Guidelines on Urinary Incontinence

M.G. Lucas, J.L.H.R. Bosch, F. Cruz, T.B. Madden,
A. Nambiar, A. Neisius, R.S. Pickard, D.J.M.K. de Ridder,
A. Tubaro, W.H. Turner

© European Association of Urology 2012

European
Association
of Urology

TABLE OF CONTENTS PAGE

1. INTRODUCTION

Urinary incontinence (UI) is an extremely common complaint in every part of the world. It causes a great deal of distress and embarrassment, as well as significant costs, to both individuals and societies. Estimates of prevalence vary according to the definition of incontinence being used and the populations being studied. However, there is universal agreement about the importance of the problem, both in terms of human suffering and economic costs.

These new Guidelines from the European Association of Urology (EAU) Working Panel on Urinary Incontinence are written by urologists for urologists, and aim to provide sensible and practical guidance on the clinical problems of UI rather than an exhaustive narrative review. Such a review is already available elsewhere, as provided by the International Consultation on Incontinence (1), and so these Guidelines do not mention topics such as the causation, basic science, epidemiology and psychology of UI. The focus of these Guidelines is entirely on assessment and treatment reflecting clinical practice. The Guidelines also do not consider patients with UI caused by neurological disease, as this is covered by complementary EAU Guidelines (2).

The EAU Panel knew that they would find only a little evidence for some issues and a lot of evidence for others. This difference largely reflects the much greater research funding needed to produce the high-quality evidence required for regulatory submissions by the regulated (pharmaceutical) industries and their marketing strategies. The situation regarding published evidence for surgical devices is different, with much more surgical experimentation. However, despite the higher potential for harm, there are far fewer high-quality studies from which to derive clear evidence. There is a high potential for bias in this situation, and so the Panel has deliberately adjusted its expectation for quality evidence, depending on the domain of management being considered, and tried to reflect this in the text.

1.1 Methodology

The Panel decided to rewrite the existing EAU Guidelines on UI using a new methodological approach and to present them in a format that most closely reflected the approach to management of UI. The current Guidelines provide:

- A clear clinical pathway (algorithm) for common clinical problems. This can provide the basis for thinking through a patient's management and also for planning and designing clinical services.
- A brief but reliable summary of the current state of evidence on clinical topics, complete with references to the original text.
- Clear guidance on what to do or not to do, in most clinical circumstances. This should be particularly helpful in those areas of practice for which there is little or no published evidence.

*1.1.1 **PICO questions***

The 'PICO' (Population, Intervention, Comparison, Outcome) framework was used to develop a series of clinical questions that would provide the basis of presentation of the guidelines (3,4). There are four elements to each clinical question:

- population;
- intervention;
- comparison;
- outcome.

The wording is important because it directs the subsequent literature research. For each element, the Panel listed every possible wording variation.

In these Guidelines, four traditional domains of urological practice are presented as separate chapters, namely assessment and diagnosis, conservative management, drug therapy and surgical treatments.

In this first edition of these new EAU Guidelines for Urinary Incontinence, the Panel has focused largely on the management of a 'standard' patient. The Panel has referred in places to patients with 'complicated incontinence', by which we mean patients with associated morbidity, a history of previous pelvic surgery, surgery for UI, radiotherapy and women with associated genitourinary prolapse. This first edition does not review the prevention of UI, the management of fistula, or the special problems of the frail elderly, but these issues will be fully addressed in future editions.

*1.1.2 **Search strategies***

A number of significant narrative reviews and major guidelines and systematic reviews have been produced within the last few years. It was agreed from the start that the literature searches carried out by these reviews

would be accepted as valid. Thus, for each PICO question, a search was carried out with a start date that was the same as the cut-off date for the search associated with the most recent systematic review for the PICO topic. This pragmatic selection approach, while being a compromise and open to criticism, made the task of searching the literature for such a large subject area possible within the available resources. For each section, the latest cut-off date for the relevant search is indicated.

Thus, for each PICO, a subsequent literature search was carried out (confined to Medline and Embase and to English language articles), which produced an initial list of abstracts (*see* Number of 'hits', Table 1). The abstracts were each assessed by two Panel members, who selected the studies relevant to the PICO question, and the full text for these was retrieved.

Table 1: Initial list of abstracts

Chapter	Latest 'cut-off' date for search	Number of 'hits'
Assessment and diagnosis	June 2010	1055
Conservative therapy	July 2010	1026
Drug therapy	February 2011	1162
Surgical therapy	May 2011	2191

Each PICO was then assigned to a Panel member, who read the paper and extracted the evidence for incorporation into standardised evidence tables, which are maintained online as an evidence resource for the Panel. This resource will continue to be available and will be continuously updated with each repeated review of the literature.

The existing evidence from previous systematic reviews and new evidence were then discussed, for each PICO in turn, at a Panel meeting before the Panel came to its conclusions. To help standardise the approach, modified process forms (data extraction and considered judgment) from the Scottish Intercollegiate Guidelines Network (SIGN) were used.

The quality of evidence for each PICO is commented on in the text, which then leads into the development of an evidence summary. This aims to synthesise the important clinical messages from the available literature and is presented as a series of 'evidence summaries', which follow the standard for levels of evidence used by the EAU (Table 2).

From the evidence summaries, the Panel then produced a series of action-based recommendations graded according to EAU standards (Table 3). These grades aim to make it clear what the clinician should or should not do in clinical practice, not merely to comment on what they might do.

The Panel has tried to avoid extensive narrative text. Instead, algorithms are presented for both initial and specialised management of men and women with non-neurogenic UI. Each decision node of these algorithms is clearly linked back to the relevant evidence and recommendations.

It must be emphasised that clinical guidelines present the best evidence available to the expert Panel at the time of writing. There remains a need for ongoing re-evaluation of the current guidelines by the Panel. However, following guidelines recommendations will not necessarily result in the best outcome. Guidelines can never replace clinical expertise when making treatment decisions for individual patients; they aim to focus decisions. Clinical decisions must also take into account the patient's personal values, preferences and specific circumstances.

1.1.3 Level of evidence and grade of recommendation

References used in the text have been assessed according to their level of scientific evidence (Table 2), which is a modification of the system used by the Oxford Centre for Evidence Based Medicine (CEBM). A similar modification has been used for Guidelines recommendations. The aim of grading recommendations is to provide transparency between the underlying evidence and the recommendation given. Diagnostic studies were assessed according to a similar modification of the CEBM evidence levels for diagnostic accuracy and prognosis.

Table 2: Level of evidence (LE)*

Type of evidence	LE
Evidence obtained from meta-analysis of randomised trials.	1a
Evidence obtained from at least one randomised trial.	1b
Evidence obtained from one well-designed controlled study without randomisation.	2a
Evidence obtained from at least one other type of well-designed quasi-experimental study.	2b
Evidence obtained from well-designed non-experimental studies, such as comparative studies, correlation studies and case reports.	3
Evidence obtained from expert committee reports or opinions or clinical experience of respected authorities.	4

**Modified from Sackett et al. (5).*

It should be noted that when recommendations are graded, there is not an automatic relationship between the level of evidence and grade of recommendation. The availability of randomised controlled trials (RCTs) may not necessarily translate into a Grade A recommendation if there are methodological limitations or a disparity in published results.

Alternatively, an absence of high-level evidence does not necessarily preclude a Grade A recommendation; if there is overwhelming clinical experience and consensus to support a high level recommendation, this can be made. In addition, there may be exceptional situations in which corroborating studies cannot be performed, perhaps for ethical or other reasons. In this case, unequivocal recommendations are considered helpful for the reader. Whenever this occurs, it has been clearly indicated in the text with an asterisk, as 'upgraded based on Panel consensus'. The quality of the underlying scientific evidence is a very important factor, but it has to be balanced against benefits and burdens, values and preferences and economic cost when a grade is assigned (6-8).

The EAU Guidelines Office does not perform cost assessments nor can they address local/national preferences in a systematic fashion.

Table 3: Grade of recommendation (GR)*

Nature of recommendations	GR
Based on clinical studies of good quality and consistency addressing the specific recommendations and including at least one randomised trial.	A
Based on well-conducted clinical studies, but without randomised clinical trials.	B
Made despite the absence of directly applicable clinical studies of good quality.	C

**Modified from Sackett et al. (5).*

1.2 Publication history

The complete update in 2009 was largely a synthesis of ICUD and NICE and so was the 2010 edition. In 2011 an addendum was added on the use of drugs, now incorporated in the full text under Chapter 4. This 2012 edition is also partly based on ICUD and NICE but new searches were conducted from June 2008 to present. An addendum to the guidelines is provided on mixed urinary incontinence (see Appendix).

1.3 References

1. Abrams P, Cardozo L, Khoury S, et al., eds. Incontinence. 4th International Consultation on Incontinence, Paris, July 5-8, 2008. Plymouth: Health Publication Ltd, 2009. http://www.icud.info/incontinence.html
2. Stöhrer M, Blok B, Castro-Diaz D, et al. EAU guidelines on neurogenic lower urinary tract dysfunction. Eur Urol 2009 Jul;56(1):81-8. http://www.uroweb.org/fileadmin/tx_eauguidelines/2009/Trans/2009_Neurogenic_LUTS.pdf
3. Higgins JPT, Green S, eds. Cochrane Handbook for Systematic Reviews of Interventions 5.1.0 [updated March 2011]. www.cochrane.org/training/cochrane-handbook

4. Richardson WS, Wilson MS, Nishikawa J, et al. The well-built clinical question: a key to evidence-based decisions. ACP Journal Club 1995;123:A12-3.
5. Oxford Centre for Evidence-based Medicine Levels of Evidence (May 2009). Produced by Bob Phillips, Chris Ball, Dave Sackett, Doug Badenoch, Sharon Straus, Brian Haynes, Martin Dawes since November 1998. Updated by Jeremy Howick March 2009. http://www.cebm.net/index.aspx?o=1025 [Access date January 2012]
6. Atkins D, Best D, Briss PA, et al; GRADE Working Group. Grading quality of evidence and strength of recommendations. BMJ 2004 Jun 19;328(7454):1490. http://www.ncbi.nlm.nih.gov/pubmed/15205295
7. Guyatt GH, Oxman AD, Vist GE, et al; GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ 2008 Apr 26;336(7650):924-6. http://www.ncbi.nlm.nih.gov/pubmed/18436948
8. Guyatt GH, Oxman AD, Kunz R, et al; GRADE Working Group. Going from evidence to recommendations. BMJ 2008 May 10;336(7652):1049-51. http://www.ncbi.nlm.nih.gov/pubmed/18467413

1.4 Use in different healthcare settings and by healthcare professionals

The Guidelines have been written for urologists and for use in any healthcare setting in Europe. However, the Panel recognises that many different health professionals besides urologists use the Guidelines. The Panel also recognises that a patient's first point of contact may not always be a urologist, and that the healthcare professional delivering treatment, e.g. physiotherapy, may also not be a urologist. For this reason, some healthcare professionals may find that the Guidelines do not explain a particular topic in enough detail for their needs, e.g. delivery modalities for pelvic floor muscle training.

1.5 Terminology

Evidence summaries provide a succinct summary of what the currently available evidence tells us about an individual clinical question. They are presented according to the levels of evidence used by the EAU.

Recommendations have been deliberately written as 'action-based' sentences. The following words or phrases are used consistently throughout the Guidelines, as follows:

- **Consider** an action. This word is used when there is not enough evidence to say whether the action causes benefit or risk to the patient. However, in the opinion of the Panel, the action may be justified in some circumstances. Action is optional.
- **Offer** an action. This word is used when there is good evidence to suggest that the action is effective, or that, in the opinion of the Panel, it is the best action. Action is advisable.
- **Carry out (perform)** an action**. Do** something. This phrase is used when there is strong evidence that this is the only best action in a certain clinical situation. Action is mandatory.
- **Avoid** an action. This phrase is used when there is high-level evidence that the action is either ineffective or is harmful to the patient. Action is contraindicated.

2. ASSESSMENT AND DIAGNOSIS

2.1 History and physical examination

Taking a careful clinical history is fundamental to the clinical process. Despite the lack of formal evidence, there is universal agreement that taking a history should be the first step in the assessment of anyone with UI. The history should include details of the type, timing and severity of incontinence, associated voiding, and other urinary symptoms. The history should allow the UI to be categorised into stress, urgency or mixed. It should also identify patients who need rapid referral to a specialist. These include patients with associated pain, haematuria, a history of recurrent urinary tract infections (UTIs), pelvic surgery (particularly prostate surgery) or radiotherapy, constant leakage suggesting a fistula, voiding difficulty or suspected neurological disease. An obstetric and gynaecological history may help to understand the underlying cause and identify factors that may impact on treatment decisions. The patient should also be asked about comorbid conditions, as these may impact on symptoms of UI, or cause it, and details of current medications.

There is little evidence for the necessity to carry out a clinical examination. However, there is wide agreement that clinical examination is essential. In a patient with UI, this should include abdominal examination, to detect an enlarged bladder or other abdominal mass, and perineal and digital examination of the rectum

and/or vagina. Examining the perineum includes an assessment of oestrogen status in women and a careful assessment of any associated genitourinary prolapse. A cough test will often reveal stress incontinence, but only if the bladder contains urine during the examination. Pelvic floor contraction is assessed by means of digital vaginal examination. In men, it is essential to perform a digital examination of the rectum and prostatic assessment.

2.2 Patient questionnaires

Questionnaires may be symptom scores, symptom questionnaires, patient-reported outcome measures (PROMS) or health-related quality of life (HRQoL) measures. Questionnaires are widely used to record patients' symptoms, including their severity and impact on the patient, and have been used to monitor the symptom scores of individual patients or groups of patients over time, e.g. in the context of changes related to treatment. During the last 10 years, many questionnaires have been developed and studied, including ones specifically designed for lower urinary tract symptoms (LUTS), pelvic organ prolapse, faecal incontinence and both condition-specific quality of life (QoL) and generic QoL. The methodology for their development was reviewed in the 4th International Consultation on Incontinence (ICI) in 2008 (1).

*2.2.1 **Questions***

- In adults with UI, does assessment using either urinary symptom or QoL questionnaires improve the treatment outcome for UI?
- In adults with UI, does assessment of the patient perspective (concerns or expectations) improve patient outcomes, regarding either urinary symptoms or QoL, compared to no patient-reported assessment?

*2.2.2 **Evidence***

Although many studies have investigated the validity and reliability of questionnaires and PROMs, most have taken place in adults without UI. This greatly limits the extent to which results and conclusions from these studies can be applied in adults with UI.

Evidence summary	**LE**
There is no evidence that the use of either questionnaires or PROMs in the assessment of adults with UI has an influence on outcome.	4

*2.2.3 **Research priorities***

There is a lack of knowledge about whether using questionnaires to assess urinary symptoms or QoL helps to improve outcomes in adults with UI. Further research is needed to compare the use of questionnaires to assess urinary symptoms and/or QoL in addition to standard clinical assessment versus clinical measures alone. Patients should be closely involved in the design of such studies.

*2.2.4 **Reference***

1. Staskin D, Kelleher C, Avery K, et al: Committee 5B. Patient reported outcome assessment. In: Abrams P, Cardozo L, Khoury S, et al., editors. Incontinence. 4th International Consultation on Incontinence, Paris July 5-8, 2008. Plymouth: Health Publication Ltd, 2009. http://www.icud.info/incontinence.html

2.3 Voiding dairies

Measurement of the frequency and severity of LUTS is an important step in the evaluation and management of lower urinary tract dysfunction, including UI. Voiding diaries are a semi-objective method of quantifying symptoms, such as daytime and night-time frequency, urgency, urgency urinary incontinence (UUI) and stress urinary incontinence (SUI) episodes. They also quantify urodynamic variables, such as voided volume and 24-hour or nocturnal total urine volume. Voiding diaries are also known as micturition time charts, frequency/volume charts and bladder diaries.

Any discrepancy between diary recordings and the patient rating of symptoms, e.g. frequency or UI, can be useful in patient management. In addition, voided volume measurement can be used to support diagnoses, such as overactive bladder (OAB) or polyuria. Diaries can also be used to monitor treatment response and are widely used in clinical trials as a semi-objective measure of treatment outcome.

*2.3.1 **Questions***

- In adults with UI, what is the reliability, the diagnostic accuracy and predictive value of a voiding diary,

compared to patient history or symptom score?
- How does the accuracy of a computerised voiding diary compare to a paper diary?

2.3.2 ***Evidence***

Two recent articles have suggested a consensus has been reached in the terminology used in voiding diaries (1,2):

- Micturition time charts record only the times of micturitions for a minimum of 24 continuous hours.
- Frequency volume charts record voided volumes and times of micturitions for a minimum of 24 hours.
- Bladder diaries include information on incontinence episodes, pad usage, fluid intake, degree of urgency and degree of incontinence.

Several studies have compared patients' preference for, and the accuracy of, electronic and paper voiding diaries in voiding dysfunction (3-7). Several studies have compared shorter (3 or 5 days) and longer diary durations (7 days) (8-14). The choice of diary duration appears to be based upon the possible behavioural therapeutic effect of keeping a diary rather than on validity or reliability.

Two studies have investigated the reproducibility of voiding diaries in both men and women (8,9). Further studies investigated the variability of diary data within a 24-hour period (15) and compared voided volumes recorded in diaries with those recorded on uroflowmetry (16). Other studies have investigated the correlation between data obtained from voided diaries and standard symptom evaluation (17-20).

One study investigated the effect of diary duration on the observed outcome of treatment of LUTS (21). Another study found that keeping a voiding diary had a therapeutic benefit (22).

In conclusion, voiding diaries give reliable data on lower urinary tract function. There remains a lack of consensus about how long a diary should be kept and how well diary data correlate with some symptoms.

Evidence summary	**LE**
Voiding diaries of 3-7 days duration are a reliable tool for quantifying mean voided volume, daytime and night-time frequency.	2b
Voiding diaries are sensitive to change and are a reliable measure of outcome.	2b

Recommendations	**GR**
Voiding diaries should be used in urinary incontinence to evaluate co-existing storage and voiding dysfunction in clinical practice and in research.	A
A diary duration of between 3 and 7 days is recommended.	B

2.3.3 ***References***

1. Abrams P, Cardozo L, Fall M, et al. The standardisation of terminology of lower urinary tract function: report from the Standardisation Sub-committee of the International Continence Society. Neurourol Urodyn 2002;21(2):167-78. http://www.ncbi.nlm.nih.gov/pubmed/11857671
2. Haylen BT, de Ridder D, Freeman RM, et al. An International Urogynecological Association (IUGA)/ International Continence Society (ICS) joint report on the terminology for female pelvic floor dysfunction. Neurourol Urodyn 2010;29(1):4-20. http://www.ncbi.nlm.nih.gov/pubmed/19941278
3. Rabin JM, McNett J, Badlani GH. Computerized voiding diary. Neurourol Urodyn 1993;12(6):541-53; discussion 553-4. http://www.ncbi.nlm.nih.gov/pubmed/8312939
4. Rabin JM, McNett J, Badlani GH. A computerized voiding diary. J Reprod Med 1996 Nov;41(11): 801-6. http://www.ncbi.nlm.nih.gov/pubmed/8951128
5. Rabin JM, McNett J, Badlani GH. "Compu-Void II": the computerized voiding diary. J Med Syst 1996 Feb;20(1):19-34. http://www.ncbi.nlm.nih.gov/pubmed/8708489
6. Quinn P, Goka J, Richardson H. Assessment of an electronic daily diary in patients with overactive bladder. BJU Int 2003 May;91(7):647-52. http://www.ncbi.nlm.nih.gov/pubmed/12699477

7. Guan ZC, Wei BL, Meng ZW. [Development of remote wireless mobile voiding diary and a report of its objective voiding in 20 young people.] Beijing Da Xue Xue Bao 2010 Aug 18;42(4):476-9. [Chinese] http://www.ncbi.nlm.nih.gov/pubmed/20721269
8. Nygaard I, Holcomb R. Reproducibility of the seven-day voiding diary in women with stress urinary incontinence. Int Urogynecol J Pelvic Floor Dysfunct 2000;11(1):15-7. http://www.ncbi.nlm.nih.gov/pubmed/10738929
9. Brown JS, McNaughton KS, Wyman JF, et al. Measurement characteristics of a voiding diary for use by men and women with overactive bladder. Urology 2003 Apr;61(4):802-9. http://www.ncbi.nlm.nih.gov/pubmed/12670569
10. Locher JL, Goode PS, Roth DL, et al. Reliability assessment of the bladder diary for urinary incontinence in older women. J Gerontol A Biol Sci Med Sci 2001 Jan;56(1):M32-5. http://www.ncbi.nlm.nih.gov/pubmed/11193230
11. Homma Y, Ando T, Yoshida M, et al. Voiding and incontinence frequencies: variability of diary data and required diary length. Neurourol Urodyn 2002;21(3):204-9. http://www.ncbi.nlm.nih.gov/pubmed/11948713
12. Ku JH, Jeong IG, Lim DJ, et al. Voiding diary for the evaluation of urinary incontinence and lower urinary tract symptoms: prospective assessment of patient compliance and burden. Neurourol Urodyn 2004;23(4):331-5. http://www.ncbi.nlm.nih.gov/pubmed/15227650
13. Gordon D, Groutz A. Evaluation of female lower urinary tract symptoms: overview and update. Curr Opin Obstet Gynecol 2001 Oct;13(5):521-7. http://www.ncbi.nlm.nih.gov/pubmed/11547034
14. Addla S, Adeyoju A, Neilson D. Assessment of reliability of 1-day, 3-day and 7-day frequency volume charts. Eur Urol Suppl 2004;2:130, abstract no. 510. http://www.europeanurology.com/article/S1569-9056(04)90507-6/pdf/
15. Ertberg P, Moller LA, Lose G. A comparison of three methods to evaluate maximum bladder capacity: cystometry, uroflowmetry and a 24-h voiding diary in women with urinary incontinence. Acta Obstet Gynecol Scand 2003 Apr:82(4):374-7. http://www.ncbi.nlm.nih.gov/pubmed/12716323
16. Fitzgerald MP, Brubaker L. Variability of 24-hour voiding diary variables among asymptomatic women. J Urol 2003 Jan;169(1):207-9. http://www.ncbi.nlm.nih.gov/pubmed/12478137
17. van Brummen HJ, Heintz AP, van der Vaart CH. The association between overactive bladder symptoms and objective parameters from bladder diary and filling cystometry. Neurourol Urodyn 2004;23(1):38-42. http://www.ncbi.nlm.nih.gov/pubmed/14694455
18. Stav K, Dwyer PL, Rosamilia A. Women overestimate daytime urinary frequency: the importance of the bladder diary. J Urol 2009 May;181(5):2176-80. http://www.ncbi.nlm.nih.gov/pubmed/19296975
19. Fayyad AM, Hill SR, Jones G. Urine production and bladder diary measurements in women with type 2 diabetes mellitus and their relation to lower urinary tract symptoms and voiding dysfunction. Neurourol Urodyn 2010 Mar;29(3):354-8. http://www.ncbi.nlm.nih.gov/pubmed/19760759
20. Homma Y, Kakizaki H, Yamaguchi O, et al. Assessment of overactive bladder symptoms: comparison of 3-day bladder diary and the overactive bladder symptoms score. Urology. 2011 Jan;77(1):60-4. http://www.ncbi.nlm.nih.gov/pubmed/20951412
21. Wein AJ, Khullar V, Wang JT, et al. Achieving continence with antimuscarinic therapy for overactive bladder: effects of baseline incontinence severity and bladder diary duration. BJU Int 2007 Feb;99(2):360-3. http://www.ncbi.nlm.nih.gov/pubmed/17155987
22. Burgio KL, Locher JL, Goode PS, et al. Behavioral vs drug treatment for urge urinary incontinence in older women: a randomized controlled trial. JAMA 1998 Dec 16;280(23):1995-2000. http://www.ncbi.nlm.nih.gov/pubmed/9863850

2.4 Urinalysis and urinary tract infection

Urinary incontinence is known to occur more commonly in women with UTIs and is also more likely in the first few days following an acute infection (1). In contrast with symptomatic UTI, asymptomatic bacteriuria appears to have little influence on UI. A study carried out in nursing home residents showed that the severity of UI was unchanged after eradication of bacteriuria (2).

Reagent strip ('dipstick') urinalysis may detect infection, proteinuria, haematuria and glycosuria:

- Nitrite and leucocyte esterase may indicate a UTI.
- Protein may indicate infection and/or renal disease.
- Blood may indicate malignancy (or infection).
- Glucose may indicate diabetes mellitus.

It is generally agreed that dipstick urinalysis provides sufficient screening information in both men and women with UI. Microscopy and other tests may be necessary to confirm any abnormalities identified on dipstick analysis. Urinalysis is usually carried out on a mid-stream urine specimen, but analysis of initial voided and terminal urine samples may be required for assessment of urethral and prostate infections.

*2.4.1 **Questions***

- In adults with UI, what is the diagnostic accuracy of urinalysis for UTIs?
- What is the benefit on UI of treating UTIs?

*2.4.2 **Evidence***

In both men and women with UI, diagnosis of a UTI by positive leucocytes or nitrites using urine culture as the reference standard had a low sensitivity and very high specificity (3,4). A negative urine dipstick test in patients with UI therefore excludes a UTI with a high degree of certainty.

There is a consensus that urinalysis should be a standard part of the basic evaluation of UI irrespective of gender, age or aetiology.

Evidence summary	**LE**
There is no evidence that a UTI causes UI.	4
There is no evidence that treating a UTI cures UI.	4
The presence of a symptomatic UTI worsens symptoms of UI.	3
Elderly nursing home patients with established UI do not benefit from treatment of asymptomatic bacteriuria.	2

Recommendations	**GR**
Do urinalysis as a part of the initial assessment of a patient with urinary incontinence.	A
In a patient with urinary incontinence, treat a symptomatic urinary tract infection appropriately *(see 'EAU Guidelines on Urological Infections' [5]).*	A
Do not treat asymptomatic bacteriuria in elderly patients to improve urinary incontinence.	B

*2.4.3 **References***

1. Moore EE, Jackson SL, Boyko EJ, et al. Urinary incontinence and urinary tract infection: temporal relationships in postmenopausal women. Obstet Gynecol 2008 Feb;111(2 Pt 1):317-23. http://www.ncbi.nlm.nih.gov/pubmed/18238968
2. Ouslander JG, Schapira M, Schnelle JF, et al. Does eradicating bacteriuria affect the severity of chronic urinary incontinence in nursing home residents? Ann Intern Med 1995 May 15;122(10):749-54. http://www.ncbi.nlm.nih.gov/pubmed/7717597
3. Semeniuk H, Church D. Evaluation of the leukocyte esterase and nitrite urine dipstick screening tests for detection of bacteriuria in women with suspected uncomplicated urinary tract infections. J Clin Microbiol 1999 Sep;37(9):3051-2. http://www.ncbi.nlm.nih.gov/pubmed/10449505
4. Buchsbaum GM, Albushies DT, Guzick DS. Utility of urine reagent strip in screening women with incontinence for urinary tract infection. Int Urogynecol J Pelvic Dysfunct 2004 Nov-Dec;15(6):391-3; discussion 393. http://www.ncbi.nlm.nih.gov/pubmed/15278254
5. Grabe M, Bjerklund-Johansen TE, Botto H, et al. EAU Guidelines on Urological Infections. http://www.uroweb.org/guidelines/online-guidelines/

2.5 Post-voiding residual volume

Post-voiding residual (PVR) volume (also known as residual urine, bladder residual) is the amount of urine that remains in the bladder after voiding. It indicates poor voiding efficiency, which may result from a number of contributing factors. It is important because it may worsen symptoms and, more rarely, may be associated with upper urinary tract dilatation and renal insufficiency. Both bladder outlet obstruction and detrusor underactivity contribute to the development of PVR.

Post-voiding residual can be measured by catheterisation or ultrasound (US). The prevalence of PVR is uncertain, partly because of the lack of a standard definition of an abnormal PVR volume.

*2.5.1 **Question***

In adults with UI, what are the diagnostic accuracy and predictive value of measurements of PVR?

*2.5.2 **Evidence***

Most studies investigating PVR have not included patients with UI. Although some studies have included women with UI and men and women with LUTS, they have also included children and adults with neurogenic UI. In general, the data on PVR can be applied with caution to adults with non-neurogenic UI. The results of studies investigating the best method of measuring PVR (1-6) have led to the consensus that US measurement of PVR is better than measurement using catheterisation.

Several studies have evaluated PVR in different subjects and patients cohorts (7-17). In peri- and post-menopausal women without significant LUTS or pelvic organ symptoms, 95% of women had a PVR < 100 mL (7). A comparison of women with and without LUTS suggested that symptomatic women had a higher incidence of elevated PVR (9). In women with UUI, a PVR > 100 mL was found in 10% of cases (8). Other research has found that a high PVR is associated with pelvic organ prolapse (> stage II), voiding symptoms and an absence of SUI (10,11,13,15). In women with SUI, the mean PVR was 38.5 mL measured by catheterisation and 62.8 mL measured by US, with 15.9% of women having a PVR > 100 mL (8). Overall, women with symptoms of lower urinary tract or pelvic floor dysfunction and pelvic organ prolapse have a higher risk of elevated PVR compared to asymptomatic subjects.

There is evidence to suggest that elevated PVR should be particularly looked for in patients with voiding symptoms (18-21). There is no evidence to define a threshold between normal and abnormal PVR values. Expert opinion has therefore been used to produce a definition of elevated PVR values (22-25).

There is a lack of evidence to support the routine measurement of PVR in patients with UI (26-30).

Evidence summary	**LE**
Ultrasonography provides an accurate estimate of post-voiding residual.	1b
Lower urinary tract dysfunction is associated with a higher risk of post-voiding residual compared to controls.	2
Elevated post-voiding residual is not a risk factor for poor outcome in the management of SUI.	2

Recommendations	**GR**
Post-voiding residual should be measured by ultrasound.	A
Measure post-voiding residual in patients with urinary incontinence who have voiding dysfunction.	B
Measure post-voiding residual when assessing patients with complicated urinary incontinence.	C
Post-voiding residual should be monitored in patients receiving treatments that may cause or worsen voiding dysfunction.	B

*2.5.3 **Research priority***

Further research is required to evaluate whether combining non-invasive tests provides greater diagnostic accuracy and prognostic value than tests viewed in isolation.

