treated.[872–875] Each study included women with stress UI, and one stated that 69% of those followed up to 1 year had urgency or urge UI. Patient numbers ranged from 24 to 200 (median 102). Three studies noted that 25–54% of women had had prior continence surgery.[872,873,875] Concomitant surgery was undertaken in 55% of women in one.[873]

Duration of follow-up ranged from a mean of 2 years to 5 years. Subjective cure rates across the studies ranged from 50% to 96% (median 84%). The objective cure rate in 26% of women with follow-up of 5 years was 94%; compared with 95% at 1 year (one study).[873]

Complications reported were:

- intra-operative: haemorrhage 2%;874 no cases of urethral or bladder injury[872]
- *de novo* urge UI or DO (two studies): 4% and 15%[872,874]
- retention or voiding difficulties (two studies): 1.5% and 15%;[873,874] surgical release for

Recommendations

Number	Recommendation
94	When offering a surgical procedure discuss with the woman the risks and benefits of the different treatment options for SUI using the information in table 9.12. **[new 2013]**
95	If conservative management for SUI has failed, offer: • synthetic mid-urethral tape (see recommendations 96–101), **or** • open colposuspension (see also recommendation 102), **or** • autologous rectus fascial sling (see also recommendation 103). **[new 2013]**
	Synthetic tapes
96	When offering a synthetic mid-urethral tape procedure, surgeons should: • use procedures and devices for which there is current high quality evidence of efficacy and safety* • only use a device that they have been trained to use (see recommendations in chapter 11) • use a device manufactured from type 1 macroporous polypropylene tape • consider using a tape coloured for high visibility, for ease of insertion and revision. **[new 2013]**
97	If women are offered a procedure involving the transobturator approach, make them aware of the lack of long-term outcome data. **[new 2013]**
98	Refer women to an alternative surgeon if their chosen procedure is not available from the consulting surgeon. **[new 2013]**
99	Use 'top-down' retropubic tape approach only as part of a clinical trial. **[new 2013]**
100	Refer to single-incision sub-urethral short tape insertion for stress urinary incontinence (NICE interventional procedure guidance 262) for guidance on single-incision procedures. **[new 2013]**
101	Offer a follow-up appointment (including vaginal examination to exclude erosion) within 6 months to all women who have had continence surgery. **[new 2013]**

Number	Research recommendations
RR16	Newer mid-urethral procedures and single incision procedures should be further investigated and compared with pelvic floor muscle training and accepted surgical interventions in the treatment of stress urinary incontinence.
RR17	What are long-term outcomes for 'top down' retropubic, transobturator proceedures?

2013 Update

* The guideline only recommends the use of tapes with proven efficacy based on robust RCT evidence. However, technological advances are frequent, therefore the choice of tape should include devices that are shown in future clinical trials to have equal or improved efficacy at equal or lower cost. At the time of publication (September 2013) the following met the Guideline Development Group criteria:

- TVT or Advantage for a 'bottom-up' retropubic approach
- TVT-O for an 'inside-out' transobturator approach
- Monarc and obtryx halo for an 'outside-in' transobturator approach.

Introduction

In order to make an informed choice about proceeding with surgery for SUI, women should be advised whether they have any additional risk factors which may influence the outcome or occurrence of adverse events. Finding specific indications to accurately predict the chances of tape success may enable multidisciplinary teams to make more informed decisions in offering specific interventions (or not offering any interventions at all).

Review question

What patient characteristics are predictors of primary tape failure?

Methodological approach for the review

The review classified patient characteristics by whether they were protective factors (odds ratio [OR] less than 1) against or risk factors (OR more than 1) for predicting primary tape failure. Characteristics were identified as statistically significant, clinically significant or both. For the purposes of this review, the odds ratio for a protective factor's lower confidence interval had to be less than 0.75 to be considered clinically significant.

Overview of the evidence

Evidence for factors are categorised according to their association with tape failure:

- factors found to be associated strongly (both statistically and clinically significant) with tape failure (Table 9.14)
- factors found not be associated (statistically but not clinically significant) with tape failure (Table 9.15)
- factors found not to be associated not statistically significant) with tape failure (Table 9.16).

Description of included studies

Six studies (Abdel-Fattah et al., 2010a; Barber et al., 2008a; Paick et al., 2004; Paick et al., 2004b; Richter et al., 2011; Schraffordt et al., 2006) were identified, three of which were prospective cohort studies (Paick et al., 2004; Paick et al., 2004b; Schraffordt et al., 2006), two ancillary analysis of data from RCTs (Abdel-Fattah et al., 2010a; Barber et al., 2008a) and one a two-arm randomised equivalence trial (Richter et al., 2011). Studies that were ancillary analyses of data from RCTs were analysed as observational studies and so the quality rating started at low.

Two studies were from the USA (Barber et al., 2008a; Richter et al., 2011), two from Korea (Paick et al., 2004; Paick et al., 2004b), one from the UK (Abdel-Fattah et al., 2010a) and one from the Netherlands (Schraffordt et al., 2006). The mean age of the participants was reported in four studies and ranged from 51.3 years (no SD, range from 20 to 82) to 57.2 years (SD 8.6). The mean number of incontinence episodes was only reported in one study (Richter et al., 2011) and ranged from 2.9 (SD 2.7) episodes per day in subjects in which treatment was successful to 3.9 (SD 3.2) episodes per day in subjects in which treatment failed. The duration of SUI was reported in two studies (Paick et al., 2004; Paick et al., 2004b) and ranged from 7 months (3–10) and 10 months (1–30) respectively for the cases (tape failure) and controls (no tape failure) of one study (Paick et al., 2004) to 103 months (2–480) in another (Paick et al., 2004b).

Evidence profile

Table 9.14 GRADE findings for all statistically and clinically significant factors

Number of studies	Number of women		Effect	Quality
	Number of women with factor / Number with tape failure	Number of women with factor / Number without tape failure	Adjusted OR (95% CI)	
Preoperative anticholinergic medication use vs no use				
1 (Barber et al., 2008a)	Not reported	Not reported	6.7 (1.6 to 22)	High
BMI > 35 compared with BMI ≤ 30 (patient reported outcome)				
1 (Abdel-Fattah et al., 2010a)	8/58 (13.79%)	10/247 (4.05%)	6.37 (1.73 to 23.44)	High
MUCP ≥ 31 compared with MUCP ≤ 30 (objective outcome)				
1 (Abdel-Fattah et al., 2010a)	25/43 (58.14%)	219/245 (89.39%)	7.06 (2.85 to 17.48)	High
Primary surgery compared with secondary surgery (objective outcome)				
1 (Abdel-Fattah et al., 2010a)	31/44 (70.45%)	223/253 (88.14%)	6.22 (2.34 to 16.52)	High

BMI body mass index, CI confidence interval, MUCP maximum urethral closure pressure, OR odds ratio

Table 9.15 GRADE findings for all statistically significant factors

Number of studies	Number of women		Effect	Quality
	Number of women with factor / Number with tape failure	Number of women with factor / Number without tape failure	Adjusted OR (95% CI)	
Age per decade (outcome: recurrent SUI)				
1 (Barber et al., 2008a)	Not reported	Not reported	1.7 (1.1 to 2.6)	Moderate
Concurrent pelvic organ prolapse surgery				
1 (Barber et al., 2008a)	Not reported	Not reported	2.7 (1.1 to 6.7)	Moderate
Secondary surgery compared with primary surgery (patient reported outcome)				
1 (Abdel-Fattah et al., 2010a)	14/61 (22.95%)	32/249 (12.85%)	2.33 (1.1 to 5.478)	Low
Nocturia compared with no nocturia (patient reported outcome)				
1 (Abdel-Fattah et al., 2010a)	44/61 (72.13%)	105/246 (42.68%)	2.18 (1.04 to 4.58)	Low
Urgency incontinence compared with no urgency incontinence (patient reported outcome)				
1 (Abdel-Fattah et al., 2010a)	44/61 (72.13%)	124/249 (49.80%)	3.35 (1.07 to 10.51)	Low

Number of studies	Number of women		Effect	Quality
	Number of women with factor / Number with tape failure	Number of women with factor / Number without tape failure	Adjusted OR (95% CI)	
Higher maximal flow rate				
1 (Paick et al., 2004)	Mean: 16ml/s (9-36) n=10	Mean: 26ml/s (11-63) n=50	0.90 (0.82 to 0.99)	Moderate
Previous UI surgery compared with no previous UI surgery				
1 (Richter et al., 2011)	49/259 (18.92%)	26/304 (8.55%)	1.99 (1.14 to 3.47)	Moderate
Q-tip maximum straining less than 30 degrees, yes compared with no				
1 (Richter et al., 2011)	59/260 (22.69%)	42/305 (13.77%)	1.89 (1.16 to 3.05)	Moderate
Urge score (per 10 points)				
1 (Richter et al., 2011)	Mean +/-SD: 7.2+/-4.0 n=260	Mean +/-SD: 5.6+/- 3.7 n=305	1.97 (1.21 to 3.21)	Moderate
Pad weight (per 10 g)				
1 (Richter et al., 2011)	Mean +/-SD: 50.2+/-88.9 n=260	Mean +/-SD: 24.7+/-39.7 n=305	1.06 (1.02 to 1.1)	Moderate
More than 20 procedures for each surgeon compared with first 10 procedures for each surgeon (Outcome 1: defined as the answer to the question 'Do you experience urinary leakage during physical activity, coughing or sneezing?' Success for SUI was defined as the answer 'no'.)				
1 (Schraffordt et al., 2006)	66/184 (35.87%)	173/381 (45.41%)	1.918 (1.24 to 2.97)	Low
More than 20 procedures for each surgeon compared with first 10 procedures for each surgeon (Outcome 2: defined as answer to the doctor's question 'Do you leak during physical activity, coughing or sneezing?' asked at 2-year follow-up. The answer 'no' was defined as success. All other answers as well as 'improved' were considered as failure.)				
1 (Schraffordt et al., 2006)	44/133 (33.08%)	220/478 (46.03%)	0.55 (0.32 to 0.96)	Low
General anesthesia when compared with local anaesthesia				
1 (Schraffordt et al., 2006)	22/122 (18.03%)	47/451 (10.42%)	2.21 (1.07 to 4.55)	Low
Urge symptoms when compared with no urge symptoms				
1 (Paick et al., 2004b)	Not reported	Not reported	5.703 (1.232 to 26.404)	Low
Lower MUCP (reference not stated)				
1 (Paick et al., 2004b)	Not reported	Not reported	0.944 (0.895 to 0.996)	Low

CI confidence interval, MUCP maximum urethral closure pressure, OR odds ratio, SUI stress urinary incontinence, UI urinary incontinence

Table 9.16 GRADE findings for factors of no statistical significance

Number of studies	Number of women		Effect	Quality
	Number of women with factor / Number with tape failure	Number of women with factor / Number without tape failure	Adjusted OR (95% CI)	
Current smoking				
1 (Barber et al., 2008a)	Not reported	Not reported	0.4 (0.1 to 1.3)	Low
Functional capacity (metabolic unit, METs)				
1 (Barber et al., 2008a)	Not reported	Not reported	2.4 (0.4 to 15)	Low
Number of vaginal deliveries				
1 (Barber et al., 2008a)	Not reported	Not reported	0.3 (0.03 to 2.4)	Low
No nocturia compared with nocturia (objective outcome)				
1 (Abdel-Fattah et al., 2010a)	16/44 (36.36%)	134/250 (53.6%)	1.23 (0.52 to 2.89)	Very low
No urgency incontinence compared with urgency incontinence (objective outcome)				
1 (Abdel-Fattah et al., 2010a)	16/44 (36.36%)	117/253 (46.25%)	1.18 (0.33 to 4.31)	Very low
Maximal cystometric capacity				
1 (Paick et al., 2004)	Mean: 411ml (293-699)	Mean: 384ml (178-549ml)	1.00 (1 to 1.02)	High
Treatment group: retropubic 'bottom-up' compared with transobturator 'outside-in'				
1 (Barber et al., 2008a)	Not reported	Not reported	1.1 (0.5 to 2.5)[4,5,6]	Low
Treatment group: transobturator 'outside-in' compared with transobturator 'inside-out' (patient reported outcome)				
1 (Abdel-Fattah et al., 2010a)	35/61 (57.38%)	119/249 (47.79%)	1.46 (0.75 to 2.82)	Very low
Treatment group: transobturator 'inside-out' compared with transobturator 'outside-in' (objective outcome)				
1 (Abdel-Fattah et al., 2010a)	19/44 (43.18%)	131/253 (51.78%)	1.48 (0.68 to 3.22)	Very low
Treatment group: transobturator midurethral sling compared with retropubic midurethral sling				
1 (Richter et al., 2011)	138/260 (53.08%)	147/305 (48.20%)	1.15 (0.81 to 1.63)	Moderate
No prolapse of cervix of vaginal vault compared with prolapse				
1 (Schraffordt et al., 2006)	82/119 (68.91%)	343/437 (78.49%)	1.25 (0.66 to 2.37)	Very low
Weekly incontinence episodes compared with daily incontinence episodes				
1 (Schraffordt et al., 2006)	4/170 (2.35%)	27/361 (7.48%)	3.01 (0.87 to 10.49)	Low

Number of studies	Number of women		Effect	Quality
	Number of women with factor / Number with tape failure	Number of women with factor / Number without tape failure	Adjusted OR (95% CI)	
Q-tip test < 30 degrees compared with ≥ 30 degrees				
1 (Paick et al., 2004)	Mean: 23 degrees (10-45)	Mean: 30 degrees (5-70)	0.55 (0.09 to 3.17)	Very low
Previous incontinence surgery compared with no previous urogynecological surgery				
1 (Schraffordt et al., 2006)	12/200 (6.00%)	20/408 (4.90%)	0.51 (0.243 to 1.071)	Very low
VLPP < 60 cmH_2O compared with ≥ 60 cmH_2O				
1 (Paick et al., 2004)	Mean: 52cm H_20 (20-104)	Mean: 72cm H_2O (20-125)	2.34 (0.42 to 12.89)	Very low
Dribbling incontinence compared with no dribbling incontinence (patient reported outcome)				
1 (Abdel-Fattah et al., 2010a)	31/61 (50.82%)	87/248 (35.08%)	0.77 (0.37 to 1.61)	Very low
No dribbling incontinence compared with dribbling incontinence (objective outcome)				
1 (Abdel-Fattah et al., 2010a)	23/43 (53.49%)	160/253 (63.24%)	0.63 (0.25 to 1.58)	Very low
Urgency compared with no urgency (patient reported outcome)				
1 (Abdel-Fattah et al., 2010a)	42/61(68.85%)	110/247 (44.53%)	3.26 (0.87 to 12.26)	Low
No urgency compared with urgency (objective outcome)				
1 (Abdel-Fattah et al., 2010a)	19/44 (43.18%)	130/251 (51.79%)	0.45 (0.08 to 2.67)	Very low
BMI 31–35 compared with ≤ 3 0 (patient reported outcome)				
1 (Abdel-Fattah et al., 2010a)	22/58 (37.93%)	65/247 (26.32%)	1.91 (0.95 to 3.87)	Low
BMI 31–35 compared with ≤ 30 (objective outcome)				
1 (Abdel-Fattah et al., 2010a)	17/43 (39.53%)	66/250 (26.4%)	1.84 (0.81 to 4.17)	Low
BMI > 35 compared with ≤ 30 (objective outcome)				
1 (Abdel-Fattah et al., 2010a)	6/43 (13.95%)	12/250 (4.80%)	3.46 (0.78 to 15.32)	Low
Age 45–65 yrs compared with ≤ 45yrs (patient reported outcome)				
1 (Abdel-Fattah et al., 2010a)	40/60 (66.67%)	137/230 (59.57%)	1.99 (0.82 to 4.87)	Very low
Age > 65 yrs compared with ≤ 45 yrs (patient reported outcome)				
1 (Abdel-Fattah et al., 2010a)	9/60 (15.00%)	29/230 (12.61%)	1.85 (0.57 to 5.94)	Very low

Number of studies	Number of women		Effect	Quality
	Number of women with factor / Number with tape failure	Number of women with factor / Number without tape failure	Adjusted OR (95% CI)	
Age 45–65 yrs compared with ≤ 45yrs (objective outcome)				
1 (Abdel-Fattah et al., 2010a)	25/42 (59.52%)	146/235 (62.13%)	0.8 (0.3 to 2.09)	Very low
Age > 65 yrs compared with ≤ 45 yrs (objective outcome)				
1 (Abdel-Fattah et al., 2010a)	7/42 (16.67%)	30/235 (12.77%)	1.32 (0.37 to 4.74)	Very low
Age per decade (outcome: any urinary incontinence)				
1 (Barber et al., 2008a)	Not reported	Not reported	1.3 (0.5 to 2.7)	Low
MUCP ≤ 30 when compared with ≤ 31 (patient reported outcome)				
1 (Abdel-Fattah et al., 2010a)	18/60 (30.00%)	28/239 (11.72%)	2.26 (0.996 to 5.124)	Low
Type of incontinence: mixed group compared with USI group (patient reported outcome)				
1 (Abdel-Fattah et al., 2010a)	23/61 (37.70%)	59/249 (23.69%)	1.06 (0.5 to 2.24)	Very low
Type of incontinence: SUI group compared with mixed group (objective outcome)				
1 (Abdel-Fattah et al., 2010a)	32/44 (72.73%)	186/253 (73.52%)	0.72 (0.28 to 1.85)	Very low
Type of incontinence: stress incontinence compared with mixed incontinence				
1 (Schraffordt et al., 2006)	84/119 (70.59%)	365/432 (84.49%)	1.84 (0.96 to 3.54)	Very low

BMI body mass index, CI confidence interval, MUCP Maximum urethral closure pressure, OR odds ratio, SUI stress urinary incontinence, UI urinary incontinence, VLPP Valsava Leak Point Pressure,

Evidence statements and overview table

Clinically and statistically significant factors

The review found that the following factors were useful in predicting primary tape failure:

- maximum urethral closure pressure (MUCP) of 31 cmH_2O or more when compared with MUCP of 30 or less (objective outcome) (1 study)
- body mass index (BMI) of more than 35 when compared with BMI of 30 or less (patient reported outcome) (1 study)
- preoperative anticholinergic medication use when compared with no use (1 study)
- primary surgery when compared with secondary surgery (objective outcome) (1 study).

The evidence was of high quality.

Statistically significant factors

The review found that the following factors may be useful in predicting primary tape failure:

- older age (per decade) (1 study, evidence was moderate quality)
- concurrent pelvic organ prolapse surgery (1 study, evidence was moderate quality)
- secondary surgery (1 study, evidence was low quality)

- nocturia as a preceding symptom (1 study, evidence was low quality)
- urgency incontinence as a preceding symptom (1 study, evidence was low quality)
- higher maximal flow rate before surgery (1 study, evidence was moderate quality)
- previous UI surgery (1 study, evidence was moderate quality)
- Q-tip maximum straining less than 30 degrees before surgery (1 study, evidence was moderate quality)
- urge score before surgery (1 study, evidence was moderate quality)
- pad weight (per 10 g) before surgery (1 study, evidence was moderate quality)
- more than 20 procedures for each surgeon when compared with first 10 procedures for each surgeon (Outcome 1: defined as the answer to the question 'Do you experience urinary leakage during physical activity, coughing or sneezing?' Success for SUI was defined as the answer 'no'.) (1 study, evidence was low quality)
- more than 20 procedures for each surgeon when compared with first 10 procedures for each surgeon (Outcome 2: defined as the answer to the doctor's question 'Do you leak during physical activity, coughing or sneezing?' asked at 2-year follow-up. Success for SUI was defined as the answer 'no'. All other answers as well as improved were considered failure.) (1 study, evidence was low quality)
- general anaesthesia when compared with local anaesthesia (1 study, evidence was low quality)
- urge symptoms when compared with no urge symptoms before surgery (1 study, evidence was low quality)
- lower MUCP (reference not stated) before surgery (1 study, evidence was low quality).

Factors that are not significant

The review found that the following factors were not useful in predicting primary tape failure:

- current smoking (1 study, evidence was low quality)
- functional capacity (metabolic equivalents) before surgery (1 study, evidence was low quality)
- number of vaginal deliveries (1 study, evidence waslow quality)
- no nocturia when compared with nocturia (objective outcome before surgery) (1 study, evidence was very low quality)
- no urgency incontinence when compared with urgency incontinence (objective outcome) before surgery (1 study, evidence was very low quality)
- maximal cystometric capacity before surgery (1 study, evidence was high quality)
- treatment group (retropubic 'bottom-up' when compared with transobturator 'outside-in' (1 study, evidence was low quality)
- treatment group: transobturator 'outside-in' when compared with transobturator 'inside-out' (patient reported outcome) (1 study, evidence was very low quality)
- treatment group: transobturator 'inside-out' when compared with transobturator 'outside-in' (objective outcome) (1 study, evidence was very low quality)
- treatment group (transobturator midurethral sling when compared with retropubic midurethral sling) (1 study, evidence was moderate quality)
- no prolapse of cervix of vaginal vault when compared with prolapse before surgery (1 study, evidence was very low quality)
- incontinence episodes, weekly when compared with daily before surgery (1 study, evidence was low quality)

- Q-tip less than 30 degrees when compared with 30 degrees or more before surgery (1 study, evidence was very low quality)
- previous incontinence surgery when compared with no previous urogynecological surgery (1 study, evidence was very low quality)
- valsalva leak point pressure less than 60 cmH_2O when compared with 60cmH_2O or more before surgery (1 study, evidence was very low quality)
- dribbling incontinence when compared with no dribbling incontinence (patient reported outcome) before surgery (1 study, evidence was very low quality)
- no dribbling incontinence when compared with dribbling incontinence (objective outcome) before surgery (1 study, evidence was very low quality)
- urgency when compared with no urgency (patient reported outcome) before surgery (1 study, evidence was low quality)
- no urgency when compared with urgency (objective outcome) before surgery (1 study, evidence was very low quality)
- BMI of 31–35 when compared with BMI of 30 or less (patient reported outcome) (1 study, evidence was low quality)
- BMI of 31–35 when compared with 30 or less (objective outcome) (1 study, evidence was low quality)
- BMI more than 35 when compared with 30 or less (objective outcome) (1 study, evidence was low quality)
- age 45–65 years when compared with age 45 years or less (patient reported outcome) (1 study, evidence was very low quality)
- age over 65 years when compared with age 45 years or less (patient reported outcome) (1 study, evidence was very low quality)
- age 45–65 years when compared with age 45 years or less (objective outcome) (1 study, evidence was very low quality)
- age over 65 years when compared with age 45 years or less (objective outcome) (1 study, evidence was very low quality)
- age per decade (outcome: any UI) (1 study, evidence was low quality)
- MUCP 30 or less when compared with 31 or more (patient reported outcome before surgery) (1 study, evidence was low quality)
- type of incontinence: mixed when compared with USI (patient reported outcome) (1 study, evidence was very low quality)
- type of incontinence: USI (urinary stress incontinence, as reported in evidence) when compared with mixed (objective outcome) (1 study, evidence was very low quality)
- type of incontinence: stress when compared with mixed (1 study, evidence was very low quality)

Table 9.17 Overview table of factors for treatment failure

Characteristics identified as statistically significant[1]	Characteristics identified as statistically significant but not clinically significant	Characteristics identified as both statistically and clinically significant
Age per decade (outcome defined as any urinary incontinence)	Age per decade (outcome defined as recurrent stress urinary incontinence)	BMI > 35 when compared with ≤ 30 (patient reported outcome)

Characteristics identified as statistically significant[1]	Characteristics identified as statistically significant but not clinically significant	Characteristics identified as both statistically and clinically significant
Age 45–65 years when compared with ≤ 45 yrs (patient reported outcome)	Lower MUCP (reference not stated)	MUCP ≥ 31 cm water when compared with ≤ 30 cm water (objective outcome)
Age >65 years when compared with ≤45 years (patient reported outcome)	Secondary surgery when compared with primary surgery (patient reported outcome)	Primary surgery when compared with secondary surgery (objective outcome)
Age 45–65 years when compared with ≤45 years (objective outcome)	Higher maximal flow rate	Preoperative anticholinergic medication use when compared with no use
Age > 65 years when compared with ≤ 45 years (objective outcome)	Concurrent pelvic organ prolapse surgery	
No nocturia when compared with nocturia (objective outcome)	Nocturia when compared with no nocturia (patient reported outcome)	
No urgency incontinence when compared with urgency incontinence (objective outcome)	Urgency incontinence when compared with no urgency incontinence (patient reported outcome)	
Treatment group (retropubic 'bottom-up' when compared with transobturator 'outside-in', transobturator 'outside-in'when compared with transobturator 'inside-out', transobturator 'inside-out' when compared with transobturator 'outside-in', transobturator midurethral sling when compared with retropubic midurethral sling).	Pad weight (per 10 g)	
Previous incontinence surgery when compared with no previous urogynecological surgery	Previous UI surgery when compared with no surgery	
Dribbling incontinence when compared with no dribbling incontinence (patient reported outcome)	Q-tip maximum straining < 30 degrees, yes when compared with no	
No dribbling incontinence when compared with dribbling incontinence (objective outcome)	Urge score (per 10 points)	
Urgency when compared with no urgency (patient reported outcome)	Urge symptoms when compared with no urge symptoms	
No urgency when compared with urgency (objective outcome)	More than 20 procedures for each surgeon when compared with first 10 procedures for each surgeon (outcome 1)[2]	
Current smoking	More than 20 procedures for each surgeon when compared with first 10 procedures for each surgeon (outcome 2)[3]	

Characteristics identified as statistically significant[1]	Characteristics identified as statistically significant but not clinically significant	Characteristics identified as both statistically and clinically significant
Functional capacity (metabolic equivalents)	General anaesthesia when compared with local anaesthesia	
Number of vaginal deliveries		
BMI 31–35 when compared with ≤30 (patient reported outcome)		
BMI 31–35 when compared with ≤30 (objective outcome)		
BMI > 35 when compared with ≤=30 (objective outcome)		
MUCP ≤ 30 when compared with ≥ 31 (patient reported outcome)		
Type of incontinence: mixed group when compared with USI (urinary stress incontinence, patient reported outcome)		
Type of incontinence: USI (urinary stress incontinence) when compared with mixed group (objective outcome)		
Type of incontinence: stress when compared with mixed		
Maximal cystometric capacity		
Valsalva leak point pressure < 60 cmH_2O when compared with ≥ 60 cmH_2O		
Incontinence episodes, weekly when compared with daily		
No prolapse of cervix of vaginal vault when compared with prolapse		
Q-tip < 30 degrees when compared with ≥ 30 degrees		

BMI body mass index, MUCP maximum urethral closure pressure, SUI stress urinary incontinence, UI urinary incontinence, VLPP valsava leak point pressure,

[1] Confidence intervals not crossing 1

[2] Defined as the answer to the question 'Do you experience urinary leakage during physical activity, coughing or sneezing?' This question was asked on the Urogenital Distress Inventory questionnaire. Success for SUI was defined as the answer 'no'.

[3] Defined as answer to the doctor's question 'Do you leak during physical activity, coughing or sneezing?' asked at 2-year follow-up. The answer 'no' was defined as success. All other answers as well as 'improved' were considered as failure.

Evidence to recommendations

Relative value placed on the outcomes considered

Tape failure was identified as the primary outcome for this review. The GDG noted that the reporting of tape failure varied in the studies identified and included both subjective measures, such as responses to the Patient Global Impression of Improvement (PFI-I) questionnaire, and objective measures, such as an urodynamic assessment.

All predictive factors identified in the literature search were reported. The GDG chose to make recommendations using only those factors demonstrating clinical significance as it was impossible to base any conclusions on statistical significance alone due to the low quality of evidence. Clinical significance was determined by an adjusted odds ratio and confidence intervals greater than 2.5 from the line of no effect. The majority of studies were either prospective cohort studies or ancillary analysis of data from RCTs.

Consideration of clinical benefits and harms

This review identified four factors associated with a clinically and statistically significant likelihood of tape failure:

- BMI greater than 35
- MUCP of 31 or more
- primary surgery versus secondary surgery
- preoperative anticholinergic medication use.

The GDG noted that the evidence for MUCP did not agree with current clinical understanding, as a higher value of MUCP reported in the evidence was associated with a higher rate of tape failure, which is contrary to the belief that a lower MUCP value indicates urethral degradation and therefore a higher rate of incontinence is expected. In clinical practice, MUCP would not be a suitable indication of failure as it is rarely considered a risk factor due to its variability with age. Tests of MUCP are not routinely undertaken in NHS clinical practice.

The evidence reporting favourable outcomes when tapes for primary surgery were compared with secondary surgery was also contrary to current clinical understanding, and the GDG concluded that the evidence on which this assumption was based was not sufficiently robust to make accurate conclusions. Patient selection and potential bias in offering secondary procedures may be the explanations for the differences observed.

The evidence for anticholinergic medication use indicated a higher chance of failure than no medication use. Anticholinergic medication use would suggest OAB, which cannot be treated by a tape procedure. This indication would not influence the choice of SUI intervention but should be included in the information given to the woman before treatment.

The GDG agreed that a BMI greater than 35 was likely to be indicator for a higher rate of failed primary tape procedures. However, the evidence was not sufficiently robust to make a specific recommendation for tapes. This would require additional information beyond the general guidance offered for all surgery and its risks related to obesity. Furthermore, there are some potential predictors of failure that can be addressed with lifestyle interventions. Obesity is one such indicator that can be addressed with successful conservative treatment before surgery is considered.

The GDG concluded that the evidence was not strong enough to make a conclusive recommendation regarding any of the four factors demonstrating clinical significance. Instead, the GDG chose to make a research recommendation for further investigation of all the clinically and statistically significant indications reported.

Consideration of health benefits and resource uses

The GDG considered that being able to predict the chances of tape success would offer potential savings as not offering treatment to women whose surgery is likely to fail would avoid the costs of the procedure and the cost of any subsequent failure. For some lifestyle factors, such as BMI, offering conservative treatments before SUI treatment was considered to be cost effective.

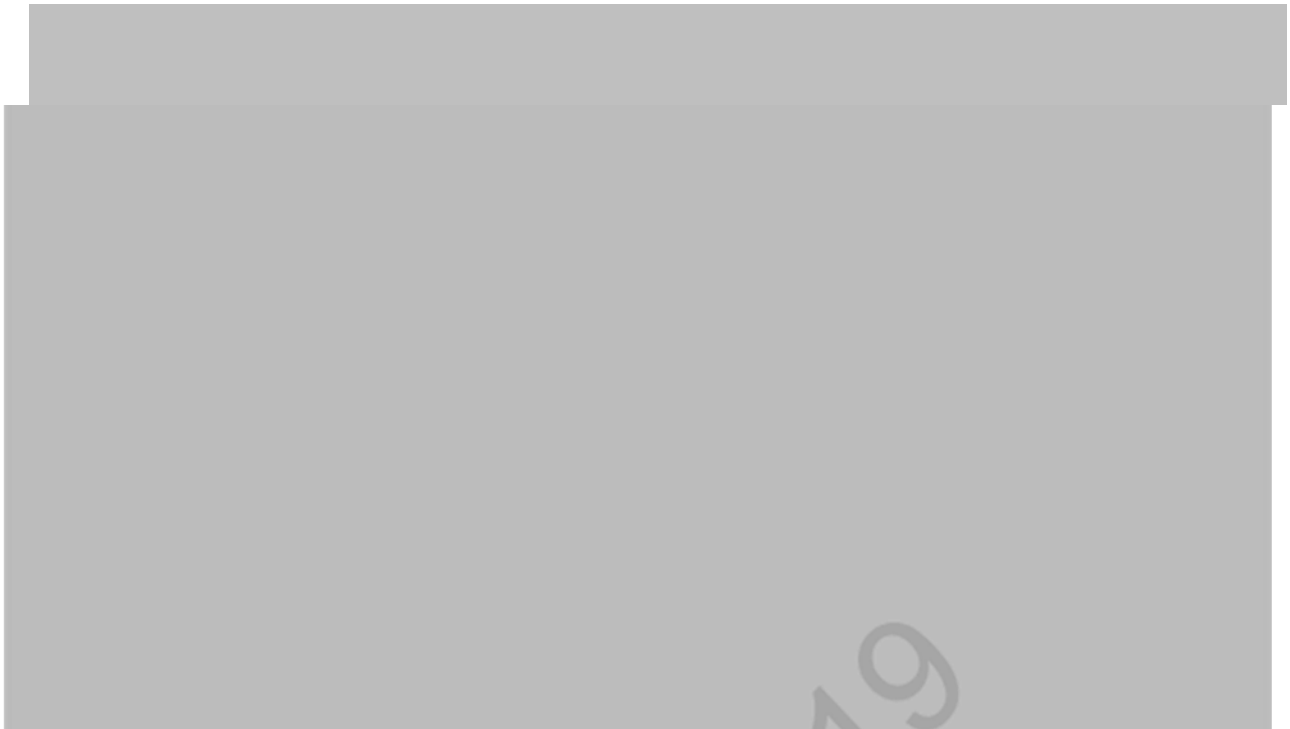
Quality of evidence

The evidence identified in this review was of varying quality, from high to very low, which did not allow the GDG to make conclusive recommendations. The review was limited to a very small pool of evidence and it was limited to small study populations. In addition, the GDG noted that the evidence for certain predictive factors contradicted current clinical experience.