2.5.4 ***References***

1. Goode PS, Locher JL, Bryant RL, et al. Measurement of postvoid residual urine with portable transabdominal bladder ultrasound scanner and urethral catheterization. Int Urogynecol J Pelvic Floor Dysfunct 2000;11(5):296-300.
http://www.ncbi.nlm.nih.gov/pubmed/11052565
2. Ouslander JG, Simmons S, Tuico E, et al. Use of a portable ultrasound device to measure post-void residual volume among incontinent nursing home residents. J Am Geriatr Soc 1994 Nov;42(11): 1189-92.
http://www.ncbi.nlm.nih.gov/pubmed/7963206
3. Nygaard IE. Postvoid residual volume cannot be accurately estimated by bimanual examination. Int Urogynecol J Pelvic Floor Dysfunct 1996;7(2):74-6.
http://www.ncbi.nlm.nih.gov/pubmed/8798090
4. Griffiths DJ, Harrison G, Moore K, et al. Variability of post-void residual urine volume in the elderly. Urol Res 1996;24(1):23-6.
http://www.ncbi.nlm.nih.gov/pubmed/8966837
5. Stoller ML, Millard RJ. The accuracy of a catheterized residual urine. J Urol 1989 Jan;141(1):15-6.
http://www.ncbi.nlm.nih.gov/pubmed/2908944
6. Marks LS, Dorey FJ, Macairan ML, et al. Three-dimensional ultrasound device for rapid determination of bladder volume. Urology 1997 Sep;50(3):341-8.
http://www.ncbi.nlm.nih.gov/pubmed/9301695
7. Gehrich A, Stany MP, Fischer JR, et al. Establishing a mean postvoid residual volume in asymptomatic perimenopausal and postmenopausal women. Obstet Gynecol 2007 Oct;110(4):827-32.
http://www.ncbi.nlm.nih.gov/pubmed/17906016
8. Tseng LH, Liang CC, Chang YL, et al. Postvoid residual urine in women with stress incontinence. Neurourol Urodyn 2008;27(1):48-51.
http://www.ncbi.nlm.nih.gov/pubmed/17563112
9. Haylen BT, Law MG, Frazer M, et al. Urine flow rates and residual urine volumes in urogynecology patients. Int Urogynecol J Pelvic Floor Dysfunct 1999;10(6):378-83.
http://www.ncbi.nlm.nih.gov/pubmed/10614974
10. Fitzgerald MP, Jaffar J, Brubaker L. Risk factors for an elevated postvoid residual urine volume in women with symptoms of urinary urgency, frequency and urge incontinence. Int Urogynecol J Pelvic Floor Dysfunct 2001;12(4):237-9; discussion 239-40.
http://www.ncbi.nlm.nih.gov/pubmed/11569651
11. Lukacz ES, DuHamel E, Menefee SA, et al. Elevated postvoid residual in women with pelvic floor disorders: prevalence and associated risk factors. Int Urogynecol J Pelvic Floor Dysfunct 2007 Apr;18(4):397-400.
http://www.ncbi.nlm.nih.gov/pubmed/16804634
12. Wu J, Baguley IJ. Urinary retention in a general rehabilitation unit: prevalence, clinical outcome, and the role of screening. Arch Phys Med Rehabil 2005 Sep;86(9):1772-7.
http://www.ncbi.nlm.nih.gov/pubmed/1618941
13. Milleman M, Langenstroer P, Guralnick ML. Post-void residual urine volume in women with overactive bladder symptoms. J Urol 2004 Nov;172(5 Pt 1):1911-4.
http://www.ncbi.nlm.nih.gov/pubmed/15540753
14. de Waal KH, Tinselboer BM, Evenhuis HM, et al. Unnoticed post-void residual urine volume in people with moderate to severe intellectual disabilities: prevalence and risk factors. J Intellect Disabil Res 2009 Sep;53(9):772-9.
http://www.ncbi.nlm.nih.gov/pubmed/19627424
15. Haylen BT, Lee J, Logan V, et al. Immediate postvoid residual volumes in women with symptoms of pelvic floor dysfunction. Obstet Gynecol 2008;111(6):1305-12.
http://www.ncbi.nlm.nih.gov/pubmed/18515513
16. Lowenstein L, Anderson C, Kenton K, et al. Obstructive voiding symptoms are not predictive of elevated postvoid residual urine volumes. Int Urogynecol J Pelvic Floor Dysfunct 2008 Jun;19(6): 801-4.
http://www.ncbi.nlm.nih.gov/pubmed/18074067
17. Gupta A, Taly AB, Srivastava A, et al. Urodynamic profile in myelopathies: a follow-up study. Ann Indian Acad Neurol 2009 Jan;12(1):35-9.
http://www.ncbi.nlm.nih.gov/pubmed/20151007
18. Fowler CJ, Panicker JN, Drake M, et al. A UK consensus on the management of the bladder in multiple sclerosis. J Neurol Neurosurg Psychiatry 2009 May;80(5):470-7.
http://www.ncbi.nlm.nih.gov/pubmed/19372287

19. Jacobsen SJ, Girman CJ, Lieber MM. Natural history of benign prostatic hyperplasia. Urology 2001 Dec;58(6 Suppl 1):5-16; discussion 16.
http://www.ncbi.nlm.nih.gov/pubmed/11750242
20. Dorflinger A, Monga A. Voiding dysfunction. Curr Opin Obstet Gynecol 2001 Oct;13(5):507-12.
http://www.ncbi.nlm.nih.gov/pubmed/11547032
21. Twiss C, Triaca V, Anger J, et al. Validating the incontinence symptom severity index: a self-assessment instrument for voiding symptom severity in women. J Urol 2009 Nov;182(5):2384-91.
http://www.ncbi.nlm.nih.gov/pubmed/19758631
22. Fantl JA, Newman DK, Colling J. Urinary incontinence in adults: acute and chronic management: 1996 update. AHCPR Clinical Practice Guidelines. No. 2. Rockville (MD): Agency for Health Care Policy and Research (AHCPR), March 1996. Report No. 96-0682.
http://www.ncbi.nlm.nih.gov/pubmed/1302135
23. AUA guideline on management of benign prostatic hyperplasia (2003). Chapter 1: Diagnosis and treatment recommendations. J Urol 2003 Aug;170(2 Pt 1):530-47.
http://www.ncbi.nlm.nih.gov/pubmed/12853821
24. Abrams P, Griffiths D, Hoefner K, et al. The urodynamic assessment of lower urinary tract symptoms. In: Chatelain C, Denis L, Foo K, et al., editors. Benign Prostatic Hyperplasia. Plymouth: Health Publication Ltd., 2001, pp. 227-81.
25. Madersbacher S, Alivizatos G, Nordling J, et al. EAU 2004 guidelines on assessment, therapy and follow-up of men with lower urinary tract symptoms suggestive of benign prostatic obstruction (BPH guidelines). Eur Urol 2004 Nov;46(5):547-54.
http://www.ncbi.nlm.nih.gov/pubmed/15474261
26. Nager CW, FitzGerald M, Kraus SR, et al. Urodynamic measures do not predict stress continence outcomes after surgery for stress urinary incontinence in selected women. J Urol 2008 Apr;179(4):1470-4.
http://www.ncbi.nlm.nih.gov/pubmed/18295276
27. Bates TS, Sugiono M, James ED, et al. Is the conservative management of chronic retention in men ever justified? BJU Int 2003 Oct;92(6):581-3.
http://www.ncbi.nlm.nih.gov/pubmed/14511038
28. Vesely S, Knutson T, Fall M, et al. Clinical diagnosis of bladder outlet obstruction in men with lower urinary tract symptoms: reliability of commonly measured parameters and the role of idiopathic detrusor overactivity. Neurourol Urodyn 2003;22(4):301-5.
http://www.ncbi.nlm.nih.gov/pubmed/12808704
29. Athanasopoulos A, Mitropoulos D, Giannitsas K, et al. Safety of anticholinergics in patients with benign prostatic hyperplasia. Expert Opin Drug Saf 2008 Jul;7(4):473-9.
http://www.ncbi.nlm.nih.gov/pubmed/18613810
30. Sahai A, Sangster P, Kalsi V, et al. Assessment of urodynamic and detrusor contractility variables in patients with overactive bladder syndrome treated with botulinum toxin-A: is incomplete bladder emptying predictable? BJU Int 2009 Mar;103(5):630-4.
http://www.ncbi.nlm.nih.gov/pubmed/18990156

2.6 Urodynamics

In clinical practice, 'urodynamics' is generally used as a collective term for all tests of bladder and urethral function. These Guidelines will review both non-invasive estimation of urine flow, i.e. uroflowmetry, and invasive tests, including multichannel cystometry, ambulatory monitoring and videourodynamics, and different tests of urethral function, such as urethral pressure profilometry, Valsalva leak point pressure estimation, and retrograde urethral resistance measurement.

Multichannel cystometry, ambulatory monitoring and videourodynamics aim to observe the effects on intravesical and intra-abdominal pressures while reproducing a patient's symptoms. Bladder filling may be artificial or physiological and voiding is prompted. Any incontinence observed may be categorised as SUI, detrusor overactivity (DO) incontinence, a mixture of SUI/DO incontinence, or, rarely, urethral relaxation incontinence. A test may fail to reproduce a patient's symptoms because of poor diagnostic accuracy or because the symptoms are not directly attributable to a urodynamically measurable phenomenon. Despite these uncertainties, urodynamic testing is still used to establish an uncertain 'diagnosis', to direct decisions about treatment and to provide prognostic information.

*2.6.1 **Question***

In adults with UI, what is the diagnostic accuracy and predictive value of uroflowmetry, i.e. the measurement of maximum urinary flow rate (Q_{max}) and urodynamic testing?

2.6.2 ***Evidence***

2.6.2.1 Repeatability

Many studies have examined test-retest reliability for a range of urodynamic parameters, including eight studies on cystometry/pressure flow studies (1-8). No published studies on the reliability of ambulatory monitoring were found.

Various techniques are used to measure urethral profilometry. Individual techniques are generally reliable in terms of repeatability, but results may vary between different techniques, so that one type of test cannot be compared meaningfully to another (9-11).

The measurement of abdominal or Valsalva leak point pressures has not been standardised. It has not been possible to correlate consistently any method of measuring Valsalva leak point pressure with either UI severity or other measures of urethral function (12-17).

Studies of technical accuracy have included adults with LUTS, with or without UI. The studies used different equipment and lacked standardised techniques (18,19). As with all physiological investigation, results have shown a wide range of variability.

Inter-rater and intra-rater reliability of videourodynamics for the severity and type of SUI is good (20).

2.6.2.2 Diagnostic accuracy

The diagnostic accuracy of urodynamics cannot be measured against a 'gold standard' since all incontinence diagnoses are defined in urodynamic terms.

Detrusor overactivity may be found in asymptomatic patients, while normal cystometry is found in patients who are clearly symptomatic. There have been many studies of variable quality, investigating the relationship between UI symptoms and subsequent urodynamic findings. For their UK-based guidance, the National Institute for Health and Clinical Evidence (NICE) reviewed 11 studies (21), which investigated the relationship between clinical diagnosis and urodynamic findings and the diagnostic accuracy of urodynamic measurement, specifically in females. The Panel found no new evidence had been published since 2005 up until July 2011.

There is a consensus that urodynamic tests should aim to reproduce the patient's symptoms. If they do not, the findings are inevitably inconclusive. There is also a consensus that attention to technical and methodological detail during urodynamic testing may increase the accuracy of urodynamics in recording usual bladder behaviour.

In clinical practice, urodynamic testing (cystometry) may help to provide, or confirm, a diagnosis, predict treatment outcome, or facilitate discussion during a consultation.

2.6.2.3 Does urodynamics influence the outcome of conservative therapy?

A meta-analysis of 129 studies of diagnostic tests for incontinence, using economic modelling, concluded that urodynamics was not cost-effective in a primary care setting (22).

A few RCTs have investigated the ability of urodynamics to predict treatment decisions or treatment outcomes following conservative management. In 2009, a Cochrane review examined three small RCT studies, two of which were reported as abstracts (23,24). A further RCT, not included in the Cochrane review, also compared patients who underwent urodynamics with those who did not, though they did have urodynamics later in their care (25). Since then, another RCT addressing the same question has been published (26). Patients who underwent urodynamics were more likely to be treated by surgery or drugs or to have a change in their treatment (23). However, urodynamic tests made no difference to the outcomes of conservative treatment, including antimuscarinic therapy (27,28).

2.6.2.4 Does urodynamics influence the outcome of surgery for SUI?

There have been no RCTs specifically addressing this question, though trials are currently underway. Several case series have examined a possible relationship between individual urodynamic parameters and the subsequent success or failure of surgical treatment for SUI. Most were low-quality small studies. Post-hoc analysis of an RCT on surgery for SUI failed to confirm a predictive value for urodynamics, though the success rate for patients with urodynamic SUI exceeded that for women without urodynamic SUI (29).

Various studies have examined the relationship between measures of poor urethral function, i.e. low maximal

urethral closure pressure, low Valsalva leak point pressure, and subsequent failure of surgery. Some studies found a correlation between low urethral pressures and surgical failure, while other studies did not (30-33). A correlation, in itself, was not necessarily predictive.

2.6.2.5 Does urodynamics help to predict complications of surgery?
There have been no RCTs. A large number of case series, or post-hoc analyses of larger studies, have examined the relationship between urodynamic parameters and surgical outcome for SUI. A low Q_{max} or low pressure voiding has been inconsistently associated with post-operative voiding difficulty (34-40). However, the predictive value has rarely been calculated.

The presence of pre-operative DO has more consistently been associated with development of post-operative UUI. Post-hoc analysis of an RCT comparing the autologous fascial sling to Burch colposuspension showed inferior outcomes for women who suffered pre-operative urgency (41). However pre-operative urodynamics had failed to predict this outcome (29). Other case series, however, have shown a consistent association of poor outcomes with pre-operative DO, though the predictive value was not calculated (42,43).

2.6.2.6 Does urodynamics influence the outcome of surgery for DO?
No studies were found on the relationship between urodynamic testing and subsequent surgical outcome for DO. However, most studies reporting surgical outcomes for DO have included only patients with urodynamically proven DO or DO incontinence. Higher-pressure DO appears to be consistently associated with surgical failure and persistent or de-novo urgency. As with other suggested 'predictors', the predictive value has not often been formally calculated (30,44,45). Pre-operative urgency was resolved in some patients (46,47).

2.6.2.7 Does urodynamics influence the outcome of treatment for post-prostatectomy UI in men?
There are no RCTs examining the clinical usefulness of urodynamics in post-prostatectomy incontinence. However, many case series have demonstrated the ability of urodynamics to distinguish between different causes of UI (48-50). The ability of urodynamic testing to predict surgical outcome for post-prostatectomy incontinence is inconsistent (51,52).

Evidence summary	**LE**
Most urodynamic parameters show a high random immediate and short-term test-retest variability of up to 15% in the same subject.	2
Test-retest variability creates an overlap between 'normal' and 'abnormal' populations, which may make it more difficult to categorise urodynamic findings in a particular individua.l	2
Different techniques of measuring urethral function may perform reliably from one test to another, but do not reliably correlate to other tests and to the severity of UI.	3
The accuracy of ambulatory urodynamics remains uncertain.	4
There may be inconsistency between history and urodynamic results.	3
Preliminary urodynamics do not affect the outcome of conservative therapy for UI.	1a
There is limited evidence about whether preliminary urodynamic testing predicts surgical outcomes in adults with UI.	3
There is conflicting low-level evidence that tests suggesting poor urethral function predict surgery failure for SUI in women.	3
There is consistent low-level evidence that pre-operative DO predicts failure of mid-urethral sling surgery in women.	3
There is no evidence about whether preliminary urodynamics predicts outcomes of treatment for UI in men.	4

Recommendations	**GR**
Clinicians carrying out urodynamics in patients with urinary incontinence should: • Ensure that the test replicates patient's symptoms • Interpret results in context of the clinical problem • Check recordings for quality control • Remember there may be physiological variability within the same individual.	C

Advise patients that the results of urodynamics may be useful in discussing treatment options, although there is limited evidence that performing urodynamics will alter the outcome of treatment for urinary incontinence.	C
Do not routinely carry out urodynamics when offering conservative treatment for urinary incontinence.	B
Perform urodynamics if the findings may change the choice of surgical treatment.	C
Perform urodynamics prior to surgery for urinary incontinence if there are either symptoms of overactive bladder, a history of previous surgery or a suspicion of voiding difficulty.	C
Do not routinely carry out urethral pressure profilometry.	C

2.6.3 ***Research priority***

Future studies should address whether any urodynamic test influences the choice between treatments or prediction of the outcome of treatment.

2.6.4 ***References***

1. Chin-Peuckert L, Komlos M, Rennick JE, et al. What is the variability between 2 consecutive cystometries in the same child? J Urol 2003 Oct;170(4 Pt 2):1614-7. http://www.ncbi.nlm.nih.gov/pubmed/14501675
2. Chou FH, Ho CH, Chir MB, et al. Normal ranges of variability for urodynamic studies of neurogenic bladders in spinal cord injury. J Spinal Cord Med 2006;29(1):26-31. http://www.ncbi.nlm.nih.gov/pubmed/16572562
3. Gupta A, Defreitas G, Lemack GE. The reproducibility of urodynamic findings in healthy female volunteers: results of repeated studies in the same setting and after short-term follow-up. Neurourol Urodyn 2004;23(4):311-6. http://www.ncbi.nlm.nih.gov/pubmed/15227647
4. Hess MJ, Lim L, Yalla SV. Reliability of cystometrically obtained intravesical pressures in patients with neurogenic bladders. J Spinal Cord Med 2002 Winter;25(4):293-6. http://www.ncbi.nlm.nih.gov/pubmed/12482172
5. Homma Y, Kondo Y, Takahashi S, et al. Reproducibility of cystometry in overactive detrusor. Eur Urol 2000 Dec;38(6):681-5. http://www.ncbi.nlm.nih.gov/pubmed/11111184
6. Mortensen S, Lose G, Thyssen H. Repeatability of cystometry and pressure-flow parameters in female patients. Int Urogynecol J Pelvic Floor Dysfunct 2002;13(2):72-5. http://www.ncbi.nlm.nih.gov/pubmed/12054185
7. Ockrim J, Laniado ME, Khoubehi B, et al. Variability of detrusor overactivity on repeated filling cystometry in men with urge symptoms: comparison with spinal cord injury patients. BJU Int 2005 Mar;95(4):587-90. http://www.ncbi.nlm.nih.gov/pubmed/15705085
8. Brostrom S, Jennum P, Lose G. Short-term reproducibility of cystometry and pressure-flow micturition studies in healthy women. Neurourol Urodyn 2002;21(5):457-60. http://www.ncbi.nlm.nih.gov/pubmed/12232880
9. Zehnder P, Roth B, Burkhard FC, et al. Air charged and microtip catheters cannot be used interchangeably for urethral pressure measurement: a prospective, single-blind, randomized trial. J Urol 2008 Sep;180(3):1013-7. http://www.ncbi.nlm.nih.gov/pubmed/18639301
10. Wang AC, Chen MC. A comparison of urethral pressure profilometry using microtip and double-lumen perfusion catheters in women with genuine stress incontinence. BJOG 2002 Mar;109(3):322-6. http://www.ncbi.nlm.nih.gov/pubmed/11950188
11. Pollak JT, Neimark M, Connor JT, et al. Air-charged and microtransducer urodynamic catheters in the evaluation of urethral function. Int Urogynecol J Pelvic Floor Dysfunct 2004 Mar-Apr;15(2):124-8; discussion 128. http://www.ncbi.nlm.nih.gov/pubmed/15014940
12. Almeida FG, Bruschini H, Srougi M. Correlation between urethral sphincter activity and Valsalva leak point pressure at different bladder distentions: revisiting the urethral pressure profile. J Urol 2005 Oct;174(4 Pt 1):1312-5; discussion 1315-6. http://www.ncbi.nlm.nih.gov/pubmed/16145410
13. Sinha D, Nallaswamy V, Arunkalaivanan AS. Value of leak point pressure study in women with incontinence. J Urol 2006 Jul;176(1):186-8; discussion 188. http://www.ncbi.nlm.nih.gov/pubmed/16753397

14. Nguyen JK, Gunn GC, Bhatia NN. The effect of patient position on leak-point pressure measurements in women with genuine stress incontinence. Int Urogynecol J Pelvic Floor Dysfunct 2002;13(1):9-14. http://www.ncbi.nlm.nih.gov/pubmed/11999213
15. Dorflinger A, Gorton E, Stanton S, et al. Urethral pressure profile: is it affected by position? Neurourol Urodyn 2002;21(6):553-7. http://www.ncbi.nlm.nih.gov/pubmed/12382246
16. Fleischmann N, Flisser AJ, Blaivas JG, et al. Sphincteric urinary incontinence: relationship of vesical leak point pressure, urethral mobility and severity of incontinence. J Urol 2003 Mar;169(3):999-1002. http://www.ncbi.nlm.nih.gov/pubmed/12576830
17. Schick E, Dupont C, Bertrand PE, et al. Predictive value of maximum urethral closure pressure, urethral hypermobility and urethral incompetence in the diagnosis of clinically significant female genuine stress incontinence. J Urol 2004 May;171(5):1871-5. http://www.ncbi.nlm.nih.gov/pubmed/15076296
18. Brown K, Hilton P. Ambulatory monitoring. Int Urogynecol J Pelvic Floor Dysfunct 1997;8(6):369-76. http://www.ncbi.nlm.nih.gov/pubmed/9609337
19. Brown K, Hilton P. The incidence of detrusor instability before and after colposuspension: a study using conventional and ambulatory urodynamic monitoring. BJU Int 1999 Dec;84(9):961-5. http://www.ncbi.nlm.nih.gov/pubmed/10571620
20. Glancz LJ, Cartwright R, Cardozo L. Inter- and intra-rater reliability of fluoroscopic cough stress testing. J Obstet Gynaecol 2010;30(5):492-5. http://www.ncbi.nlm.nih.gov/pubmed/20604654
21. Urinary incontinence: the management of urinary incontinence in women. Clinical guidelines CG40. National Institute for Health and Clinical Excellence, October 2006. http://guidance.nice.org.uk/CG40
22. Martin JL, Williams KS, Abrams KR, et al. Systematic review and evaluation of methods of assessing urinary incontinence. Health Technol Assess 2006 Feb;10(6):1-132, iii-iv. http://www.ncbi.nlm.nih.gov/pubmed/16487456
23. Khullar V, Salvatore S, Cardozo Let al. Randomised study of ambulatory urodynamics versus symptomatic treatment of symptomatic women without a urodynamic diagnosis. 30th Annual Meeting of the International Continence Society (ICS). Tampere, Finland, 28-31 August 2000. Neurourol Urodyn 2000;19(4)379-547, abstract no. 274. http://www.icsoffice.org/Abstracts/Publish/38/000274.pdf
24. Dowling CR, O'Connell HE, Kurczyki L, et al. Randomised control trial of bladder pressure management versus management based on symptoms and residual volumes in patients with established multiple sclerosis (Abstract). In: Abstracts of the Urological Society of Australasia, Annual Scientific Meeting 2005, Melbourne, Victoria, Australia, 13-17 February 2005. BJU Int 2005;95(Suppl s1):5, abstract no. U018. http://onlinelibrary.wiley.com/doi/10.1111/bju.2005.95.issue-s1/issuetoc
25. Holtedahl K, Verelst M, Schiefloe A, et al. Usefulness of urodynamic examination in female urinary incontinence-lessons from a population-based, randomized, controlled study of conservative treatment. Scand J Urol Nephrol 2000 Jun;34(3):169-74. http://www.ncbi.nlm.nih.gov/pubmed/10961470
26. Malone-Lee JG, Al-Buheissi S. Does urodynamic verification of overactive bladder determine treatment success? Results from a randomized placebo controlled study. BJU Int 2009 Apr;103(7):931-7. http://www.ncbi.nlm.nih.gov/pubmed/19281469
27. Ramsay IN, Ali HM, Hunter M, et al. A randomized controlled trial of urodynamic investigations prior to conservative treatment of urinary incontinence in the female. Int Urogynecol J Pelvic Floor Dysfunct 1995;6(5):277-81.
28. Ward RM, Hampton BS, Blume JD, et al. The impact of multichannel urodynamics upon treatment recommendations for female urinary incontinence. Int Urogynecol J Pelvic Floor Dysfunct 2008 Sep;19(9):1235-41. http://www.ncbi.nlm.nih.gov/pubmed/18425401
29. Nager CW, FitzGerald M, Kraus SR, et al. Urodynamic measures do not predict stress continence outcomes after surgery for stress urinary incontinence in selected women. J Urol 2008 Apr;179(4):1470-4. http://www.ncbi.nlm.nih.gov/pubmed/18295276

30. Hsiao SM, Chang TC, Lin HH. Risk factors affecting cure after mid-urethral tape procedure for female urodynamic stress incontinence: comparison of retropubic and transobturator routes. Urology 2009 May;73(5):981-6.
http://www.ncbi.nlm.nih.gov/pubmed/19285713
31. McLennan MT, Melick CF, Bent AE. Leak-point pressure: clinical application of values at two different volumes. Int Urogynecol J Pelvic Floor Dysfunct 2000 Jun;11(3):136-41.
http://www.ncbi.nlm.nih.gov/pubmed/11484740
32. Wadie BS, El-Hefnawy AS. Urethral pressure measurement in stress incontinence: does it help? Int Urol Nephrol 2009;41(3):491-5.
http://www.ncbi.nlm.nih.gov/pubmed/19048384
33. Roderick T, Paul M, Christopher M, et al. Urethral retro-resistance pressure: association with established measures of incontinence severity and change after midurethral tape insertion. Neurourol Urodyn 2009;28(1):86-9.
http://www.ncbi.nlm.nih.gov/pubmed/18671296
34. Lemack GE, Krauss S, Litman H, et al. Normal preoperative urodynamic testing does not predict voiding dysfunction after Burch colposuspension versus pubovaginal sling. J Urol 2008 Nov;180(5):2076-80.
http://www.ncbi.nlm.nih.gov/pubmed/18804239
35. Dawson T, Lawton V, Adams E, et al. Factors predictive of post-TVT voiding dysfunction. Int Urogynecol J Pelvic Floor Dysfunct 2007 Nov;18(11):1297-302.
http://www.ncbi.nlm.nih.gov/pubmed/17347790
36. Hong B, Park S, Kim HS, et al. Factors predictive of urinary retention after a tension-free vaginal tape procedure for female stress urinary incontinence. J Urol 2003 Sep;170(3):852-6.
http://www.ncbi.nlm.nih.gov/pubmed/12913715
37. Lose G, Jorgensen L, Mortensen SO, et al. Voiding difficulties after colposuspension. Obstet Gynecol 1987 Jan;69(1):33-8.
http://www.ncbi.nlm.nih.gov/pubmed/3796917
38. Iglesia CB, Shott S, Fenner DE, et al. Effect of preoperative voiding mechanism on success rate of autologous rectus fascia suburethral sling procedure. Obstet Gynecol 1998 Apr;91(4):577-81.
http://www.ncbi.nlm.nih.gov/pubmed/9540944
39. Wheeler TL 2nd, Richter HE, Greer WJ, et al. Predictors of success with postoperative voiding trials after a mid urethral sling procedure. J Urol 2008;179(2):600-4.
http://www.ncbi.nlm.nih.gov/pubmed/18082219
40. Gravina GL, Costa AM, Ronchi P, et al. Bladder outlet obstruction index and maximal flow rate during urodynamic study as powerful predictors for the detection of urodynamic obstruction in women. Neurourol Urodyn 2007;26(2):247-53.
http://www.ncbi.nlm.nih.gov/pubmed/17219400
41. Richter HE, Diokno A, Kenton K, et al. Predictors of treatment failure 24 months after surgery for stress urinary incontinence. J Urol 2008 Mar;179(3):1024-30.
http://www.ncbi.nlm.nih.gov/pubmed/18206917
42. Kuo HC. Effect of detrusor function on the therapeutic outcome of a suburethral sling procedure using a polypropylene sling for stress urinary incontinence in women. Scand J Urol Nephrol 2007;41(2): 138-43.
http://www.ncbi.nlm.nih.gov/pubmed/17454953
43. Colombo M, Milani R, Vitobello D, et al. A randomized comparison of Burch colposuspension and abdominal paravaginal defect repair for female stress urinary incontinence. Am J Obstet Gynecol 1996 Jul;175(1):78-84.
http://www.ncbi.nlm.nih.gov/pubmed/8694079
44. Sahai A, Sangster P, Kalsi V, et al. Assessment of urodynamic and detrusor contractility variables in patients with overactive bladder syndrome treated with botulinum toxin-A: is incomplete bladder emptying predictable? BJU Int 2009 Mar;103(5):630-4.
http://www.ncbi.nlm.nih.gov/pubmed/18990156
45. Houwert RM, Venema PL, Aquarius AE, et al. Predictive value of urodynamics on outcome after midurethral sling surgery for female stress urinary incontinence. Am J Obstet Gynecol 2009 Jun;200(6):649.e1-12.
http://www.ncbi.nlm.nih.gov/pubmed/19344879
46. Nilsson CG, Kuuva N, Falconer C, et al. Long-term results of the tension-free vaginal tape (TVT) procedure for surgical treatment of female stress urinary incontinence. Int Urogynecol J Pelvic Floor Dysfunct 2001;12 Suppl 2:S5-8.
http://www.ncbi.nlm.nih.gov/pubmed/11450979

47. Ward K, Hilton P. Prospective multicentre randomised trial of tension-free vaginal tape and colposuspension as primary treatment for stress incontinence. BMJ 2002 Jul;325(7355):67. http://www.ncbi.nlm.nih.gov/pubmed/12114234
48. Kuo HC. Analysis of the pathophysiology of lower urinary tract symptoms in patients after prostatectomy. Urol Int 2002;68(2):99-104. http://www.ncbi.nlm.nih.gov/pubmed/11834899
49. Groutz A, Blaivas JG, Chaikin DC, et al. The pathophysiology of post-radical prostatectomy incontinence: a clinical and video urodynamic study. J Urol 2000 Jun;163(6):1767-70. http://www.ncbi.nlm.nih.gov/pubmed/10799178
50. Huckabay C, Twiss C, Berger A, et al. A urodynamics protocol to optimally assess men with post-prostatectomy incontinence. Neurourol Urodyn 2005;24(7):622-6. http://www.ncbi.nlm.nih.gov/pubmed/16208638
51. Gomha MA, Boone TB. Artificial urinary sphincter for post-prostatectomy incontinence in men who had prior radiotherapy: a risk and outcome analysis. J Urol 2002 Feb;167(2 Pt 1):591-6. http://www.ncbi.nlm.nih.gov/pubmed/11792924
52. Thiel DD, Young PR, Broderick GA, et al. Do clinical or urodynamic parameters predict artificial urinary sphincter outcome in post-radical prostatectomy incontinence? Urology 2007 Feb;69(2):315-9. http://www.ncbi.nlm.nih.gov/pubmed/17320671

2.7 Pad testing

A well-designed continence pad will contain any urine leaked within a period of time and this has therefore been used as a way of quantifying leakage. Although the International Continence Society has attempted to standardise pad testing, there remains variation in the duration of the test and the physical activity undertaken during the test.

2.7.1 ***Question***

In adults with UI, what are the reliability, the diagnostic accuracy and predictive value of pad testing?

2.7.2 ***Evidence***

The use of pad tests has been reviewed in the 4th International Consultation on Incontinence. Many studies have investigated the use of short-term and long-term pad tests to diagnose UI (1). Several other studies have investigated the correlation between pad test results and symptom scores for UI or LUTS (2-6). In addition, several studies have analysed the reproducibility of pad tests (6,7-11).

A few studies have tried to use pad testing to predict the outcome of treatment for UI with variable results (12,13). Currently, pad tests are mostly used as objective outcomes in clinical trials. However, pad tests may be helpful in daily clinical practice, and most guidelines already include the use of pad testing to evaluate treatment outcome (14,15). There is good evidence to show that repeat pad testing can detect change following treatment for UI (16-18).

Evidence summary	**LE**
A pad test can diagnose UI accurately, is reproducible and correlates with patients' symptoms.	1b
A pad test cannot differentiate between causes of UI.	4
An office-based pad test requires standardisation of bladder volume and a predefined set of exercises to improve diagnostic accuracy.	1b
A pad weight gain > 1 g in a 1-hour test can be used as a threshold to diagnose UI.	2b
Patient adherence to home pad testing protocols is poor.	1b
A weight gain > 1.3 g in a 24-hour home-based test can be used as a diagnostic threshold for UI.	1b
Home-based pad tests longer than 24 hours provide no additional benefit.	2b
Repeat pad tests can indicate treatment outcome.	1b

Recommendations	**GR**
Use a pad test when quantification of urinary incontinence is required.	C
Use repeat pad test if objective treatment outcome measure is required.	C

2.7.3 ***Research recommendation***

A systematic review of pad testing at home and in the office would clarify its role in routine care.

2.7.4 ***References***

1. Abrams P, Cardozo L, Khoury S, et al., editors. Incontinence. 4th International Consultation on Incontinence, Paris July 5-8, 2008. Plymouth: Health Publication Ltd, 2009. http://www.icud.info/incontinence.html
2. Aslan E, Beji NK, Coskun A, et al. An assessment of the importance of pad testing in stress urinary incontinence and the effects of incontinence on the life quality of women. Int Urogynecol J Pelvic Floor Dysfunct 2003 Nov;14(5):316-9; discussion 320. http://www.ncbi.nlm.nih.gov/pubmed/14618307
3. Harvey MA, Kristjansson B, Griffith D, et al. The Incontinence Impact Questionnaire and the Urogenital Distress Inventory: a revisit of their validity in women without a urodynamic diagnosis. Am J Obstet Gynecol 2001 Jul;185(1):25-31. http://www.ncbi.nlm.nih.gov/pubmed/11483899
4. Singh M, Bushman W, Clemens JQ. Do pad tests and voiding diaries affect patient willingness to participate in studies of incontinence treatment outcomes? J Urol 2004 Jan;171(1):316-8; discussion 318-9. http://www.ncbi.nlm.nih.gov/pubmed/14665904
5. Franco AV, Lee F, Fynes MM. Is there an alternative to pad tests? Correlation of subjective variables of severity of urinary loss to the 1-h pad test in women with stress urinary incontinence. BJU Int 2008 Aug 5;102(5):586-90. http://www.ncbi.nlm.nih.gov/pubmed/18384632
6. Albo M, Wruck L, Baker J, et al. The relationships among measures of incontinence severity in women undergoing surgery for stress urinary incontinence. J Urol 2007 May;177(5):1810-4. http://www.ncbi.nlm.nih.gov/pubmed/17437826
7. Simons AM, Yoong WC, Buckland S, et al. Inadequate repeatability of the one-hour pad test: the need for a new incontinence outcome measure. BJOG 2001 Mar;108(3):315-9. http://www.ncbi.nlm.nih.gov/pubmed/11281474
8. Jakobsen H, Kromann-Andersen B, Nielsen KK, et al. Pad weighing tests with 50% or 75% bladder filling. Does it matter? Acta Obstet Gynecol Scand 1993;72(5):377-81. http://www.ncbi.nlm.nih.gov/pubmed/8392270
9. Groutz A, Blaivas JG, Chaikin DC, et al. Noninvasive outcome measures of urinary incontinence and lower urinary tract symptoms: a multicenter study of micturition diary and pad tests. J Urol 2000 Sep;164(3 Pt 1):698-701. http://www.ncbi.nlm.nih.gov/pubmed/10953128
10. Karantanis E, O'Sullivan R, Moore KH. The 24-hour pad test in continent women and men: normal values and cyclical alterations. BJOG 2003 Jun;110(6):567-71. http://www.ncbi.nlm.nih.gov/pubmed/12798473
11. Kromann-Andersen B, Jakobsen H, Thorup Andersen J. Pad-weighing tests: a literature survey on test accuracy and reproducibility. Neurourol Urodyn 1989;8(3):237-42. http://onlinelibrary.wiley.com/doi/10.1002/nau.1930080309/abstract
12. Richter HE, Diokno A, Kenton K, et al. Predictors of treatment failure 24 months after surgery for stress urinary incontinence. J Urol 2008 Mar;179(3):1024-30. http://www.ncbi.nlm.nih.gov/pubmed/18206917
13. Foster RT, Sr., Anoia EJ, Webster GD, et al. In patients undergoing neuromodulation for intractable urge incontinence a reduction in 24-hr pad weight after the initial test stimulation best predicts long-term patient satisfaction. Neurourol Urodyn 2007;26(2):213-7. http://www.ncbi.nlm.nih.gov/pubmed/17009252
14. Leach GE, Dmochowski RR, Appell RA, et al. Female Stress Urinary Incontinence Clinical Guidelines Panel summary report on surgical management of female stress urinary incontinence. The American Urological Association. J Urol 1997 Sep;158(3 Pt 1):875-80. http://www.ncbi.nlm.nih.gov/pubmed/9258103
15. Blaivas JG, Appell RA, Fantl JA, et al. Standards of efficacy for evaluation of treatment outcomes in urinary incontinence: recommendations of the Urodynamic Society. Neurourol Urodyn 1997;16(3): 145-7. http://www.ncbi.nlm.nih.gov/pubmed/9136135

16. Floratos DL, Sonke GS, Rapidou CA, et al. Biofeedback vs verbal feedback as learning tools for pelvic muscle exercises in the early management of urinary incontinence after radical prostatectomy. BJU Int 2002 May;89(7):714-9. http://www.ncbi.nlm.nih.gov/pubmed/11966630
17. Blackwell AL, Yoong W, Moore KH. Criterion validity, test-retest reliability and sensitivity to change of the St George Urinary Incontinence Score. BJU Int 2004 Feb;93(3):331-5. http://www.ncbi.nlm.nih.gov/pubmed/14764131
18. Ward KL, Hilton P; UK and Ireland TVT Trial Group. A prospective multicenter randomized trial of tension-free vaginal tape and colposuspension for primary urodynamic stress incontinence: two-year follow-up. Am J Obstet Gynecol 2004 Feb;190(2):324-31. http://www.ncbi.nlm.nih.gov/pubmed/14981369

2.8 Imaging

Imaging improves our understanding of the anatomical and functional abnormalities that may cause UI. In clinical research, imaging is used to understand the relationship between conditions of the central nervous system (CNS) and of the lower urinary tract in causing UI, and to investigate the relationship between conditions of the lower urinary tract and treatment outcome.

Ultrasonography and magnetic resonance imaging (MRI) have replaced X-ray imaging as both procedures are safer than X-ray imaging and can provide both qualitative and quantitative data on the kidneys, bladder neck and pelvic floor.

Ultrasound is preferred to MRI because of its ability to produce three-dimensional and four-dimensional (dynamic) images at lower cost and wider availability. The current lack of knowledge about the pathophysiology of UI makes it difficult to carry out research in the imaging of UI. Studies on lower urinary tract imaging in patients with UI often include an evaluation of surgical outcomes, making design and conduct of these trials particularly challenging.

*2.8.1 **Questions***

- Can imaging aid selection of surgical procedure for SUI?
- How accurate is imaging in evaluating the outcome of UI surgery?

*2.8.2 **Evidence***

Several imaging studies have investigated the relationship between sphincter volume and function in women (1) and between sphincter volume and surgery outcome in men and women (2,3). Imaging of urethral anastomosis following radical prostatectomy has been used to investigate continence status (4). However, no imaging test has been shown to predict the outcome of treatment for UI.

Many studies have evaluated the imaging of bladder neck mobility by US and MRI, and concluded that UI cannot be identified by a particular pattern of urethrovesical movements (5). In addition, the generalised increase in urethral mobility after childbirth does not appear to be associated with de-novo SUI (6).

There is a general consensus that MRI provides good global pelvic floor assessment, including pelvic organ prolapse, defecatory function and integrity of the pelvic floor support structure (7). However, there is a large variation in MRI interpretation between institutions (8) and little evidence to support its clinical usefulness.

Studies have assessed the use of imaging to effect of mid-urethral sling insertion for SUI. One study suggested that mid-urethral sling placement decreased mobility of the mid-urethra, but not of the bladder neck (9). In addition, the position of mid-urethral slings with respect to the pubis has been associated with the cure of UI (10).

However, in conclusion, no studies were found which specifically addressed the PICO questions for this section. Lower urinary tract imaging does not appear to provide any clinical benefit in patients with UI (11). Despite this, however, some experts continue to recommend imaging (12-15).

Evidence summary	LE
Imaging can reliably measure bladder neck and urethral mobility, although there is no evidence of any clinical benefit in patients with UI.	2b
Imaging of the pelvic floor can identify levator ani detachment and hiatus, although there is little evidence of clinical benefit.	2b
Ultrasonography can image mid-urethral slings, although more research is needed into the relationship between sling position and surgical outcome.	2b

Recommendation	GR
Do not routinely carry out imaging of the upper or lower urinary tract as part of the assessment of uncomplicated SUI in women.	A

2.8.3 ***References***

1. Morgan DM, Umek W, Guire K, et al. Urethral sphincter morphology and function with and without stress incontinence. J Urol 2009 Jul;182(1):203-9. http://www.ncbi.nlm.nih.gov/pubmed/19450822
2. Digesu GA, Robinson D, Cardozo L, et al. Three-dimensional ultrasound of the urethral sphincter predicts continence surgery outcome. Neurourol Urodyn 2009;28(1):90-4. http://www.ncbi.nlm.nih.gov/pubmed/18726938
3. Nguyen L, Jhaveri J, Tewari A. Surgical technique to overcome anatomical shortcoming: balancing post-prostatectomy continence outcomes of urethral sphincter lengths on preoperative magnetic resonance imaging. J Urol 2008 May;179(5):1907-11. http://www.ncbi.nlm.nih.gov/pubmed/18353395
4. Paparel P, Akin O, Sandhu JS, et al. Recovery of urinary continence after radical prostatectomy: association with urethral length and urethral fibrosis measured by preoperative and postoperative endorectal magnetic resonance imaging. Eur Urol 2009 Mar;55(3):629-37. http://www.ncbi.nlm.nih.gov/pubmed/18801612
5. Lewicky-Gaupp C, Blaivas J, Clark A, et al. "The cough game": are there characteristic urethrovesical movement patterns associated with stress incontinence? Int Urogynecol J Pelvic Floor Dysfunct 2009 Feb;20(2):171-5. http://www.ncbi.nlm.nih.gov/pubmed/18850057
6. Shek KL, Dietz HP, Kirby A. The effect of childbirth on urethral mobility: a prospective observational study. J Urol 2010 Aug;184(2):629-34. http://www.ncbi.nlm.nih.gov/pubmed/20639028
7. Woodfield CA, Krishnamoorthy S, Hampton BS, et al. Imaging pelvic floor disorders: trend toward comprehensive MRI. AJR Am J Roentgenol 2010 Jun;194(6):1640-9. http://www.ncbi.nlm.nih.gov/pubmed/20489108
8. Lockhart ME, Fielding JR, Richter HE, et al. Reproducibility of dynamic MR imaging pelvic measurements: a multi-institutional study. Radiology 2008 Nov;249(2):534-40. http://www.ncbi.nlm.nih.gov/pubmed/18796659
9. Shek KL, Chantarasorn V, Dietz HP. The urethral motion profile before and after suburethral sling placement. J Urol 2010 Apr;183(4):1450-4. http://www.ncbi.nlm.nih.gov/pubmed/20171657
10. Chantarasorn V, Shek KL, Dietz HP. Sonographic appearance of transobturator slings: implications for function and dysfunction. Int Urogynecol J 2011 Apr;22(4):493-8. http://www.ncbi.nlm.nih.gov/pubmed/20967418
11. Thuroff JW, Abrams P, Andersson KE, et al. EAU guidelines on urinary incontinence. Eur Urol 2011 Mar;59(3):387-400. http://www.ncbi.nlm.nih.gov/pubmed/21130559
12. Doumouchtsis SK, Jeffery S, Fynes M. Female voiding dysfunction. Obstet Gynecol Surv 2008 Aug;63(8):519-26. http://www.ncbi.nlm.nih.gov/pubmed/18631408
13. Dietz HP. Pelvic floor ultrasound: a review. Am J Obstet Gynecol 2010 Apr;202(4):321-34. http://www.ncbi.nlm.nih.gov/pubmed/20350640
14. Savoye-Collet C, Koning E, Dacher JN. Radiologic evaluation of pelvic floor disorders. Gastroenterol Clin North Am 2008 Sep;37(3):553-67, viii. http://www.ncbi.nlm.nih.gov/pubmed/18793996

15. Santoro GA, Wieczorek AP, Dietz HP, et al. State of the art: an integrated approach to pelvic floor ultrasonography. Ultrasound Obstet Gynecol 2011 Apr;37(4):381-96. http://www.ncbi.nlm.nih.gov/pubmed/20814874

3. CONSERVATIVE TREATMENT

In clinical practice, it is a convention that non-surgical therapies are tried first because they usually carry the least risk of harm.

The Panel has grouped together simple clinical interventions, which are likely to be initiated by the healthcare professional at the first point of contact. These are followed by a series of treatments described as 'lifestyle interventions' because they are changes that a patient can make to improve symptoms. These are then followed by behavioural treatments, which require some form of training or instruction, and physical therapies, which require instruction and use some form of physical intervention. Drug treatment is described separately. The Panel recognises that in clinical practice a combination of these interventions may be recommended as a care package. Consequently, recommendations have been linked together in places where this reflects the way that care is often 'packaged'.

3.1 Simple clinical interventions

*3.1.1 **Underlying disease/cognitive impairment***

Urinary Incontinence, especially in the elderly, can be worsened or caused by underlying diseases, especially conditions that cause polyuria, nocturia, increased abdominal pressure or CNS disturbances. These conditions include:

- cardiac failure (1);
- chronic renal failure;
- diabetes (1,2);
- chronic obstructive pulmonary disease (3);
- neurological disorders;
- stroke;
- dementia;
- multiple sclerosis;
- general cognitive impairment;
- sleep disturbances e.g. sleep apnoea.

It is possible that correction of the underlying disease may reduce the severity of urinary symptoms. However, this is often difficult to assess as patients often suffer from more than one condition. In addition, interventions may be combined and individualised, making it impossible to decide which change in an underlying disease has affected a patient's UI.

3.1.1.1 Question

In adults with UI, does correcting an underlying disease or cognitive impairment improve UI or QoL compared to no correction of underlying disease?

3.1.1.2 Evidence

We found only one study that directly addressed the question. The study was a follow-up of an earlier RCT. The study found no correlation between earlier intensive treatment of type 1 diabetes mellitus and the prevalence of UI in later life versus conventional treatment (4). This was despite the known benefit of close control of blood glucose levels on other known consequences of type 1 diabetes mellitus, including renal and visual impairment. A higher prevalence of UI was associated with an increase in age and body mass index in this study.

Evidence summary	**LE**
Improved diabetic control neither resolves nor improves UI.	3

3.1.1.3 References

1. Lee PG, Cigolle C, Blaum C, et al. The co-occurrence of chronic diseases and geriatric syndromes: the health and retirement study. J Am Geriatr Soc 2009 Mar;57(3):511-6. http://www.ncbi.nlm.nih.gov/pubmed/19187416
2. Vischer UM, Bauduceau B, Bourdel-Marchasson I, et al. A call to incorporate the prevention and treatment of geriatric disorders in the management of diabetes in the elderly. Diabetes Metab 2009 Jun;35(3):168-77. http://www.ncbi.nlm.nih.gov/pubmed/19446486
3. Hirayama F, Lee AH, Binns CW, et al. Urinary incontinence in men with chronic obstructive pulmonary disease. Int J Urol 2008 Aug;15(8):751-3. http://www.ncbi.nlm.nih.gov/pubmed/18786199
4. Sarma AV, Kanaya A, Nyberg LM, et al. Risk factors for urinary incontinence among women with type 1 diabetes: findings from the epidemiology of diabetes interventions and complications study. Urology 2009 Jun;73(6):1203-9. http://www.ncbi.nlm.nih.gov/pubmed/19362350

3.1.2 ***Adjustment of medication***

Although UI is listed as an adverse effect in many drug compendiums, e.g. *British National Formulary*, this is mainly due to uncontrolled individual patient reports and post-marketing surveillance. Few controlled studies have used the occurrence of UI as a primary outcome or were powered to assess the occurrence of statistically significant UI or worsening rates against placebo. It is therefore not possible in most cases to be sure that a drug causes incontinence.

In patients with existing UI, particularly the elderly, it may be difficult or impossible to distinguish between the effects on UI of medication, comorbidity, or ageing.

Although changing drug regimens for underlying disease may be considered a possible early intervention for UI, there is very little evidence of benefit (1). There is also a theoretical risk that stopping or altering medication may result in more harm than benefit.

3.1.2.1 Question

In adults with UI, does adjustment of medication improve UI or QoL compared to no change in treatment?

3.1.2.2 Evidence

A structured narrative review found there was only weak evidence for a causative effect for most medications associated with the adverse effect of new, or worsening, UI (2). A case-control study found that women with hypertension started on alpha-blockers were more likely to develop UI than untreated controls (3).

Several case series have suggested a link between drugs with a CNS site of action and UI (2). A secondary analysis of a large observational database of elderly Italians found a higher risk of UI among those taking benzodiazepines. In addition, a retrospective analysis of a large Dutch database of dispensed prescriptions found that patients started on a selective serotonin re-uptake inhibitor were more likely to require a subsequent prescription of antimuscarinic drugs or absorbent urinary pads, suggesting the development of UI (4). Limited evidence from case series and case-control studies suggests that diuretic therapy is not associated with a higher incidence or worsening of UI (2). It is possible that SUI may be worsened by the development of the chronic cough sometimes associated with ACE inhibitors prescribed for heart failure or hypertension.

Systemic oestrogen therapy for post-menopausal women was shown by a meta-analysis (5) to be associated with the development and worsening of UI. Systemic oestrogen, compared to placebo, worsened symptoms of UI, both in women who had undergone a hysterectomy, and in those who had not (5). In addition, data from a single large RCT (6) showed that previously continent women treated with systemic oestrogen were more likely to develop symptoms of UI compared to women given a placebo.

These more recent analyses have superseded conflicting results from earlier and smaller studies of the effect of oestrogen replacement therapy on UI. However, the number of women who gain relief from UI through stopping systemic oestrogen replacement is likely to be small, as there has been a decline in the use of oestrogen replacement therapy by post-menopausal women, due to concerns about developing cancer and the association of oestrogen replacement therapy with UI.

Evidence summary	LE
Alpha-blockers used to treat hypertension in women may cause or exacerbate UI, and stopping them may relieve UI.	3
Individuals taking drugs acting on the central nervous system may experience UI as a side effect.	3
Diuretics in elderly patients does not cause or worsen UI.	3
Systemic oestrogen replacement therapy in previously continent women approximately doubles the prevalence of UI at 12 months compared to placebo.	1b
Women with pre-existing UI, who use systemic oestrogen replacement therapy, are 30% more likely to experience worsening UI compared to placebo.	1a

Recommendations	GR
Take a drug history from all patients with urinary incontinence.	A
Inform women with urinary incontinence that begins or worsens after starting systemic oestrogen replacement therapy that it may cause urinary incontinence.	A
Review any new medication associated with the development or worsening of urinary incontinence.	C

3.1.2.3 References

1. Urinary incontinence: the management of urinary incontinence in women. Clinical guidelines CG40. National Institute for Health and Clinical Excellence, October 2006. http://guidance.nice.org.uk/CG40
2. Tsakiris P, de la Rosette JJ, Michel MC, et al. Pharmacologic treatment of male stress urinary incontinence: systematic review of the literature and levels of evidence. Eur Urol 2008 Jan;53(1):53-9. http://www.ncbi.nlm.nih.gov/pubmed/17920183
3. Marshall HJ, Beevers DG. Alpha-adrenoceptor blocking drugs and female urinary incontinence: prevalence and reversibility. Br J Clin Pharmacol 1996 Oct;42(4):507-9. http://www.ncbi.nlm.nih.gov/pubmed/8904625
4. Movig KL, Leufkens HG, Belitser SV, et al. Selective serotonin reuptake inhibitor-induced urinary incontinence. Pharmacoepidemiol Drug Saf 2002 Jun;11(4):271-9. http://www.ncbi.nlm.nih.gov/pubmed/12138594
5. Cody JD, Richardson K, Moehrer B, et al. Oestrogen therapy for urinary incontinence in post-menopausal women. Cochrane Database Syst Rev 2009 Oct 7;(4):CD001405. http://www.ncbi.nlm.nih.gov/pubmed/19821277
6. Hendrix SL, Cochrane BB, Nygaard IE, et al. Effects of estrogen with and without progestin on urinary incontinence. JAMA 2005 Feb 23;293(8):935-48. http://www.ncbi.nlm.nih.gov/pubmed/15728164

*3.1.3 **Constipation***

Several studies have shown strong associations between constipation, UI and OAB. Constipation can be improved by behavioural and medical treatments.

3.1.3.1 Question

Does treatment for constipation therapy improve symptoms or QoL in patients with UI?

3.1.3.2 Evidence

One RCT found that a multimodal intervention in elderly patients, involving assisted toileting, fluid intake, etc., reduced the occurrence of UI and constipation, while behavioural therapy appeared to improve both constipation and UI (1). Another study found bowel function improved after successful treatment of voiding problems with sacral nerve stimulation (2). A different study recommended the simultaneous treatment of constipation and urinary disorders in children and adolescents with LUTS.

An observational study comparing women with UI and women with pelvic organ prolapse to controls found that a history of constipation was associated with both prolapse and UI (3). Two large cross-sectional population-based studies (4,5) and two longitudinal studies (6,7) showed constipation was a risk factor for LUTS.

In conclusion, constipation appears to be associated with LUTS. However, there is no evidence to show whether or not treating constipation improves LUTS, although both constipation and UI appear to be improved by certain behavioural interventions.

Evidence summary	LE
There is a consistent association between a history of constipation and the development of UI and pelvic organ prolapse.	3
There is no evidence that treatment of constipation improves UI.	4
Multimodal behavioural therapy improves both constipation and UI in the elderly.	1b
Simultaneous treatment of constipation and urinary incontinence in adolescents is beneficial.	3

Recommendation	GR
For adults with UI, treat co-existing constipation.	C

3.1.3.3 References

1. Schnelle JF, Leung FW, Rao SS, et al. A controlled trial of an intervention to improve urinary and fecal incontinence and constipation. J Am Geriatr Soc 2010;58(8):1504-11. http://www.ncbi.nlm.nih.gov/pubmed/20653804
2. Killinger KA, Kangas JR, Wolfert C, et al. Secondary changes in bowel function after successful treatment of voiding symptoms with neuromodulation. Neurourol Urodyn 2011 Jan;30(1):133-7. http://www.ncbi.nlm.nih.gov/pubmed/20928914
3. Spence-Jones C, Kamm MA, Henry MM, et al. Bowel dysfunction: a pathogenic factor in uterovaginal prolapse and urinary stress incontinence. Br J Obstet Gynaecol 1994 Feb;101(2):147-52. http://www.ncbi.nlm.nih.gov/pubmed/8305390
4. Coyne KS, Cash B, Kopp Z, et al. The prevalence of chronic constipation and faecal incontinence among men and women with symptoms of overactive bladder. BJU Int 2011 Jan;107(2):254-61. http://www.ncbi.nlm.nih.gov/pubmed/20590548
5. Diokno AC, Brock BM, Herzog AR, et al. Medical correlates of urinary incontinence in the elderly. Urology 1990 Aug;36(2):129-38. http://www.ncbi.nlm.nih.gov/pubmed/2385880
6. Alling Moller L, Lose G, Jorgensen T. Risk factors for lower urinary tract symptoms in women 40 to 60 years of age. Obstet Gynecol 2000 Sep;96(3):446-51. http://www.ncbi.nlm.nih.gov/pubmed/10960640
7. Byles J, Millar CJ, Sibbritt DW, et al. Living with urinary incontinence: a longitudinal study of older women. Age Ageing 2009 May;38(3):333-8; discussion 251. http://www.ncbi.nlm.nih.gov/pubmed/19258398

*3.1.4 **Containment***

Although initiation of assessment and treatment of UI should be the main priority for healthcare professionals, containment is of great practical importance to many patients with UI. Absorbent pads are predominantly used to absorb or collect leakage. However, if these are inadequate, an indwelling urethral or suprapubic catheter may then be used after taking into account the complications associated with catheter use, e.g. infection, bladder spasm, stone formation, etc.

3.1.4.1 Question

In adults with UI, does urinary containment improve patient outcomes, regarding either urinary symptoms or QoL, compared with no containment?

3.1.4.2 Evidence

There was a lack of consistency in the evidence reviewed. There have been two consensus statements in the 4th International Consultation on Incontinence (1) and one RCT comparing conservative treatment with urinary pads (2). There have been Cochrane reviews of devices (3) and pads (4), and three small trials of devices with differing outcomes (5-7). Few studies have been carried out in urinary catheterisation; these included an RCT comparing condom catheters with indwelling urinary catheters (8). A small open crossover RCT (11) evaluated different penile clamps and showed that none completely controlled urine leakage, but penile blood flow was reduced.

Evidence summary	LE
Pads are not effective as a treatment for UI.	1b
Different pads have different advantages and disadvantages.	1b
Intermittent catheterisation carries a lower risk of urinary tract infection and bacteriuria than indwelling catheterisation.	1b
Containment devices are better than no treatment.	4
There is not enough evidence to conclude which containment device is best.	4
Condom catheters are better than indwelling catheters if no residual urine is present.	1b
There is no evidence to compare mechanical devices with other forms of treatment.	4

Recommendations	GR
Offer pads when containment of urinary incontinence is needed.	B
Adapt the choice of pad to the type and severity of urinary incontinence and the patient's needs.	A
Offer catheterisation to manage urinary incontinence when no other treatments can be considered.	B
Offer condom catheters to men with urinary incontinence without significant residual urine.	A
Offer to teach intermittent catheterisation to manage UI associated with retention of urine.	A
Do not routinely offer intravaginal devices as treatment for incontinence.	B
Do not use penile clamps for control of UI in men.	A

3.1.4.3 References

1. Cottenden A, Bliss DZ, Buckley B, et al: Committee 20. Management using continence products. In: Abrams P, Cardozo L, Khoury S, et al., editors. Incontinence. 4th International Consultation on Incontinence, Paris, July 5-8, 2008. Plymouth: Health Publication Ltd, 2009, pp. 1519-1642. http://www.icud.info/incontinence.html
2. Fader M, Cottenden A, Getliffe K, et al. Absorbent products for urinary/faecal incontinence: a comparative evaluation of key product designs. Health Technol Assess 2008 Jul;12(29):iii-iv, ix-185. http://www.ncbi.nlm.nih.gov/pubmed/18547500
3. Shaikh S, Ong EK, Glavind K, et al. Mechanical devices for urinary incontinence in women. Cochrane Database Syst Rev 2006 Jul 19;(3):CD001756. Update in: Cochrane Database Syst Rev 2011;(7):CD001756. http://www.ncbi.nlm.nih.gov/pubmed/16855977
4. Fader M, Cottenden AM, Getliffe K. Absorbent products for moderate-heavy urinary and/or faecal incontinence in women and men. Cochrane Database Syst Rev 2008 Oct 8;(4):CD007408. http://www.ncbi.nlm.nih.gov/pubmed/18843748
5. Allen WA, Leek H, Izurieta A, Moore KH. Update: the "Contiform" intravaginal device in four sizes for the treatment of stress incontinence. Int Urogynecol J Pelvic Floor Dysfunct 2008 June;19(6):757-61. http://www.ncbi.nlm.nih.gov/pubmed/18183342
6. Richter HE, Burgio KL, Brubaker L, et al. Continence pessary compared with behavioral therapy or combined therapy for stress incontinence: a randomized controlled trial. Obstet Gynecol 2010 Mar;115(3):609-17. http://www.ncbi.nlm.nih.gov/pubmed/20177294
7. Ziv E, Stanton SL, Abarbanel J. Significant improvement in the quality of life in women treated with a novel disposable intravaginal device for stress urinary incontinence. Int Urogynecol J Pelvic Floor Dysfunct 2009 Jun;20(6):651-8. http://www.ncbi.nlm.nih.gov/pubmed/19434384
8. Saint S, Kaufman SR, Rogers MA, et al. Condom versus indwelling urinary catheters: a randomized trial. J Am Geriatr Soc 2006 Jul;54(7):1055-61. http://www.ncbi.nlm.nih.gov/pubmed/16866675
9. Jamison J, Maguire S, McCann J. Catheter policies for management of long term voiding problems in adults with neurogenic bladder disorders. Cochrane Database Syst Rev 2004;(2):CD004375. http://www.ncbi.nlm.nih.gov/pubmed/15106248
10. Hagen S, Sinclair L, Cross S. Washout policies in long-term indwelling urinary catheterisation in adults. Cochrane Database Syst Rev 2010 Mar 17;(3):CD004012. http://www.ncbi.nlm.nih.gov/pubmed/20238325

11. Moore KN, Schieman S, Ackerman T, et al. Assessing comfort, safety and patient satisfaction with three commonly used penile compression devices. Urology 2004 Jan;63(1):150-4. http://www.ncbi.nlm.nih.gov/pubmed/14751370

3.2 Lifestyle interventions

Examples of lifestyle factors that may be associated with incontinence include obesity, smoking, level of physical activity and diet. It may therefore be possible to improve UI by beginning lifestyle interventions, such as weight loss, fluid restriction, reduction of caffeine or alcohol intake, limiting heavy activity and stopping smoking.