Recommendations

Number	Research recommendations
RR18	What are the effects of the following predictors on tape failure? • Age per decade • Lower maximum urethral closure pressure • Secondary surgery versus primary surgery • Higher maximal flow rate • Concurrent pelvic organ prolapse surgery • Nocturia versus no nocturia • Urgency versus no urgency • Pad weight (per 10 g) • Previous urinary incontinence surgery versus no surgery • Q-tip maximum straining less than 30 degrees, yes versus no • Urge score (per 10 points) • Urgency symptoms versus no urgency symptoms • More than 20 procedures for each surgeon versus first 10 procedures for each surgeon • General anaesthesia versus local anaesthesia • BMI over 35 versus 30 or less • Maximum urethral closure pressure of 31 or more versus 30 or less • Primary surgery versus secondary surgery • Preoperative anticholinergic medication use versus no use **Why this is important** The factors identified for this research question are thought anecdotally by surgeons to have an impact on the outcome of tape surgery but there is little robust evidence in the literature. Certain patient factors such as older age and increased weight are thought to produce a higher chance of recurrent symptoms. Similarly, the effect of previous incontinence surgery, concomitant prolapse surgery and the 'learning curve' of the surgeon are all thought to have adverse effects on outcome (including an increased chance of urgency incontinence). In addition there is little robust evidence regarding the effect of previous urgency incontinence, higher maximum flow rates, nocturia or preoperative use of anticholinergics on the occurrence of post-operative urgency and bladder overactivity. It would be useful to be able to individualise treatment by understanding these risks in more detail.

9.2.3 Colposuspension



Each study considered objective cure rates, using varying methods, including pad testing, stress test or urodynamic assessment. Four studies found no significant differences between open and laparoscopic colposuspension in this outcome,[624,626–629] one found a significantly higher cure rate with open colposuspension at 6 months (96% versus 80%; provocative testing on urodynamics),[628] and the other a higher cure with laparoscopic suspension at 18 months (78% versus 85%; stress test), with no difference between groups if objective and subjective cure were considered together.[625] Three studies considered subjective success and satisfaction, which were similar with both interventions.[624,626,629] In the study that evaluated open colposuspension, and laparoscopic suspension with sutures or mesh and staples, objective cure rates were significantly higher at 1 year with open than laparoscopic colposuspension with mesh and staples by the stress test (92% versus 63%), with no difference between groups when assessed by a 48 hour pad test (92% versus 91% versus 76%) (n = 211).[624] [EL = 1−]

Peri- and postoperative complications were reported for each study. Significantly fewer women in the laparoscopic colposuspension group using mesh and staples had urinary retention for longer than 5 days.[624] No other significant differences in complications were seen with open and laparoscopic colposuspension, which were bladder injury, urinary obstruction, *de novo* DO, haematuria, UTI, wound complications, haematoma, dyspareunia, urinary retention and enterocele.[625–628]

Operating time was significantly shorter in the open colposuspension group in four studies,[624–627] with one not identifying a significant difference between groups.[628] Conversion to open colposuspension was required in 1% and 5% of women undergoing the laparoscopic procedure in two studies.[624,626] Duration of hospital stay was longer in the open group in three studies,[624,625,627] and not significantly different in two.[626,629] The UK MRC study also reported no significant difference between open and laparoscopic groups in the time to return to work, which applied to about half of the women studied.[629]

Studies comparing different suturing methods for laparoscopic suspension

Four RCTs compared different suturing methods for laparoscopic suspension.[624,630–635] Sutures were compared with mesh and staples in three studies,[624,631–635] while the remaining study compared the use of double- with single-bite sutures.[630]

In the study that evaluated open colposuspension, and laparoscopic suspension with sutures or mesh and staples, objective cure rates were significantly higher at 1 year with open than laparoscopic suspension with mesh and staples by the stress test (92% versus 63%), with no difference between groups when assessed by a 48 hour pad test (92% versus 91% versus 76%). No other significant differences were identified (subjective cure, ‘quality of life’ assessed on a visual analogue scale, or satisfaction). Duration of hospital stay and bladder drainage were significantly shorter in the mesh and staples group and fewer people had retention; no other differences in complication rates were noted (n = 211).[624] [EL = 1−] While another RCT found no significant differences in objective cure rates at 1 year (n = 69),[631] the third study comparing sutures with mesh and staples reported significantly higher objective and subjective cure rates at 1, 2 and 3 years in the sutures group; cure rates declined with time in both groups. No significant differences were noted in operating time or hospital stay or in complications (bladder injury or DO) (n = 60).[632–635] [EL = 1+]

Recruitment to the RCT comparing double- with single-bite sutures was terminated early because of a notably higher cure rate in the double-grip group. Those who were treated were all evaluated at 1 year; both objective and subjective cure rates were significantly higher in the double-grip suture group. No significant differences in immediate or subsequent postoperative complications were reported between

Objective and/or subjective cure or improvement rates were reported in each study. In the study with three treatment arms, the rate of combined objective and subjective cure (not precisely defined) at 4 years was significantly higher with colposuspension than with MMK or anterior colporrhaphy (n = 170; 91% analysed).[639] [EL = 1−] A study that only reported subjective cure or improvement also found that significantly more women failed MMK than colposuspension at mean follow-up of 2 years (range 6 months to 5 years), when analysed using intention-to-treat (36% versus 15%) or for completers only (25% versus 7%) (n = 138).[636] [EL = 1+]

The remaining two studies both reported objective cure by negative stress test.[637,638] [EL = 1+] One found no significant differences between colposuspension andMMKin objective (80% versus 65%) or subjective cure rates (92% versus 85%), at a minimum of 2 years follow-up (mean ~3 years) (n = 80).[637] The second study, in women with stress UI with low urethral pressure and hypermobility, reported significantly higher objective (53% versus 93%) and subjective (66% versus 100%) cure rates in the MMK group at 1 year (n = 30).[638]

Three of the four studies reported complications.[637–639] *De novo* DO and urge UI were common with both procedures, and with anterior colporrhaphy.[637,639] Time to normal voiding was significantly longer with MMK in one study (mean 21 versus 7 days),[638] as were hospital stay and duration of catheterisation in another.[637]

Colposuspension or vagino-obturator shelf versus bladder neck needle suspension or anterior colporrhaphy

Open colposuspension was compared with anterior colporrhaphy in two RCTs[640,641] and in a further two which also had a Pereyra needle suspension treatment arm.[642–645] Four studies compared open colposuspension or the vagino-obturator shelf procedure with needle suspension alone,[646–649] one of which also had a transvaginal colposuspension arm.[648]

Open colposuspension or vagino-obturator shelf versus anterior colporrhaphy

The four studies that compared open colposuspension with anterior colporrhaphy included women with stress UI without prior continence surgery; two specifically included women with prolapse.[640,642,643] In women with stress UI and prolapse, one study found significantly higher objective (74% versus 42%, negative stress test) and subjective cure rates (86% versus 52%) in the colposuspension group, compared with colporrhaphy after a minimum of 8 years followup. Recurrence of cystocele was significantly higher in the colposuspension group (34% versus 3%). Hysterectomy was also undertaken in all women in this study (n = 71; 96% analysed).[640] [EL = 1+] The second study compared colposuspension with the Pereyra procedure and with anterior colporrhaphy. Only women with complete data were analysed at 1 year, with only limited information on baseline characteristics of the women across groups. This study also reported significantly higher combined objective and subjective cure rates with colposuspension compared with Pereyra and anterior colporrhaphy; 87% versus 70% versus 69%, defined as negative stress test with no history of UI, and no urine loss observed at any

Open colposuspension or vagino-obturator shelf procedure versus bladder neck needle suspension

Four RCTs compared open colposuspension or the vagino-obturator shelf procedure with needle suspension in women with stress UI,[646–649] one of which also had a transvaginal colposuspension arm.[648] One study noted that 42% had had prior continence surgery.[649] Three of the four studies, which compared Burch with Stamey procedures, were considered to be of poor quality because of the use of alternate allocation rather than true randomisation, or not describing randomisation, and were additionally lacking in baseline data to enable consideration of whether groups were similar other than in the intervention.[646,647,649] [EL = 1−] Patient numbers were 50 or 51 in the three studies; all reported higher cure rates (subjective in two, objective in one) with colposuspension at varying durations of follow-up (minimum 8–12 months). The remaining study was of better quality, although only 74% of the women were followed up to 3 years. No significant differences in objective (urodynamics) or subjective cure rates were reported between retropubic Burch, transvaginal Burch or Raz procedures at 1, 2 or 3 years follow-up (n = 204).[648] [EL = 1+]

One RCT noted that there were no complications.[647] Common complications were haematoma, retention, abscess,[646] urgency or *de novo* DO,[646,648,649] wound infection, and postoperative pain in both groups, and voiding problems (not defined) in the vagino-obturator shelf procedure group.[649] Hospital stay was longer with colposuspension compared with Stamey needle suspension in two studies.[646,649]

Data from six RCTs were pooled in the Cochrane review[642,644,646–648,650] to calculate risk of failure with colposuspension (open or laparoscopic) compared with needle suspension (any).[616] The relative risk (RR) of subjective failure was significantly lower with colposuspension compared with needle suspension both up to and after 5 years follow-up (RR 0.56, 95% CI 0.39 to 0.81 after the first year and up to 5 years, and RR 0.32, 95% CI 0.15 to 0.71 after 5 years[616]).

Other colposuspension RCTs

One RCT compared Burch colposuspension with abdominal paravaginal defect repair in women with stress UI and grade 1 urethrocystocele. At mean follow-up of about 2 years, objective (negative stress test) and subjective cure rates were significantly higher in the colposuspension group (100% versus 61% and 100% versus 72%, respectively). The majority of women in both groups also underwent hysterectomy and culdoplasty. Recruitment to the trial was stopped after 36 women as it was considered that paravaginal defect repair was no longer ethical in the treatment of stress UI. Persisting voiding difficulties were very common, and recurrent urethrocystocele common in both groups; *de novo* DO was common in the colposuspension group (n = 36).[651] [EL = 1+]

Open colposuspension and pubococcygeal repair were compared in one RCT in women undergoing primary surgery for stress UI. Women with poor or absent pelvic floor contraction were excluded from the pubococcygeal repair group. At 1 year, objective cure rates were 67% with colposuspension versus 47% with repair. Subjective cure rates were 73% and 80% at 1 year, and 43% and 60% at between 5 and 7 years. Postoperative UTI was common. The median hospital stay was longer in the pubococcygeal repair group although the range of durations was similar in both groups (n = 45).[652–654] [EL = 1−]

Other needle suspension RCTs

One RCT compared the Raz suspension procedure with anterior colporrhaphy in women with grade 3 or 4 cystocele, about half of whom also had urge UI. Hysterectomy was undertaken in the majority of women alongside the continence procedure. At follow-up (between 10 months and about 4 years) the failure rate was significantly higher in the anterior colporrhaphy group (27% versus 14%). Postoperative urinary retention of between 5 and 10 days was common in both groups. No other complications were

Colposuspension versus slings or synthetic tapes

Open colposuspension versus biological slings

Open colposuspension was compared with dura mater sling in one RCT of women with recurrent stress UI after hysterectomy.[657] The combined objective and subjective cure rates were 86% with colposuspension versus 92% with dura mater sling at follow-up of about 3 years (n = 72). Significantly more women in the sling group had voiding difficulty or retention postoperatively, both of which were common; and more in the colposuspension group developed rectocele. Bladder perforation and *de novo* urgency were common in both groups. Time to spontaneous voiding was significantly longer in the sling group.[657] [EL = 1+]

One RCT compared colposuspension with autologous rectus fascial sling and retropubic 'bottom-up' tape.[658] Higher cure rates (negative stress test and symptom-free) were reported in the sling group at 1 year (93%) compared with open colposuspension or a retropubic 'bottom-up' tape (88% versus 87%). *De novo* DO and hesitancy were common in the colposuspension group, and retention common in the other groups (n = 92).[658] [EL = 1+]

Colposuspension versus synthetic slings

As well as the study of colposuspension, retropubic 'bottom-up' tape and rectus fascial sling described above,[658] a further seven RCTs compared colposuspension with retropubic 'bottom-up' tape: open colposuspension in four studies[659–663] and laparoscopic colposuspension in three.[664–667] Another RCT compared open colposuspension with a polypropylene soft tissue patch sling.[668,669]

Open colposuspension versus tension-free vaginal tape

Five RCTs studies compared open colposuspension with retropubic 'bottom-up' tapes in women undergoing primary surgery for urodynamic stress UI.[658–663] Overall, 627 women were randomised to either intervention (range of numbers across studies 50–344). One study also evaluated an autologous fascial sling.[658] [EL = 1+] Duration of follow-up ranged from 1 to a maximum of 3 years and was mostly about 2 years, although one study only provided results at 3–6 months.[663] In the largest study, 8% of the women withdrew consent after randomisation. Further losses to follow-up occurred by the 2 year analysis, the impact of which was considered in the analysis of results.[659,660] [EL = 1++] A second study also lost 17% of the women from the colposuspension arm before the end of follow-up.[662] [EL = 1+] The other two studies did not use true randomisation[661] or did not describe randomisation or consider whether groups were balanced at baseline in key parameters.[663] [EL = 1−]

The study with 3–6 months follow-up reported that 72% were subjectively 'completely' cured at that time point.[663] Of the other studies, each considered objective cure as an outcome, which was defined as less than 1 g[659–661] or 2 g[662] change in pad weight during a 1 hour pad test. The individual studies reported objective cure rates for colposuspension versus retropubic 'bottom-up' tapes of 80% versus 81%[659,660] and 86% versus 84%[661] at 2 years, with the third study reporting 76% versus 82% at median follow-up of 22 months.[662] While none of the trials identified significant differences between groups when women with complete data were analysed at follow-up, the impact of losses to follow-up were considered in the largest study. Assuming that all losses were failures or with the last observation carried forward (LOCF), the cure rate would be significantly higher with retropubic 'bottom-up' tapes. If all losses were assumed to be cured, or both presurgery withdrawals cured, and LOCF used for post-surgery withdrawals, there would be no significant difference between the interventions. In these analyses, the best and worst case cure rates were 51–87% for colposuspension and 63–85% with retropubic 'bottom-up' tapes.[659,660] [EL = 1++]

Other outcomes evaluated were QOL,[659,660] satisfaction[659,660] and subjective success.[662] Significant improvements in two-thirds of questions on the BFLUTS questionnaire were seen in both groups, and similar proportions were satisfied with treatment (82% versus 85%). The rate of subjective cure or

procedure in each study, and was noted to be significantly higher than with colposuspension in one.[659] No other significant differences in complications were reported (*de novo* DO, wound infection, fever, sensory urgency). Complications reported with retropubic 'bottom-up' tapes were vaginal perforation, retropubic haematoma, vascular injury and tape erosion, and in the colposuspension arm were incisional hernia, haematoma, retention and pain at incision site.

During the 2 year follow-up period of the largest study, significantly more women in the colposuspension group required surgery for uterovaginal prolapse (5% versus none).[659] No other significant differences were identified in further procedures required (surgery for stress UI, cystoscopy, hysterectomy, urethral dilatation). Division or trimming of the tape was undertaken in 2% of the retropubic 'bottom-up' tape group, and incisional hernia repair in 3% of the colposuspension group.[660]

Time to return to work[659,660] and to normal activities[659–661] was significantly longer with colposuspension, as were hospital stay, operating time and duration of catheterisation.[659–661,665]

Laparoscopic colposuspension versus tension-free vaginal tape

Three studies compared laparoscopic colposuspension with retropubic 'bottom-up' tapes in women with stress UI.[664–667] Prior continence surgery was an exclusion criterion in two studies (except colporrhaphy in one); the third reported that 17% in the retropubic 'bottom-up' tape group had had prior continence surgery.[667] The numbers of women randomised were 46, 72 and 128. Duration of follow-up in two studies was 1 year, and a mean of 11 months in the third. In two studies, one or more women withdrew after randomisation (1% and 5%),[664–666] and only 88% of those treated in one study were followed-up to 1 year.[666] One study had sparse methodological data, and had different mean duration of follow-up in groups, which was not adjusted for in the analysis of results.[667] [EL = 1−]

Objective cure at 1 year was reported in two studies, with the third reporting combined subjective and objective cure. Within one study, the significance of the results depended on the definition of cure, with cure in significantly more women in the retropubic 'bottom-up' tape group assessed by a stress test (86% versus 57%), but not with a 48 hour pad test (73% versus 59%).[664] Severity and KHQ scores were significantly lower with retropubic 'bottom-up' tape at 1 year, and satisfaction higher. In the second study, objective cure rates (urodynamics) were 97% versus 81% in the retropubic 'bottom-up' tape and colposuspension groups at mean follow-up of 21 months. No significant differences were found in UDI or IIQ scores, in leakage episodes or in satisfaction at 1 or 2 years. The majority of women in the study underwent another gynaecological procedure at the same time as the continence surgery.[666] In the third study, 83% of women in both groups were cured at mean follow-up of 11 or 13 months (minimum 3 months).