*3.2.1 **Caffeine reduction***

Many drinks contain caffeine, particularly tea, coffee and cola. The pharmacological actions of caffeine include CNS stimulation, diuresis and smooth muscle relaxation. Anecdotal evidence of urinary symptoms being aggravated by excessive caffeine intake has focussed attention on whether caffeine reduction may improve UI. However, a cross-sectional population survey found no statistical association between caffeine intake and UI (1). A lack of knowledge about the caffeine content of different drinks has made the role of caffeine reduction in alleviating UI more complex.

3.2.1.1 Question

In adults with UI, does caffeine reduction improve UI or QoL, compared to no caffeine reduction?

3.2.1.2 Evidence

Four studies were found on the effect of caffeine reduction on UI (2-5). They were of moderate quality and the results were inconsistent. The studies were mainly in women, so results can only be cautiously generalised to all adults. There were two RCTs investigating caffeine reduction (3,4). One RCT showed that reducing caffeine intake resulted in reduced urgency but not reduced UI (3). However, the study was not powered for UI and compared the interventions of bladder training (BT) and caffeine reduction against BT alone. Another RCT found that reducing caffeine had no benefit for UI (4). An uncontrolled study suggested that people with OAB and high caffeine intake were more likely to show DO on filling during conventional cystometry (2). A further interventional study in the elderly showed borderline significance for the benefit of reducing caffeine intake on UI (5).

Evidence summary	**LE**
Reduction of caffeine intake does not improve UI.	2
Reduction in caffeine intake may improve symptoms of urgency and frequency.	2

3.2.1.3 References

1. Hannestad YS, Rortveit G, Daltveit AK, et al. Are smoking and other lifestyle factors associated with female urinary incontinence? The Norwegian EPINCONT Study. BJOG 2003 Mar;110(3):247-54. http://www.ncbi.nlm.nih.gov/pubmed/12628262
2. Arya LA, Myers DL, Jackson ND. Dietary caffeine intake and the risk for detrusor instability: a case-control study. Obstet Gynecol 2000 Jul;96(1):85-9. http://www.ncbi.nlm.nih.gov/pubmed/10862848
3. Bryant CM, Dowell CJ, Fairbrother G. Caffeine reduction education to improve urinary symptoms. Br J Nurs 2002 Apr 25-May 8;11(8):560-5. http://www.ncbi.nlm.nih.gov/pubmed/11979209
4. Swithinbank L, Hashim H, Abrams P. The effect of fluid intake on urinary symptoms in women. J Urol 2005 Jul;174(1):187-9. http://www.ncbi.nlm.nih.gov/pubmed/15947624
5. Tomlinson BU, Dougherty MC, Pendergast JF, et al. Dietary caffeine, fluid intake and urinary incontinence in older rural women. Int Urogynecol J Pelvic Floor Dysfunct 1999;10(1):22-8. http://www.ncbi.nlm.nih.gov/pubmed/10207763

*3.2.2 **Physical exercise***

Regular physical activity may strengthen the pelvic floor musculature and possibly decrease the risk of developing UI, especially SUI. However, it is also possible that heavy physical exercise may aggravate UI.

3.2.2.1 Question

Does physical exercise cause, improve or exacerbate UI in adults?

3.2.2.2 Evidence

The association between exercise and UI is unclear. Four studies (1-4) in differing populations concluded that strenuous physical exercise increases the risk of SUI during periods of physical activity and there is consistent evidence that physically active females and elite athletes experience higher levels of SUI than control populations (5-10). On the other hand, the presence of UI may prevent women from taking exercise (11). There is no evidence that strenuous exercise predisposes athletes to the development of SUI later in life (12). Lower levels of UI have been observed in cohorts of women who undertake moderate exercise, but it remains unclear whether taking exercise can prevent development of UI (13,14).

Evidence summary	**LE**
Female athletes may experience UI during intense physical activity but not during common activities.	3
Strenuous physical activity does not predispose to UI for women later in life.	3
Although moderate exercise is associated with lower rates of UI in middle-aged or older women, there is no evidence that starting moderate exercise improves established UI in women.	2b

3.2.2.3 References

1. Jorgensen S, Hein HO, Gyntelberg F. Heavy lifting at work and risk of genital prolapse and herniated lumbar disc in assistant nurses. Occup Med (Lond) 1994 Feb;44(1):47-9. http://www.ncbi.nlm.nih.gov/pubmed/8167320
2. Nygaard IE, Thompson FL, Svengalis SL, et al. Urinary incontinence in elite nulliparous athletes. Obstet Gynecol 1994 Aug;84(2):183-7. http://www.ncbi.nlm.nih.gov/pubmed/8041527
3. Hannestad YS, Rortveit G, Daltveit AK, et al. Are smoking and other lifestyle factors associated with female urinary incontinence? The Norwegian EPINCONT Study. BJOG 2003 Mar;110(3):247-54. http://www.ncbi.nlm.nih.gov/pubmed/12628262
4. Nygaard I, DeLancey JO, Arnsdorf L, et al. Exercise and incontinence. Obstet Gynecol Nygaard 1990 May;75(5):848-51. http://www.ncbi.nlm.nih.gov/pubmed/2325968
5. Kruger JA, Dietz HP, Murphy BA. Pelvic floor function in elite nulliparous athletes. Ultrasound Obstet Gynecol 2007 Jul;30(1):81-5. http://www.ncbi.nlm.nih.gov/pubmed/17497753
6. Bo K, Borgen JS. Prevalence of stress and urge urinary incontinence in elite athletes and controls. Med Sci Sports Exerc 2001 Nov;33(11):1797-802. http://www.ncbi.nlm.nih.gov/pubmed/11689727
7. Bo K, Maehlum S, Oseid S, et al. The prevalence of stress urinary incontinence amongst physically active and sedentary female students. Scand J Sports Sci 1989;11(3):113-6.
8. Caylet N, Fabbro-Peray P, Mares P, et al. Prevalence and occurrence of stress urinary incontinence in elite women athletes. Can J Urol 2006 Aug;13(4):3174-9. http://www.ncbi.nlm.nih.gov/pubmed/16953954
9. Thyssen HH, Clevin L, Olesen S, et al. Urinary incontinence in elite female athletes and dancers. Int Urogynecol J Pelvic Floor Dysfunct. 2002;13(1):15-7. http://www.ncbi.nlm.nih.gov/pubmed/11999199
10. Bø K, Sundgot-Borgen J. Are former female elite athletes more likely to experience urinary incontinence later in life than non-athletes? Scand J Med Sci Sports. 2010 Feb;20(1):100-4. http://www.ncbi.nlm.nih.gov/pubmed/19000097
11. Brown WJ, Miller YD. Too wet to exercise? Leaking urine as a barrier to physical activity in women. J Sci Med Sport. 2001 Dec;4(4):373-8. http://www.ncbi.nlm.nih.gov/pubmed/11905931
12. Nygaard IE. Does prolonged high-impact activity contribute to later urinary incontinence? A retrospective cohort study of female Olympians. Obstet Gynecol 1997 Nov;90(5):718-22. http://www.ncbi.nlm.nih.gov/pubmed/9351751
13. Eliasson K, Nordlander I, Larson B, et al. Influence of physical activity on urinary leakage in primiparous women. Scand J Med Sci Sports 2005 Apr;15(2):87-94. http://www.ncbi.nlm.nih.gov/pubmed/15773862
14. Kikuchi A, Niu K, Ikeda Y, et al. Association between physical activity and urinary incontinence in a community-based elderly population aged 70 years and over. Eur Urol 2007 Sep;52(3):868-74. http://www.ncbi.nlm.nih.gov/pubmed/17412488

3.2.3 ***Fluid intake***

It is generally assumed that reduction in total volume of fluid intake may be beneficial for UI. Fluid restriction is a widely used, inexpensive and non-invasive intervention that is easily recommended. It is usually advised that fluid intake and output is monitored using a frequency volume chart. Daily urine output should not be less than 1500 mL and not more than 3000 mL. The restriction of fluid intake may have adverse effects, including a predisposition to UTI, dehydration, urinary tract stone formation and constipation. The cause of a high fluid intake should be investigated.

3.2.3.1 Question

In adults with UI, what is the effect of modifying fluid intake compared to not modifying fluid intake on symptoms and QoL?

3.2.3.2 Evidence

The few RCTs provide inconsistent evidence. In most studies, the instructions for fluid intake are individualised and it is difficult to assess participant adherence to protocol. All available studies are in women.

Two RCTs of limited quality due to high drop-out rates and small sample size (1,2) produced conflicting results regarding recommendations for fluid intake. One study found that increased fluid intake improved symptoms, while the other study, which was limited to patients with DO, found that decreased fluid intake improved QoL. A more recent RCT (3) showed that a reduction in fluid intake by 25% improved symptoms in patients with OAB but not incontinence. An observational study also addressed fluid intake as part of a behavioural regime (4).

Evidence summary	**LE**
There is conflicting evidence on whether fluid modification changes symptoms of urinary incontinence and quality of life.	2

3.2.3.3 References

1. Dowd TT, Campbell JM, Jones JA. Fluid intake and urinary incontinence in older community-dwelling women. J Community Health Nurs 1996;13(3):179-86. http://www.ncbi.nlm.nih.gov/pubmed/8916607
2. Swithinbank L, Hashim H, Abrams P. The effect of fluid intake on urinary symptoms in women. J Urol 2005 Jul;174(1):187-9. http://www.ncbi.nlm.nih.gov/pubmed/15947624
3. Wyman JF, Fantl JA, McClish DK, et al. Comparative efficacy of behavioral interventions in the management of female urinary incontinence. Continence Program for Women Research Group. Am J Obstet Gynecol 1998 Oct;179(4):999-1007. http://www.ncbi.nlm.nih.gov/pubmed/9790388
4. Fantl JA, Wyman JF, McClish DK, et al. Efficacy of bladder training in older women with urinary incontinence. JAMA 1991 Feb 6;265(5):609-13. http://www.ncbi.nlm.nih.gov/pubmed/1987410

3.2.4 ***Obesity and weight loss***

In most developed countries, nearly one-quarter to more than one-third of adult women are obese. Obesity and UI are serious health problems, adversely affecting QoL. Obesity has been identified as a risk factor for UI in many epidemiological studies (1,2). There is evidence that the prevalence of both UUI and SUI increases proportionately with rising body mass index. A significant proportion of patients who undergo surgery for incontinence are overweight or obese. In 2009, the 4th International Consultation on Incontinence recommended that the role of obesity in UI should be a research priority.

3.2.4.1 Question

In adults with UI, does weight loss lead to an improvement in symptoms of UI or QoL?

3.2.4.2 Evidence

All the available evidence relates to women. The prevalence of UI in overweight individuals is well established (1,2). Obesity appears to confer a four-fold increased risk of UI (3).

Two systematic reviews concluded that weight loss was beneficial in improving symptoms of UI (4,5). Four further RCTs reported a similar benefit beneficial effect on incontinence following surgical weight reduction

programmes (6-9). The largest study was in diabetic women, for whom weight loss was the main lifestyle intervention (9). There have been other cohort studies and case-control studies suggesting similar effects, including surgery for the morbidly obese (10-17). For example, in a longitudinal cohort study, a weight loss of 5-10% was associated with a significant reduction in pad test loss of urine (18).

Evidence summary	**LE**
Obesity is a risk factor for UI in women.	1b
Weight loss (> 5%) in obese women improves UI.	1b

3.4.2.3 References

1. Danforth KN, Townsend MK, Lifford K, et al. Risk factors for urinary incontinence among middle-aged women. Am J Obstet Gynecol 2006 Feb;194(2):339-45. http://www.ncbi.nlm.nih.gov/pubmed/16458626
2. Hannestad YS, Rortveit G, Daltveit AK, et al. Are smoking and other lifestyle factors associated with female urinary incontinence? The Norwegian EPINCONT Study. BJOG 2003 Mar;110(3):247-54. http://www.ncbi.nlm.nih.gov/pubmed/12628262
3. Chen CC, Gatmaitan P, Koepp S, et al. Obesity is associated with increased prevalence and severity of pelvic floor disorders in women considering bariatric surgery. Surg Obes Relat Dis 2009 Jul-Aug;5(4):411-5. http://www.ncbi.nlm.nih.gov/pubmed/19136310
4. Hunskaar S. A systematic review of overweight and obesity as risk factors and targets for clinical intervention for urinary incontinence in women. Neurourol Urodyn 2008;27(8):749-57. http://www.ncbi.nlm.nih.gov/pubmed/18951445
5. Imamura M, Abrams P, Bain C, et al. Systematic review and economic modelling of the effectiveness and cost-effectiveness of non-surgical treatments for women with stress urinary incontinence. Health Technol Assess 2010 Aug;14(40):1-188, iii-iv. http://www.ncbi.nlm.nih.gov/pubmed/20738930
6. Bump RC, Sugerman HJ, Fantl JA, et al. Obesity and lower urinary tract function in women: effect of surgically induced weight loss. Am J Obstet Gynecol 1992 Aug;167(2):392-7; discussion 397-9. http://www.ncbi.nlm.nih.gov/pubmed/1497041
7. Subak LL, Johnson C, Whitcomb E, et al. Does weight loss improve incontinence in moderately obese women? Int Urogynecol J Pelvic Floor Dysfunct 2002;13(1):40-3. http://www.ncbi.nlm.nih.gov/pubmed/11999205
8. Subak LL, Whitcomb E, Shen H, et al. Weight loss: a novel and effective treatment for urinary incontinence. J Urol 2005 Jul;174(1):190-5. http://www.ncbi.nlm.nih.gov/pubmed/15947625
9. Brown JS, Wing R, Barrett-Connor E, et al. Lifestyle intervention is associated with lower prevalence of urinary incontinence: the Diabetes Prevention Program. Diabetes Care 2006 Feb;29(2):385-90. http://www.ncbi.nlm.nih.gov/pubmed/16443892
10. Subak LL, Wing R, West DS, et al; PRIDE Investigators. Weight loss to treat urinary incontinence in overweight and obese women. N Engl J Med 2009 Jan 29;360(5):481-90. http://www.ncbi.nlm.nih.gov/pubmed/19179316
11. Deitel M, Stone E, Kassam HA, et al. Gynecologic-obstetric changes after loss of massive excess weight following bariatric surgery. J Am Coll Nutr 1988 Apr;7(2):147-53. http://www.ncbi.nlm.nih.gov/pubmed/3361039
12. Burgio KL, Richter HE, Clements RH, et al. Changes in urinary and fecal incontinence symptoms with weight loss surgery in morbidly obese women. Obstet Gynecol 2007 Nov;110(5):1034-40. http://www.ncbi.nlm.nih.gov/pubmed/17978117
13. Laungani RG, Seleno N, Carlin AM. Effect of laparoscopic gastric bypass surgery on urinary incontinence in morbidly obese women. Surg Obes Relat Dis 2009 May-Jun;5(3):334-8. http://www.ncbi.nlm.nih.gov/pubmed/19342304
14. López M, Ortiz AP, Vargas R. Prevalence of urinary incontinence and its association with body mass index among women in Puerto Rico. J Womens Health (Larchmt) 2009 Oct;18(10):1607-14. http://www.ncbi.nlm.nih.gov/pubmed/19788409
15. Mishra GD, Hardy R, Cardozo L, et al. Body weight through adult life and risk of urinary incontinence in middle-aged women: results from a British prospective cohort. Int J Obes (Lond) 2008 Sep;32(9):1415-22. http://www.ncbi.nlm.nih.gov/pubmed/18626483

16. Richter HE, Kenton K, Huang L, et al. The impact of obesity on urinary incontinence symptoms, severity, urodynamic characteristics and quality of life. J Urol 2010 Feb;183(2):622-8. http://www.ncbi.nlm.nih.gov/pubmed/20018326
17. Sarma AV, Kanaya A, Nyberg LM, et al; Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Research Group. Risk factors for urinary incontinence among women with type 1 diabetes: findings from the epidemiology of diabetes interventions and complications study. Urology 2009 Jun;73(6):1203-9. http://www.ncbi.nlm.nih.gov/pubmed/19362350
18. Auwad W, Steggles P, Bombieri L, et al. Moderate weight loss in obese women with urinary incontinence: a prospective longitudinal study. Int Urogynecol J Pelvic Floor Dysfunct 2008 Sep;19(9):1251-9. http://www.ncbi.nlm.nih.gov/pubmed/18421406

*3.2.5 **Smoking***

The role of smoking and the importance of smoking cessation are discussed in the management of almost every disease. Smoking, especially if > 20 cigarettes per day, is considered to intensify UI.

3.2.5.1 Question

In adults with UI, does smoking cessation improve patient outcomes regarding either urinary symptoms or QoL versus continued smoking?

3.2.5.2 Evidence

Seven published articles were found, all in women, on whether smoking cessation improved patient outcome. There was no RCT, but several population studies were found, including a study including 83,500 people. The studies only provided a comparison of smoking rates between different populations and did not examine the role of smoking cessation.

Four of these studies, totalling more than 110,000 subjects, found an association between smoking and UI, for people smoking > 20 cigarettes per day (1-4). Both former and current cigarette smoking was positively associated with frequent and severe UI, with a stronger relationship in women who were current smokers (2). Other studies involving similar large populations have not shown an association. The effect of smoking cessation on UI was described as uncertain in the latest Cochrane review (5).

Evidence summary	**LE**
There is no consistent evidence that smokers are more likely to suffer from UI.	3
There is some evidence that smoking may be associated with more severe UI, but not mild UI.	3
There is no evidence that smoking cessation will improve the symptoms of UI.	4

Recommendations for lifestyle interventions	**GR**
Encourage obese women suffering from any urinary incontinence to lose weight (> 5%).	A
Advise adults with urinary incontinence that reducing caffeine intake may improve symptoms of urgency and frequency but not incontinence.	B
Patients with abnormally high or abnormally low fluid intake should be advised to modify their fluid intake appropriately.	C
Counsel female athletes experiencing urinary incontinence with intense physical activity that it will not predispose to urinary incontinence in later life.	C
Patients with urinary incontinence who smoke should be given smoking cessation advice in line with good medical practice although there is no definite effect on urinary incontinence.	A

3.2.5.3 References

1. Sampselle CM, Harlow SD, Skurnick J, et al. Urinary incontinence predictors and life impact in ethnically diverse perimenopausal women. Obstet Gynecol 2002;100(6):1230-8. http://www.ncbi.nlm.nih.gov/pubmed/12468167
2. Danforth KN, Townsend MK, Lifford K, et al. Risk factors for urinary incontinence among middle-aged women. Am J Obstet Gynecol 2006;194(2):339-45. http://www.ncbi.nlm.nih.gov/pubmed/12628262

3. Hannestad YS, Rortveit G, Daltveit AK, et al. Are smoking and other lifestyle factors associated with female urinary incontinence? The Norwegian EPINCONT Study. BJOG 2003 Mar;110(3):247-54. http://www.ncbi.nlm.nih.gov/pubmed/12628262
4. Hojberg KE, Salvig JD, Winslow NA, et al. Urinary incontinence: prevalence and risk factors at 16 weeks of gestation. Br J Obstet Gynaecol 1999 Aug;106(8):842-50. http://www.ncbi.nlm.nih.gov/pubmed/10453836
5. Imamura M, Abrams P, Bain C, et al. Systematic review and economic modelling of the effectiveness and cost-effectiveness of non-surgical treatments for women with stress urinary incontinence. Health Technol Assess 2010 Aug;14(40):1-188, iii-iv. http://www.ncbi.nlm.nih.gov/pubmed/20738930

3.3 Behavioural therapy/scheduled voiding

Scheduled voiding is a treatment programme designed to gradually increase a person's control over voiding function and urgency and to reduce episodes of incontinence. It is also known as bladder drill, bladder discipline, bladder re-education, or BT. The programme also aims to increase a person's self-confidence in bladder function, though this can take months to achieve and may not persist long term unless the programme is maintained.

Different strategies may be used since no single regimen has yet been proven ideal. As well as following a voiding pattern, the patient is instructed on bladder function and fluid intake, including caffeine restriction and bowel habits. Patients may be asked to void according to a fixed voiding schedule. Alternatively, patients may be encouraged to follow a schedule established by their own bladder diary/voiding chart (habit training). 'Timed voiding' is voiding initiated by the patient, while 'prompted voiding' is voiding initiated by the caregiver. Timed and habit voiding are recommended to patients who can void independently.

Bladder training can be offered to any patient with any form of UI, as a first-line therapy for at least a short period of time. The ideal form or intensity of a BT programme for UI is unclear. It is also unclear whether or not BT can prevent the development of UI.

*3.3.1 **Questions***

- Is BT better than no treatment for cure or improvement of UI?
- Is BT better than other conservative treatments for cure or improvement of UI?
- Is BT useful as an adjunct to other conservative treatments for UI?
- Are the benefits of BT durable in the longer term?
- Are there any patient groups for whom BT is more effective?

*3.3.2 **Evidence***

There have been four systematic reviews covering the effect of BT compared to standard care (1-4). Two key RCTs, which compared BT with no intervention, found that UI was improved, but not cured, by timed bladder voiding at intervals of between 2.5 and 4 hours (5,6). However, it is unclear whether these findings also applied to specific groups of individuals with UI. However, another two RCTs reported inconsistent findings regarding treatment adherence(7).

Bladder training has been compared with other treatments for UI in a number of other RCTs. BT alone is as effective in controlling UUI and nocturnal incontinence as oxybutynin, tolterodine and solifenacin (8-13).

Studies have shown that the addition of BT to antimuscarinic therapy gives either no (10,11) or minimal (12) added benefit in terms of improvement of UI compared with antimuscarinic treatment alone. BT combined with antimuscarinic therapy does provide a greater benefit in reducing urinary frequency and nocturia (10,14). BT does not improve an individual's capacity to discontinue drug therapy and maintain improvement of UUI (12). However, the addition of BT to antimuscarinic drugs may increase patient satisfaction with pharmacological treatment (15), including in patients previously dissatisfied with the antimuscarinic treatment (16).

Bladder training combined with pelvic floor muscle training (PFMT) is better than standard care for controlling UI in elderly women living in institutions (17). However, BT alone is inferior to a high-intensity programme of PFMT to improve SUI in elderly women (18). BT is better than intravaginal pessaries to control SUI, although the improvement may only be short term.

Whatever the method of training used, any benefit of BT on UI is likely to be of short duration unless the BT programme is practised repeatedly. No adverse events have been reported with BT.

Evidence summary	LE
There is limited evidence that supervised bladder training is better than no treatment in women with UUI and mixed urinary incontinence.	1b
The effectiveness of bladder training diminishes after the treatment has ceased.	2
There is inconsistent evidence to show whether bladder training is better than drug therapy.	2
The combination of bladder training with antimuscarinic drugs does not result in greater in improvement of UI but may have other benefits.	2
Bladder training is better than pessary alone.	1b
Timed voiding reduces leakage episodes in cognitively impaired men and women.	1b

For recommendations see page 46.

3.3.3 References

1. Abrams P, Andersson KE, Birder L, et al. Fourth International Consultation on Incontinence Recommendations of the International Scientific Committee: evaluation and treatment of urinary incontinence, pelvic organ prolapse, and fecal incontinence. Neurourol Urodyn 2010;29(1):213-40. http://www.ncbi.nlm.nih.gov/pubmed/20025020
2. Shamliyan TA, Kane RL, Wyman J, et al. Systematic review: randomized, controlled trials of nonsurgical treatments for urinary incontinence in women. Ann Intern Med 2008 Mar 18;148(6):459-73. http://www.ncbi.nlm.nih.gov/pubmed/18268288
3. Imamura M, Abrams P, Bain C, et al. Systematic review and economic modelling of the effectiveness and cost-effectiveness of non-surgical treatments for women with stress urinary incontinence. Health Technol Assess 2010;14(40):1-188, iii-iv. http://www.ncbi.nlm.nih.gov/pubmed/20738930
4. National Collaborating Centre for Women's and Children's Health (UK). Urinary incontinence. The management of urinary incontinence in women. NICE Clinical Guidelines. No. 40. London: RCOG Press, October 2006. http://www.ncbi.nlm.nih.gov/books/NBK57205/
5. Jarvis GJ, Millar DR. Controlled trial of bladder drill for detrusor instability. Br Med J 1980 Nov 15;281(6251):1322-3. http://www.ncbi.nlm.nih.gov/pubmed/7002250
6. Fantl JA, Wyman JF, McClish DK, et al. Efficacy of bladder training in older women with urinary incontinence. JAMA 1991 Feb 6;265(5):609-13. http://www.ncbi.nlm.nih.gov/pubmed/1987410
7. Colombo M, Zanetta G, Scalambrino S, et al. Oxybutynin and bladder training in the management of female urinary urge incontinence: a randomized study. Int Urogynecol J 1995;6(2):63-7. http://www.springerlink.com/content/p75435j280072j72/
8. Lauti M, Herbison P, Hay-Smith J, et al. Anticholinergic drugs, bladder retraining and their combination for urge urinary incontinence: a pilot randomised trial. Int Urogynecol J Pelvic Floor Dysfunct 2008 Nov;19(11):1533-43. http://www.ncbi.nlm.nih.gov/pubmed/18654731
9. Mattiasson A, Blaakaer J, Hoye K, et al; Tolterodine Scandinavian Study Group. Simplified bladder training augments the effectiveness of tolterodine in patients with an overactive bladder. BJU Int 2003 Jan;91(1):54-60. http://www.ncbi.nlm.nih.gov/pubmed/12614251
10. MattiassonA, Masala A, Morton R, et al. Efficacy of simplified bladder training in patients with overactive bladder receiving a solifenacin flexible-dose regimen: results from a randomized study. BJU Int 2009 Oct 10. http://www.ncbi.nlm.nih.gov/pubmed/19818077
11. Fitzgerald MP, Lemack G, Wheeler T, et al; Urinary Incontinence Treatment Network. Nocturia, nocturnal incontinence prevalence, and response to anticholinergic and behavioral therapy. Int Urogynecol J Pelvic Floor Dysfunct 2008 Nov;19(11):1545-50. http://www.ncbi.nlm.nih.gov/pubmed/18704249
12. Burgio KL, Locher JL, Goode PS, et al. Behavioral vs drug treatment for urge urinary incontinence in older women: a randomized controlled trial. JAMA 1998 Dec 16;280(23):1995-2000. http://www.ncbi.nlm.nih.gov/pubmed/9863850
13. Goode PS, Burgio KL, Locher JJ, et al. Effect of behavioral training with or without pelvic floor electrical stimulation on stress incontinence in women: a randomized controlled trial. JAMA 2003 Jul 16;290(3):345-52. http://www.ncbi.nlm.nih.gov/pubmed/12865375

14. Song C, Park JT, Heo KO, et al. Effects of bladder training and/or tolterodine in female patients with overactive bladder syndrome: a prospective, randomized study. J Korean Med Sci 2006 Dec;21(6):1060-3. http://www.ncbi.nlm.nih.gov/pubmed/17179687
15. Wallace SA, Roe B, Williams K, et al. Bladder training for urinary incontinence in adults. Cochrane Database Syst Rev 2004;(1):CD001308. http://www.ncbi.nlm.nih.gov/pubmed/14973967
16. Klutke CG, Burgio KL, Wyman JF, et al. Combined effects of behavioral intervention and tolterodine in patients dissatisfied with overactive bladder medication. J Urol 2009 Jun;181(6):2599-607. http://www.ncbi.nlm.nih.gov/pubmed/19375110
17. Aslan E, Komurcu N, Beji NK, et al. Bladder training and Kegel exercises for women with urinary complaints living in a rest home. Gerontology 2008;54(4):224-31. http://www.ncbi.nlm.nih.gov/pubmed/18483451
18. Sherburn M, Bird M, Carey M, et al. Incontinence improves in older women after intensive pelvic floor muscle training: an assessor-blinded randomized controlled trial. Neurourol Urodyn 2011 Mar;30(3):317-24. http://www.ncbi.nlm.nih.gov/pubmed/21284022

3.4 Physical therapies

*3.4.1 **Pelvic floor muscle training (PFMT)***

Pelvic floor muscle training is used to increase the strength and durability of contraction of the pelvic floor muscles. This increases urethral closure pressure and stabilises the urethra, preventing downward movement during moments of increased activity. Patients are sometimes taught to perform 'the knack' of contracting the pelvic floor at moments when predictable UI is likely to occur. Otherwise regular training aims to increase pelvic floor muscle strength. There is some evidence that increasing pelvic floor strength may help to inhibit bladder contraction in patients with an OAB.

Traditionally, following vaginal examination and pelvic floor assessment by a trained professional, patients are taught to contract their pelvic floor muscles, as hard as they can and for as long as they can, and to repeat these exercises a number of times every day. This training can be delivered in many ways, including women teaching themselves (e.g. using an information leaflet), group training in classes, or intensive one-to-one supervision from a highly trained physical therapist. PFMT may be used to prevent UI, e.g. in childbearing women before birth, in men about to undergo radical prostatectomy, or as part of a planned recovery programme after childbirth or surgery. Most often, PFMT is used to treat existing UI, and may be augmented with biofeedback, electrical stimulation or vaginal cones.

3.4.1.1 Methods used to augment PFMT

Biofeedback increases patient awareness of the pelvic floor muscles, using visual, tactile or auditory stimuli, e.g. vaginal manometry or electromyography, and is used to help teach patients to exercise their pelvic floor muscles more effectively. However, there is no guarantee that the signals recorded come from the pelvic floor and digital palpation or ultrasound may provide better reassurance of correct contraction. Biofeedback can be used at home or in an office setting.