Intra- or postoperative complications common in both groups across the studies were bladder perforation, prolonged retention, wound infection, UTI, haematoma and pelvic abscess.[665,666] In two studies 9% of the women required conversion from laparoscopic to open colposuspension.[666,667] Other complications occurring less commonly were *de novo* DO,[667] vaginal erosion of mesh,[666] transection for voiding[666] and urge symptoms[665] with retropubic 'bottom-up' tape, and port-site infection,[665] postoperative ileus, pulmonary embolism and pyelonephritis with laparoscopic colposuspension.[666]

Hospital stay, duration of catheterisation and operating time were significantly longer with laparoscopic colposuspension than retropubic 'bottom-up' tape.[665–667]

Eleven cohort studies comparing long-term outcomes with colposuspension (Burch or MMK) and anterior colporrhaphy or needle suspension were identified.[670–681] Most were retrospective reviews of cases undertaken, some with questionnaire follow-up. The duration of follow-up of these studies ranged from a minimum of 2 years to a maximum of 17 years; most had follow-up of within 5–10 years. Losses to follow-up were noted in most studies, ranging from 2% to 76% (median 40%). Patient numbers ranged from 90 to 742, with a total of 3,306. Procedures were selected for specific indications, typically with colporrhaphy undertaken in women with stress UI and prolapsed of a higher grade. Those who underwent colposuspension usually had more severe stress UI. None of the studies considered the impact of potential confounding factors on the statistical significance of continence outcomes. Owing to losses to follow-up, and because of differences between groups in terms of patient characteristics, comparative outcome data derived should be viewed with caution and are not considered here. [EL = 2−]

Of the 18 case series identified for retropubic suspension procedures, most were in the form of retrospective reviews of case notes, with telephone or mailed questionnaires used for further follow-up (total n = 2568, range 48–374).[682–702] The majority of the studies evaluated the Burch colposuspension procedure, with the others being laparoscopic colposuspension or the MMK procedure. The duration of follow-up ranged from a minimum of 1 year to a maximum of 18 years; two-thirds had 5 years follow-up or more. Between 32% and 91% of those originally treated provided follow-up data. Concomitant procedures were undertaken alongside colposuspension in many of the studies, such as hysterectomy or correction of prolapse.

Long-term complications noted with colposuspension across the cohort and case series studies were:

- prolapse (cystocele, rectocele or enterocele; 16 studies): median 4% (range 0–60%)
- voiding difficulties/chronic retention (13 studies): median 6% (range 4–43%)
- *de novo* urgency or urge UI (nine studies): median 22% (range 3–40%)
- dyspareunia (seven studies): median 3% (range 1–12%)
- recurrent UTI (five studies): median 5% (range 4–11%)
- suprapubic pain/pain at site of suture (five studies): median 2% (range 0–12%).

Case series of needle suspension procedures

Twelve case series reporting long-term complications of needle suspension procedures were considered.[703–715] Patient numbers ranged from 55 to 206 (total treated 1346), with the majority including fewer than 100 women. Two described the Raz procedure,[703,704,706] one study each the Pereyra[707] and Gittes[708] procedures, and seven the Stamey procedure.[709–715] The duration of follow-up was about 4–5 years in most studies, ranging from 1 year to over 8 years.

Long-term complications reported with needle suspension procedures across the cohort and case series studies were:

- suprapubic pain/pain at site of suture (nine studies): median 6% (range 2–10%)
- surgery to release or remove sutures (eight studies): median 3% (range 1–10%)
- *de novo* urgency or urge UI (seven studies): median 13% (range 0–30%)
- recurrent UTI (five studies): median 2% (range 1–13%)
- voiding difficulty (four studies): median 6% (range 2–17%)

Recommendations

Number	Recommendations
94	When offering a surgical procedure discuss with the woman the risks and benefits of the different treatment options for SUI using the information in table 9.12. **[new 2013]**
95	If conservative management for SUI has failed, offer: • synthetic mid-urethral tape (see recommendations 96 – 101) **or** • open colposuspension (see also recommendation 102), **or** • autologous rectus fascial sling (see also recommendation 103). **[new 2013]**
102	Do not offer laparoscopic colposuspension as a routine procedure for the treatment of stress UI in women. Only an experienced laparoscopic surgeon working in an MDT with expertise in the assessment and treatment of UI should perform the procedure. **[2006]**

9.2.4 Biological slings

Other relevant guidance

NICE IP guidance on biological slings states that:

> "Current evidence on the safety and efficacy of the insertion of biological slings for stress urinary incontinence in women is adequate to support the use of this procedure provided that normal arrangements are in place for consent and clinical governance. Data on the long-term efficacy of the insertion of biological slings for stress urinary incontinence in women are limited to autologous slings. Clinicians should therefore audit patients in the longer term."[29]

A Cochrane systematic review considered traditional suburethral slings; the review included studies evaluating synthetic as well as biological materials.[876] Therefore, the relevant studies included in the review are considered individually within this section.

Controlled trials evaluating biological slings

Nearly all RCTs of biological slings compare the autologous rectus fascial sling procedure with a range of other surgical interventions. RCTs evaluating dura mater and porcine dermal slings were also identified. Non-randomised comparisons of autologous and allograft rectus fascial or fascia lata slings were also considered.

Tension-free vaginal tape versus porcine dermal collagen sling

In an RCT of women who had failed conservative treatment, no significant differences were seen between retropubic 'bottom-up' tape and porcine dermal collagen in subjective cure or improvement at 1 or 3 years, nor in satisfaction at 3 years (assessed by mailed questionnaire). Operating time, hospital stay and complication rates were not significantly different. The complications seen were haemorrhage (3% retropubic 'bottom-up' tape versus 4% porcine dermal sling), infection (0% versus 2%), the need for sling release or urethral dilatation (5% versus 10%), intermittent self-catheterisation (ISC) (3% versus 3%), *de novo* urgency or urge UI (15% versus 18%) and dyspareunia (3% versus 0%) (n =

at 5 years found no statistically significant differences between groups in urinary symptoms or in satisfaction with surgery (n = 45).[557] [EL = 1+]

Continence surgery versus periurethral collagen

Open continence surgery (a suspension procedure in 46% and fascial sling in 54%) was compared with periurethral collagen in women with stress or mixed UI in one RCT, which found no differences in satisfaction or QOL (SF-36, IIQ) between groups at 1 year. Using intention-to-treat analysis (where treatment was considered to have failed in women with missing data), there was no significant difference in continence rates at 1 year (52% collagen, 55% surgery). If only the 89% of women who underwent the randomised intervention were considered, the continence rate with surgery was significantly higher (72% versus 53%). The incidence of adverse effects was significantly higher in the surgery group: urinary retention 13% versus 2%, transient voiding difficulty 36% versus 17%, UTI 6% versus 0% (n = 133).[560] [EL = 1+]

Rectus fascial sling versus tension-free vaginal tape

Two small RCTs compared retropubic 'bottom-up' tapes with an autologous rectus fascial sling, one of which also had a colposuspension arm (total n = 145). In the study with three arms, cure rates (negative stress test and symptom-free) were 87%, 88% and 93%, with retropubic 'bottom-up' tape, open colposuspension and rectus fascial sling, respectively, at 1 year (n = 92).[658] [EL = 1+] The second study reported cure rates (using the same criteria) of 92% in both groups at 6 months. Complications reported were *de novo* DO (0% with retropubic 'bottom-up' tape versus 0% or 4% with rectus fascial sling), wound pain (7% versus 28%), or urinary retention (13% versus 7%).[658,717] [EL = 1+]

Rectus fascial sling versus self-fashioned polypropylene mesh sling

A quasi-RCT compared a rectus fascial sling with a self-fashioned polypropylene mesh sling. At median follow-up of about 2 years, cure and satisfaction rates were similar but operating time and hospital stay were significantly shorter in the synthetic sling group. Delayed voiding occurred in more women in the fascial sling group. No other significant differences were seen between groups in complications (haematoma, dysuria, *de novo* urgency or urge UI) (n = 50).[848] [EL = 1−] Rectus fascial sling versus polytetrafluoroethylene One RCT compared rectus fascial and PTFE slings in women with stress UI, 92% of whom had had prior continence surgery. Combined objective and subjective cure rates were 81% and 88%, respectively, at 6 months. No complications were reported in the fascial sling group, whereas urethral erosion, recurrent UTI and *de novo* DO were very common with PTFE (n = 48).[861] [EL = 1−]

Rectus fascial sling versus vaginal wall sling

Rectus fascial and vaginal wall slings were compared in one RCT and in two non-randomised retrospective studies involving women with stress UI.[877–879] All women in the non-randomised studies had had prior continence surgery. Each study was considered to be of poor quality. The RCT reported high subjective cure, and satisfaction rates (80–100%), with median follow-up of 7 months (n = 26). Transient urinary retention and *de novo* urge UI were very common.[877] [EL = 1−] The retrospective studies reported similar 'success' rates with both interventions, ranging from 80% to 97%, with follow-up of 21 months, and 70 months versus 45 months (n = 232, n = 79). Other than the proportions requiring ISC (2% fascial versus 0% vaginal wall), no other significant differences were reported in the complications listed (voiding dysfunction, wound infection, urgency, *de novo* DO, bladder or urethral perforation, pain, seroma formation, rectocele).[878,879] [EL = 2−]

A retrospective cohort study compared a rectus fascial sling with one reinforced with polyglactin mesh in women with urodynamic stress UI, one-third of whom also had urge UI (n = 51). Followup differed between groups (mean 8 versus 5 months). Overall, no clear difference was seen between groups in success rates, although results depended on the definition of success used (patient-determined, urodynamics or based on weekly leakage episodes). No significant differences between groups were noted in complications (wound infection, incisional hernia, voiding dysfunction, *de novo* DO).[881] [EL = 2−]

Dura mater sling versus open colposuspension

One RCT compared dura mater sling with open colposuspension in women with recurrent stress UI after hysterectomy. The cure rates (combined objective/subjective) were 92% versus 86%, at about 3 years. Significantly more women in the sling group had voiding difficulty or retention postoperatively, both of which were common, and more women developed rectocele in the colposuspension group. Bladder perforation and *de novo* urgency were common in both groups. Time to spontaneous voiding was significantly longer in the sling group (n = 72).[657] [EL = 1+]

Porcine dermis sling versus Stamey needle suspension

One RCT compared a porcine dermis suburethral sling with the Stamey needle suspension procedure in women with stress UI who were considered unsuitable for colposuspension; overall 60% had had prior continence surgery. At 2 years, subjective cure rates were 90% versus 70%. Intraoperative blood loss and postoperative infection were significantly more common in the sling group. Other common complications in both groups were bladder injury and *de novo* DO (n = 20).[656] [EL = 1+]

Porcine dermal collagen sling versus tension-free vaginal tape

In an RCT of women who had failed conservative treatment, no significant differences were seen between porcine dermal collagen sling and retropubic 'bottom-up' tape in subjective cure or improvement at 1 or 3 years, nor in satisfaction at 3 years (assessed by mailed questionnaire). Operating time and hospital stay were not significantly different, nor was the rate of complications. The complications seen were haemorrhage (4% versus 3%), infection (2% versus 0%), the need for sling release or urethral dilatation (10% versus 5%), ISC (3% versus 3%), *de novo* urgency or urge UI (18% versus 15%), and dyspareunia (0% versus 3%) (n = 142).[719,720] [EL = 1+]

Autologous versus allograft slings

Seven non-randomised studies compared the outcomes of autologous and allograft slings in women with stress UI (54–60% in two studies having mixed UI). One also compared both interventions with a xenograft material (porcine dermis). All were retrospective reviews of cases undertaken, each with differences in duration of follow-up for the interventions evaluated, with drop-out rates of 4–34% of those treated in four studies; all were therefore considered to be of poor quality.[180,882–889] [EL = 2−] Women in six studies had had prior continence surgery (19– 57%). Across four studies, 16–82% underwent concomitant surgery. Between 45 and 167 women were followed up (total 786) with duration of follow-up of between 3 months and about 3 years.

Four studies compared autologous with allograft (cadaveric) fascia lata,[883,885–888] three of which reported similar results for all outcomes (subjective cure, satisfaction, and UDI-6, IIQ-7 and SEAPI scores). The fourth study reported significantly higher cure rates in the autologous group.[883] In three studies that compared autologous rectus fascia (or fascia lata in one) with allograft fascia lata, two found a significantly higher cure rate in the autologous group.[180,884,889] The other did not report significant differences between groups in cure rate, although satisfaction rates were higher in the autologous group after 2 years follow-up. Operating time and hospital stay were shorter in the allograft group.[882] In the

- between 2% and 5% of autologous, allograft and xenograft groups underwent urethrolysis for persistent voiding dysfunction.[889]

Case series of biological slings

Autologous slings

Ten case series reported outcomes of the autologous rectus fascial sling.[890–899] Patient numbers in the studies ranged from 32 to 251 (total 1280). In six studies, only 67–95% of those treated were followed up. Six studies included women with mixed UI (34–58%). Prior continence surgery was documented for between 26% and 70% of women in six studies. Concomitant surgery was undertaken in 15–65% of women across six studies.

Each study reported a mean or median duration of follow-up ranging from about 2 to 6 years; in three studies, maximum follow-up of 15–18 years was reported.[894,896,897] Subjective cure rates ranged from 26% to 97% (median 81%); objective cure rate (one study) 93%; and cure that included subjective and objective elements 73% and 95% (two studies). Satisfaction rates of 86% and 92% were reported in two studies.

Intra-operative complications reported were:

- haemorrhage requiring transfusion: 4%[894]
- pelvic haematoma: 0.8%[895]
- retropubic haematoma or wound infection: 2%[897]
- wound infection: 3%[894]
- bladder perforation/injury: 0–7% (median 1.3%)[894,896,897,899]
- urethral injury: no cases.[896,899]

Postoperative complications were:

- *de novo* urgency, urge UI or DO (seven studies): median 14% (range 2–23%)
- voiding difficulty or retention either requiring intervention (sling removal or release, urethrolysis, ISC) or described as prolonged (eight studies): median 2% (range 1–9%)
- transient retention (five studies): median 33% (range 1.3–94%)
- lower abdominal pain (five studies): median 2.5% (range 0–25%)
- UTI (three studies): median 13% (range 4–41%); recurrent UTI (two studies): 4% and 22%
- sling erosion into urethra (two studies): 0% and 3%
- pelvic organ prolapse (two studies): 3–4%
- incisional hernia (two studies): 0.8–4.5%
- abdominal wall hernia (one study): 2%.

- sling division or urethrolysis for retention (1% and 4%);[900]
- ISC at 1 year in 3%[904]
- *de novo* urge UI (15%)901 or urgency (8%)[902]
- surgery for new onset or recurrent POP (2%);[901]
- another noted no cases of recurrent cystocele[902]
- vaginal pain, pressure or protrusion, and bladder or kidney infection very common in one study.[905]

No cases of bleeding, wound infection, or erosion were reported in one study.[904]

Slings made of other biological materials

Case series reporting the outcomes of slings made from other materials were identified: porcine dermal sling procedures,[906–908] vaginal wall slings[909–913] lyophilised dura mater,[914] and cadaveric dermal grafts.[915,916] The use of cadaveric human dermal sling, and bovine pericardium were described in two studies, but these studies are not considered further as both procedures used bone-anchors.[917,918]

The studies evaluating the porcine dermal or small intestinal mucosa slings were small (between 25 and 50 women), and had relatively short duration of follow-up. All reported cure, improvement and failure rates, using varying definitions, and complications. The three studies that evaluated the porcine dermal sling in women with stress UI (14% mixed UI in one)[908] had follow-up of 6 months or a mean of about 21 months.[906–908] In one study, all women had had prior continence surgery, compared with 18–26% in the other two studies. In one, 43% underwent concomitant prolapse surgery.[907] The cure rates ranged from 68% to 78%, with 9–15% improved, and failure rates of 10–25%. Common complications (1% or more and less than 10%) across the studies were UTI, wound infection, transient retention, and persisting or *de novo* urge UI.[906,907] Cases of sling erosion into the urethral wall,[907] retention requiring sling removal,[907] deep vein thrombosis[907] and bladder injury[908] were also reported. In one study pelvic pain for up to 3 months was common.

The case series evaluating the porcine small intestinal mucosa sling (32% of whom had concomitant surgery) reported cure and improvement rates of 79% and 9%, respectively, at 2 years. There was one case of *de novo* urge UI and three of suprapubic inflammation; no women had prolonged retention (n = 34).[919] [EL = 3]

In women who had stress UI and POP who underwent a lyophilised dura mater sling procedure, objective success (pad test) was seen in 89% at 6 months. There was a case each of the sling passing through the bladder and of haemorrhage requiring surgery (n = 36).[914] [EL = 3]

Two case series reported 6 or 12 month outcomes of cadaveric dermal grafts, in a total of 50 women with stress UI (28% had mixed in one study). The cure rate in both studies was 68%. Complications included a case of bladder perforation, suprapubic or vaginal infection (12%), and *de novo* urgency

Recommendations

Number	Recommendations
94	When offering a surgical procedure discuss with the woman the risks and benefits of the different treatment options for SUI using the information in table 9.12. **[new 2013]**
95	If conservative management for SUI has failed, offer: • synthetic mid-urethral tape (see recommendations 96– 101) **or** • open colposuspension (see also recommendation 102), **or** • autologous rectus fascial sling (see also recommendation 103). **[new 2013]**
103	Do not offer anterior colporrhaphy, needle suspensions, paravaginal defect repair and the Marshall–Marchetti–Krantz procedure for the treatment of stress UI. **[2006]**

9.3 Operations to augment sphincter closure

9.3.1 Introduction

Procedures in this section include injection of urethral bulking agents and implants that aim to occlude the urethra.

Studies considered for this section

Evidence described in this section is derived where possible from RCTs; where RCTs were not identified or had only short duration of follow-up, case series were considered. A systematic review of periurethral injection therapy for UI has been published on the Cochrane library.[554] Because most of the studies included in the review were published only as abstracts, and owing to publication of further studies, all relevant studies were considered individually. A further systematic review considered studies evaluating the silicone implantable product, which are considered individually in this section.[555]

The Interventional Procedures Programme of NICE has published guidance on two procedures of relevance to this area of practice:

- Intramural Urethral Bulking Procedures for Stress Urinary Incontinence in Women (2005). The guidance states that “Current evidence on the safety and short-term efficacy of intramural urethral bulking procedures for stress urinary incontinence is adequate to support the use of these procedures provided that normal arrangements are in place for clinical governance and for audit and research’ and that ‘clinicians should ensure that patients understand that the benefits of the procedures diminish in the long-term and provide them with clear written information”.[27]
- Insertion of Extraurethral (Non-Circumferential) Retropubic Adjustable Compression Devices for Stress Urinary Incontinence in Women (2005), which applies to the adjustable compression therapy balloon. The guidance states that “Current evidence on the safety and efficacy of insertion of extraurethral (non-circumferential) retropubic adjustable compression devices for stress urinary incontinence in women does not appear adequate for this procedure to be used without special arrangements for consent and for audit or research”.[28] Such devices are therefore not considered further in this guideline.

9.3.2 Intramural urethral bulking agents

and then passing it parallel to the urethra, while visualising the area around the bladder neck by cystoscope. A variety of biological and synthetic materials are available.

Controlled trials

Six RCTs[556–561] and two cohort studies[562,563] compared the effectiveness of a urethral bulking agent with other bulking agents, surgical interventions or placebo in women with stress UI. A further RCT and cohort study compared different routes of urethral injection of the same products (collagen[564] or hyaluronic acid/dextran copolymer[565]).

Silicone versus sling

One RCT compared periurethral silicone injection with an autologous rectus fascial sling in women with stress UI secondary to ISD in whom conservative treatment had failed. At 6 months, no significant differences were seen between groups in subjective cure or satisfaction, QOL (UDI-6, IIQ) or on a 1 hour pad test. Significantly fewer women undergoing injection therapy were objectively cured (no leakage on urodynamic assessment), but duration of the procedure, catheterisation, inpatient stay, and time to return to normal activities were significantly shorter compared with the sling. No significant differences in other adverse effects were noted (voiding dysfunction, *de novo* DO, UTI). A telephone survey of two-thirds of the women at 5 years found no significant differences between groups in urinary symptoms or in satisfaction with surgery, although fewer women in the silicone group were satisfied (29% versus 69%) (n = 45).[557] [EL = 1+]

Different injection routes of the same product

One RCT compared outcomes of transurethral and paraurethral placement of hyaluronic acid/dextran copolymer in women with stress UI who had failed conservative treatment. Up to three injections were given within 3 months (mean 1.7 months). No significant differences were seen between groups in subjective cure or improvement at follow-up to 1 year. Significantly more women in the paraurethral group experienced postoperative urinary retention (30% versus 5%) (n = 40).[565] [EL = 1+]

A retrospective review of women who had either trans- or paraurethral collagen injections for stress UI also found no differences between groups in any outcome (continence status, pad usage, transient haematuria or UTI), although mean duration of follow-up differed between groups (6 versus 9 months) (n = 45).[564] [EL = 2−]

Case series of silicone bulking agent

Nine case series evaluating the outcomes of silicone were evaluated (total n = 379; range 21– 102).[566–575] Eight studies included 60 women or less. Duration of follow-up ranged from 3 months to 3 years, with most between 1 and 2 years. All included women with stress UI, some of whom had had prior continence surgery (median 62%, range 19–100% across all studies).

Silicone was injected transurethrally in most studies. A single injection was given to women in two studies, while between 10% and 45% (median 18%) of women received a second injection after 3 months in the other studies. A third injection was given to 3% of women in one.[570] Each study reported continence status although the way in which this was reported varied widely across the studies. Given the difference in definitions, the results at maximum duration of follow-up in individual studies were:

- success rates (three studies): median 48% (range 48–74%)[566,567,569]
- objective cure (two studies): range 48–59%[571,572,574]
- cure or improvement in four studies that reported both: cure median 30% (range

- acute retention (six studies): median 11% (range 3–18%)[566–572]
- UTI (two studies): 6%.[570,574]

Case series of hyaluronic acid/dextranomer copolymer bulking agent

Three case series of the hyaluronic acid/dextranomer copolymer in women with stress UI were identified (total n = 204). Women in two studies had failed conservative treatment. One reported subjective cure or improvement by about 80% of the women at 3–6 months. Of 80% followed up to 5–6 years, 56% had continued response. Overall, 55% had two or three injections (n = 20; 16 followed up to 5–6 years).[595,596] [EL = 3] In the other two studies, women were followed for 1 year. A repeat injection was given to 43%. In the smaller study, 69% of women reported improvement, while objective cure or improvement was seen in 82% of those assessed (n = 22). Significant improvement in QOL (seven of ten KHQ domains) was reported (n = 42).[597,598] [EL = 3] In the larger study, 77% reported at least 50% improvement, with significant reductions in leakage episodes and in 24 hour pad weight, and improvements in six of nine domains of the KHQ (n = 142).[599] [EL = 3]

No adverse effects were reported in one study.[595,596] Adverse effects reported across the other two, which were mainly transient, included UTI (12%), urgency (12%), haematuria (10%), dysuria (8%), urethral disorder, reduced urine flow, vaginal discomfort (all 7%), urinary retention (7–20%) and injection-site pain (4%) or infection (2%) (n = 42).[597–599] [EL = 3]

Case series of carbon-coated zirconium beads bulking agent

Two case series reporting the use of carbon-coated zirconium beads were identified, which had mean follow-up duration of 9 or 10 months. One study that included men and women reported efficacy data for women separately (n = 20; 13 women).[600] The other included women only, with follow-up data for only 66% of those treated (n = 46).[601] Across both studies, 65% and 77% of women reported subjective cure or improvement: in the study that reported this outcome at 6 and 12 months, the proportion improved fell to one-third at 12 months.[600] No cases of urinary retention were seen in one study.[601] The other reported transient effects (skin reactions, urine retention in one case each).[600] [EL = 3]

Case series of polytetrafluoroethylene bulking agent

Only case series studies evaluating the use of para- or transurethral PTFE in women with stress UI were identified. The outcomes considered were subjective cure or improvement, and complications.[135,602–607] Mean duration of follow-up ranged from 1 to 5 years. Across the seven studies, 14–73% had had prior continence surgery. Between 22 and 56 patients were included in each study; one included men and women with results reported separately for women.[604]

In six studies the median subjective cure rate was 36% (range 7–70%), and median improvement rate 19% (range 11–41%).[135,602–607] The remaining study reported a combined cure or improvement rate of 32% at 1 year, which fell to 18% at 5 years.[607]

Five of the studies considered complications. Those reported in two or more studies were:

- acute retention (three studies): median 11% (range 3–31%)[135,603,605]
- UTI (two studies): 3% and 4%[135,605]

2013 update

Glutaraldehyde cross-linked collagen has been removed from the recommendations. This update has been made as the use of collagen for this procedure is no longer undertaken in the UK.

Recommendations

Number	Recommendations
104	Consider intramural bulking agents (silicone, carbon-coated zirconium beads or hyaluronic acid/dextran copolymer) for the management of stress UI if conservative management has failed. Women should be made aware that: • repeat injections may be needed to achieve efficacy • efficacy diminishes with time • efficacy is inferior to that of synthetic tapes or autologous rectus fascial slings. **[2006, amended 2013]**
105	Do not offer autologous fat and polytetrafluoroethylene used as intramural bulking agents for the treatment of stress UI. **[2006]**

9.3.3 Artificial urinary sphincters

The artificial urinary sphincter is a complex device that comprises an occlusive cuff inserted around the urethra which, while inflated, will exert a constant closure pressure. Pressure is maintained by means of an inflated pressure-regulating balloon. A small pump located in the labium is manually operated by the woman whenever she wishes to pass urine.

Most studies evaluating the AUS were conducted in populations outside the scope of this guideline (men and/or patients with neurogenic bladder), or studies included a mixed population but did not report data separately for women with idiopathic UI.

Six case series reported the outcomes of AUS in women with idiopathic stress UI. Across the studies 51–100% had failed prior continence surgery. The largest study included 206 women, 82% of whom had idiopathic UI, with results reported separately for this group.[609] The other studies included between 25 and 55 women.[610–613] The AUS device used was stated in five studies; except for a minority of women in two studies who received AS 791/792 or AS 742/761 sphincter, all received AS 800.

Duration of follow-up varied, with most being about 2–3 years (minimum 4 months, maximum about 9 years). Between 84% and 100% of women were subjectively cured. The largest study noted peri-operative complications, which were injuries to the vagina, bladder neck or urethra (all common) (n = 168).[609]

One series reported the duration and aetiology of device failure. At mean follow-up of about 9 years, 56% of women still had the same device *in situ*, 35% had revisions, and the median duration of the

has failed. Life-long follow-up is recommended. **[2006]**

9.4 The effect of hysterectomy on continence

No evidence was identified that addressed the question of whether hysterectomy is an effective treatment for UI. While the procedure is often undertaken at the same time as surgery for UI, it is not possible to evaluate the independent impact of hysterectomy on continence.

There is some evidence regarding the influence of hysterectomy for reasons other than treatment of UI on continence status, but the data are inconsistent. A systematic review of studies found no increase in UI within the first 2 years after hysterectomy; although there was an increase in the risk of UI in women over 60 years of age who had undergone the procedure many years earlier; this was not found in younger women.[920]

Evidence statements for procedures for stress urinary incontinence

There has been little consistency between trials of continence surgery in the types of patients recruited, the incidence of previous surgery or concomitant procedures, and the prevalence of pre-existing urge incontinence or voiding difficulty. [EL = 3]

Outcome measures have been inconsistent so comparisons between studies are difficult. Some procedures may be indistinguishable in anything other than name. There is no strong evidence of superior effectiveness for any one surgical procedure. [EL = 3]

Procedures to augment sphincter pressure

Controlled trials evaluating urethral bulking agents (collagen, silicone, carbon-coated zirconium beads, hyaluronic acid/dextran copolymer) for the treatment of women with stress UI are few, enrol relatively small numbers of patients and are of mixed quality. Bulking agents may be less effective than open surgery for UI, but they are associated with fewer postoperative complications. [EL = 1+] Autologous fat is no better than placebo in effecting cure or improvement of incontinence, and is significantly less effective than collagen. [EL = 2+] Otherwise, there is no evidence of greater efficacy of one injectable over another. Polytetrafluoroethylene has not been assessed in controlled trials.

Repeat injections are required in the majority of patients to achieve initial benefit. [EL = 3] There are no data on the outcome of subsequent courses of treatment.

Controlled trials show that urethral bulking agents have relatively poor efficacy. Case series show that any benefit observed declines with time, and that complications, though common or very common, are mainly transient, and include acute retention, dysuria, haematuria, frequency, and UTI. *De novo* DO with urge UI was the only long-term complication documented. Uncommon but serious complications have been reported with autologous fat. [EL = 3]

Data supporting the use of artificial urinary sphincter in women with idiopathic UI are limited to case series. Subjective cure rates are high although complications requiring removal or revision are common. [EL = 3]

Retropubic suspension procedures

Open colposuspension is an effective treatment for stress UI in women and has longevity. There is no consistent difference in effectiveness between laparoscopic and open colposuspension for any outcome measures. [EL = 1+] However, laparoscopic colposuspension consumes more resources, and skills take longer to acquire than with open colposuspension. [EL = 4]

In general, most suspension procedures are effective in the short term but the longer term outcomes for anterior colporrhaphy, abdominal paravaginal repair and needle suspension are poor when used for stress incontinence alone. [EL = 3]

Complications are common for all suspension procedures; these include voiding difficulty, urgency syndrome or development of vaginal vault and posterior wall prolapse. There is no evidence that the Marshall–Marchetti–Krantz (MMK) procedure offers any significant advantage over open colposuspension. [EL = 1+] The MMK procedure is no longer in routine clinical practice owing to the serious additional complication of osteitis pubis. [EL = 4]

Synthetic slings

Most RCT data regarding synthetic slings for the treatment of stress UI relate to a macroporous (type 1) polypropylene mesh inserted through the retropubic space using a bottom-up approach (e.g. TVT).

This has been shown to have comparable efficacy to colposuspension (open or laparoscopic) with follow-up to 3 years. Hospital resource use is less and recovery time is shorter when compared with colposuspension. [EL = 1+] Limited data are available on outcomes beyond 3 years. [EL = 3]

Results from an economic model conducted alongside a systematic review suggest that a synthetic sling using a macroporous (type 1) polypropylene mesh, inserted through the retropubic space using a bottom-up approach (e.g. TVT) for the treatment of stress UI is more cost effective than other surgical procedures, open colposuspension in particular. This result is based on limited follow-up data and assumes that the relative differences between treatments do not change over time. Case series suggest that cure rates for retropubic 'bottom-up' tapes are sustained. Higher prevalence of prolapse in open colposuspension would increase the relative cost effectiveness of retropubic 'bottom-up' tape. Numerous alternative synthetic sling materials and techniques have been described where the tape may be inserted by a retropubic route, bottom-up or top-down, or via the obturator foramina, outside-in or inside-out. Based on case series, these techniques appear to be effective, but there are only limited comparative data. [EL = 3] Slings using a retropubic top-down approach appear to be as effective as bottom-up retropubic techniques. [EL = 1+] Slings inserted through the obturator foramen appear to be effective in the short term but there is limited high-level evidence of their effectiveness compared with more established techniques. [EL = 1+] Long-term outcomes are unknown.

Slings using materials other than a wholly macroporous construction (e.g. type 2, 3 or 4 meshes [made of polyester, polytetrafluoroethylene, or silicone]), cannot be assumed to be of comparable efficacy and safety to those using a macroporous (type 1) polypropylene mesh inserted through the retropubic space using a bottom-up approach (e.g. TVT). [EL = 4]

Intra-operative complications are rare except for bladder perforation, which, although common, appears to have no long-term sequelae provided it is recognised and remedied at the time of surgery. Long-term complications with synthetic slings include voiding difficulties and development of urgency and urge UI. There is a lack of high-level evidence on the relative safety of sling materials or techniques. Slings employing materials other than the wholly macroporous (type 1) appear to have higher rates of erosion and infection. [EL = 3]

Patients who have undergone prior surgery are more likely to have intra-operative complications. [EL = 3]

Biological slings

Autologous rectus fascial sling is the most widely evaluated biological sling, which is an effective treatment for stress UI and has longevity. [EL = 1+] Short-length suspended autologous fascial sling achieves similar outcomes to full-length slings at 1 year. [EL = 1+]

Limited data show that pubovaginal sling using porcine dermis is effective. [EL = 1+] Data relating to other biological slings (autologous or allograft fascia lata, vaginal wall sling, dura mater, porcine small intestinal mucosa) are few, and generally of low evidence level and poor quality. Complications with all slings are common and include voiding difficulties and development of urgency and urge UI.

9.5 Secondary procedures for women who have had previous surgery

- conservative management, specifically looking at:
    - lifestyle interventions, specifically weight loss, fluid management and smoking cessation
    - physical therapy, specifically pelvic floor muscle training
- repeat tape procedure
- fascial sling
- colposuspension.

Methodological approach for the review

No comparative studies were identified for this question. Therefore the evidence was identified from the data available, which was primarily case–series data. The GDG agreed a threshold of effectiveness for a secondary procedure. Any procedure that reported a cure rate of 60% or more was considered an adequately effective treatment option after a failed primary tape procedure.