In electrical stimulation, surface electrodes supply electrical current to stimulate the pelvic floor muscles via their nerve supply. Electrodes are available in several formats, including vaginal, anal, or skin. Electrical stimulation is often used to help patients recognise their pelvic floor muscles though there is no evidence supporting this concept. It is also used to exercise muscles in the hope of increasing pelvic floor strength. Electrical stimulation can also be used to inhibit overactive detrusor contractions.

Weighted vaginal cones are cone-shaped vaginal inserts of graduated weights. A woman learns first to insert the lightest cone and retain it using pelvic floor contraction. Gradually, she is able to hold increasingly heavy cones as her pelvic floor muscles become stronger.

3.4.1.2 Question

In adult men and women suffering from UI, does treatment with PFMT (given either alone or augmented with biofeedback, electrical stimulation or vaginal cones) improve or cure UI or improve QoL, compared to no treatment, sham treatment or other conservative treatments, e.g. bladder training, electrical stimulation or vaginal cones?

3.4.1.3 Evidence

Although there have been many randomised trials of PFMT, the trials vary widely in terms of quality, mode of delivery, intensity and duration of treatment, and the details of contractions and repetitions.

In a recent UK Health Technology Appraisal, the role of PFMT in the care of women with SUI was analysed in both direct comparisons and a mixed treatment comparison model, which compared different 'packages' of care (1). This extensive meta-analysis reviewed data from 37 interventions and 68 direct comparisons, while the mixed treatment comparisons examined combinations of 14 different types of intervention from 55 separate trials. The mixed treatment comparison used both indirect and direct comparisons and has probably provided more accurate estimates of effect. Where relevant, the Technology Appraisal has influenced the evidence and recommendations in these Guidelines.

3.4.1.4 Efficacy of PFMT in SUI, UUI and MUI in women

This question has been addressed by one Cochrane systematic review (2), which included six RCTs comparing PFMT to no treatment. Three RCTs evaluated PFMT for mixed urinary incontinence (MUI), while the other three RCTs compared a programme of treatment supervised by a professional versus either self-taught PFMT or unsupervised PFMT. There was inconsistency between studies because of poor reporting of technique and different outcome measures. Meta-analysis showed that PFMT achieved cure or improvement of incontinence more often compared to no treatment.

One recent RCT compared interpersonal support and digital vaginal palpation to PFMT and an instruction leaflet, finding superior efficacy for the former group (3). Another recent RCT found that PFMT delivered in a group setting can be as effective as individual treatment (4). Another RCT reported 15-year follow-up outcomes of an earlier RCT, showing that long-term adherence to treatment was poor. Half of patients had progressed to surgery, though the functional outcomes in those who had undergone surgery were less satisfactory than those who did not have surgery (5).

The 4th International Consultation on Incontinence 2009 (6) reviewed studies up to June 2008. This review included the following comparisons:

- vaginal cones: 8 RCTs
- different types of electrical stimulation: 8 RCTs
- BT: 3 RCTs
- different drugs: 4 RCTs
- surgery in which the operation was 'selected' by the surgeon (i.e. inconsistent): 1 RCT.

None of these RCTs were of good quality. In addition, inconsistent reporting of techniques and outcomes makes it difficult to compare studies.

The same review also included comparisons of PFMT with other therapies in women with SUI:

- PFMT versus PFTM + vaginal cones: 2 RCTs
- PFMT versus PFMT + electrical stimulation: 2 small RCTs
- PFMT versus PFMT + biofeedback: 9 RCTs of mixed quality, of which 5 RCTs were clinic-based and 4 RCTs used a home-based biofeedback device. Potential bias was caused by the inconsistent supervision of women between different treatment groups.

There has been one further RCT comparing PFMT + duloxetine versus duloxetine alone versus PFMT alone versus no treatment (6).

These studies, and two additional studies (8,9) were reviewed as part of the 2010 UK Health Technology Appraisal (1), which considered additional data as part of a mixed treatment comparison. The Appraisal resulted in a number of different findings from those based solely on direct comparisons. In conclusion, the Appraisal, using a revised methodology, supported the general principle that greater efficacy was achieved by adding together different types of treatment and increasing intensity.

3.4.1.5 Efficacy of PFMT in childbearing women

The Cochrane review in 2008 (10) reviewed sixteen RCTs in pregnant or post partum women which included PFMT in one arm of the trial. Five of these trials were in post partum women who had developed urinary incontinence. Eight trials reported mixed treatment and prevention groups. Treatment of UI with PFMT in the post partum period inreased the chances of continence at 12 months post partum.

3.4.1.6 Efficacy of PFMT in men with SUI following radical prostatectomy

There has been one systematic review of eleven RCTs. There have been three further RCTs of reasonable quality (11-13). These trials consistently demonstrated improved continence within the first few months after

radical prostatectomy (RP), but not thereafter, suggesting that PFMT speeds the recovery of UI. Two additional RCTs have shown that written instructions alone can achieve the same result (14,15).

3.4.1.7 Preventive value of PFMT in childbearing women and post-RP men

The Cochrane review by Hay Smith (10) reviews five RCTs in which PFMT was started in continent pregnant women. A number of other trials included both prevention and treatment groups in their comparisons. PFMT was found to reduce the risk of incontinence in late pregancny and up to 6 months post partum.

Ten RCTs of variable quality compared the preventative effect of PFMT prior to RP versus various different types of control treatments. These were generally small studies, which were difficult to compare with each other because of different times of delivery and different outcomes (16-24). However, one study was well designed and provided level 2 evidence confirming that pre-operative PFMT speeds recovery of continence post-operatively (25).

PFMT as monotherapy	**LE**
PFMT is better than no treatment for reducing incontinence episodes and improving quality of life in women with SUI, and MUI. There is no evidence that PFMT is better than no treatment in providing a cure.	1
Higher-intensity regimes, or the addition of biofeedback, confer greater benefit, but differences are not sustained long term.	1
A taught/supervised programme of PFMT is more effective than self-taught PFMT.	1
Group-based PFMT is as effective as treatment delivered individually.	1
Short-term benefits of intensive PFMT are not maintained at 15 years' follow-up.	2
PFMT compared with other conservative treatments	**LE**
PFMT results in better reduction in leakage episodes than training using vaginal cones, but no difference in self-reported cure or improvement.	1
PFMT results in fewer incontinence episodes than electrical stimulation.	1
PFMT does not result in measurable improvement in quality of life.	2
PFMT is better than bladder training for improvement of leakage and quality of life, in women with SUI.	2
There is no consistent difference between PFMT and bladder training for women with UUI or MUI.	2
PFMT is as effective as duloxetine in women with SUI and has fewer side effects.	2
PFMT is better tolerated than oxybutynin for UUI.	2
PFMT is better than alpha-blockers for women with SUI.	2
PFMT for UI in childbearing women	**LE**
PFMT commencing in early pregnancy reduces the risk of incontinence in late pregnancy, and up to 6 months post partum.	1
PFMT commencing in the early post partum period improves UI in women for up to 12 months.	1
PFMT for post-prostatectomy incontinence	**LE**
Men undergoing some form of PFMT, before or after radical prostatectomy achieve continence more quickly than non-treated men.	2
There is conflicting evidence on whether the addition of electrical stimulation or biofeedback or supervised training increases the effectiveness of PFMT alone.	2
There is no evidence that pre-operative PFMT prevents UI following radical prostatectomy. As with post-operative PFMT, it appears to lead to earlier recovery of continence.	2
What remains unproven about PFMT	**LE**
There is a lack of evidence about what is the most effective regimen for PFMT.	4
The long-term durability of PFMT, augmented or not by other therapies, remains uncertain in all clinical situations.	4
There is insufficient evidence that adding electrical stimulation or vaginal cones to PFMT alters the efficacy of PFMT alone.	2

3.4.1.8 References

1. Imamura M, Abrams P, Bain C, et al. Systematic review and economic modelling of the effectiveness and cost-effectiveness of non-surgical treatments for women with stress urinary incontinence. Health Technol Assess 2010;14(40):1-188, iii-iv. http://www.ncbi.nlm.nih.gov/pubmed/20738930
2. Dumoulin C, Hay-Smith J. Pelvic floor muscle training versus no treatment for urinary incontinence in women. A Cochrane systematic review. Eur J Phys Rehabil Med 2008 Mar;44(1):47-63. http://www.ncbi.nlm.nih.gov/pubmed/18385628
3. Tsai YC, Liu CH. The effectiveness of pelvic floor exercises, digital vaginal palpation and interpersonal support on stress urinary incontinence: an experimental study. Int J Nurs Stud 2009;46(9):1181-6. http://www.ncbi.nlm.nih.gov/pubmed/19361800
4. de Oliveira Camargo F, Rodrigues AM, Arruda RM, et al. Pelvic floor muscle training in female stress urinary incontinence: comparison between group training and individual treatment using PERFECT assessment scheme. Int Urogynecol J Pelvic Floor Dysfunct 2009 Dec;20(12):1455-62. http://www.ncbi.nlm.nih.gov/pubmed/19690792
5. Bo K, Kvarstein B, Nygaard I. Lower urinary tract symptoms and pelvic floor muscle exercise adherence after 15 years. Obstet Gynecol 2005 May;105(5 Pt 1):999-1005. http://www.ncbi.nlm.nih.gov/pubmed/15863536
6. Abrams P, Cardozo L, Khoury S, et al., editors. Incontinence. 4th International Consultation on Incontinence, Paris, July 5-8, 2008. Plymouth: Health Publication Ltd, 2009. http://www.icud.info/incontinence.html
7. Ghoniem GM, Van Leeuwen JS, Elser DM, et al. Duloxetine/Pelvic Floor Muscle Training Clinical Trial Group. A randomized controlled trial of duloxetine alone, pelvic floor muscle training alone, combined treatment and no active treatment in women with stress urinary incontinence. J Urol 2005;173(5): 1647-53. http://www.ncbi.nlm.nih.gov/pubmed/15821528
8. Aukee P, Immonen P, Penttinen J, et al. Increase in pelvic floor muscle activity after 12 weeks' training: a randomized prospective pilot study. Urology 2002;60(6):1020-3; discussion 1023-4. http://www.ncbi.nlm.nih.gov/pubmed/12475661
9. Ferguson KL, McKey P, Bishop KR, et al. Stress urinary incontinence: effect of pelvic muscle exercise. Obstet Gynecol 1990 Apr;75(4):671-5. http://www.ncbi.nlm.nih.gov/pubmed/2314786
10. Hay-Smith J, Mørkved S, Fairbrother KA, et al. Pelvic floor muscle training for prevention and treatment of urinary and faecal incontinence in antenatal and postnatal women. Cochrane Database Syst Rev. 2008 Oct 8;(4):CD007471. http://www.ncbi.nlm.nih.gov/pubmed/18843750
11. Manassero F, Traversi C, Ales V, et al. Contribution of early intensive prolonged pelvic floor exercises on urinary continence recovery after bladder neck-sparing radical prostatectomy: results of a prospective controlled randomized trial. Neurourol Urodyn 2007;26(7):985-9. http://www.ncbi.nlm.nih.gov/pubmed/17487874
12. Marchiori D, Bertaccini A, Manferrari F, et al. Pelvic floor rehabilitation for continence recovery after radical prostatectomy: role of a personal training re-educational program. Anticancer Res 2010 Feb;30(2):553-6. http://www.ncbi.nlm.nih.gov/pubmed/20332469
13. Ribeiro LH, Prota C, Gomes CM, et al. Long-term effect of early postoperative pelvic floor biofeedback on continence in men undergoing radical prostatectomy: a prospective, randomized, controlled trial. J Urol 2010 Sep;184(3):1034-9. http://www.ncbi.nlm.nih.gov/pubmed/20643454
14. Moore KN, Valiquette L, Chetner MP, et al. Return to continence after radical retropubic prostatectomy: a randomized trial of verbal and written instructions versus therapist-directed pelvic floor muscle therapy. Urology 2008 Dec;72(6):1280-6. http://www.ncbi.nlm.nih.gov/pubmed/18384853
15. Dubbelman Y, Groen J, Wildhagen M, et al. The recovery of urinary continence after radical retropubic prostatectomy: a randomized trial comparing the effect of physiotherapist-guided pelvic floor muscle exercises with guidance by an instruction folder only. BJU Int 2010 Aug;106(4):515-22. http://www.ncbi.nlm.nih.gov/pubmed/20201841
16. Bales GT, Gerber GS, Minor TX, et al. Effect of preoperative biofeedback/pelvic floor training on continence in men undergoing radical prostatectomy. Urology 2000 Oct 1;56(4):627-30. http://www.ncbi.nlm.nih.gov/pubmed/11018619

17. Mathewson-Chapman M. Pelvic muscle exercise/biofeedback for urinary incontinence after prostatectomy: an education program. J Cancer Educ 1997 Winter;12(4):218-23. http://www.ncbi.nlm.nih.gov/pubmed/9440013
18. Sueppel C, Kreder K, See W. Improved continence outcomes with preoperative pelvic floor muscle strengthening exercises. Urol Nurs 2001 Jun;21(3):201-10. http://www.ncbi.nlm.nih.gov/pubmed/11998651
19. Parekh AR, Feng MI, Kirages D, et al. The role of pelvic floor exercises on post-prostatectomy incontinence. J Urol 2003 Jul;170(1):130-3. http://www.ncbi.nlm.nih.gov/pubmed/12796664
20. Burgio KL, Goode PS, Urban DA, et al. Preoperative biofeedback assisted behavioral training to decrease post-prostatectomy incontinence: a randomized, controlled trial. J Urol 2006 Jan;175(1): 196-201; discussion 201. http://www.ncbi.nlm.nih.gov/pubmed/16406909
21. Filocamo MT, Li Marzi V, Del Popolo G, et al. Effectiveness of early pelvic floor rehabilitation treatment for post-prostatectomy incontinence. Eur Urol 2005 Nov;48(5):734-8. http://www.ncbi.nlm.nih.gov/pubmed/16002204
22. Overgard M, Angelsen A, Lydersen S, et al. Does physiotherapist-guided pelvic floor muscle training reduce urinary incontinence after radical prostatectomy? A randomised controlled trial. Eur Urol 2008 Aug;54(2):438-48. http://www.ncbi.nlm.nih.gov/pubmed/18448233
23. Lilli P, Mercuriali M, Fiori M, et al. Impact of preoperative biofeedback on incontinence in cancer patients undergoing radical prostatectomy. Arch Ital Urol Androl 2006 Sep;78(3):92-6. http://www.ncbi.nlm.nih.gov/pubmed/17137022
24. Wille S, Sobottka A, Heidenreich A, et al. Pelvic floor exercises, electrical stimulation and biofeedback after radical prostatectomy: results of a prospective randomized trial. J Urol 2003 Aug;170(2 Pt 1): 490-3. http://www.ncbi.nlm.nih.gov/pubmed/12853806
25. Centemero A, Rigatti L, Giraudo D, et al. Preoperative pelvic floor muscle exercise for early continence after radical prostatectomy: a randomised controlled study. Eur Urol 2010 Jun;57(6):1039-43. http://www.ncbi.nlm.nih.gov/pubmed/20227168

3.4.2 ***Electrical stimulation (surface electrodes)***

Electrical stimulation with surface electrodes can be delivered vaginally, anally or with skin electrodes on the perineum or suprapubic region. Stimulation parameters vary considerably from one study to another. Generally, low-intensity levels are used in home-based, self-administered therapy and high-intensity levels in clinic-based settings. Maximal stimulation under general anaesthesia has been described. The treatment regimes (number and frequency of sessions) vary considerably.

Electrical stimulation can also be combined with other forms of conservative therapy, e.g. PFMT and biofeedback. Electrical stimulation is often used to assist women who cannot initiate contractions to identify their pelvic floor muscles.

3.4.2.1 Question

In adults with UI, does treatment with electrical stimulation improve or cure symptoms of UI or QoL compared to no treatment or sham treatment?

3.4.2.2 Evidence

Most evidence on electrical stimulation refers to women. Five recent systematic reviews of electrical stimulation were found (1-5), although there was no specific Cochrane review. The five reviews included analysis of 15 RCTs, of which eight were comparisons to no treatment or sham treatment - seven studies were comparisons to other physical or behavioural therapies - and a further eight studies were comparisons of electrical stimulation combined with other therapies, usually PFMT.

The studies were considered to be of generally low quality, with small sample size and a variety of stimulation parameters, treatment regimes and outcome parameters. In addition, most of the studies lacked detail of the statistical methods used, e.g. power calculation. Due to the lack of consistency in the parameters used for electrical stimulation and in the outcome measures, it has not been possible to compare or pool data from most of these studies.

The role of electrical stimulation is complicated by a lack of knowledge of how it might work in UI.

Physiotherapists have used electrical stimulation to help women identify and contract pelvic floor muscles during PFMT. It has been suggested that electrical stimulation probably targets the pelvic floor directly in SUI, and the detrusor muscle or pelvic floor muscle or afferent innervation in UUI.

Evidence summary	LE
The evidence is inconsistent for whether electrical stimulation alone can improve UI.	2

3.4.2.3 References

1. Berghmans LC, Hendriks HJ, Bo K, et al. Conservative treatment of stress urinary incontinence in women: a systematic review of randomized clinical trials. Br J Urol 1998 Aug;82(2):181-91. http://www.ncbi.nlm.nih.gov/pubmed/9722751
2. Berghmans LC, Hendriks HJ, De Bie RA, et al. Conservative treatment of urge urinary incontinence in women: a systematic review of randomized clinical trials. BJU Int 2000 Feb;85(3):254-63. http://www.ncbi.nlm.nih.gov/pubmed/10671878
3. Imamura M, Abrams P, Bain C, et al. Systematic review and economic modelling of the effectiveness and cost-effectiveness of non-surgical treatments for women with stress urinary incontinence. Health Technol Assess 2010 Aug;14(40):1-188, iii-iv. http://www.ncbi.nlm.nih.gov/pubmed/20738930
4. Shamliyan TA, Kane RL, Wyman J, et al. Systematic review: randomized, controlled trials of nonsurgical treatments for urinary incontinence in women. Ann Intern Med 2008 Mar 18;148(6):459-73. http://www.ncbi.nlm.nih.gov/pubmed/18268288
5. Abrams P, Andersson KE, Birder L, et al. Fourth International Consultation on Incontinence Recommendations of the International Scientific Committee: Evaluation and treatment of urinary incontinence, pelvic organ prolapse, and fecal incontinence. Neurourol Urodyn. 2010;29(1):213-40. http://www.ncbi.nlm.nih.gov/pubmed/20025020

*3.4.3 **Magnetic stimulation***

(Extracorporeal) magnetic stimulation stimulates the pelvic floor musculature and/or the sacral roots in a non-invasive way. The patient is seated over a magnetic field generator. This produces a steep gradient magnetic field, which may stimulate the pelvic floor muscles and sphincters. Magnetic stimulation can also be given via a portable electromagnetic device. Magnetic stimulation may be effective in SUI and UUI. The mechanism of action is not understood.

3.4.3.1 Question

In adults with SUI or UUI or MUI, what is the clinical effectiveness of magnetic stimulation versus sham treatment?

3.4.3.2 Evidence

Eight RCTs and two cohort studies have investigated the question of whether magnetic stimulation is effective in UI. The RCTs were mostly of poor quality. The technique of electromagnetic stimulation was poorly standardised and involved different devices, mode of delivery, and stimulation parameters. Blinding was difficult to achieve and this resulted in a high risk of bias in some trials.

Three RCTs induced magnetic stimulation in women with UI, using a coil placed over the sacral foramina. Two were poor-quality RCTs, with a short follow-up and an inconclusive effect in SUI and UUI or OAB (1,2). The third better-quality RCT observed no improvement in UUI or OAB after a longer 12-week follow-up and did not recommend treatment with magnetic stimulation (3).

A portable device (Pulsegen) was compared in two RCTs to sham treatment in women with UI. Inconclusive effects were obtained. Both trials were poor quality with a short follow-up (4,5).

In adult women with SUI, an RCT using the NeoControl chair found no improvement (6). A cohort study for 6 weeks, but with a follow-up of 2 years, showed a moderate improvement in incontinence measured by pad test (7), while another cohort study found no improvement (8). A further poor-quality RCT using the NeoControl chair also found no benefit in women with UUI or OAB (9). No clinical benefits were reported when magnetic stimulation using the NeoControl chair was also compared to functional electrical stimulation with surface electrodes (10).

The negative or inconclusive effects obtained from the reviewed literature were considered to be consistent

and generally applicable to adult women with SUI or UUI. There was a lack of evidence in men with UI.

Evidence summary	LE
There is no consistent evidence of efficacy of magnetic stimulation for the cure or improvement of UI.	2a
There are no reports of adverse events for magnetic stimulation.	1b

3.4.3.3 References

1. Fujishiro T, Enomoto H, Ugawa Y, et al. Magnetic stimulation of the sacral roots for the treatment of stress incontinence: an investigational study and placebo controlled trial. J Urol 2000 Oct;164(4): 1277-9. http://www.ncbi.nlm.nih.gov/pubmed/10992380
2. Fujishiro T, Takahashi S, Enomoto H, et al. Magnetic stimulation of the sacral roots for the treatment of urinary frequency and urge incontinence: an investigational study and placebo controlled trial. J Urol 2002 Sep;168(3):1036-9. http://www.ncbi.nlm.nih.gov/pubmed/12187217
3. O'Reilly BA, Fynes M, Achtari C, et al. A prospective randomised double-blind controlled trial evaluating the effect of trans-sacral magnetic stimulation in women with overactive bladder. Int Urogynecol J Pelvic Floor Dysfunct 2008 Apr;19(4):497-502. http://www.ncbi.nlm.nih.gov/pubmed/17932613
4. But I. Conservative treatment of female urinary incontinence with functional magnetic stimulation. Urology 2003 Mar;61(3):558-61. http://www.ncbi.nlm.nih.gov/pubmed/12639647
5. But I, Faganelj M, Sostaric A. Functional magnetic stimulation for mixed urinary incontinence. J Urol 2005 May;173(5):1644-6. http://www.ncbi.nlm.nih.gov/pubmed/15821527
6. Gilling PJ, Wilson LC, Westenberg AM, et al. A double-blind randomized controlled trial of electromagnetic stimulation of the pelvic floor vs sham therapy in the treatment of women with stress urinary incontinence. BJU Int 2009 May;103(10):1386-90. http://www.ncbi.nlm.nih.gov/pubmed/19154474
7. Hoscan MB, Dilmen C, Perk H, et al. Extracorporeal magnetic innervation for the treatment of stress urinary incontinence: results of two-year follow-up. Urol Int 2008;81(2):167-72. http://www.ncbi.nlm.nih.gov/pubmed/18758214
8. Ismail SI, Forward G, Bastin L, et al. Extracorporeal magnetic energy stimulation of pelvic floor muscles for urodynamic stress incontinence of urine in women. J Obstet Gynaecol 2009 Jan;29(1): 35-9. http://www.ncbi.nlm.nih.gov/pubmed/19280493
9. Morris AR, O'Sullivan R, Dunkley P, et al. Extracorporeal magnetic stimulation is of limited clinical benefit to women with idiopathic detrusor overactivity: a randomized sham controlled trial. Eur Urol 2007 Sep;52(3):876-81. http://www.ncbi.nlm.nih.gov/pubmed/17335962
10. Yamanishi T, Sakakibara R, Uchiyama T, et al. Comparative study of the effects of magnetic versus electrical stimulation on inhibition of detrusor overactivity. Urology 2000 Nov;56(5):777-81. http://www.ncbi.nlm.nih.gov/pubmed/11068300

*3.4.4 **Posterior (percutaneous) tibial nerve stimulation***

Electrical stimulation of the posterior tibial nerve (PTNS) delivers electrical stimuli to the sacral micturition centre via the S2-S4 sacral nerve plexus. The PTNS is stimulated with a fine, 34-G, needle, which is inserted just above the medial aspect of the ankle (equivalent to the SP6 acupuncture point). Treatment cycles typically consist of 12-weekly treatments of 30 minutes. PTNS may be effective in patients with UUI.

3.4.4.1 Question

In adults suffering from UUI, what is the clinical effectiveness of PTNS compared to sham treatment or antimuscarinic drug treatment?

3.4.4.2 Evidence

The reviewed studies included 2 RCTs of PTNS against sham treatment (1,2) and one comparing PTNS to tolterodine in patients with UUI (3).

The results of studies of PTNS in women with refractory UUI are consistent. Considered together, these results

allow the conclusion that PTNS has a benefit in women with UUI who have had no benefit from antimuscarinic therapy or who are not able to tolerate these drugs. However, there is no evidence that PTNS cures UUI in women. In men there is insufficient data to make a conclusion about efficacy.

Evidence summary	**LE**
There are not enough data to make a conclusion about the effectiveness of PTNS in men.	4
PTNS is effective for improvement of UUI, but not curing UUI in some women who have had no benefit from antimuscarinic medication.	1b
PTNS is no more effective than tolterodine for improvement of UUI in women.	2b
No serious adverse events have been reported for PTNS in UUI.	3

Recommendations for behavioural and physical therapies	**GR**
Offer supervised PFMT, lasting at least 3 months, as a first-line therapy to women with stress or mixed urinary incontinence.	A
PFMT programmes should be as intensive as possible.	A
Consider using biofeedback as an adjunct in women with stress urinary incontinence.	A
Offer supervised PFMT to continent women in their first pregnancy to help prevent incontinence in the postnatal period.	A
Offer instruction on pelvic floor exercises to men undergoing radical prostatectomy to speed recovery of urinary incontinence.	B
Offer bladder training as a first-line therapy to adults with urgency urinary incontinence or mixed urinary incontinence.	A
Offer timed voiding to adults with urinary incontinence, who are cognitively impaired.	A
Do not offer electrical stimulation with surface electrodes (skin, vaginal, anal) alone for the treatment of urinary incontinence.	A
Do not offer magnetic stimulation for the treatment of urinary incontinence or overactive bladder in adult women.	B
Do not offer PTNS to women or men who are seeking a cure for urgency urinary incontinence	A
Offer, if available, PTNS as an option for improvement of urgency urinary incontinence in women, but not men, who have not benefited from antimuscarinic medication.	B

PFMT = pelvic floor muscle training; PTNS = posterior tibial nerve stimulation.

3.4.4.3 Research priorities

There is a need for well-designed studies of both electrical stimulation and magnetic stimulation in adults with UI.

3.4.4.4 References

1. Finazzi-Agro E, Petta F, Sciobica F, et al. Percutaneous tibial nerve stimulation effects on detrusor overactivity incontinence are not due to a placebo effect: a randomized, double-blind, placebo controlled trial. J Urol 2010 Nov;184(5):2001-6. http://www.ncbi.nlm.nih.gov/pubmed/20850833
2. Peters KM, Carrico DJ, Perez-Marrero RA, et al. Randomized trial of percutaneous tibial nerve stimulation versus Sham efficacy in the treatment of overactive bladder syndrome: results from the SUmiT trial. J Urol 2010 Apr;183(4):1438-43. http://www.ncbi.nlm.nih.gov/pubmed/20171677
3. Peters KM, Macdiarmid SA, Wooldridge LS, et al. Randomized trial of percutaneous tibial nerve stimulation versus extended-release tolterodine: results from the overactive bladder innovative therapy trial. J Urol 2009 Sep;182(3):1055-61. http://www.ncbi.nlm.nih.gov/pubmed/19616802

4. DRUG TREATMENT

4.1 Antimuscarinic drugs

Antimuscarinic drugs are currently the mainstay of treatment for UUI. They act by blocking muscarinic receptors in the bladder wall. This reduces detrusor contractility and also alters sensation. Antimuscarinic agents differ in their pharmacological profiles, e.g. muscarinic receptor affinity and other modes of action, in their pharmacokinetic properties, e.g. lipid solubility and half-life, and in their formulation, e.g. immediate release (IR) or extended release (ER) and transdermal.

The evaluation of cure/improvement of UI using oxybutynin and tolterodine IR formulations is made harder by the lack of a standard definition of improvement. Outcome measures vary and are not standardised, and never use 'cure' as a primary outcome. Meta-analysis of the published evidence is therefore not always possible.

There have been many publications of variable quality about the pharmacological treatment of the overactive bladder (OAB), including several systematic reviews and meta-analyses. The systematic reviews, published in 2009 (1), on behalf of the US Agency for Healthcare Research and Quality (AHRQ) and the Oregon Health and Science University (2), have collated together much of the relevant evidence. As well as the studies included in these reviews, the Panel have examined studies published since these reviews up until July 2010.

Dry mouth is the commonest side effect though others include constipation, blurred vision, fatigue and congnitive dysfuction. When people have a dry mouth they may be inclined to drink more but it is not clear whether this adversely influences the effect of the drug.

*4.1.1 **Immediate-release antimuscarinic agents***

The IR formulation of oxybutynin is the prototype drug in the treatment of UUI. Oxybutynin IR provides maximum dosage flexibility, including an off-label 'on-demand' use. Immediate-release drugs have been the only available formulation for many years. They have a greater risk of side effects than ER formulations because of their higher plasma peak levels. A transdermal delivery system (TDS) and gel developed for oxybutynin has improved its safety profile while maintaining efficacy.

4.1.1.1 Question

In adults with UI, are IR formulations of antimuscarinic drugs, and TDS application of oxybutynin, more effective than placebo in reducing UI episodes and achieving continence?

4.1.1.2 Evidence

Four systematic reviews of individual antimuscarinic drugs versus placebo were included by the Panel for this section (1-4).

A systematic review and meta-analysis by Chapple et al. in 2008 (2), which updated previous reviews, showed that oxybutynin IR versus placebo was better for improvement and cure of UUI. In patients receiving oxybutynin IR, 15 mg daily, there were statistically significant improvements compared to placebo. However, the absolute changes in incontinence episodes were small. Treated patients were 3.53 times more likely to achieve complete continence than controls (7-11). Similar changes have been reported for tolterodine IR, 4 mg daily, versus placebo (12-20), although the changes reported for tolterodine IR, 2 mg daily, were smaller than for the higher dose (15-19). With propiverine IR, a cure of incontinence was 1.8 times more likely than with placebo (21-23). For trospium IR, no cure rates were available (24).

Randomised controlled trials of oxybutynin TDS versus placebo and other oral formulations have shown a significant improvement in the number of incontinence episodes and micturitions per day.

In Staskin et al. oxybutynin topical gel was superior to placebo for improvement of UUI with a higher proportion of participants being cured (25).