The evidence on secondary procedures was separated into two categories:

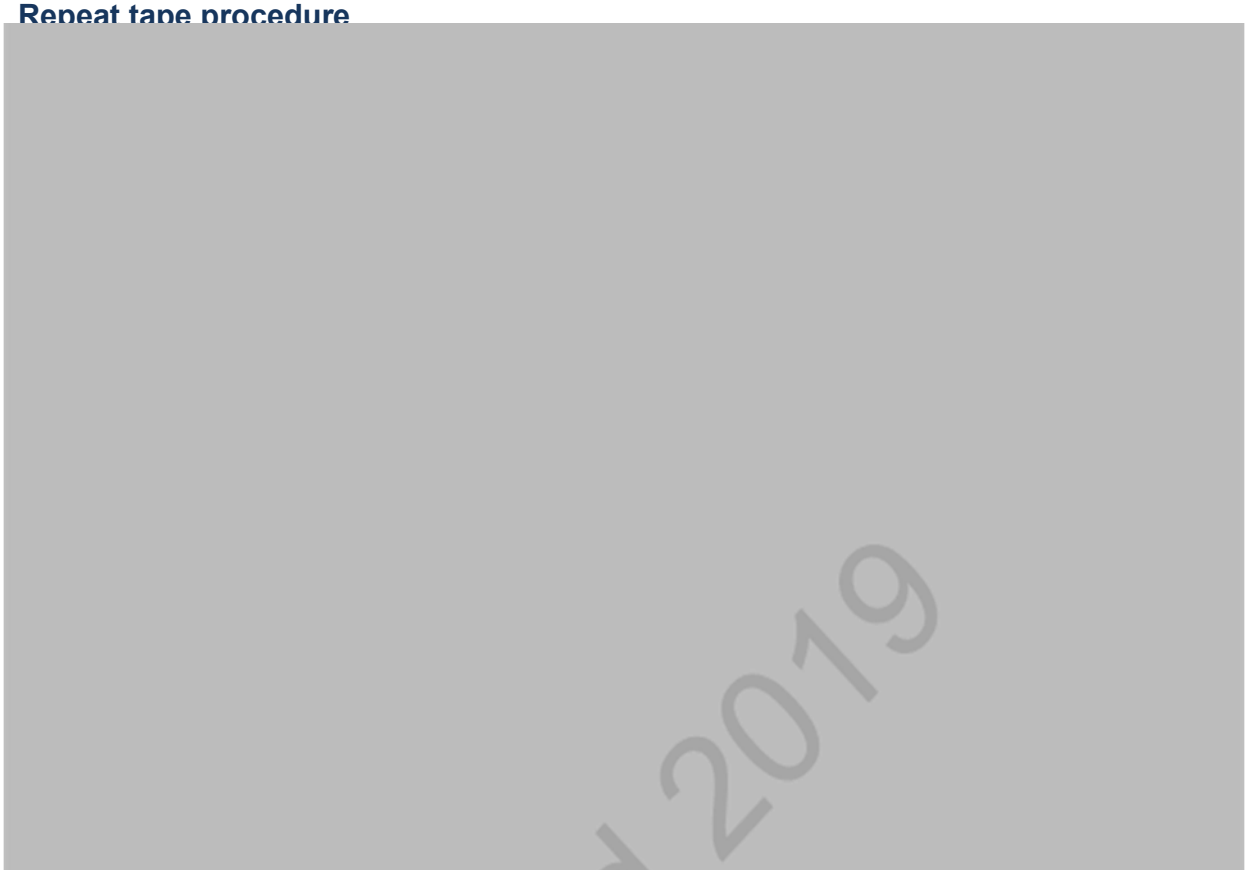
- secondary procedures following primary tape failure
- secondary procedures following complications of the primary tape.

The evidence is presented in GRADE tables with accompanying descriptions of included studies and evidence statements:

- repeat tape procedure (seven studies)
- laparoscopic Burch colposuspension (one study)
- open Burch colposuspension (one study)
- bulking agent injection (one study)
- tape shortening procedure (two studies)
- re-suturing following erosion (one study)
- tape adjustment for voiding problems or retention (three studies).

9.5.1 Secondary procedures following primary tape failure

Repeat tape procedure



No of studies	Relative effects (range of events)	Quality
No studies identified		
Self-reported rate of absolute reduction in symptoms		
No studies identified		
Continence status		
7 (Eandi et al., 2008; Han et al., 2012; Lee et al., 2007; Liapis et al., 2009; Palva & Nilsson, 2009; Sabadell et al., 2011; VanBaelen & Delaere, 2009)	52% to 84%	Very low
Incontinence-specific quality of life – urinary incontinence severity score (better indicated by lower values)		
1 (Palva & Nilsson, 2009)	Median scores changed from 60 (15 to 85) to 5 (0 to 60)	Very low
Incontinence-specific quality of life – incontinence – quality of life (better indicated by higher values)		
1 (VanBaelen & Delaere, 2009)	Median scores changed from 18 (no range reported) to 6 (no range reported)	Very low
Adverse effects – Tissue injury		
1 (Liapis et al., 2009)	3.2%	Very low
Adverse effects – Tape erosion		
1 (VanBaelen & Delaere, 2009)	0%	Very low
Adverse effects – Urinary retention		
1 (Lee et al., 2007)	0%	Very low
Adverse effects – Voiding dysfunction		
4 (Han et al., 2012; Lee et al., 2007; Liapis et al., 2009; Sabadell et al., 2011)	2.8% to 10.3%	Very low
Adverse effects – de novo OAB symptoms		
5 (Han et al., 2012; Lee et al., 2007; Liapis et al., 2009; Sabadell et al., 2011; VanBaelen & Delaere, 2009)	9.1% to 21.7%	Very low

- psychological outcomes
- clinical outcomes.

Continence status

A review of seven studies reported that up to 84% of women were continent after the repeat tape procedure. The evidence was very low quality.

Incontinence specific quality of life

Two studies found conflicting evidence of improved quality of life from the repeat tape procedure. The evidence was very low quality

Adverse effect – Tissue injury

A single study found up to 3% of women suffered tissue injury due to the repeat tape procedure. The evidence was very low quality.

Adverse effects – Tape erosion

A single study reported no instances of tape erosion following the repeat tape procedure. The evidence was very low quality.

Adverse effects – Urinary retention

A single study reported no instances of urinary retention following the repeat tape procedure. The evidence was very low quality.

Adverse effects – Voiding dysfunction

A review of four studies found that up to 10% of women suffered from voiding dysfunction after the repeat tape procedure. The evidence was very low quality.

Adverse effects – De novo OAB symptoms

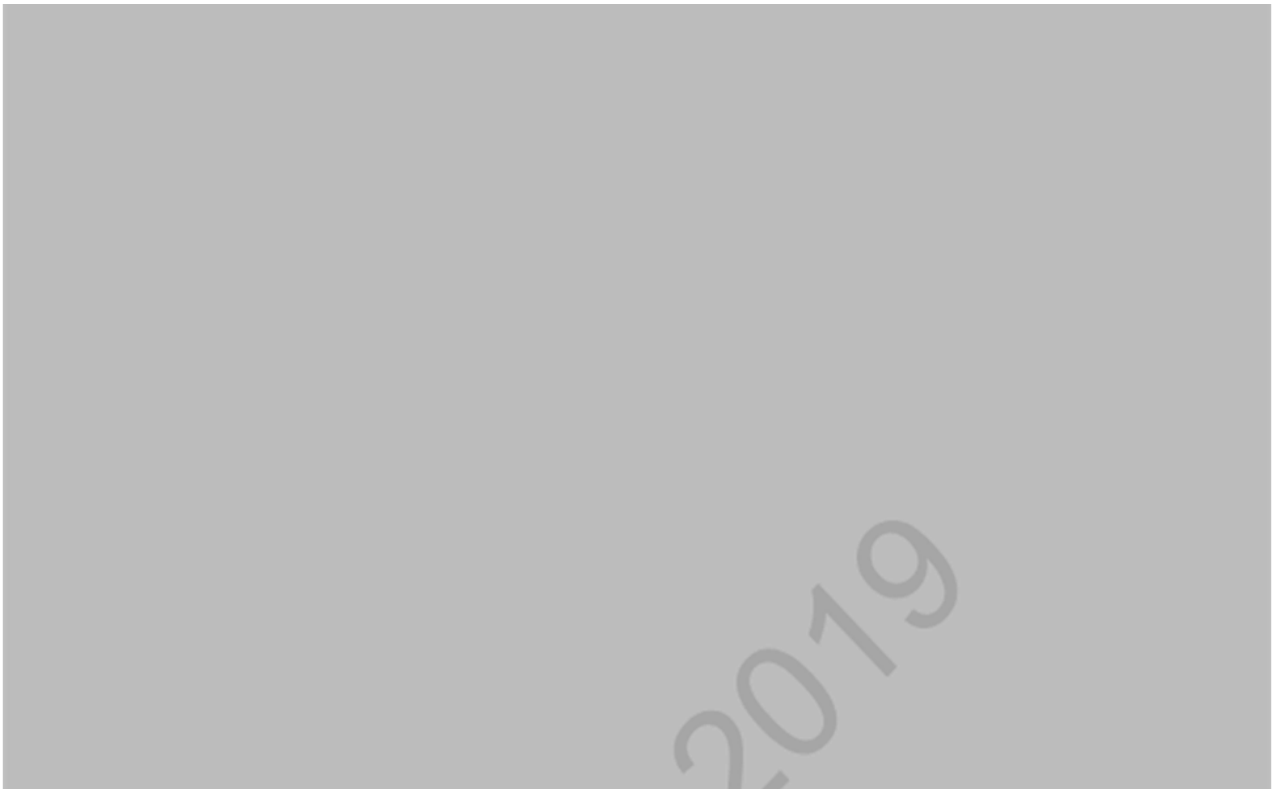
A review of five studies found that up to 21% of women developed *de novo* OAB symptoms after the repeat tape procedure. The evidence was very low quality.

Laparoscopic Burch colposuspension

Description of included studies

One study (de Cuyper, 2008) was identified. The mean age of participants was 51.9 years (SD 8.9). The mean number of incontinence episodes and mean duration of symptoms were not reported in any of the four studies. Seven (50.0%) woman had occasional (less than 1 per week) urge incontinence symptoms in the pre-operative period while six (42.9%) women had frequent (more than 1 per week) urge incontinence symptoms in the pre-operative period.

The primary procedure was retropubic ‘bottom-up’ in eight (50.0%) women, transobturator ‘inside-out’ in two (12.5%) of women and intravaginal slingplasty (IVS) in six (37.5%) women.



No of studies	Relative effects (range of events)	Quality
urinary stress incontinence: a prospective randomised multicentre study comparing the retropubic and transobturator routes, European Urology, 51, 795-802, 2007 David-Montefiore et al., 2006 David-Montefiore,E., Frobert,J.L., Grisard-Anaf,M., Lienhart,J., Bonnet,K., Poncelet,C., Darai,E., Peri-operative complications and pain after the suburethral sling procedure for urinary stress incontinence: a French prospective randomised multicentre study comparing the retropubic and transobturator routes, European Urology, 49, 133-138, 2006 deCuyper et al., 2008)		
Self-reported rate of absolute reduction in symptoms		
No evidence reported		
Continence status		
1 (Darai et al., 2007 Darai,E., Frobert,J.L., Grisard-Anaf,M., Lienhart,J., Fernandez, H., Duberand, G,.David-Montefiore,E. Functional results after the suburethral sling procedure for urinary stress incontinence: a prospective randomised multicentre study comparing the retropubic and transobturator routes, European Urology, 51, 795-802, 2007 David-Montefiore et al., 2006 David-Montefiore,E., Frobert,J.L., Grisard-Anaf,M., Lienhart,J., Bonnet,K., Poncelet,C., Darai,E., Peri-operative complications and pain after the suburethral sling procedure for urinary stress incontinence: a French prospective randomised multicentre study comparing the retropubic and transobturator	55.0%	Very low

No of studies	Relative effects (range of events)	Quality
routes, European Urology, 49, 133-138, 2006 deCuyper et al., 2008)		
Incontinence-specific quality of life		
No evidence reported		
Adverse effect – Tissue injury		
No evidence reported		
Adverse effect – Tape erosion		
No evidence reported		
Adverse effects – Urinary retention		
1 (Darai et al., 2007 Darai,E., Frobert,J.L., Grisard-Anaf,M., Lienhart,J., Fernandez, H., Duberand, G,.David-Montefiore,E. Functional results after the suburethral sling procedure for urinary stress incontinence: a prospective randomised multicentre study comparing the retropubic and transobturator routes, European Urology, 51, 795-802, 2007 David-Montefiore et al., 2006 David-Montefiore,E., Frobert,J.L., Grisard-Anaf,M., Lienhart,J., Bonnet,K., Poncelet,C., Darai,E., Peri-operative complications and pain after the suburethral sling procedure for urinary stress incontinence: a French prospective randomised multicentre study comparing the retropubic and transobturator routes, European Urology, 49, 133-138, 2006 deCuyper et al., 2008)	9.1%	Very low
Adverse effects – Voiding dysfunction		
No evidence reported		
Adverse effects – *de novo* OAB symptoms		
1 (Darai et al., 2007 Darai,E., Frobert,J.L., Grisard-Anaf,M., Lienhart,J., Fernandez, H., Duberand,	9.1%	Very low

No of studies	Relative effects (range of events)	Quality
G,.David-Montefiore,E. Functional results after the suburethral sling procedure for urinary stress incontinence: a prospective randomised multicentre study comparing the retropubic and transobturator routes, European Urology, 51, 795-802, 2007 David-Montefiore et al., 2006 David-Montefiore,E., Frobert,J.L., Grisard-Anaf,M., Lienhart,J., Bonnet,K., Poncelet,C., Darai,E., Peri-operative complications and pain after the suburethral sling procedure for urinary stress incontinence: a French prospective randomised multicentre study comparing the retropubic and transobturator routes, European Urology, 49, 133-138, 2006 deCuyper et al., 2008)		
Psychological outcomes		
No evidence reported		
Clinical outcomes		
No evidence reported		

OAB overactive bladder, SD standard deviation

Evidence statements

No studies were identified which reported the following outcomes:

- self-reported rate of absolute symptom reduction
- incontinence-specific quality of life
- tissue injury
- tape erosion
- voiding dysfunction
- psychological outcomes

Adverse effect – Urinary retention

One study reported that up to 9% of women suffered from urinary retention following laparoscopic Burch colposuspension after a failed primary tape procedure. The evidence was very low quality.

Adverse effect – De novo OAB symptoms

One study reported that up to 9% of women developed *de novo* OAB symptoms following laparoscopic Burch colposuspension after a failed primary tape procedure. The evidence was very low quality.

Open Burch colposuspension

Description of included studies

One study (Giarenis et al., 2012) was identified. The mean age of participants was 55.3 years (SD 9.61) years. The mean number of incontinence episodes and mean duration of symptoms were not reported. Three (23%) of the women had detrusor overactivity symptoms.

The primary procedure was retropubic 'bottom-up' in eight (61%) women and transobturator 'inside-out' in five (39%) of women.

No funding source was reported for this study.

Evidence profile

Table 9.20 GRADE findings for a Burch colposuspension

No of studies	Relative effects (range of events)	Quality
Patient satisfaction with treatment – using a 0–10 visual analogue scale		
No evidence reported		
Self-reported rate of absolute reduction in symptoms		
No evidence reported		
Continence status (zero episodes per day)		
1 (Giarenis et al., 2012)	76.9%	Very low
Incontinence-specific quality of life		
No evidence reported		
Adverse effect – Tissue injury		
No evidence reported		
Adverse effect – Tape erosion		
No evidence reported		
Adverse effect – Urinary retention		
No evidence reported		
Adverse effect – Voiding dysfunction		
1 (Giarenis et al., 2012)	7.7%	Very low
Adverse effects – de novo OAB symptoms		
1 (Giarenis et al., 2012)	40%	Very low
Psychological outcomes		
No studies identified		
Clinical outcomes		

Number of studies	Number of women		Relative effects (range of events)	Quality
	Comparator	Control		
No evidence reported				
Continence status				
1 (Lee et al., 2010a)	8	23	34.6%	Very low
Incontinence-specific quality of life (better indicated by lower values)				
1 (Lee et al., 2010a)	Increased by a mean of 19.2 points (no SD reported)			Very low
Psychological outcomes				
No evidence reported				
Clinical outcomes – post-void residual volume				
1 (Lee et al., 2010a)	Changed from a mean of 31.0 (SD 50.7) to 30.8 (SD 41.8)			Very low
Tissue injury				
No evidence reported				
Erosion rate				
No evidence reported				
Retention				
No evidence reported				
***De novo* overactive bladder symptoms**				
No evidence reported				
Voiding dysfunction				
No evidence reported				

SD standard deviation

Evidence statements

No studies were identified which reported the following outcomes:

- self-reported rate of absolute symptom reduction
- tissue injury
- urinary retention
- voiding dysfunction
- *de novo* OAB symptoms

Incontinence-specific quality of life

One study contributed data to this analysis. The injection of bulking agents resulted in an improvement that met the published minimal important difference (MID) for the scale. The evidence was of low quality.

Clinical outcomes

One study contributed data to this analysis. The injection of bulking agents did not lead to a significant change in post-void residual volume. The evidence was of low quality.

Tape shortening

Description of included studies

Two studies (Han et al., 2012, Lo et al., 2006) met the inclusion criteria for this analysis. The mean age of women ranged from 48.7 years (no SD, range 41 to 57) to 53.4 years (SD 7.6). The mean number of incontinence episodes and mean duration of symptoms were not reported. There were no reported urge incontinence symptoms in the pre-operative period.

The primary tape procedure was retropubic 'outside-in' in one study (Lo et al., 2006) and varied in the second (Han et al., 2012).

The funding source was not reported for either study.

Evidence profile

Table 9.22 GRADE findings for a tape shortening procedure

No of studies	Relative effects (range of events)	Quality
Patient satisfaction with treatment		
No evidence reported		
Self-reported rate of absolute reduction in symptoms		
No evidence reported		
Continence status (zero episodes per day)		
2 (Han et al., 2012; Lo et al., 2006)	47% to 71%	Very low
Incontinence-specific quality of life		
No evidence reported		
Adverse effects – Tissue injury		
No evidence reported		
Adverse effects – Urinary retention		

Evidence statements

No studies were identified which reported the following outcomes:

- patient satisfaction with treatment
- self-reported rate of absolute symptom reduction
- incontinence-specific quality of life
- tissue injury
- urinary retention
- voiding dysfunction
- psychological outcomes
- clinical outcomes.

Continence status

Two studies contributed data to this analysis. The findings did not meet the GDG's agreed threshold for effectiveness. The evidence was of very low quality.