Evidence summary	**LE**
Oxybutynin IR and transdermal, tolterodine IR, and propiverine IR provide a significantly better rate of cure/improvement compared to placebo.	1a
Trospium IR provides significantly better reduction in incontinence episodes than placebo.	1a

4.1.1.3 References

1. Chapple CR, Khullar V, Gabriel Z, et al. The effects of antimuscarinic treatments in overactive bladder: a systematic review and meta-analysis. Eur Urol 2005 Jul;48(1):5-26. http://www.ncbi.nlm.nih.gov/pubmed/15885877
2. Chapple CR, Khullar V, Gabriel Z, et al. The effects of antimuscarinic treatments in overactive bladder: an update of a systematic review and meta-analysis. Eur Urol 2008;54(3):543-62. http://www.ncbi.nlm.nih.gov/pubmed/18599186
3. Hartmann KE, McPheeters ML, Biller DH, et al. Treatment of overactive bladder in women. Evid Rep Technol Assess (Full Rep). 2009 Aug;(187):1-120, v. [Comparative study review] http://www.ncbi.nlm.nih.gov/pubmed/19947666
4. Herbison P, Hay-Smith J, Ellis G, et al. Effectiveness of anticholinergic drugs compared with placebo in the treatment of overactive bladder: systematic review. BMJ 2003 Apr 19;326(7394):841-4. http://www.ncbi.nlm.nih.gov/pubmed/12702614
5. Nabi G, Cody JD, Ellis G, et al. Anticholinergic drugs versus placebo for overactive bladder syndrome in adults. [Meta-analysis review.] Cochrane Database Syst Rev 2006 Oct 18;(4):CD003781. http://www.ncbi.nlm.nih.gov/pubmed/17054185
6. McDonagh MS, Selover D, Santa J, et al. Drug class review: agents for overactive bladder. Final report. Update 4. Portland, Oregon: Oregon Health & Science University, 2009 Mar. http://www.ncbi.nlm.nih.gov/books/NBK47183/
7. Homma Y, Paick JS, Lee JG, et al. Clinical efficacy and tolerability of extended-release tolterodine and immediate-release oxybutynin in Japanese and Korean patients with an overactive bladder: a randomized, placebo-controlled trial. BJU Int 2003 Nov;92(7):741-7. http://www.ncbi.nlm.nih.gov/pubmed/14616458
8. Moore KH, Goldstein M, Hay D. The treatment of detrusor instability in postmenopausal women with oxybutynin chloride: a double blind placebo controlled study. Br J Obstet Gynaecol 1990 Nov;97(11):1063-4. http://www.ncbi.nlm.nih.gov/pubmed/2082973
9. Szonyi G, Collas DM, Ding YY, et al. Oxybutynin with bladder retraining for detrusor instability in elderly people: a randomized controlled trial. Age Ageing 1995 Jul;24(4):287-91. http://www.ncbi.nlm.nih.gov/pubmed/7484484
10. Tapp AJ, Cardozo LD, Versi E, et al. The treatment of detrusor instability in post-menopausal women with oxybutynin chloride: a double blind placebo controlled study. Br J Obstet Gynaecol 1990 Jun;97(6):521-6. http://www.ncbi.nlm.nih.gov/pubmed/2198921
11. Thuroff JW, Bunke B, Ebner A, et al. Randomized, double-blind, multicenter trial on treatment of frequency, urgency and incontinence related to detrusor hyperactivity: oxybutynin versus propantheline versus placebo. J Urol 1991 Apr;145(4):813-6; discussion 816-7. http://www.ncbi.nlm.nih.gov/pubmed/2005707
12. Abrams P, Freeman R, Anderstrom C, et al. Tolterodine, a new antimuscarinic agent: as effective but better tolerated than oxybutynin in patients with an overactive bladder. Br J Urol 1998 Jun;81(6): 801-10. http://www.ncbi.nlm.nih.gov/pubmed/9666761
13. Abrams P, Malone-Lee J, Jacquetin B, et al. Twelve-month treatment of overactive bladder: efficacy and tolerability of tolterodine. Drugs Aging 2001;18(7):551-60. http://www.ncbi.nlm.nih.gov/pubmed/11482747
14. Drutz HP, Appell RA, Gleason D, et al. Clinical efficacy and safety of tolterodine compared to oxybutynin and placebo in patients with overactive bladder. Int Urogynecol J Pelvic Floor Dysfunct 1999;10(5):283-9. http://www.ncbi.nlm.nih.gov/pubmed/10543335
15. Jacquetin B, Wyndaele J. Tolterodine reduces the number of urge incontinence episodes in patients with an overactive bladder. Eur J Obstet Gynecol Reprod Biol 2001 Sep;98(1):97-102. http://www.ncbi.nlm.nih.gov/pubmed/11516807
16. Jonas U, Hofner K, Madersbacher H, et al. Efficacy and safety of two doses of tolterodine versus placebo in patients with detrusor overactivity and symptoms of frequency, urge incontinence, and urgency: urodynamic evaluation. The International Study Group. World J Urol 1997;15(2):144-51. http://www.ncbi.nlm.nih.gov/pubmed/9144906
17. Malone-Lee JG, Walsh JB, Maugourd MF. Tolterodine: a safe and effective treatment for older patients with overactive bladder. J Am Geriatr Soc 2001 Jun;49(6):700-5. http://www.ncbi.nlm.nih.gov/pubmed/11454106

18. Millard R, Tuttle J, Moore K, et al. Clinical efficacy and safety of tolterodine compared to placebo in detrusor overactivity. J Urol 1999 May;161(5):1551-5. http://www.ncbi.nlm.nih.gov/pubmed/10210394
19. Rentzhog L, Stanton SL, Cardozo L, et al. Efficacy and safety of tolterodine in patients with detrusor instability: a dose-ranging study. Br J Urol 1998 Jan;81(1):42-8. http://www.ncbi.nlm.nih.gov/pubmed/9467475
20. Van Kerrebroeck P, Kreder K, Jonas U, et al; Tolterodine Study Group. Tolterodine once-daily: superior efficacy and tolerability in the treatment of the overactive bladder. Urology 2001 Mar;57(3):414-21. http://www.ncbi.nlm.nih.gov/pubed/11248608
21. Dorschner W, Stolzenburg JU, Griebenow R, et al. Efficacy and cardiac safety of propiverine in elderly patients-a double-blind, placebo-controlled clinical study. Eur Urol 2000 Jun;37(6):702-8. http://www.ncbi.nlm.nih.gov/pubmed/10828671
22. Halaska M, Martan A, Voigt R, et al. [Tolerance and effectiveness of propiverine hydrochloride in 752 patients with symptoms of detrusor hyperactivity and increased sensitivity and irritability of the urinary bladder: results of a study monitoring drug utilization]. Ceska Gynekol 1997 Oct;62(5):259-64. [Czech] http://www.ncbi.nlm.nih.gov/pubmed/9600163
23. Junemann KP, Hessdorfer E, Unamba-Oparah I, et al. Propiverine hydrochloride immediate and extended release: comparison of efficacy and tolerability in patients with overactive bladder. Urol Int 2006;77(4):334-9. http://www.ncbi.nlm.nih.gov/pubmed/17135784
24. Zinner N, Gittelman M, Harris R, et al. Trospium chloride improves overactive bladder symptoms: a multicenter phase III trial. J Urol 2004 Jun;171(6 Pt 1):2311-5. http://www.ncbi.nlm.nih.gov/pubmed/15126811
25. Staskin DR, Dmochowski RR, Sand PK, et al. Efficacy and safety of oxybutynin chloride topical gel for overactive bladder: a randomized, double-blind, placebo controlled, multicenter study. J Urol 2009 Apr;181(4):1764-72. http://www.ncbi.nlm.nih.gov/pubmed/19233423

4.1.2 ***Extended-release and longer-acting antimuscarinic agents***

4.1.2.1 Question

In men and women with UUI, do oral extended-release and longer-acting antimuscarinic drugs cure or improve the symptoms of UUI compared with no treatment?

4.1.2.2 Evidence

Most studies included patients with OAB, with a mean age of 55-60 years. Because most patients were women, the results can be generalised to women, but not to men. The reported rates for improvement or cure of UUI were only short term (up to 12 weeks). The evidence reviewed was consistent, indicating that ER formulations of antimuscarinics offer clinically significant short-term cure rates and improvement rates for UUI. A comprehensive review of antimuscarinic therapy by the AHRQ was published in 2009. The references to individual RCTs included in this review have not been listed separately for this section (1).

Darifenacin

Two RCTs compared darifenacin to placebo, involving 838 patients (681 women). One study included only patients older than 65 years. The second study by Hill et al. found that darifenacin was superior to placebo for cure of UUI. No new data comparing darifenacin with placebo have been published since the AHRQ and Oregon Health and Science University systematic reviews, published in 2009 (1,2).

Fesoterodine

Two randomised trials have been reported since the AHRQ review (4,5). Both trials compared fesoterodine, 8 mg/day, versus tolterodine ER, 4 mg/day, versus placebo. The first study reported higher cure rates with fesoterodine than with placebo, but also higher rates of dry mouth. In the second study, the cure rates were also higher than with placebo, but again with higher rates of dry mouth. These trials are consistent with previous reports showing the effectiveness of fesoterodine compared to no treatment (placebo) described in the AHRQ and Oregon systematic reviews (1-3).

Oxybutynin

None of the identified studies that compared oxybutynin ER with placebo included incontinence as a measured outcome. One study reported that oxybutynin ER produced less cognitive disturbance than placebo (6).

Tolterodine
A study of mostly women (n = 361) compared tolterodine ER, transcutaneous oxybutynin, and placebo (7). Tolterodine ER resulted in a significantly higher chance of cure than placebo. Another study (8) in 337 incontinent men and women calculated the daytime incontinence outcomes in a secondary analysis of data from a previous study of tolterodine ER in OAB with nocturia. The analysis found higher cure rates of UUI using tolterodine ER. These data are consistent with the studies summarised in the AHRQ and Oregon systematic reviews (1,2) showing that tolterodine was effective for improvement of UUI compared to placebo.

Propiverine
We found three RCTs comparing propiverine ER with placebo, all with improvement of UUI as an outcome (9-11). All trials showed propiverine ER had a significant benefit over placebo in terms of improvement (11) and cure (9,10). Adverse effects reported included dry mouth and a prolonged QTc interval (9,10).

Solifenacin
Karram et al. reported a study in 707 patients comparing solifenacin and placebo, although their primary outcome measure was urgency rather than incontinence (12). Cure rates for urgency were 58% for solifenacin and 42% for placebo. Concerning an improvement in UUI, there have been no high-quality studies published since the AHRQ and Oregon systematic reviews (1,2), which already contained useful data on improvement in UI with solifenacin.

Trospium
Several authors (13-15) have done a secondary analysis of two previously published studies of trospium ER versus placebo (16,17). Cure rates for UUI were reported as 21% with trospium ER and 11% with placebo (14).

Evidence summary	**LE**
ER formulations of antimuscarinic agents are effective for improvement and cure of UUI.	1b
ER formulations of antimuscarinic agents result in higher rates of dry mouth compared to placebo.	1b

4.1.2.3 References

1. Hartmann KE, McPeeters ML, Biller DH, et al. Treatment of overactive bladder in women. Evid Rep Technol Assess (Full Rep). 2009 Aug;(187):1-120, v. http://www.ncbi.nlm.nih.gov/pubmed/19947666
2. McDonagh MS, Selover D, Santa J, et al. Drug class review: agents for overactive bladder. Final report. Update 4. Portland, Oregon: Oregon Health & Science University, 2009 Mar. http://www.ncbi.nlm.nih.gov/pubmed/21089246
3. Dmochowski RR, Peters KM, Morrow JD, et al. Randomized, double-blind, placebo-controlled trial of flexible-dose fesoterodine in subjects with overactive bladder. Urology 2010 Jan;75(1):62-8. http://www.ncbi.nlm.nih.gov/pubmed/19931895
4. Herschorn S, Swift S, Guan Z, et al. Comparison of fesoterodine and tolterodine extended release for the treatment of overactive bladder: a head-to-head placebo-controlled trial. BJU Int 2010;105(1): 58-66. http://www.ncbi.nlm.nih.gov/pubmed/20132103
5. Kaplan SA, Schneider T, Foote JE, et al. Superior efficacy of fesoterodine over tolterodine extended release with rapid onset: a prospective, head-to-head, placebo-controlled trial. BJU Int 2011 May;107(9):1432-40. http://www.ncbi.nlm.nih.gov/pubmed/20860717
6. Lackner TE, Wyman JF, McCarthy TC, et al. Randomized, placebo-controlled trial of the cognitive effect, safety, and tolerability of oral extended-release oxybutynin in cognitively impaired nursing home residents with urge urinary incontinence. J Am Geriatr Soc 2008 May;56(5):862-70. http://www.ncbi.nlm.nih.gov/pubmed/18410326
7. Dmochowski RR, Sand PK, Zinner NR, et al.; Transdermal Oxybutynin Study Group. Comparative efficacy and safety of transdermal oxybutynin and oral tolterodine versus placebo in previously treated patients with urge and mixed urinary incontinence. Urology 2003 Aug;62(2):237-42. http://www.ncbi.nlm.nih.gov/pubmed/12893326
8. Rovner ES, Rackley R, Nitti VW, et al. Tolterodine extended release is efficacious in continent and incontinent subjects with overactive bladder. Urology 2008 Sep;72(3):488-93. http://www.ncbi.nlm.nih.gov/pubmed/18639327

9. Junemann KP, Hessdorfer E, Unamba-Oparah I, et al. Propiverine hydrochloride immediate and extended release: comparison of efficacy and tolerability in patients with overactive bladder. Urol Int 2006;77(4):334-9.
http://www.ncbi.nlm.nih.gov/pubmed/17135784
10. Yamaguchi O, Marui E, Kakizaki H, et al. Randomized, double-blind, placebo- and propiverine-controlled trial of the once-daily antimuscarinic agent solifenacin in Japanese patients with overactive bladder. BJU Int 2007 Sep;100(3):579-87.
http://www.ncbi.nlm.nih.gov/pubmed/17669143
11. Homma Y, Yamaguchi O; Imidafenacin Study Group. A randomized, double-blind, placebo- and propiverine-controlled trial of the novel antimuscarinic agent imidafenacin in Japanese patients with overactive bladder. Int J Urol 2009 May;16(5):499-506.
http://www.ncbi.nlm.nih.gov/pubmed/19389083
12. Karram MM, Toglia MR, Serels SR, et al. Treatment with solifenacin increases warning time and improves symptoms of overactive bladder: results from VENUS, a randomized, double-blind, placebo-controlled trial. Urology 2009 Jan;73(1):14-8.
http://www.ncbi.nlm.nih.gov/pubmed/18995887
13. Staskin DR, Rosenberg MT, Sand PK, et al. Trospium chloride once-daily extended release is effective and well tolerated for the treatment of overactive bladder syndrome: an integrated analysis of two randomised, phase III trials. Int J Clin Pract 2009;63(12):1715-23.
http://www.ncbi.nlm.nih.gov/pubmed/19930332
14. Staskin DR, Cardozo L. Baseline incontinence severity is predictive of the percentage of patients continent after receiving once-daily trospium chloride extended release. Int J Clin Pract 2009;63(6):973-6.
http://www.ncbi.nlm.nih.gov/pubmed/19459997
15. Sand PK, Dmochowski RR, Zinner NR, et al. Trospium chloride extended release is effective and well tolerated in women with overactive bladder syndrome. Int Urogynecol J Pelvic Floor Dysfunct 2009 Dec;20(12):1431-8.
http://www.ncbi.nlm.nih.gov/pubmed/19727537
16. Dmochowski RR, Sand PK, Zinner NR, et al. Trospium 60 mg once daily (QD) for overactive bladder syndrome: results from a placebo-controlled interventional study. Urology 2008 Mar;71(3):449-54.
http://www.ncbi.nlm.nih.gov/pubmed/18342185
17. Staskin D, Sand P, Zinner N, et al. Once daily trospium chloride is effective and well tolerated for the treatment of overactive bladder: results from a multicenter phase III trial. J Urol 2007 Sep;178(3 Pt 1):978-83; discussion 983-4.
http://www.ncbi.nlm.nih.gov/pubmed/17632131

4.2 Comparison of antimuscarinic agents

Head-to-head comparison trials of the efficacy and side effects of different antimuscarinic agents can help clinicians and patients to decide on the best initial agent to use, and the most appropriate second-line agent to try if the initial agent provides little benefit or has troublesome side effects.

4.2.1 ***Question***

In adults with UUI, does one type of antimuscarinic drug result in a greater likelihood of cure or improvement in UUI, and/or a greater improvement in QoL, and/or a lesser likelihood of adverse effects compared to an alternative antimuscarinic drug?

4.2.2 ***Evidence***

There is a considerable body of evidence covering this question, comprising over 40 RCTs and five systematic reviews. Nearly all the primary studies have been funded and sponsored by the manufacturer of the newer drug under evaluation, which forms the experimental arm of the RCT. It was noted that upward dose titration is often included in the protocol for the experimental arm, but not for the comparator arm (Table 4).

Table 4: Description of trials comparing antimuscarinic agents

Comparison of agents	No. of trials
Experimental IR agent vs. standard IR drug	11
Experimental ER agents vs. standard IR drug	19
Experimental ER agents vs. standard ER drug	12
Transcutaneous oxybutynin vs. standard IR oral drug	1
Transcutaneous oxybutynin vs. standard oral ER drug	1

In general, these studies have been designed for regulatory approval. They have a short treatment duration of typically 12 weeks and a primary outcome of a change in OAB symptoms rather than a cure of, or an improvement in, UUI, which were generally analysed as secondary outcomes. It is therefore difficult to use the results from these trials in daily clinical practice to select the best first-line drug or second-line alternative following the failure of initial treatment. A quality assessment carried out as part of the most recent systematic review (1) found that all the trials were of low or moderate quality.

Two, recent, high-quality systematic reviews from the USA included RCTs published up to the end of October 2008 (1,2). One review specifically addressed evidence of the comparative efficacy of antimuscarinic drugs (2). A European review included drugs not available in the USA and included literature published up to the end of August 2008 (3). Both reviews broadly agreed with two earlier reviews (4,5). Between December 2008 and July 2010 (the literature search cut-off date for the present review), two further relevant trials were published (6,9).

For cure of UI, there was weak evidence that oxybutynin ER was more effective than tolterodine ER (1,7). Three recent studies found some evidence that fesoterodine, 8 mg daily, was better than tolterodine ER, 4 mg daily, for cure of UI (6,8,9).

For improvement in UI, there was weak evidence that both oxybutynin ER and tolterodine ER were superior to tolterodine IR (2,3), and that oxybutynin ER was superior to tolterodine ER (3,7). The meta-analysis by Chapple et al. (4), which concluded that solifenacin was better than tolterodine IR for improving UI, has been challenged by more recent systematic reviews, which have concluded that there is no difference (1,2). Evidence from two trials where improvement in UI was the primary outcome suggests greater benefit is obtained with fesoterodine, 8 mg daily, compared with tolterodine ER, 4 mg daily (6,10). All other comparisons showed no difference in efficacy for improvement of UI.

There was no evidence that any one antimuscarinic agent improved QoL more than another agent (1).

Dry mouth is the most prevalent and most studied adverse effect of antimuscarinic agents. Good evidence indicates that, in general, ER formulations of both short-acting drugs and longer-acting drugs are associated with lower rates of dry mouth than IR preparations (1,3). Oxybutynin IR showed higher rates of dry mouth than tolterodine IR and trospium IR, but lower rates of dry mouth than darifenacin, 15 mg daily (1,3). Overall, oxybutynin ER had higher rates of dry mouth than tolterodine ER, but generally oxybutynin did not have higher rates for moderate or severe dry mouth. Transdermal oxybutynin was associated with a lower rate of dry mouth than oxybutynin IR and tolterodine ER, but had an overall higher rate of withdrawal due to an adverse skin reaction (1). Solifenacin, 10 mg daily, had higher rates of dry mouth than tolterodine ER (1). Fesoterodine, 8 mg daily, had a higher rate of dry mouth than tolterodine, 4 mg daily (6,10). In general, discontinuation rates were similar for each treatment arm in comparative RCTs, irrespective of differences in the occurrence of dry mouth.

In conclusion, there is no consistent evidence for the superiority of one antimuscarinic agent over another for the cure or improvement of UI. Recent trials with incontinence as the primary outcome suggest that fesoterodine, 8 mg daily, is superior to tolterodine ER, 4 mg daily, but meta-analysis is required to determine the size of effect. There is good evidence that ER, once-daily, and transdermal preparations, are associated with lower rates of dry mouth than ER preparations, although discontinuation rates are similar.

Evidence summary	LE
There is no consistent evidence that one antimuscarinic drug is superior to an alternative antimuscarinic drug for cure or improvement of UUI.	1a
The ER formulation of oxybutynin is superior to the ER and IR formulations of tolterodine for improvement of UUI.	1b
Fesoterodine, 8 mg daily, is more effective than tolterodine ER, 4 mg daily, for cure and improvement of UUI.	1b
ER and once-daily formulations of antimuscarinic drugs are generally associated with lower rates of dry mouth than IR preparations, although discontinuation rates are similar.	1b
A transdermal oxybutynin (patch) is associated with lower rates of dry mouth than oral antimuscarinic drugs, but has a high rate of withdrawal due to skin reaction.	1b
Oxybutynin IR or ER shows higher rates of dry mouth than the equivalent formulation of tolterodine.	1a
There is no evidence that any particular antimuscarinic agent is superior to another for improvement in QoL.	1a

4.2.3 ***References***

1. McDonagh MS, Selover D, Santa J, et al. Drug Class Review. Agents for overactive bladder. Final report. Update 4. Portland, Oregon: Oregon Health & Science University, 2009 Mar. http://www.ncbi.nlm.nih.gov/pubmed/21089246
2. Hartmann KE, McPeeters ML, Biller DH, et al. Treatment of overactive bladder in women. Evid Rep Technol Assess (Full Rep). 2009 Aug;(187):1-120, v. http://www.ncbi.nlm.nih.gov/pubmed/19947666
3. Novara G. Galfano A, Secco S, et al. A systematic review and meta-analysis of randomized controlled trials with antimuscarinic drugs for overactive bladder. Eur Urol 2008 Oct;54(4):740-63. http://www.ncbi.nlm.nih.gov/pubmed/18632201
4. Chapple C, Khullar V, Gabriel Z, et al. The effects of antimuscarinic treatments in overactive bladder: a systematic review and meta-analysis. Eur Urol 2005 Jul;48(1):5-26. http://www.ncbi.nlm.nih.gov/pubmed/15885877
5. Hay-Smith J, Herbison P, Ellis G, et al. Which anticholinergic drug for overactive bladder symptoms in adults. Cochrane Database Syst Rev 2005 Jul 20;(3):CD005429. http://www.ncbi.nlm.nih.gov/pubmed/16034974
6. Herschorn S, Swift S, Guan Z, et al. Comparison of fesoterodine and tolterodine extended release for the treatment of overactive bladder: a head-to-head placebo-controlled trial. BJU Int 2010 Jan;105(1):58-66. http://www.ncbi.nlm.nih.gov/pubmed/20132103
7. Chapple CR, Khullar V, Gabriel Z, et al. The effects of antimuscarinic treatments in overactive bladder: an update of a systematic review and meta-analysis. Eur Urol 2008 Sep;54(3):543-62. http://www.ncbi.nlm.nih.gov/pubmed/18599186
8. Chapple CR, Van Kerrebroeck PE, Junemann KP, et al. Comparison of fesoterodine and tolterodine in patients with overactive bladder. BJU Int 2008 Nov;102(9):1128-32. http://www.ncbi.nlm.nih.gov/pubmed/18647298
9. Kaplan SA, Schneider T, Foote JE, et al. Superior efficacy of fesoterodine over tolterodine extended release with rapid onset: a prospective, head-to-head, placebo-controlled trial. BJU Int 2011 May;107(9):1432-40. http://www.ncbi.nlm.nih.gov/pubmed/20860717
10. Chapple CR, Van Kerrebroeck P, Tubaro A. Clinical efficacy, safety, and tolerability of once-daily fesoterodine in subjects with overactive bladder. Eur Urol 2007 Oct;52(4):1204-12. http://www.ncbi.nlm.nih.gov/pubmed/17651893

4.3 Antimuscarinic drugs versus non-drug treatment

The choice of drug versus non-drug treatment of UUI is an important question for many clinicians. Especially in less economically developed countries, conservative treatment remains a cheap, effective alternative treatment to drug therapy, with a low risk of side effects.

4.3.1 ***Question***

In adults with UUI, does one type of antimuscarinic drug result in a greater likelihood of cure or improvement in UUI and/or greater improvement in QoL, and/or lesser likelihood of adverse effects compared to an alternative non-drug treatment?

4.3.2 ***Evidence***

There is a large body of evidence comparing non-drug and drug treatment, including more than 100 RCTs and four, recently published, high-quality reviews (1-4). Most of these studies were not funded by the pharmaceutical industry, whose main focus is on drug treatment rather than on conservative treatment.

The US Health Technology Appraisal found that trials were of low- or moderate-quality with none categorised as high quality. The main focus of the review was to compare the different drugs used to treat UUI. Non-drug treatments were mentioned only in the evidence tables for the treatment of UUI. This review included studies comparing behavioural and pharmacological treatments. Nine studies, including one prospective cohort study and eight RCTs, provided direct comparisons between behavioural and pharmacological treatment arms. The behavioural approaches included bladder training, multicomponent behavioural approaches and electrical stimulation. Only one of these studies showed superiority for behavioural therapy. In one study, multicomponent behavioural modification produced significantly greater reductions in incontinence episodes compared to oxybutynin, and higher patient satisfaction for behavioural versus drug treatment.

The Health Technology Appraisal included a comparison between procedural and pharmaceutical treatments, including one RCT that showed a substantial benefit for sacral neuromodulation compared with medical therapy (5).

The most recently published systematic review in 2010 (3) found that medication was less effective than behavioural therapy in a comparative effectiveness trial (81% vs. 69% reduction in UI episodes). In addition, the use of antimuscarinic agents had side effects.

Two older RCTs (6,7), in only small patient groups, reported a similar improvement in subjective parameters with either transcutaneous electrical nerve stimulation or Stoller afferent nerve stimulation. However, only oxybutynin-treated patients showed significant improvements in objective urodynamic parameters (capacity). The oxybutynin-treated group had more side effects.

An important question addressed by multiple studies is how well the combination of antimuscarinic drugs and behavioural therapy compare to either treatment alone. This has been previously discussed in Section 3.3 Behavioural therapy/scheduled voiding. In summary, although medication may enhance the effect of behavioural therapy, there is no evidence that behavioural therapy enhances the effect of drugs.

In conclusion, there is no consistent evidence for the superiority of antimuscarinic drugs over non-drug treatments, especially behavioural treatment. More side effects have been reported for drug therapy compared to non-drug treatment. Electrical stimulation appears to be inferior to other treatment alternatives. Several trials have suggested that a combination of drug and behavioural therapy produce the best results, including in long-term follow-up.

Evidence summary	**LE**
There is no consistent evidence to show superiority of drug therapy or behavioural therapy.	1b
Behavioural treatment results in increased patient satisfaction versus drug treatment alone.	1b

4.3.3 ***References***

1. McDonagh MS, Selover D, Santa J, et al. Drug class review: agents for overactive bladder. Final report. Update 4. Portland, Oregon: Oregon Health & Science University, 2009 Mar. http://www.ncbi.nlm.nih.gov/pubmed/21089246
2. Hartmann KE, McPeeters ML, Biller DH, et al. Treatment of overactive bladder in women. Evid Rep Technol Assess (Full Rep) 2009 Aug;(187):1-120, v. http://www.ncbi.nlm.nih.gov/pubmed/19947666
3. Goode PS, Burgio KL, Richter HE, et al. Incontinence in older women. JAMA 2010 Jun 2;303(21): 2172-81. http://www.ncbi.nlm.nih.gov/pubmed/20516418

4. Shamliyan TA, Kane RL, Wyman J, et al. Systematic review: randomized, controlled trials of nonsurgical treatments for urinary incontinence in women. Ann Intern Med 2008 Mar 18;148(6):459-73. http://www.ncbi.nlm.nih.gov/pubmed/18268288
5. Schmidt RA, Jonas U, Oleson KA, et al. Sacral nerve stimulation for treatment of refractory urinary urge incontinence. Sacral Nerve Stimulation Study Group. J Urol 1999 Aug;162(2):352-7. http://www.ncbi.nlm.nih.gov/pubmed/10411037
6. Soomro NA, Khadra MH, Robson W, et al. A crossover randomized controlled trial of transcutaneous electrical nerve stimulation and oxybutynin in patients with detrusor instability. J Urol 2001 Jul;166(1):146-9. http://www.ncbi.nlm.nih.gov/pubmed/11435843
7. Svihra J, Kurca E, Luptak J, et al. Neuromodulative treatment of overactive bladder-noninvasive tibial nerve stimulation. Bratisl Lek Listy 2002;103(12):480-3. http://www.ncbi.nlm.nih.gov/pubmed/12696778

4.4 Antimuscarinic agents: adherence and persistence

Most studies on antimuscarinic medication provide information only about short-term outcomes (12 weeks), with a smaller number of trials providing longer-term follow-up data. However, it is recognised that in clinical practice many patients stop taking their medication rather more readily than tends to occur in RCTs, where the methodology tends to enhance adherence to allocated medication.

4.4.1 ***Question***

Do patients with UUI adhere to antimuscarinic drug treatment and persist with prescribed treatment everyday clinical practice?

4.4.2 ***Evidence***

Twelve papers have been published on adherence/persistence to antimuscarinic medication in everyday clinical practice (1-12). Ten papers used established pharmaco-epidemiological parameters (1-7,9-11), including:

- Persistence. This is calculated from the index date until the patient discontinues treatment or is lost to follow-up, or the maximum follow-up period has ended, whichever occurs first.
- Medication possession rate (MPR). This is the total days of medication dispensed, except for the last refill, divided by the number of days between the first date on which medication was dispensed and the last refill date.
- Adherence ratio (MPR $\geq$ 0.8). This is the percentage of patients with MPR $\geq$ 0.8.

One study was in an open-label extension population (8). One study used only self-reports of patients and did not follow patients from the start of treatment (12). Most of the data was not derived from RCTs, but from pharmacy refill records. Pharmacy records are likely to overestimate adherence and persistence, because it is often not clear whether patients have been monitored from the start of treatment or whether monitoring (for the purpose of the study) was started in patients already taking the drug for some time and therefore defined as persistent users.