Adverse effect – De novo OAB symptoms

One study reported that up to 15% of women developed *de novo* OAB symptoms following tape shortening after a failed primary tape procedure. The evidence was very low quality

9.5.3 Secondary procedure following complications of primary tape procedure

Re-suturing following erosion

Description of included studies

One case-series (Kuhn et al., 2003) met the inclusion criteria for this analysis. The median (range) age of participants was 52 years (range 43 to 79). The mean number of incontinence episodes and mean duration of symptoms were not reported. There were no reported urge incontinence symptoms in the pre-operative period.

The primary tape procedure was retropubic 'bottom-up' in five (23.8%) of women, transobturator 'outside-in' in six (28.6%) women, transobturator 'inside-out' in five (23.8%) women, subrapubic arc sling (SPARC) in four (19.0%) of women and was not specified in one (4.8%) woman.

Adverse effects
No evidence reported
Psychological outcomes
No evidence reported
Clinical outcomes
No evidence reported

Evidence statements

No studies were identified which reported the following outcomes:

- patient satisfaction with treatment
- self-reported rate of absolute symptom reduction
- incontinence-specific quality of life
- adverse effects
- psychological outcomes
- clinical outcomes.

Continence status

One study was identified. The study reported that re-suturing to rectify erosion was effective. The evidence was of very low quality.

Tape adjustment following voiding problems or retention

Description of included studies

Three studies (Agnew et al., 2012, Molden et al., 2010, Schmid et al., 2010) met the inclusion criteria for this analysis. The age ranged from a mean of 57.7 years (SD 13.7) to a median (range) of 64 years (range 43 to 85), however age was not reported in Agnew et al., 2012. The mean number of incontinence episodes and mean duration of symptoms were not reported. There were no reported urge incontinence symptoms in the pre-operative period.

The primary tape procedure was varied in the three studies.

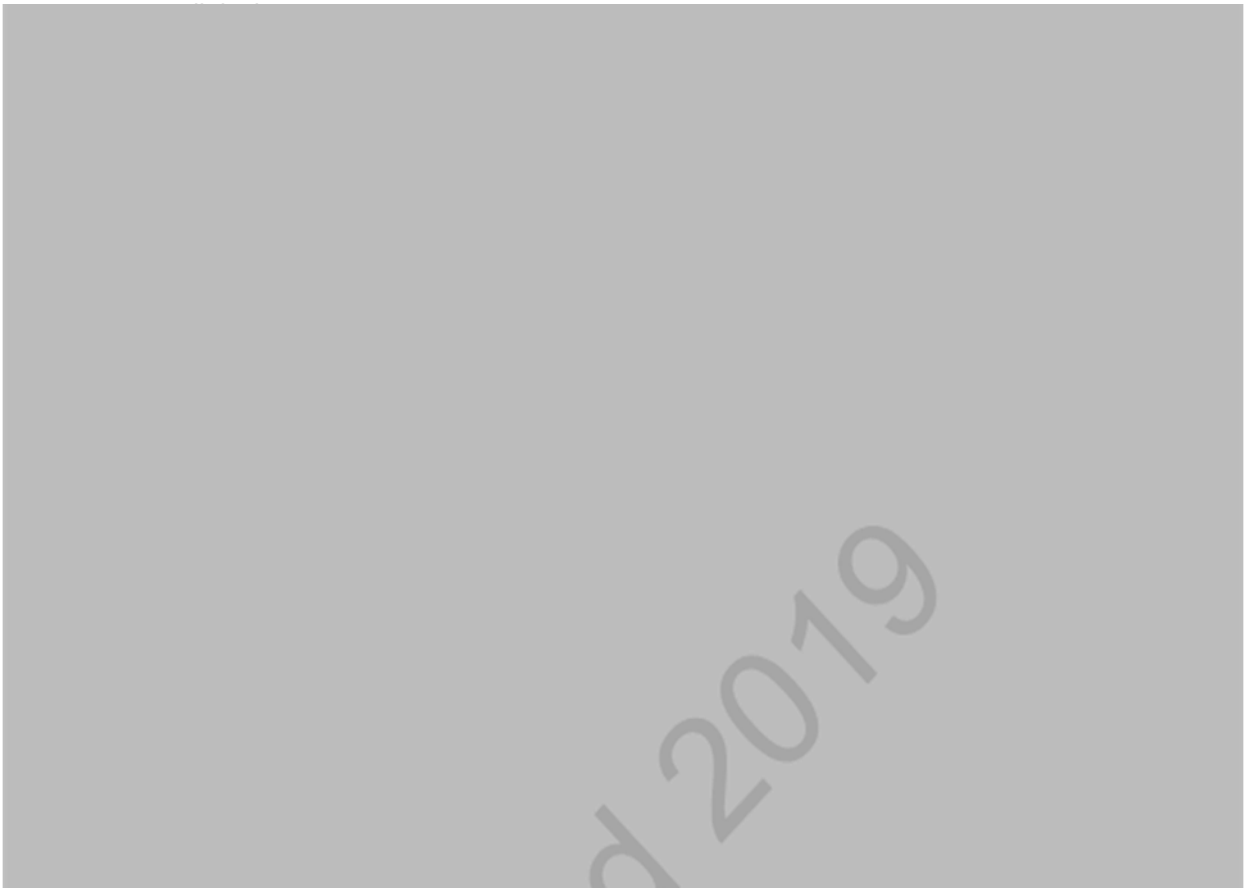
No evidence reported		
Adverse effects – Tissue injury		
No evidence reported		
Adverse effects – Urinary retention		
No evidence reported		
Adverse effects – Voiding dysfunction		
2 (Agnew et al., 2012; Molden et al., 2010)	12.7% to 19.1%	Very low
Adverse effects de novo OAB symptoms		
No evidence reported		
Psychological outcomes		
No evidence reported		
Clinical outcomes		
No evidence reported		

OAB overactive bladder

Evidence statements

No studies were identified which reported the following outcomes:

- patient satisfaction with treatment
- self-reported rate of absolute symptom reduction
- incontinence-specific quality of life
- tissue injury
- urinary retention
- *de novo* OAB symptoms
- psychological outcomes



Consideration of clinical benefits and harms

Surgical procedures for the treatment for SUI following an unsuccessful period of expectant management) have been shown to be effective (see Section 9.2). Despite high success rates for these procedures, a proportion of women will require secondary procedures following unsuccessful initial treatment. For example, the most common initial procedure, the mid-urethral tape, has an estimated 5% revision rate of which 2% of women require a secondary surgical procedure.

Only retropubic 'bottom-up' and tape-shortening procedures were effective after a primary procedure had failed. Where a secondary procedure was required due to complications rather than failure, resuturing and tape adjustment were effective. However, the evidence was not sufficiently robust to recommend which secondary procedure should be offered following any unsuccessful primary procedure. Furthermore, the GDG could not recommend a procedure after a specific primary procedure failure because of the evidence limitations (see below).

Consideration of health benefits and resource uses

The GDG concluded that the cost of the procedures would not differ widely as they all require similar resources and surgical theatre time. This rationale was based on the similar discussion for primary surgical options, where the costs, time and chance of revision would be similar for the different options.

The GDG considered that the decision to continue treatment would have a wider-reaching health economic impact than the choice of intervention. The GDG felt that a tertiary MDT will look at complex cases involving bladder, urethral, prolapse disorders including recurrent disease and complications following invasive therapy for OAB and/or SUI treatments. The considerations of the tertiary MDT should include the risk of the procedure, particularly if it is deemed that the women has had numerous surgeries previously or there is a clinical concern that any subsequent procedures have a reduced chance of success or a carry a potential risk to the woman requiring life-long care. However, it was not possible to quantify these differences with the current state of knowledge about the use of these procedures in repeat operations.

procedures. The MDT should have enough experience to assist the patient's choice of treatment appropriately. Therefore each team should expect to see a minimum of 20 secondary SUI cases per year to qualify for this role. The centralisation of such cases would also enable robust research into the optimal care for such patients. MDTs should be working within an established regional clinical network to ensure that all patients are offered the appropriate options and high quality care.

Conservative management

No data were found on the effectiveness of conservative management following unsuccessful primary tape procedure. The GDG was therefore unable to recommend offering conservative treatment again and agreed that more research is required. The GDG has, therefore, made a research recommendation to explore the role of conservative management as an alternative to further invasive treatment following an unsuccessful initial surgical procedure for SUI.

Recommendations

Number	Recommendation
107	Women whose primary surgical procedure for SUI has failed (including women whose symptoms have returned) should be: • referred to tertiary care for assessment (such as repeat urodynamic testing including additional tests such as imaging and urethral function studies) and discussion of treatment options by the MDT, **or** • offered advice as described in recommendation 51 if the woman does not want continued invasive SUI procedures. **[new 2013]**

Number	Research recommendations
RR19	What is the effectiveness of a repeat procedure following primary tape failure?
RR20	What is the effectiveness of re-suturing following vaginal tape erosion?

2013

Knowledge

- specific indications for surgery
- required preparation for surgery including preoperative investigations
- outcomes and complications of proposed procedure
- anatomy relevant to procedure
- steps involved in procedure
- alternative management options
- likely postoperative progress.

Other generic skills

- be able to explain procedures and possible outcomes to patients and family and to obtain informed consent
- possess the necessary hand–eye dexterity to complete the procedure safely and efficiently, with appropriate use of assistance
- be able to communicate with and manage the operative team effectively
- be able to prioritise interventions.

Attitude

- be able to recognise when to ask for advice from others
- demonstrate commitment to multidisciplinary team working with other health professionals involved in the care of women with UI.

A surgeon is expected to be able to perform an operation without supervision and be able to deal with the complications of that operation before he/she can be considered competent to perform it. The procedure should form part of his/her routine practice.

Existing surgeons should be able to demonstrate that their training, experience and current practice equates to the standards laid out for newly trained surgeons. They should work within the context of an integrated continence service, as recommended in the Department of Health's *Good Practice in Continence Services* (2000).[34]

Some aspects of continence surgery are likely to require a higher level of training than other procedures, which applies particularly to secondary surgical procedures. These procedures should be carried out in centres that are able to maintain their expertise and achieve good outcome for their patients[34] e.g. artificial urinary sphincter, urinary diversion, sacral nerve stimulation, augmentation cystoplasty and complex stress incontinence surgery.

10.3 Maintaining and measuring expertise and standards for practice

Surgeons undertaking continence surgery should be aware of and follow best practice in the management of UI, as laid out in this guideline. Surgeons should conform to standards of good medical practice (General Medical Council) and good surgical practice (Royal College of Surgeons). They should also conform to the standards of good practice as laid out by the British Association of Urological Surgeons Section of Female and Reconstructive Urology (BAUS-SFRU) and the British Society of Urogynaecology (BSUG), namely:

- Before undertaking new procedures surgeons must notify their trust's clinical governance committee.
- Before utilising new materials or devices in previously established procedures, the trust's clinical governance committee should be informed.
- Any intention to undertake an evaluation of a new procedure should be registered with a relevant clinical trials database.
- The development of new techniques or modifications of established techniques should receive appropriate local ethical and clinical governance approval. New techniques are defined by NICE (Department of Health *Health Services Circular* 2003/011, 13/11/03) as one where 'a doctor no longer in a training post is using it for the first time in his or her NHS clinical practice'.
- A surgeon who encounters a serious adverse event related to the use of a device or implant, in the treatment of incontinence, should notify the Medicines and Healthcare products Regulatory Agency (MHRA) through its Serious Adverse Event (SAE) reporting process.
- New procedures/classes of procedure should be notified to the Interventional Procedures Programme at NICE through the NICE website.

Measuring competence

For established surgeons, the best way to measure continuing competence is through comparative audit. All surgeons should have access to information about their personal results for continence surgery. This should include data on perioperative complications and long-term outcomes. They should also be able to compare those outcomes with the experience of others through national audit.

Examples of this include the databases set up by BSUG and BAUS-SFRU. Both systems offer the facility for surgeons to record every operation they do for incontinence, and are freely available for members of those organisations, although neither is well utilised at present.

Volume–outcome research

The necessary surgical volume of any operation required to maintain competence is inadequately defined. The volume–outcome relationship has been considered in many clinical areas, such as cardiology, gastroenterology, orthopaedics, ophthalmology and breast cancer surgery, but little evaluation has been undertaken in relation to continence surgery. In systematic reviews of this research, many methodological concerns have been raised over what is considered to be a heterogeneous body of research, consisting of observational studies. Most studies retrospectively analyse routinely collected data and are not designed to analyse the complex volume–outcome relationship, which leads to many problems when interpreting the data, namely:[921–923]

- inadequate consideration of confounders such as the effects of differences in case-mix and appropriateness of case selection on outcomes
- volume can relate to hospital or surgeon
- narrow outcomes are used in most studies, usually adverse (e.g. inpatient or 30 day mortality)
- thresholds for, or definitions of, high and low volume across and within procedures differ
- causality – it is unclear whether high volume–improved outcome relationships result from greater experience or whether the highest referral rate tends to be to those surgeons or

Although the evidence tends to suggest that higher volume is associated with better outcomes, the consistency and size of the effect varies for different procedures. A systematic review of 135 studies found a significant association between higher volume (hospital or surgeon) and better outcomes in about 70% of studies; none of the studies found a significant association between higher volume of any type of surgery and poorer outcome.[922] In these studies, the definition of low or high volume varied according to the procedure, with median low volumes of up to 100–200 for coronary angioplasty or coronary artery bypass graft surgery; and median low volume values ranging from 1 to 73 for other procedures described (mainly in the region of 10–30).[922]

Secondary surgery is unusual and can be technically challenging, and a centralisation argument probably applies. The centralisation argument holds that 'practice makes perfect' so concentration of cases into one centre that can carry out larger numbers of procedures will result in higher standards, not just in surgical technique, but also postoperative care.

Evidence for the effects of volume or hospital status on outcome of continence surgery

A few studies have reported the outcomes of continence surgery according to the volume of surgery undertaken. With the methodological issues relating to such studies in mind, the findings are described below.

A UK cohort study attempted to identify risk factors predictive of successful outcome 1 year after surgery for stress UI (colposuspension, anterior colporrhaphy or needle suspension). The outcomes considered were complications, symptom severity index, symptom impact index and activities of daily living. The number of cases performed by surgeons per year (20–42 versus 1–19) was not found to be associated with risk of a better or worse outcome (n = 232).[125,126] [EL = 2+]

Some information on volume–outcomes is available for retropubic 'bottom-up' tapes. One case series considered the cure rates for each of the ten surgeons who undertook the retropubic 'bottom-up' tape procedure, which ranged from 72% to 92% and were not significantly associated with the number of procedures performed (11–250 per surgeon).[812] From the Finnish national data on retropubic 'bottom-up' tapes, it was estimated that the incidence of complications was 40% in hospitals where 15 or fewer operations had been undertaken, and about 14% in centres performing more than 15 operations.[813] [EL = 3]

Subgroup analysis of some aspects of the UK retropubic 'bottom-up' tape /colposuspension RCT[659,660] was undertaken, including volume–outcome and recruitment numbers, although the study was not powered to do so.[924] It is difficult to put the numbers into context because those cases represent only a proportion of the continence surgery undertaken in those centres. Objective cure rates were higher for centres recruiting most patients; the categories analysed being more than 30 patients, 21–30, or fewer than 20. While it must be conceded that the effect of drop-outs on an intention-to-treat analysis is greater on units recruiting small numbers of patients, it may nevertheless be the case that there is a minimum workload consistent with optimal surgical outcome.

Other studies reflected on the learning curve with the retropubic 'bottom-up' tape procedure. Three studies observed that the complication rate,[744,772,804] or specifically bladder injury,[925] was relatively higher during the surgeon's learning curve, the threshold/definition for which differed across the studies, from the first 5, 10–20, 50 or 100 procedures.

A survey of consultants performing continence surgery in the UK in 2001 was carried out in order to establish the type and volume of surgery undertaken, the nature of postoperative complications, investigations, and follow-up (n = 578; 54% response rate). The profile of respondents was general gynaecologists (40%), gynaecologists with a special interest in urogynaecology (31%), urologists (25%), subspecialist urogynaecologists (3%), with 2% not classified. Half the respondents stated that fewer than 50 procedures per year were adequate for good surgical results, whereas the other half considered that more than 50 procedures a year were necessary. The majority specialty view was 10–20 procedures per year (61% general gynaecologists and 59% urologists), or 20–50 per procedures per year (68% urogynaecology subspecialists and 61% gynaecologists with a special interest).[926] [EL =

and 28% performed over 25 during that year. Performing 10–20 cases of retropubic 'bottom-up' tape under supervision was considered by 46% of surgeons in this survey to constitute adequate training, and 43% suggested that 20–50 cases of retropubic 'bottom-up' tape are required to gain competence.[817] [EL = 3]

Hospital status

There is some conflicting evidence that outcomes relate in part to the training status of the institution in which they are performed. In the USA, teaching centres have been shown to have higher 30-day morbidity (predominantly wound complications) across a range of specialties (general surgery, orthopaedics, urology, and vascular surgery) than non-teaching centres. Mortality was not significantly different between centres for any of the seven specialties evaluated.[927] [EL = 2+]

Two studies considered outcome of continence surgery by hospital status (teaching versus nonteaching); exactly what is meant by 'teaching' hospitals is not clear. The risk of having complications from continence surgery was not significantly associated with hospital status in a UK cohort study (on multivariate analysis).[125,126] [EL = 2+] A case series of retropubic 'bottom-up' tape reported that the risk of postoperative complications with a retropubic 'bottom-up' tape was higher when undertaken in teaching hospitals than in non-teaching hospitals (24% versus 16%; OR 0.55, 95% CI 0.35 to 0.85) (n = 809).[804] [EL = 3] While the studies report these observations, they do not explain the possible causes of the results seen. This may relate to overall case load, case mix (i.e. number of complex or secondary cases) or the impact of training on outcomes.