The main drugs studied in adherence/persistence trials were oxybutynin IR and ER and tolterodine IR and ER. These reviews demonstrated high non-persistence rates for tolterodine at 12 months, and particularly high rates (68-95%) for oxybutynin (1-3,5,6).

Five articles reported ‘median days to discontinuation’ as between < 30 days and 50 days (2,3,5,6,10), with one study reporting 273 days in a military health system (which provides patients with free medication) (6).

Only one RCT (8) included solifenacin, darifenacin and trospium. The only open-label extension study included in the review also studied solifenacin, darifenacin and trospium. However, determining adherence/persistence in an open-label extension population is not the preferred methodology, as these patients will not have been monitored from the start of treatment and are therefore self-selected as persistent patients.

Several of the RCT trials tried to identify the factors associated with a lower, or low, adherence or persistence of antimuscarinic agents (2,6,7,9). These were identified in order of importance as:

- low level of efficacy (41.3%);
- adverse events (22.4%);
- cost (18.7%), as most adherence measures were higher in populations, which did not pay for medication, e.g. patients with health insurance (6).

Other reasons for poor adherence included:

- IR versus ER formulations;
- age, with persistence lower among younger adults;
- unrealistic expectations of treatment;
- gender distribution, because adherence/persistence was better in studies that include relatively more female patients;
- ethnic group because African-Americans and other minorities were more likely to discontinue or switch treatment;
- effectiveness of treatment because in Campbell et al. only 52% were somewhat satisfied to very satisfied with treatment.

In addition, the source of data influenced the adherence figures.

Evidence summary	**LE**
More than half of patients will stop antimuscarinic agents within the first 3 months because of ineffectiveness, adverse events and cost.	2

4.4.3 ***References***

1. Lawrence M, Guay DR, Benson SR, et al. Immediate-release oxybutynin versus tolterodine in detrusor overactivity: a population analysis. Pharmacotherapy 2000;20(4):470-5. http://www.ncbi.nlm.nih.gov/pubmed/10772377
2. Shaya FT, Blume S, Gu A, et al. Persistence with overactive bladder pharmacotherapy in a Medicaid population. Am J Manag Care 2005 Jul;11(4 Suppl):S121-9. http://www.ncbi.nlm.nih.gov/pubmed/16161385
3. Yu YF, Nichol MB, Yu AP, et al. Persistence and adherence of medications for chronic overactive bladder/urinary incontinence in the california medicaid program. Value Health 2005 Jul-Aug;8(4): 495-505. http://www.ncbi.nlm.nih.gov/pubmed/16091027
4. Balkrishnan R, Bhosle MJ, Camacho FT, et al. Predictors of medication adherence and associated health care costs in an older population with overactive bladder syndrome: a longitudinal cohort study. J Urol 2006;175(3 Pt 1):1067-71; discussion 1071-2. http://www.ncbi.nlm.nih.gov/pubmed/16469620
5. D'Souza AO, Smith MJ, Miller LA, et al. Persistence, adherence, and switch rates among extended-release and immediate-release overactive bladder medications in a regional managed care plan. J Manag Care Pharm 2008 Apr;14(3):291-301. http://www.ncbi.nlm.nih.gov/pubmed/18439051
6. Sears CL, Lewis C, Noel K, et al. Overactive bladder medication adherence when medication is free to patients. J Urol 2010 Mar;183(3):1077-81. http://www.ncbi.nlm.nih.gov/pubmed/20092838
7. Campbell UB, Stang P, Barron R. Survey assessment of continuation of and satisfaction with pharmacological treatment for urinary incontinence. Value Health 2008 Jul-Aug;11(4):726-32. http://www.ncbi.nlm.nih.gov/pubmed/18179666
8. Basra RK, Wagg A, Chapple C, et al. A review of adherence to drug therapy in patients with overactive bladder. BJU Int 2008 Sep;102(7):774-9. http://www.ncbi.nlm.nih.gov/pubmed/18616691
9. Benner JS, Nichol MB, Rovner ES, et al. Patient-reported reasons for discontinuing overactive bladder medication. BJU Int 2010 Sep;105(9):1276-82. http://www.ncbi.nlm.nih.gov/pubmed/19912188
10. Yeaw J, Benner J, Walt JG, et al. Comparing adherence and persistence across 6 chronic medication classes. J Manag Care Pharm 2009 Nov-Dec;15(9):728-40. http://www.ncbi.nlm.nih.gov/pubmed/19954264
11. Varadharajan S, Jumadilova Z, Girase P, et al. Economic impact of extended-release tolterodine versus immediate- and extended-release oxybutynin among commercially insured persons with overactive bladder. Am J Manag Care 2005 Jul;11(4 Suppl):S140-9. http://www.ncbi.nlm.nih.gov/pubmed/16161387
12. Brubaker L, Fanning K, Goldberg EL, et al. Predictors of discontinuing overactive bladder medications. BJU Int 2010 May;105(9):1283-90. http://www.ncbi.nlm.nih.gov/pubmed/19912189

4.5 Antimuscarinic agents, the elderly and cognition

Although the prevalence of UI increases with age, this is not reflected by research targeted to elderly people with UI. Drug trials usually exclude patients with several comorbidities and those taking multiple medications. However, the mechanisms underlying UI in the elderly are more likely to be multifactorial than in younger patients. The elderly are also likely to be taking medications that may affect the efficacy or adverse effects of a new drug.

Muscarinic receptors exist throughout the body and are involved in many physiological processes. Most anticholinergics used to treat OAB are directed against the M2 and M3 receptors. The M1 receptor is involved in memory processes. The specificity of a drug for one or another receptor and the degree of penetration into the CNS through the blood-brain barrier may impact on cognitive function. In recent years, the effects of antimuscarinic agents on cognition have been studied in more detail.

4.5.1 ***Question***

What is the comparative efficacy, and risk of adverse effects, particularly the cognitive impact, of treatment with antimuscarinic medication in elderly men and women with UUI compared to younger patients?

4.5.2 ***Evidence***

There have been two systematic reviews of antimuscarinic agents in elderly patients (1,2). One review was confined to evidence on nursing home residents with UUI (2). A community-based cohort study on the burden of antimuscarinic drugs in an elderly population (n = 372) found a high incidence of cognitive dysfunction (3). The Oregon systematic review of treatments for OAB reported specifically on outcomes in elderly patients (4).

There have been very few trials specifically investigating the cognitive changes that might occur with the use of antimuscarinic agents. Most trials have been done in healthy volunteers of different age groups and only for a short period (varying from a single dose to 12 weeks). Other publications describe post-hoc analyses of other trials or reviewed only a number of selected publications. In general, these trials have measured CNS side effects in a non-specific way that does not allow the impact on cognition to be considered in a particular patient population (5,6). Meta-analyses have been limited by study heterogeneity, dosing inconsistency and reporting bias. There is a need for more detailed, standardised measurement of age-stratified CNS outcomes in clinical trials to provide better information to patients and clinicians about the CNS risks associated with antimuscarinic agents.

Studies on antimuscarinic effects have been done in elderly persons (7), and in people with dementia with UUI (8). There have been no specific studies in vulnerable patient populations, who are likely to have cognitive dysfunction and might suffer deterioration of their cognitive function due to using antimuscarinic medication.

Although there have been no RCTs specifically designed to examine the impact of antimuscarinic medication on elderly patients compared with younger patients, it is possible to extract relevant evidence from several RCTs, which have provided outcomes for specific age groups, and other studies of the risks/benefits of antimuscarinic agents in an elderly population. There are many case studies that report adverse effects of antimuscarinic agents in elderly patients, particularly those with serious cognitive dysfunction. There are also a number of studies that address the cardiovascular risk, which is mainly associated with antimuscarinic agents, in this age group. It should be noted that the definition of an elderly patient and the exclusion criteria vary from study to study.

Oxybutynin

There is substantial evidence that oxybutynin may cause or worsen cognitive dysfunction in adults (5,7,9).

A crossover RCT in elderly volunteers given oxybutynin IR reported increased cognitive dysfunction with oxybutynin, while a short-term RCT of oxybutynin ER in elderly women with cognitive dysfunction observed no increase in delirium (10).Two studies in the elderly demonstrated additional benefit from oxybutynin IR combined with scheduled voiding versus scheduled voiding alone. Another study found no differences between oxybutynin ER and IR in elderly patients, although the study did not reach its recruitment target (11).

A large observational study (n = 3536) suggested that more rapid functional deterioration might result from the combined use of cholinesterase inhibitors with antimuscarinic agents in elderly patients with cognitive dysfunction (12). However, the nature of the interaction with cholinesterase inhibitors is unclear. No general conclusions can be made, but caution is advised in prescribing these combinations.

Solifenacin
One pooled analysis from several RCTs (13) has shown that solifenacin has good efficacy and does not increase cognitive impairment in the elderly. Another RCT found no age-related differences in the pharmacokinetics of solifenacin between elderly, middle-aged or younger patients. One post-marketing surveillance study reported more frequent adverse events in subjects over 80 years old. Another study on healthy elderly volunteers showed no cognitive effect (9).

Tolterodine
Pooled data from RCTs showed no change in efficacy or side effects related to age, but reported a higher discontinuation rate for both tolterodine and placebo in elderly patients (5). Two RCTs of tolterodine specifically designed in the elderly found that tolterodine showed a similar efficacy and side effect profile, as in younger patients. Post-hoc analysis from other RCTs has shown little effect on cognition.

Darifenacin
Two RCTs carried out specifically in the elderly population (one RCT in patients with UUI and the other RCT in volunteers) concluded that darifenacin was effective and had no cognitive side effects (16,17). Another comparison between darifenacin and oxybutynin ER in elderly subjects concluded that the two agents had a similar efficacy, but that cognitive function was more often affected in patients receiving oxybutynin ER (7).

Trospium chloride and fesoterodine
No published evidence was found regarding the comparative efficacy and side effect profiles of trospium or fesoterodine in the elderly compared with younger patients. However, there is good evidence that trospium does not impair cognitive function.

Applicability of evidence to general elderly population
It is not clear how much the data from pooled analyses and subgroup analyses from large RCTs can be extrapolated to a general ageing population. The community-based studies of the prevalence of antimuscarinic side effects in this age group may be the most helpful (3).

When starting anticholinergic medication in patients at risk of worsening cognitive function, it has been suggested that mental function is assessed objectively and monitored to detect any significant changes during treatment (18).

Evidence summary	**LE**
Oxybutynin IR may worsen cognitive function.	1b
Trospium chloride has not been reported to affect cognitive function.	1b
Solifenacin, tolterodine and darifenacin have not been shown to impair cognitive function in healthy volunteers.	3
Oxybutynin ER, 5 mg/day, does not cause delirium in the short term in cognitively impaired elderly women.	1b
Oxybutynin IR is less effective in people with impaired orientation, cerebral cortical underperfusion and reduced bladder sensation.	2
The effectiveness and risk of adverse events of solifenacin, tolterodine and darifenacin do not differ with patient age.	3
There is conflicting evidence about whether the efficacy of antimuscarinic drugs is different in elderly people compared to younger populations.	3

Recommendations for antimuscarinic drugs	**GR**
Offer IR or ER formulations of antimuscarinic drugs as initial drug therapy for adults with urgency urinary incontinence.	A
If IR formulations of antimuscarinic drugs are unsuccessful for adults with urgency urinary incontinence, offer ER formulations or longer-acting antimuscarinic agents.	A
Consider using transdermal oxybutynin if oral antimuscarinic agents cannot be tolerated due to dry mouth.	B
Offer and encourage early review (of efficacy and side effects) of patients on antimuscarinic medication for urgency urinary incontinence (< 30 days).	A

When prescribing antimuscarinic drugs to elderly patients, be aware of the risk of cognitive side effects, especially in those receiving cholinesterase inhibitors.	C
Avoid using oxybutynin IR in patients who are at risk of cognitive dysfunction.	A
Consider use of trospium chloride in patients known to have cognitive dysfunction.	B
Use solifenacin, tolterodine and darifenacin with caution in patients with cognitive dysfunction.	B
Do an objective assessment of mental function before treating patients whose cognitive function may be at risk.	C
Check mental function in patients on antimuscarinic medication if they are at risk of cognitive dysfunction.	C

IR = Immediate release; ER = extended release.

4.5.3 ***Research priority***

As it is difficult to predict the longer-term benefit from the effect seen in short-term trials, it is recommended that cure of UUI should be a primary outcome measure in future research.

4.5.4 ***References***

1. DuBeau CE, Kuchel GA, Johnson T 2nd, et al. Incontinence in the frail elderly: report from the 4th International Consultation on Incontinence. Neurourol Urodyn 2010;29(1):165-78. http://www.ncbi.nlm.nih.gov/pubmed/20025027
2. Fink HA, Taylor BC, Tacklind JW, et al. Treatment interventions in nursing home residents with urinary incontinence: a systematic review of randomized trials. Mayo Clin Proc 2008 Dec;83(12):1332-43. http://www.ncbi.nlm.nih.gov/pubmed/19046552
3. Ancelin ML, Artero S, Portet F, et al. Non-degenerative mild cognitive impairment in elderly people and use of anticholinergic drugs: longitudinal cohort study. BMJ 2006 Feb 25;332(7539):455-9. http://www.ncbi.nlm.nih.gov/pubmed/16452102
4. McDonagh MS, Selover D, Santa J, et al. Drug class review: agents for overactive bladder. Final report. Update 4. Portland, Oregon: Oregon Health & Science University, 2009. http://www.ncbi.nlm.nih.gov/pubmed/21089246
5. Kessler TM, Bachmann LM, Minder C, et al. Adverse event assessment of antimuscarinics for treating overactive bladder: a network meta-analytic approach. PLoS One 2011 Feb 23;6(2):e16718. http://www.ncbi.nlm.nih.gov/pubmed/21373193
6. Paquette A, Gou P, Tannenbaum C. Systematic review and meta-analysis: do clinical trials testing antimuscarinic agents for overactive bladder adequately measure central nervous system adverse events? J Am Geriatr Soc 2011 Jul;59(7):1332-9. http://www.ncbi.nlm.nih.gov/pubmed/21718264
7. Kay G, Crook T, Rekeda L, et al. Differential effects of the antimuscarinic agents darifenacin and oxybutynin ER on memory in older subjects. Eur Urol 2006 Aug;50(2):317-26. http://www.ncbi.nlm.nih.gov/pubmed/16687205
8. Isik AT, Celik T, Bozoglu E, et al. Trospium and cognition in patients with late onset Alzheimer disease. J Nutr Health Aging 2009 Oct;13(8):672-6. http://www.ncbi.nlm.nih.gov/pubmed/19657549
9. Wesnes KA, Edgar C, Tretter RN, et al. Exploratory pilot study assessing the risk of cognitive impairment or sedation in the elderly following single doses of solifenacin 10 mg. Expert Opin Drug Saf 2009 Nov;8(6):615-26. http://www.ncbi.nlm.nih.gov/pubmed/19747069
10. Lackner TE, Wyman JF, McCarthy TC, et al. Randomized, placebo-controlled trial of the cognitive effect, safety, and tolerability of oral extended-release oxybutynin in cognitively impaired nursing home residents with urge urinary incontinence. J Am Geriatr Soc 2008 May;56(5):862-70. http://www.ncbi.nlm.nih.gov/pubmed/18410326
11. Minassian VA, Ross S, Sumabat O, et al. Randomized trial of oxybutynin extended versus immediate release for women aged 65 and older with overactive bladder: lessons learned from conducting a trial. J Obstet Gynaecol Can 2007 Sep;29(9):726-32. http://www.ncbi.nlm.nih.gov/pubmed/17825137
12. Sink KM, Thomas J 3rd, Xu H, et al. Dual use of bladder anticholinergics and cholinesterase inhibitors: long-term functional and cognitive outcomes. J Am Geriatr Soc 2008 May;56(5):847-53. http://www.ncbi.nlm.nih.gov/pubmed/18384584

13. Wagg A, Wyndaele JJ, Sieber P. Efficacy and tolerability of solifenacin in elderly subjects with overactive bladder syndrome: a pooled analysis. Am J Geriatr Pharmacother 2006 Mar;4(1):14-24. http://www.ncbi.nlm.nih.gov/pubmed/16730617
14. Michel MC, Wetteraurer U, Vogel M, et al. Cardiovascular safety and overall tolerability of solifenacin in routine clinical use: a 12-week, open-label, post-marketing surveillance study. Drug Saf 2008;31(6):505-14. http://www.ncbi.nlm.nih.gov/pubmed/18484784
15. Griebling TL, Kraus SR, Richter HE, et al. Tolterodine extended release is well tolerated in older subjects. Int J Clin Pract 2009 Aug;63(8):1198-204. http://www.ncbi.nlm.nih.gov/pubmed/19624787
16. Chapple C, DuBeau C, Ebinger U, et al. Darifenacin treatment of patients >or= 65 years with overactive bladder: results of a randomized, controlled, 12-week trial. Curr Med Res Opin 2007 Oct;23(10):2347-58. http://www.ncbi.nlm.nih.gov/pubmed/17706004
17. Lipton RB, Kolodner K, Wesnes K. Assessment of cognitive function of the elderly population: effects of darifenacin. J Urol 2005 Feb;173(2):493-8. http://www.ncbi.nlm.nih.gov/pubmed/15643227
18. Wagg A, Verdejo C, Molander U. Review of cognitive impairment with antimuscarinic agents in elderly patients with overactive bladder. Int J Clin Pract 2010 Aug;64(9):1279-86. http://www.ncbi.nlm.nih.gov/pubmed/20529135

4.6 Duloxetine

Duloxetine inhibits the presynaptic re-uptake of the neurotransmitters, serotonin (5-HT) and norepinephrine (NE) leading to an increase in levels of these neurotransmitters in the synaptic cleft. In the sacral spinal cord, an increased concentration of 5-HT and NE in the synaptic cleft increases stimulation of 5-HT and NE receptors on the pudendal motor neurones, which in turn increases the resting tone and contraction strength of the urethral striated sphincter.

*4.6.1 **Questions***

- In adults with SUI, does duloxetine cure or reduce UI and/or improve QoL compared to no treatment?
- In adults with SUI, does duloxetine result in a greater cure or improvement of incontinence, or a greater improvement in QoL or a lesser likelihood of adverse effects, compared to any other intervention?

*4.6.2 **Evidence***

Duloxetine was evaluated as a treatment for female SUI or MUI in two systematic reviews (1,2) including 10 RCTs (3-12). The typical dose of duloxetine was 80 mg daily, with dose escalation up to 120 mg daily allowed in one study (4), over a period of 8-12 weeks. One RCT extended the observation period up to 36 weeks and used the Incontinence Quality of Life (I-QoL) score as a primary outcome (6).

The studies provided reasonably consistent results demonstrating improvement in UI compared to placebo. There were no clear differences between SUI and MUI. One study reported cure for UI in about 10% of patients (3). An improvement in I-QoL was not found in the study using I-QoL as a primary endpoint (6). A further study compared duloxetine, 80 mg daily, with PFMT alone, PFMT + duloxetine, and placebo (13). Duloxetine reduced leakage compared to PFMT or no treatment. Global improvement and QoL were better for combined therapy than no treatment. There was no significant difference between PFMT and no treatment.

The long-term effect of duloxetine in controlling SUI was evaluated by two open-label studies with a follow-up of 1 year or more (14,15). However, the studies had high rates of discontinuation.

Duloxetine, 80 mg daily, which could be increased up to 120 mg daily, was investigated in a 12-week study in patients, who had OAB but not SUI (16). Episodes of UUI were also significantly reduced by duloxetine.

One study (17) compared PFMT + duloxetine versus PFMT + placebo, for 16 weeks, followed by 8 weeks of PFMT alone in males with post-prostatectomy incontinence. Duloxetine + PFMT significantly improved UI, but the effect did not last to the end of the study, indicating that duloxetine only accelerates cure and does not increase the percentage of patients cured.

In general, all studies had a high patient withdrawal rate of about 20-40% of patients in short-term studies and up to 90% in long-term studies. The high withdrawal rate was caused by a combination of a lack of efficacy

and a high incidence of adverse events, including nausea and vomiting (40% or more of patients), dry mouth, constipation, dizziness, insomnia, somnolence and fatigue.

Evidence summary	LE
Duloxetine does not cure incontinence.	1b
Duloxetine, 80 mg daily, can modestly improve episodes of SUI and UUI in women and men.	1b
Duloxetine causes significant gastrointestinal and CNS side effects leading to a high rate of treatment discontinuation.	1b

Recommendations	GR
Duloxetine should not be offered to women or men who are seeking a cure for their incontinence.	A
Duloxetine can be offered to women or men who are seeking temporary improvement in incontinence symptoms.	A
Duloxetine should be initiated using dose titration because of high adverse effect rates.	A

*4.6.3 **References***

1. Mariappan P, Alhasso A, Ballantyne Z, et al. Duloxetine, a serotonin and noradrenaline reuptake inhibitor (SNRI) for the treatment of stress urinary incontinence: a systematic review. Eur Urol 2007 Jan;51(1):67-74. http://www.ncbi.nlm.nih.gov/pubmed/17014950
2. Shamliyan TA, Kane RL, Wyman J, et al. Systematic review: randomized, controlled trials of nonsurgical treatments for urinary incontinence in women. Ann Intern Med 2008 Mar 18;148(6):459-73. http://www.ncbi.nlm.nih.gov/pubmed/18268288
3. Bent AE, Gousse SL, Hendrix SL, et al. Duloxetine compared with placebo for the treatment of women with mixed urinary incontinence. Neurourol Urodyn 2008;27(3):212-21. http://www.ncbi.nlm.nih.gov/pubmed/17580357
4. Cardozo L, Drutz HP, Baygani SK, et al. Pharmacological treatment of women awaiting surgery for stress urinary incontinence. Obstet Gynecol 2004 Sep;104(3):511-9. http://www.ncbi.nlm.nih.gov/pubmed/15339761
5. Dmochowski RR, Miklos JR, Norton PA, et al; Duloxetine Urinary Incontinence Study Group. Duloxetine versus placebo for the treatment of North American women with stress urinary incontinence. J Urol 2003 Oct;170(4 Pt 1):1259-63. http://www.ncbi.nlm.nih.gov/pubmed/14501737
6. Kinchen KS, Obenchain R, Swindle R. Impact of duloxetine on quality of life for women with symptoms of urinary incontinence. Int Urogynecol J Pelvic Floor Dysfunct 2005 Sep-Oct;16(5):337-44. http://www.ncbi.nlm.nih.gov/pubmed/15662490
7. Millard RJ, Moore K, Rencken R, et al; Duloxetine UI Study Group. Duloxetine vs placebo in the treatment of stress urinary incontinence: a four-continent randomized clinical trial. BJU Int 2004 Feb;93(3):311-8. http://www.ncbi.nlm.nih.gov/pubmed/14764128
8. Norton PA, Zinner NR, Yalcin I, et al; Duloxetine Urinary Incontinence Study Group. Duloxetine versus placebo in the treatment of stress urinary incontinence. Am J Obstet Gynecol 2002 Jul;187(1):40-8. http://www.ncbi.nlm.nih.gov/pubmed/12114886
9. Schagen van Leeuwen JH, Lange RR, Jonasson AF, et al. Efficacy and safety of duloxetine in elderly women with stress urinary incontinence or stress-predominant mixed urinary incontinence. Maturitas 2008 Jun 20;60(2):138-47. http://www.ncbi.nlm.nih.gov/pubmed/18547757
10. Cardozo L, Lange R, Voss S, et al. Short- and long-term efficacy and safety of duloxetine in women with predominant stress urinary incontinence. Curr Med Res Opin 2010 Feb;26(2):253-61. http://www.ncbi.nlm.nih.gov/pubmed/19929591
11. Lin AT, Sun MJ, Tai HL, et al. Duloxetine versus placebo for the treatment of women with stress predominant urinary incontinence in Taiwan: a double-blind, randomized, placebo-controlled trial. BMC Urol 2008 Jan 25;8:2. http://www.ncbi.nlm.nih.gov/pubmed/18221532
12. Van Kerrebroeck P, Abrams P, Lange R, et al. Duloxetine versus placebo in the treatment of European and Canadian women with stress urinary incontinence. BJOG 2004 Mar;111(3):249-57. http://www.ncbi.nlm.nih.gov/pubmed/14961887

13. Ghoniem GM, Van Leeuwen JS, Elser DM, et al; Duloxetine/Pelvic Floor Muscle Training Clinical Trial Group. A randomized controlled trial of duloxetine alone, pelvic floor muscle training alone, combined treatment and no active treatment in women with stress urinary incontinence. J Urol 2005 May;173(5):1647-5.
http://www.ncbi.nlm.nih.gov/pubmed/15821528
14. Bump RC, Voss S, Beardsworth A, et al. Long-term efficacy of duloxetine in women with stress urinary incontinence. BJU Int 2008 Jul;102(2):214-8.
http://www.ncbi.nlm.nih.gov/pubmed/18422764
15. Vella M, Duckett J, Basu M. Duloxetine 1 year on: the long-term outcome of a cohort of women prescribed duloxetine. Int Urogynecol J Pelvic Floor Dysfunct 2008 Jul;19(7):961-4.
http://www.ncbi.nlm.nih.gov/pubmed/18231697
16. Steers WD, Herschorn S, Kreder KJ, et al. Duloxetine compared with placebo for treating women with symptoms of overactive bladder. BJU Int 2007 Aug;100(2):337-45.
http://www.ncbi.nlm.nih.gov/pubmed/17511767
17. Filocamo MT, Li Marzi V, Del Popolo G, et al. Pharmacologic treatment in postprostatectomy stress urinary incontinence. Eur Urol 2007 Jun;51(6):1559-64.
http://www.ncbi.nlm.nih.gov/pubmed/16942833

4.7 Intravaginal oestrogen

Oestrogen treatment for UI can be given orally, vaginally or even intravesically. Oral oestrogen has been shown to worsen UI. Topical oestrogen treatment has less systemic effect and is not associated with an increased risk for cancer or thromboembolism. Topical treatment is used to treat urogenital disorders in post-menopausal women.

4.7.1 ***Question***

In women with UI, does intravaginal oestrogen cure or improve UI compared to no treatment?

4.7.2 ***Evidence***

A recent Cochrane systematic review looked at the use of oestrogen therapy in post-menopausal women (1). The review identified 33 trials, with a total of 19,313 incontinent women, including 1,262 women who were given local oestrogen therapy. There is also a more recent narrative review of oestrogen therapy in urogenital diseases (2). However, since the Cochrane review, no new RCTs have been published up to July 2010. Evidence from a large RCT showed that systemic oestrogen therapy leads to an increased incidence of UI in post-menopausal women, including both SUI and UUI (3).

Local oestrogen therapy can be given as conjugated equine, oestriol or oestradiol in vaginal pessaries, vaginal rings or creams. Besides improving vaginal atrophy (4), local oestrogen therapy reduces incontinence and frequency and urgency in OAB. Local oestrogens were more effective than placebo at improving or curing UI, and reducing frequency (1). The current data do not allow differentiation among the various types of oestrogens or delivery methods. Moreover, the ideal duration of this type of therapy and the long-term effects have been poorly studied.

In conclusion, the evidence for the use of oestrogens in UI is consistent, but is only available in post-menopausal women. This means that any conclusions can only be applied to post-menopausal women with UI. Thus, post-menopausal women taking oral oestrogens should be advised that they have an increased risk for developing or worsening UI. Local oestrogens can be used to reduce incontinence, urgency and frequency in post-menopausal women.

Evidence summary	**LE**
Systemic oestrogen therapy can worsen existing UI and carries an increased risk of UI developing in post-menopausal women.	1a
Local oestrogen therapy in post-menopausal women can at least temporarily improve or cure UI.	1a
There is no evidence available on the neoadjuvant or adjuvant use of local oestrogens at the time of surgery for UI.	1a

Recommendations	GR
Women using systemic oestrogen should be counselled that they have an increased risk for developing urinary incontinence or worsening of their existing incontinence.	A
Offer post-menopausal women with urinary incontinence local oestrogen therapy, although the ideal duration of therapy and best delivery method are unknown.	A
Advise post-menopausal women who are taking oral oestrogens that they have an increased risk for developing urinary incontinence or worsening of their existing urinary incontinence.	A

4.7.3 ***References***

1. Cody JD, Richardson K, Moehrer B, et al. Oestrogen therapy for urinary incontinence in post-menopausal women. Cochrane Database Syst Rev 2009 Oct 7;(4):CD001405. http://www.ncbi.nlm.nih.gov/pubmed/19821277
2. Robinson D, Cardozo L. Estrogens and the lower urinary tract. Neurourol Urodyn 2011 Jun;30(5): 754-7. http://www.ncbi.nlm.nih.gov/pubmed/21661025
3. Hendrix SL, Cochrane BB, Nygaard IE, et al. Effects of estrogen with and without progestin on urinary incontinence. JAMA 2005 Feb 23;293(8):935-48. http://www.ncbi.nlm.nih.gov/pubmed/15728164
6. Suckling J, Lethaby A, Kennedy R. Local oestrogen for vaginal atrophy in postmenopausal women. Cochrane Database Syst Rev 2006 Oct 18;(4):CD001500. http://www.ncbi.nlm.nih.gov/pubmed/17054136

4.8 Desmopressin

Desmopressin is a synthetic analogue of vasopressin (also known as antidiuretic hormone), which increases water re-absorbtion in the renal collecting ducts without increasing blood pressure. It can be taken orally, nasally or by injection. Desmopressin is most commonly used to treat diabetes insipidus and, when used at night, to treat nocturnal enuresis.

4.8.1 ***Questions***

- In adults with nocturnal UI, does desmopressin cure or reduce nocturnal UI and/or improve QoL compared to no treatment?
- In adults with nocturnal UI, does desmopressin result in a greater cure or improvement in nocturnal UI, or a greater improvement in QoL or a lesser likelihood of adverse effects, compared to any other intervention?

4.8.2 ***Evidence***

4.8.2.1 Improvement of incontinence

Most studies of desmopressin in UI have been designed to investigate its effect on nocturia. Few studies have examined the use of desmopressin exclusively for the treatment of UI. Only two RCTS have compared desmopressin to placebo with UI as an outcome measure. A pilot RCT study (n = 128) in women demonstrated improved incontinence during the first 4 hours after taking desmopressin (1). An RCT in 176 men and women with OAB concluded that continuous use of desmopressin improved frequency and urgency, but did not improve UI (2). There is no published evidence reporting desmopressin cure rates for UI and no evidence that compares desmopressin with other non-drug treatments for UI.