Evidence statements for competence of surgeons

There are limited data regarding the number of procedures required to learn any particular operation used in the management of urinary incontinence. There is similarly little evidence on annual workload required to maintain skills, optimise outcome and minimise morbidity. [EL = 4] From a survey of consultants performing continence surgery in the UK, the majority specialty view was that either 10–20 or 20–50 procedures per year are adequate for good surgical results. [EL = 3]

From evidence to recommendations

The GDG drew on the requirements for training schemes in gynaecology and urology in the UK to develop recommendations for training standards. The BAUS-SFRU and BSUG are currently developing training schemes and structured assessment methods specific for those undertaking continence surgery.

Cystourethroscopy is considered an integral part of several procedures used in the treatment of UI. Training in this technique is therefore deemed crucial to surgical competence in this area.

In relation to maintaining competence, the GDG agreed by consensus that a workload of 20 cases per procedure per annum was an appropriate volume, which was also supported by the survey of UK consultants. A volume of cases per procedure was recommended because a workload in one procedure does not necessarily maintain skills for other procedures. The minimum volume recommended was also agreed by GDG consensus.

Audit is an integral part of clinical governance. Regular audit of outcomes of continence surgery is considered essential to maintaining standards of practice.

Recommendations

Number	Recommendation
108	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 an MDT with this training, and who regularly carry out surgery for UI in women. [**2006]**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12 Abbreviations and glossary

12.1 Abbreviations

ADL	activities of daily living
AE	adverse effects
AFR	acceleration of flow rate
ALPP	abdominal leak point pressure
AM	ambulatory monitoring
AUS	artificial urinary sphincter
BAUS–SFRU	British Association of Urological Surgeons Section of Female and Reconstructive Urology
b.d.	to be taken twice a day (bis die)
BFLUTS	Bristol Female Urinary Tract Symptoms (questionnaire)
BMI	body mass index
BNF	British National Formulary
BOA	basic office assessment
BSUG	British Society of Urogynaecology
CEE	conjugated equine oestrogens
CI	confidence interval
CIC	clean intermittent catheterisation
CISC	clean intermittent self-catheterisation
CNS	central nervous system
CT	computed tomography
DB	double-blind
DDAVP	desmopressin
DO	detrusor overactivity
DS	diagnostic study
EL	evidence level (level of evidence)
EMG	electromyography
ER	extended release
ES	electrical stimulation
FB	Fluid-Bridge
GA	general anaesthesia

GDG	guideline development group
GP	general practitioner
GPP	good practice point
HRT	hormone replacement therapy
HTA	health technology assessment
ICER	incremental cost effectiveness ratio
ICI	International Consultation on Incontinence
ICIQ	International Consultation on Incontinence questionnaire
ICS	International Continence Society
IIQ	incontinence impact questionnaire
IP	Interventional Procedures (see IPAC)
IPAC	Interventional Procedures Advisory Committee (of NICE)
I-QOL	Incontinence Quality-of-Life (questionnaire)
IQR	interquartile range
IR	Immediate release
ISC	intermittent self-catheterisation
ISD	intrinsic sphincter deficiency
ISI	incontinence severity index
ITT	intention-to-treat analysis
IVS	intravaginal slingplasty
KHQ	King's Health Questionnaire
LA	local anaesthesia
LOCF	last observation carried forward
LPP	leak point pressure
LUTS	lower urinary tract symptoms
MC	multichannel (cystometry)
MDT	multidisciplinary team
MHRA	Medicines and Healthcare products Regulatory Agency
MMK	Marshall–Marchetti–Krantz
MMSE	Mini Mental State Examination
MPA	medroxyprogesterone acetate
MRI	magnetic resonance imaging
MUCP	maximum urethral closure pressure
MUI	mixed urinary incontinence
n	number of patients
NA	not applicable
NCC-WCH	National Collaborating Centre for Women's and Children's Health
NHS	National Health Service

NICE	National Institute for Health and Care Excellence
NPV	negative predictive value
NS	not statistically significant
OAB	overactive bladder
OAB-q	overactive bladder questionnaire
o.d.	to be taken once daily
OR	odds ratio
PCT	primary care trust
PFMT	pelvic floor muscle training
PFM	pelvic floor muscle
PGI-I	patients global impression of improvement
PNE	percutaneous nerve evaluation
POP	pelvic organ prolapse
POP-Q	pelvic organ prolapse quantification system
PPIP	Patient and Public Involvement Programme
PPV	positive predictive value
PTFE	polytetrafluoroethylene
P-PTNS	percutaneous posterior tibial nerve stimulation
P-SNS	percutaneous sacral nerve stimulation
PTR	pressure transmission ratio
PVR	post void residual
pt(s)	patient(s)
QALY	quality adjusted life year
q.d.s.	to be taken four times a day (quarter die sumendus)
QOL	quality of life
r	correlation coefficient
RCT	randomised controlled trial
RR	relative risk
SA	spinal anaesthesia
SB	single-blind
SD	standard deviation
SE	standard error
SF-36	Short form 36
SIGN	Scottish Intercollegiate Guidelines Network
SII	symptom impact index
SNS	sacral nerve stimulation
SPARC	suprapubic arc sling
SSI	symptom severity index

SUI	stress urinary incontinence
SUIQQ	stress and urge incontinence quality of life questionnaire
t.d.s.	to be taken three times a day (ter die sumendus)
TENS	transcutaneous electrical nerve stimulation
TOT	transobturator tape
TVT	tension-free vaginal tape
T-PTNS	transcutaneous postier tibial nerve stimulation
T-SNS	transcutaneous sacral nerve stimulaiton
UCP	urethral closure pressure
UD	urodynamics
UDI	urogenital distress inventory (questionnaire)
UI	urinary incontinence
UISS	urinary incontinence severity score
UPP	urethral pressure profile or profilometry
USI	urodynamic stress urinary incontinence
UTI	urinary tract infection
UUI	urge urinary incontinence
VAS	visual analogue scale
VCU	videocystourethrography
VLPP	valsalva leak point pressure
WVC	weighted vaginal cone

12.2 Glossary


Updated 2019


Updated 2019


Updated 2019


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Generalisability	The extent to which the results of a study hold true for a population of patients beyond those who participated in the research. See also external validity.

	usually regarded as homogeneous when differences between studies could reasonably be expected to occur by chance. See also consistency.
Idiopathic	Having no defined cause.

measured, it may be inappropriate or even misleading to statistically pool results in this way. See also systematic review and heterogeneity.

condition or disease for which it is not specifically licensed.

treatment will produce a different point estimate of treatment effect.

P value	If a study is done to compare two treatments then the *P* value is the probability of obtaining the results of that study, or something more extreme, if there really was no difference between treatments. (The assumption that there really is no difference between treatments is called the 'null hypothesis'.) Suppose the *P* value was 0.03. What this means is that if there really was no difference between treatments then there would only be a 3% chance of getting the kind of results obtained. Since this chance seems quite low we should question the validity of the assumption that there really is no difference between treatments. We would conclude that there probably is a difference between treatments. By convention, where the value of *P* is below 0.05 (i.e. less than 5%) the result is seen as statistically significant. Where the value of *P* is 0.001 or less, the result is seen as highly significant. *P* values just tell us whether an effect can be regarded as statistically significant or not. In no way do they relate to how big the effect might be, for which we need the confidence interval.
Quality adjusted life years (QALYs)	A measure of health outcome which looks at both length of life and quality of life. QALYs are calculated by estimating the years of life remaining for a patient following a particular care pathway and weighting each year with a quality of life score (on a zero to one scale). One QALY is equal to 1 year of life in perfect health, or 2 years at 50% health, and so on.
Quantitative research	Research that generates numerical data or data that can be converted into numbers, such as clinical trials or the national census that counts people and households.
Quasi experimental study	A study designed to test whether a treatment or intervention has an effect on the course or outcome of disease. It differs from a controlled clinical trial and a randomised controlled trial in that: (a) the assignment of patients to treatment and comparison groups is not done randomly, or patients are not given equal probabilities of selection; or (b) the investigator does not have full control over the allocation and/or timing of the intervention, but nonetheless conducts the study as if it were an experiment, allocating subjects to treatment and comparison groups.
Random allocation or randomisation	A method that uses the play of chance to assign participants to comparison groups in a research study, such as by using a random numbers table or a computer-generated random sequence. Random allocation implies that each individual (or each unit in the case of cluster randomisation) being entered into a study has the same chance of receiving each of the possible interventions.
Randomised controlled trial (RCT)	A study to test a specific drug or other treatment in which people are randomly assigned to two (or more) groups, with one (the experimental group) receiving the treatment that is being tested and the other (the comparison or control group) receiving an alternative treatment, a placebo (dummy treatment) or no treatment. The two groups are followed up to compare differences in outcomes to see how effective the experimental treatment was. (Through randomisation, the groups should be similar in all aspects apart from the treatment they receive during the study.)
Rectocele	Herniation (protrusion) of the rectum into the vagina.

	With physical assessments it is possible for different clinicians to make independent assessments in quick succession – and if their assessments tend to agree then the method of assessment is said to be reliable.
Retrospective study	A retrospective study deals with the present/past and does not involve studying future events. This contrasts with studies that are prospective.
Review	A summary of the main points and trends in the research literature on a specified topic. A review is considered non-systematic unless an extensive literature search has been carried out to ensure that all aspects of the topic are covered and an objective appraisal made of the quality of the studies.
Risk ratio (RR)	Ratio of the risk of an undesirable event or outcome occurring in a group of patients receiving experimental treatment compared with a comparison (control) group. The term relative risk is sometimes used as a synonym for risk ratio.
Royal Colleges	In the UK medical/nursing world the term Royal Colleges, as for example in 'The Royal College of . . . ' refers to organisations that usually combine an educational standards and examination role with the promotion of professional standards.
Sample	A part of the study's target population from which the subjects of the study will be recruited. If subjects are drawn in an unbiased way from a particular population, the results can be generalised from the sample to the population as a whole.
Sampling	Refers to the way participants are selected for inclusion in a study.
Scottish Intercollegiate Guidelines Network (SIGN)	SIGN was established in 1993 to sponsor and support the development of evidence-based clinical guidelines for the NHS in Scotland.
Secondary care	Care provided in hospitals.
Secondary surgery for stress UI	Surgery for stress urinary incontinence undertaken in a woman who has previously undergone surgery for this condition.
Selection bias	Selection bias has occurred if the characteristics of the sample differ from those of the wider population from which the sample has been drawn or if there are systematic differences between comparison groups of patients in a study in terms of prognosis or responsiveness to treatment.
Selection criteria	Explicit standards used by guideline development groups to decide which studies should be included and excluded from consideration as potential sources of evidence.
Sensitivity	In diagnostic testing, this refers to the chance of having a positive test result given that you have the disease. 100% sensitivity means that all those with the disease will test positive, but this is not the same the other way around. A patient could have a positive test result but not have the disease – this is called a 'false positive'. The sensitivity of a test is also related to its negative predictive value (true negatives) – a test with a sensitivity of 100% means that all those who get a negative test result do not have the disease. To fully judge the accuracy of a test, its specificity must also be considered.
Short form 36 (SF-36)	A generic multipurpose 36-item survey that measures eight domains of health: physical functioning, role limitations due to physical health, bodily pain, general health perceptions, vitality, social functioning, role limitations due to emotional problems, and mental health.

Specialist	A specialist is any healthcare professional who has received appropriate training to be able to provide the particular range of specialist services he or she undertakes, and who works within the context of an integrated, multidisciplinary continence team. Particular service profiles will differ from one place to another.
Specific indication	When a drug or a device has a specific remit to treat a specific condition and is not licensed for use in treating other conditions or diseases.
Specificity	In diagnostic testing, this refers to the chance of having a negative test result given that you do not have the disease. 100% specificity means that all those without the disease will test negative, but this is not the same the other way around. A patient could have a negative test result yet still have the disease – this is called a 'false negative'. The specificity of a test is also related to its positive predictive value (true positives) – a test with a specificity of 100% means that all those who get a positive test result definitely have the disease. To fully judge the accuracy of a test, its sensitivity must also be considered.
Stamey grading of urinary incontinence	Grade 1: urine loss only with coughing/sneezing/lifting heavy objects. Grade 2: urine loss with minimal activities, such as walking or rising from sitting position. Grade 3: totally incontinent in upright position.
Standard deviation (SD)	A measure of the spread, scatter or variability of a set of measurements. Usually used with the mean (average) to describe numerical data.
Statistical power	The ability of a study to demonstrate an association or causal relationship between two variables, given that an association exists. For example, 80% power in a clinical trial means that the study has a 80% chance of ending up with a P value of less than 5% in a statistical test (i.e. a statistically significant treatment effect) if there really was an important difference (e.g. 10% versus 5% mortality) between treatments. If the statistical power of a study is low, the study results will be questionable (the study might have been too small to detect any differences). By convention, 80% is an acceptable level of power. See also P value.
Stress test	A clinical test for the demonstration of stress urinary incontinence. The woman is asked to cough while the observer visualises the external urethral meatus. The test may be undertaken either after filling to a known volume, or prior to micturition, the volume being recorded thereafter. It may be undertaken supine or standing.
Stress urinary incontinence (SUI)	The complaint of involuntary leakage on effort or exertion or on sneezing or coughing.
Structured interview	A research technique where the interviewer controls the interview by adhering strictly to a questionnaire or interview schedule with pre-set questions.
Study checklist	A list of questions addressing the key aspects of the research methodology that must be in place if a study is to be accepted as valid. A different checklist is required for each study type. These checklists are used to ensure a degree of consistency in the way that studies are evaluated.
Study population	People who have been identified as the subjects of a study.
Study quality	See methodological quality.
Study type	The kind of design used for a study. Randomised controlled trials, case–control studies and cohort studies are all examples of study types.
Subject	A person who takes part in an experiment or research study.

Systematic	Methodical, according to plan; not random.
Systematic error	Refers to the various errors or biases inherent in a study. See also bias.
Systematic review	A review in which evidence from scientific studies has been identified, appraised and synthesised in a methodical way according to predetermined criteria. May or may not include a meta-analysis.
Systemic	Involving the whole body.
Target population	The people to whom guideline recommendations are intended to apply. Recommendations may be less valid if applied to a population with different characteristics from the participants in the research study – for example in terms of age, disease state, social background.
Tertiary centre	A major medical centre providing complex treatments which receives referrals from both primary and secondary care. Sometimes called a tertiary referral centre. See also primary care and secondary care.
Timed voiding	Timed voiding (scheduled, routine or regular toileting) is a passive toileting assistance programme that is initiated and maintained by a caregiver, for example for patients who cannot participate in independent toileting. Toileting is fixed by time or event, on a regular schedule, or a schedule to match the patient's voiding pattern.
Trust	A trust is an NHS organisation responsible for providing a group of healthcare services. An acute trust provides hospital services. A primary care trust buys hospital care on behalf of the local population, as well as being responsible for the provision of community health services.
Urethral competence	The ability of the urethral sphincter mechanisms to retain urine in the bladder at all times other than during normal micturition.
Urethral hypermobility	Incompetence of the urethral sphincter mechanisms usually associated with stress incontinence symptoms, due to failure of urethral support.
Urethral pain	Pain felt in the urethra and the patient indicates the urethra as the site.
Urgency urinary incontinence (UUI)	Involuntary urine leakage accompanied by or immediately preceded by urgency (formally known as urge urinary incontinence).
Urgency	The complaint of a sudden compelling desire to pass urine which is difficult to defer.
Urgency-frequency syndrome	Another name for overactive bladder.
Urinary incontinence (UI)	The complaint of any involuntary urinary leakage.
Urodynamics (UD)	The term 'urodynamics' encompasses a number of varied physiological tests of bladder and urethral function that aim to demonstrate an underlying abnormality of storage or voiding. The term is often used loosely to mean multichannel cystometry. See also cystometry and uroflowmetry. Videourodynamics involves synchronous radiographic screening of the bladder with multichannel cystometry and is so called because originally the information was recorded to videotape. Ambulatory urodynamics involves multichannel cystometry carried out with physiological bladder filling rates and using portable recording devices that enable to patient to remain ambulant during the test.
Urodynamic stress urinary incontinence (USI)	The demonstration of involuntary leakage of urine during increased abdominal pressure but in the absence of detrusor contraction during filling cystometry.
Uroflowmetry	Uroflowmetry entails a free-flow void into a recording device that provides the practitioner with information about the volume of urine passed, and the rate of urine flow.


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