4.8.2.2 Monitoring for hyponatraemia

Importantly, the use of desmopressin carries a risk of developing hyponatraemia (12%) (3). Elderly patients started on this drug should have their serum sodium checked regularly, beginning in the first few days after starting treatment.

Evidence summary	LE
The risk of UI is reduced within 4 hours of taking oral desmopressin, but not after 4 hours.	1b
Continuous use of desmopressin does not improve or cure UI.	1b
Regular use of desmopressin may lead to hyponatraemia.	3

Recommendations	GR
Offer desmopressin to patients requiring occasional short-term relief from urinary incontinence, inform them that this drug is not licensed for this indication.	B
Do not use desmopressin for long-term control of urinary incontinence.	A

4.8.3 References

1. Lose G, Mattiasson A, Walter S, et al. Clinical experiences with desmopressin for long-term treatment of nocturia. J Urol 2004 Sep;172(3):1021-5. http://www.ncbi.nlm.nih.gov/pubmed/15311028
2. Robinson D, Cardozo L, Akeson M, et al. Antidiuresis: a new concept in managing female daytime urinary incontinence. BJU Int 2004 May;93(7):996-1000. http://www.ncbi.nlm.nih.gov/pubmed/15142150
3. Hashim H, Malmberg L, Graugaard-Jensen C, et al. Desmopressin, as a “designer-drug”, in the treatment of overactive bladder syndrome. Neurourol Urodyn 2009;28(1):40-6. http://www.ncbi.nlm.nih.gov/pubmed/18726947

5. SURGICAL TREATMENT

Surgery for the treatment of UI is usually considered as an option in pathways of care only after the failure of conservative therapy or drug treatment, although the emergence of minimally invasive procedures with low rates of adverse effects may modify this principle in the future. The aim of all operations for incontinence is to make patients continent, usually by allowing them to store urine normally. However, the mechanisms for achieving this vary widely.

Some generic principles apply to good surgical practice. Any operation for UI should be preceded by a discussion with the patient and/or carers, about the purpose of the operation, the likely benefits and possible risks. It is also important to explain when there are alternative approaches, even if these procedures are not available locally. Surgeons performing operations for UI should be properly trained and perform an adequate number of procedures to maintain expertise. Most importantly, they should be able to demonstrate their competence by being aware of the outcomes of individual operations in their own hands, and should share this information with their patients.

Some newer surgical interventions can be very costly. The Panel is well aware that the availability of devices varies from one healthcare system to another. We have tried to recognise this in the recommendations by suggesting that procedures should be offered ‘when available’.

The section considers surgical options for the following situations:

- Women with uncomplicated SUI. This means no history of previous surgery, no neurological LUTD, no bothersome genitourinary prolapse, and not considering further pregnancy.
- Women with complicated SUI. Neurogenic LUTD is reviewed in the EAU Guidelines on Neurogenic Lower Urinary Tract Dysfunction (1).
- Associated genitourinary prolapse has not been included in these Guidelines, but will be reviewed for 2013.
- Men with SUI. This applies mainly to post-prostatectomy incontinence in men without neurological disease affecting the lower urinary tract.
- Patients with refractory DO incontinence.

5.1 Women with uncomplicated SUI

5.1.1 Open and laparoscopic surgery for SUI

The open ‘Burch’ colposuspension aims to approximate the lateral tissues of the vaginal vault to the pectineal ligament by means of insertion of several, interrupted, non-absorbable sutures. The operation has been much modified over the years, most notably as the vagino-obturator shelf procedure. This has provided less elevation of the vaginal wall by inserting suspensory sutures into the obturator fascia instead of the pectineal ligament.

Autologous fascial slings have been used for many years to provide support or elevation to the mid- or proximal urethra. Again, there have been many different descriptions of this technique.

For decades, open colposuspension has been considered the gold standard surgical intervention for SUI, and has often been used as the comparator in RCTs of new, less invasive, surgical techniques. These include laparoscopic techniques, which have enabled colposuspension to be performed with a minimally invasive approach.

Although the outcome of open and laparoscopic procedures should be considered in absolute terms, it is also important to consider any associated complications, adverse events and costs. The outcome parameters used to evaluate surgery for SUI have included:

- continence rate and number of incontinence episodes;
- general and procedure-specific complications;
- generic, specific (UI) and correlated (sexual and bowel) QoL.

The large number of RCTs available for standard review and meta-analysis suggest that the evidence can be generalised to all women with SUI. There is also a good degree of consistency between the different RCTs.

5.1.1.1 Question

In women with SUI, what is effectiveness of open and laparoscopic surgery, compared to no treatment or compared to other surgical procedures, measured in terms of cure or improvement of incontinence or QoL, or the risk of adverse events?

5.1.1.2 Evidence

Four systematic reviews were found, which covered the subject of open surgery for SUI, including 46 RCTs (1-4), but no RCTs comparing any operation to a sham procedure.

Open colposuspension

The Cochrane review (6) included 46 trials (4738 women) having open colposuspension. In most of these trials, open colposuspension was used as the comparator to an experimental procedure. Consequently, for this review we have only considered the absolute effect of colposuspension but have not reviewed all of these comparisons. No additional trials have been reported since this review.

Within the first year, complete continence rates of approximately 85-90% were achieved for open colposuspension, while failure rates for incontinence were 17% up to 5 years and 21% over 5 years. The re-operation rate for incontinence was 2%, but there was a higher rate of development of genitourinary prolapse than for other open operations.

Seven trials, covered by the review, compared open colposuspension to needle suspension. These trials found similar levels of effectiveness at 85-90% and lower rates of failure at 5 years for the Marshall Marchetti Krantz procedure.

Open colposuspension was compared with conservative treatment in one small study (7). One trial compared open colposuspension with antimuscarinic treatment, while another compared it with periurethral injection of bulking agents. Colposuspension resulted in superior outcomes, but had significantly higher rates of adverse events.

Four trials compared Burch colposuspension to the Marshall Marchetti Krantz procedure and one trial evaluated Burch colposuspension with paravaginal repair in both cases showing fewer surgical failures up to 5 years but otherwise similar outcomes.

Anterior colporrhaphy

Anterior colporrhaphy is now mainly considered to be an obsolete operation for UI. In a Cochrane review (3), 10 trials compared anterior colporrhaphy (385 women) with colposuspension (627 women). The failure rate for incontinence at follow-up of up to 5 years was worse for anterior colporrhaphy with a higher requirement for re-operation for incontinence.

Autologous fascial sling

The Cochrane review (5) described 26 RCTs, including 2284 women undergoing autologous sling procedure in comparison to other operations. The trials did not identify those women undergoing repeat surgery for recurrent UI. No further studies have been reported.

There were seven trials of autologous fascial sling versus colposuspension. Except for one very high-quality

study (8), most of the studies were of variable quality, with a few very small studies, and a short follow-up. The meta-analysis showed that fascial sling and colposuspension had a similar efficacy at 1 year. Colposuspension had a lower risk of voiding difficulty and UTIs, but a higher risk of bladder perforation.

In 12 trials of autologous fascial sling versus mid-urethral synthetic slings, the procedures showed similar efficacy. However, use of the synthetic sling resulted in shorter operating times and lower rates of complications, including voiding difficulty. Six trials compared autologous fascial slings with other materials of different origins, with results favouring traditional autologous fascial slings. There were no trials compared traditional suburethral slings with anterior colporrhaphy, laparoscopic retropubic colposuspension or the artificial urinary sphincter device.

Laparoscopic colposuspension
The Cochrane review (2) identified 22 RCTs, of which 10 trials compared laparoscopic colposuspension to open colposuspension. No other trials have been identified. Although these procedures had a similar subjective cure rate, there was limited evidence suggesting the objective outcomes were less good for laparoscopic colposuspension. However, laparoscopic colposuspension had a lower risk of complications and shorter duration of hospital stay.

In eight RCTs comparing laparoscopic colposuspension to self-fixing slings, the subjective cure rates were similar, while the objective cure rate favoured the mid-urethral sling at 18 months. Complication rates were similar for the two procedures and operating times were shorter for the mid-urethal sling.

Evidence summary	**LE**
Anterior colporrhaphy has lower rates of cure for UI especially in the longer term.	1a
Open colposuspension and autologous fascial sling are similarly effective for cure of SUI in women.	1b
Laparoscopic colposuspension has similar efficacy to open colposuspension for cure of SUI and a similar risk of voiding difficulty or de-novo urgency.	1a
Laparoscopic colposuspension has a lower risk of other complications and shorter hospital stay than open colposuspension.	1a
Autologous fascial sling has a higher risk of operative complications than open colposuspension, particularly voiding dysfunction and post-operative UTI.	1b

5.1.1.3 References

1. Stöhrer M, Blok B, Castro-Diaz D, et al. EAU guidelines on neurogenic lower urinary tract dysfunction. Eur Urol 2009 Jul;56(1):81-8. http://www.uroweb.org/fileadmin/tx_eauguidelines/2009/Trans/2009_Neurogenic_LUTS.pdf
2. Dean N, Ellis G, Wilson D, et al. Laparoscopic colposuspension for urinary incontinence in women. Cochrane Database Syst Rev 2006 Jul 19;(3):CD002239. http://www.ncbi.nlm.nih.gov/pubmed/16855989
3. Glazener CM, Cooper K. Anterior vaginal repair for urinary incontinence in women. Cochrane Database Syst Rev 2001;(1):CD001755. http://www.ncbi.nlm.nih.gov/pubmed/11279728
4. Lapitan MC, Cody JD, Grant A. Open retropubic colposuspension for urinary incontinence in women: a short version Cochrane review. Neurourol Urodyn 2009;28(6):472-80. http://www.ncbi.nlm.nih.gov/pubmed/19591206
5. Rehman H, Bezerra CCB, Bruschini H, et al. Traditional suburethral sling operations for urinary incontinence in women. Cochrane Database Syst Rev 2011 Jan 19;(1):CD001754. http://www.ncbi.nlm.nih.gov/pubmed/21249648
6. Lapitan MC, Cody JD, Grant A. Open retropubic colposuspension for urinary incontinence in women. Cochrane Database Syst Rev 2009 Oct 7;(4):CD002912. http://www.ncbi.nlm.nih.gov/pubmed/19821297
7. Klarskov P, Belving D, Bischoff N, et al. Pelvic floor exercise versus surgery for female urinary stress incontinence. Urol Int 1986;41(2):129-32. http://www.ncbi.nlm.nih.gov/pubmed/3727190
8. Albo ME, Richter HE, Brubaker L, et al: Urinary Incontinent Treatment Network. Burch colposuspension versus fascial sling to reduce urinary stress incontinence. N Engl J Med 2007 May 24;356(21):2143-55. http://www.ncbi.nlm.nih.gov/pubmed/17517855

5.1.2 ***Mid-urethral slings***

The description of tension-free support for mid-urethra using a synthetic sling was an important new concept in the treatment of women with urodynamic SUI, which led to the development of synthetic mesh materials and devices to allow minimally invasive insertion (1). Early clinical studies identified that slings should be made from monofilament, non-absorbable material, typically polypropylene, and constructed as a 1-2 cm wide mesh with a relatively large pore size (macroporous). Mid-urethral slings are now the most frequently used surgical intervention in Europe for women with SUI.

5.1.2.1 ***Questions***

In women with SUI, what is the effectiveness in curing SUI and adverse effects at 1 year of:

- mid-urethral synthetic sling insertion compared to Burch colposuspension?
- one method of insertion of a mid-urethral synthetic sling compared to another method?
- one direction of insertion of a mid-urethral synthetic sling compared to another direction of insertion?

5.1.2.2 Evidence

For the purposes of this guideline, a new meta-analysis was performed.

Mid-urethral sling insertion compared to colposuspension

Thirteen RCTs (n = 1037) compared mid-urethral sling (retropubic) and colposuspension (open and laparoscopic). The meta-analysis found no difference in patient-reported cure rates at 12 months (2-15). The overall patient-reported cure rate was 75%. There was weak evidence of higher clinician-reported cure rates at 12 months after mid-urethral sling (83%) compared to colposuspension (78%) (7-15). However, longer-term follow-up for up to 5 years reported no difference in effectiveness, though the numbers of participants lost to follow-up was high (5,12,13). Voiding dysfunction was more likely for colposuspension (relative risk 0.34; 95%CI 0.16-0.7) whilst bladder perforation was higher for the mid-urethral sling (15% vs. 9%, and 7% vs. 2%, respectively) (3,4,14,16,17).

A single randomised trial, comparing the mid-urethral sling (transobturator) with open colposuspension, reporting similar rates of patient-reported and clinician-reported cure and no evidence of differential harms (18). In all the trials, operative time and duration of hospital stay was shorter for women randomised to insertion of the mid-urethral synthetic sling.

Transobturator route versus retropubic route

Thirty-four RCTs (5786 women) compared insertion of the mid-urethral sling by the retropubic and transobturator routes. There was no difference in cure rates at 12 months in either patient-reported or clinically reported cure rates (77% and 85%, respectively) (20-49). Voiding dysfunction was less common (4%) following transobturator insertion compared to retropubic insertion (7%), as was the risk of bladder perforation (0.3%) or urethral perforation (5%). Similarly, the risks of de-novo urgency and vaginal perforation were 6% and 1.7%, respectively. Chronic perineal pain at 12 months after surgery was reported by 21 trials and meta-analysis of these data showed strong evidence of a higher rate in women undergoing transobturator insertion (7%) compared to retropubic insertion (3%).

Insertion using a skin-to-vagina direction versus a vagina-to-skin direction

A Cochrane systematic review and meta-analysis found that the skin-to-vagina direction (outside in) for retropubic insertion of mid-urethral slings was less effective than the vagina-to-skin (inside out) direction and was associated with higher rates of voiding dysfunction, bladder perforation, and vaginal erosion (50). A further systematic review and meta-analysis found that the skin-to-vagina (outside in) direction of transobturator insertion of mid-urethral slings was equally effective compared to the vagina-to-skin route (inside out) using direct comparison. However, indirect comparative analysis gave weak evidence for a higher rate of voiding dysfunction and bladder injury (51). These differences in adverse effects were not found in the Cochrane review, which only used the limited amount of direct head-to-head comparative data and found no differences in effectiveness or adverse effects (50).

Generalisability of evidence to adult women with SUI

Analysis of the heterogeneity of trials in this meta-analysis suggests that the evidence is generalisable to women, who have predominantly SUI, and no other clinically severe lower genitourinary tract dysfunction. The evidence is not adequate to guide choice of surgical treatment for those women with MUI, severe pelvic organ prolapse, or a history of previous surgery for SUI.

The results of the EAU Panel meta-analysis were consistent with those of the Cochrane systematic review

(52), except that in our meta-analysis the objective cure rates appeared slightly higher for retropubic (88%) compared to transobturator insertion (84%). The Panel finding is consistent with an additional systematic review and meta-analysis (53), and the difference may result from the Panel's decision to only consider trial data with at least 12 months of follow-up. The cure rates at 12 months in our meta-analysis for mid-urethral sling were similar to those calculated in the meta-analysis for the American Urological Association guidelines (54). In addition, our results and recommendations are consistent with those of the Society of Obstetricians and Gynaecologists of Canada (55) and those of the UK National Institute for Health and Clinical Excellence (66).

Evidence summary	**LE**
Compared to colposuspension, the retropubic insertion of a mid-urethral synthetic sling gives equivalent patient-reported cure of SUI and superior clinician-reported cure of SUI at 12 months.	1a
Compared to colposuspension, the transobturator insertion of a mid-urethral synthetic sling gives equivalent patient-reported and clinician-reported cure of SUI at 12 months.	2
Insertion of a mid-urethral synthetic sling by the transobturator route gives equivalent patient-reported and clinician-reported cure rates at 12 months compared to retropubic insertion.	1a
The skin-to-vagina direction of retropubic insertion of mid-urethral sling is less effective than a vagina-to-skin direction.	1a
Mid-urethral sling insertion is associated with a lower rate of a new symptom of urgency, and voiding dysfunction, compared to colposuspension.	1a
The retropubic route of insertion is associated with a higher intra-operative risk of bladder perforation and a higher rate of voiding dysfunction than the transobturator route.	1a
The transobturator route of insertion is associated with a higher risk of chronic perineal pain at 12 months than the retropubic route.	1a
The skin-to-vagina direction of both retropubic and transobturator insertion is associated with a higher risk of post-operative voiding dysfunction.	1b

5.1.2.3 References

1. Ulmsten U, Petros P. Intravaginal slingplasty (IVS): an ambulatory surgical procedure for treatment of stress urinary incontinence. Scand J Urol Nephrol 1995 Mar;29(1):75-82. http://www.ncbi.nlm.nih.gov/pubmed/7618052
2. Bai SW, Sohn WH, Chung DJ, et al. Comparison of the efficacy of Burch colposuspension, pubovaginal sling, and tension-free vaginal tape for stress urinary incontinence. Int J Gynaecol Obstet 2005 Dec;91(3):246-51. http://www.ncbi.nlm.nih.gov/pubmed/16242695
3. Drahoradova PI, Masata JI, Martan AI, et al. Comparative development of quality of life between TVT and Burch colposuspension. Joint Meeting of the International Continence Society and the International UroGynecological Association, 34rd Annual Meeting, Paris, France, 25th-27th August 2004. Neurourol Urodyn 2004;23(5/6):387-616, abstract no. 278. http://www.icsoffice.org/Abstracts/Publish/42/000278.pdf
4. Foote AJ, Maughan V, Carne C. Laparoscopic colposuspension versus vaginal suburethral slingplasty: a randomised prospective trial. Aust N Z J Obstet Gynaecol 2006 Dec;46(6):517-20. http://www.ncbi.nlm.nih.gov/pubmed/17116057
5. Jelovsek JE, Barber MD, Karram MM, et al. Randomised trial of laparoscopic Burch colposuspension versus tension-free vaginal tape: long-term follow up. BJOG 2008 Jan;115(2):219-25; discussion 225. http://www.ncbi.nlm.nih.gov/pubmed/18081602
6. Mirosh M, Epp A. TVT vs laparoscopic Burch colposuspension for the treatment of stress urinary incontinence. 35th Annual Meeting of the International Continence Society, Montreal, Canada, 28th August-2nd September, 2005. Neurourology Urodyn 2005;24(5/6):401-598, abstract number 640. http://www.icsoffice.org/Abstracts/AbstractsSearch.aspx?EventID=43
7. Paraiso MF, Walters MD, Karram MM, et al. Laparoscopic Burch colposuspension versus tension-free vaginal tape: a randomized trial. Obstet Gynecol 2004 Dec;104(6):1249-58. http://www.ncbi.nlm.nih.gov/pubmed/15572485
8. Persson J, Teleman P, Etén-Bergquist C, et al. Cost-analyzes based on a prospective, randomized study comparing laparoscopic colposuspension with a tension-free vaginal tape procedure. Acta Obstet Gynecol Scand 2002 Nov;81(11):1066-73. http://www.ncbi.nlm.nih.gov/pubmed/12421176

9. Ustun Y, Engin-Ustun Y, Gungor M, et al. Tension-free vaginal tape compared with laparoscopic Burch urethropexy. J Am Assoc Gynecol Laparosc 2003 Aug;10(3):386-9. http://www.ncbi.nlm.nih.gov/pubmed/14567818
10. Valpas A, Kivela A, Penttinen J, et al. Tension-free vaginal tape and laparoscopic mesh colposuspension for stress urinary incontinence. Obstet Gynecol 2004 Jul;104(1):42-9. http://www.ncbi.nlm.nih.gov/pubmed/15228999
11. Wang AC, Chen MC. Comparison of tension-free vaginal taping versus modified Burch colposuspension on urethral obstruction: a randomized controlled trial. Neurourol Urodyn 2003;22(3):185-90. http://www.ncbi.nlm.nih.gov/pubmed/12707868
12. Ward K, Hilton P; United Kingdom and Ireland Tension-free Vaginal Tape Trial Group. Prospective multicentre randomised trial of tension-free vaginal tape and colposuspension as primary treatment for stress incontinence. BMJ 2002 Jul 13;325(7355):67. http://www.ncbi.nlm.nih.gov/pubmed/12114234
13. Adile B, Granese R, Lo Bue A, et al. A prospective randomized study comparing laparoscopic Burch versus TVT. Short and long term follow-up. Proceedings of the International Continence Society, 33rd Annual Meeting, Florence, Italy, 5th-9th October 2003. Neurourol Urodyn 2003;22(5):357-548, abstract 550. http://www.icsoffice.org/Abstracts/Publish/41/000550.pdf
14. Liapis A, Bakas P, Creatsas G. Burch colposuspension and tension-free vaginal tape in the management of stress urinary incontinence in women. Eur Urol 2002 Apr;41(4):469-73. http://www.ncbi.nlm.nih.gov/pubmed/12074820
15. Tellez Martinez-Fonres M, Fernandez Perez C, Fouz Lopez C, et al. A three year follow-up of a prospective open randomized trial to compare tension-free vaginal tape with Burch colposuspension for treatment of female stress urinary incontinence. Actas Urol Esp 2009 Nov;33(10):1088-96. [English, Spanish] http://www.ncbi.nlm.nih.gov/pubmed/20096179
16. El-Barky E, El-Shazly A, El-Wahab OA, et al. Tension free vaginal tape versus Burch colposuspension for treatment of female stress urinary incontinence. Int Urol Nephrol 2005;37(2):277-81. http://www.ncbi.nlm.nih.gov/pubmed/16142556
17. Maher C, Qatawneh A, Baessler K, et al. Laparoscopic colposuspension or tension-free vaginal tape for recurrent stress urinary incontinence and/or intrinsic sphincter deficiency-a randomised controlled trial (Abstract). Joint Meeting of the International Continence Society and the International UroGynecological Association, 34rd Annual Meeting, Paris, France, 25th-27th August 2004. Neurourol Urodyn 2004;23(5/6):433. http://www.icsoffice.org/Abstracts/Publish/42/000025.pdf
18. Sivaslioglu AA, Caliskan E, Dolen I, et al. A randomized comparison of transobturator tape and Burch colposuspension in the treatment of female stress urinary incontinence. Int Urogynecol J Pelvic Floor Dysfunct 2007 Sep;18(9):1015-9. http://www.ncbi.nlm.nih.gov/pubmed/17180553
19. Barber MD, Kleeman S, Karram MM, et al. Transobturator tape compared with tension-free vaginal tape for the treatment of stress urinary incontinence: a randomized controlled trial. Obstet Gynecol 2008 Mar;111(3):611-21. http://www.ncbi.nlm.nih.gov/pubmed/18310363
20. Barber MD, Kleeman, Karram MM, et al. Risk factors associated with failure 1 year after retropubic or transobturator midurethral slings. Am J Obstet Gynecol 2008 Dec;199(6):666.e1-7. http://www.ncbi.nlm.nih.gov/pubmed/19084098
21. Deffieux X, Daher H, Mansoor A, et al. Transobturator TVT-O versus retropubic TVT: results of a multicenter randomized controlled trial at 24 months follow-up. Int Urogynecol J 2010 Nov;21(11):1337-45. http://www.ncbi.nlm.nih.gov/pubmed/20552165
22. Krofta L, Feyereisl J, Otcenasek M, et al. TVT and TVT-O for surgical treatment of primary stress urinary incontinence: prospective randomized trial. Int Urogynecol J 2010 Feb;21(2):141-8. http://www.ncbi.nlm.nih.gov/pubmed/19907913
23. Lee KS, Han DH, Choi YS, et al. A prospective trial comparing tension-free vaginal tape and transobturator vaginal tape inside-out for the surgical treatment of female stress urinary incontinence: 1-year followup. J Urol 2007 Jan;177(1):214-8. http://www.ncbi.nlm.nih.gov/pubmed/17162048

24. Liapis A, Bakas P, Giner M, et al. Tension-free vaginal tape versus tension-free vaginal tape obturator in women with stress urinary incontinence. Gynecol Obstet Invest 2006;62(3):160-4. http://www.ncbi.nlm.nih.gov/pubmed/16707901
25. Nerli RB, Kumar AG, Koura A, et al. Transobturator vaginal tape in comparison to tension-free vaginal tape: a prospective trial with a minimum 12 months follow-up. Indian J Urol 2009 Jul;25(3):321-5. http://www.ncbi.nlm.nih.gov/pubmed/19881123
26. Palva K, Rinne K, Aukee P, et al. A randomized trial comparing tension-free vaginal tape with tension-free vaginal tape-obturator: 36-month results. Int Urogynecol J 2010 Sep;21(9):1049-55. http://www.ncbi.nlm.nih.gov/pubmed/20440474
27. Porena M, Costantini E, Frea B, et al. Tension-free vaginal tape versus transobturator tape as surgery for stress urinary incontinence: results of a multicentre randomised trial. Eur Urol 2007 Nov;52(5): 1481-90. http://www.ncbi.nlm.nih.gov/pubmed/17482343
28. Richter HE, Albo ME, Zyczynski HM, et al. Retropubic versus transobturator midurethral slings for stress incontinence. N Engl J Med 2010 Jun 3;362(22):2066-76. http://www.ncbi.nlm.nih.gov/pubmed/20479459
29. Riva D, Sacca V, Tonta A, et al. T.V.T versus T.O.T. A randomised study at 1-year follow up. 31st Annual IUGA Meeting, Athens, Greece, 6-9 September 2006. Int Urogynecol J 2006;17(Suppl 2):S93, abstract no. 060. http://www.springerlink.com/content/102824/
30. Ross S, Robert M, Swaby C, et al. Transobturator tape compared with tension-free vaginal tape for stress incontinence: a randomized controlled trial. Obstet Gynecol 2009 Dec;114(6):1287-94. http://www.ncbi.nlm.nih.gov/pubmed/19935032
31. Teo R, Moran P, Mayne C, et al. Randomized trial of tension-free vaginal tape and tension-free vaginal tape-obturator for urodynamic stress incontinence in women. J Urol 2011 Apr;185(4):1350-5. http://www.ncbi.nlm.nih.gov/pubmed/21334654
32. Wang F, Song Y, Huang H. Prospective randomized trial of TVT and TOT as primary treatment for female stress urinary incontinence with or without pelvic organ prolapse in Southeast China. Arch Gynecol Obstet 2010 Feb;281(2):279-86. http://www.ncbi.nlm.nih.gov/pubmed/19404656
33. Zhu L, Lang J, Hai N, et al. Comparing vaginal tape and transobturator tape for the treatment of mild and moderate stress incontinence. Int J Gynaecol Obstet 2007 Oct;99(1):14-7. http://www.ncbi.nlm.nih.gov/pubmed/17707822
34. Andonian S, St-Denis B, Lemieux MC, et al. Prospective clinical trial comparing Obtape and DUPS to TVT: one-year safety and efficacy results. Eur Urol 2007 Jul;52(1):245-51. http://www.ncbi.nlm.nih.gov/pubmed/17234331
35. Aniuliene R. Tension-free vaginal tape versus tension-free vaginal tape obturator (inside-outside) in the surgical treatment of female stress urinary incontinence. Medicina (Kaunas) 2009;45(8):639-43. http://www.ncbi.nlm.nih.gov/pubmed/19773623
36. Araco F, Gravante G, Sorge R, et al. TVT-O vs TVT: a randomized trial in patients with different degrees of urinary stress incontinence. Int Urogynecol J Pelvic Floor Dysfunct 2008 Jul;19(7):917-26. http://www.ncbi.nlm.nih.gov/pubmed/18217177
37. Castillo-Pino E, Sasson A, Pons JE. Comparison of retropubic and transobturator tension-free vaginal implants for the treatment of stress urinary incontinence. Int J Gynaecol Obstet 2010 Jul;110(1):23-6. http://www.ncbi.nlm.nih.gov/pubmed/20409546
38. Chen Z, Chen Y, Du GH, et al. Comparison of three kinds of mid-urethral slings for surgical treatment of female stress urinary incontinence. Urologia 2010 Jan-Mar;77(1):37-41; discussion 42. http://www.ncbi.nlm.nih.gov/pubmed/20890856
39. Costantini E, Lazzeri M, Bini V, et al. Burch colposuspension does not provide any additional benefit to pelvic organ prolapse repair in patients with urinary incontinence: a randomized surgical trial. J Urol 2008 Sep;180(3):1007-12. http://www.ncbi.nlm.nih.gov/pubmed/18639302
40. Darai E, Frobert JL, Grisard-Anaf M, et al. Functional results after the suburethral sling procedure for urinary stress incontinence: a prospective randomized multicentre study comparing the retropubic and transobturator routes. Eur Urol 2007 Mar;51(3):795-801; discussion 801-2. http://www.ncbi.nlm.nih.gov/pubmed/17010507
41. El-Hefnawy AS, Wadie BS, El Mekresh M, et al. TOT for treatment of stress urinary incontinence: how should we assess its equivalence with TVT? Int Urogynecol J 2010 Aug;21(8):947-53. http://www.ncbi.nlm.nih.gov/pubmed/20424826

42. Enzelsberger H, Schalupny J, Heider R, et al. TVT versus TOT-A prospective randomized study for the treatment of female stress urinary incontinence at a follow-up of 1 year. Geburts Frauenheilk 2005;65(5):506-11. [German]
https://www.thieme-connect.de/ejournals/abstract/gebfra/doi/10.1055/s-2005-837654
43. Karateke A, Haliloglu B, Cam C, et al. Comparison of TVT and TVT-O in patients with stress urinary incontinence: short-term cure rates and factors influencing the outcome. A prospective randomised study. Aust N Z J Obstet Gynaecol 2009 Feb;49(1):99-105.
http://www.ncbi.nlm.nih.gov/pubmed/19281588
44. Oliveira LM, Girao MJBC, Sartori MGF, et al. Comparison of retro pubic TVT, pre pubic TVT and TVT obturator in surgical treatment of women with stress urinary incontinence. Int Urogynecol J 2006;17(Suppl 2):S253, abstract no. 354.
45. Rechberger T, Jankiewicz K, Skorupski P, et al. Transobturator vs retropubic vaginal tape for female stress urinary incontinence: one year follow-up in 296 patients. 37th Annual Meeting of the International Continence Society, Rotterdam, The Netherlands, 20th-24th August. Neurourol Urodyn 2007;26(5):595-748, abstract no. 288.
http://www.icsoffice.org/Abstracts/AuthorIndex.aspx?EventID=45
46. Rechberger T, Futyma K, Jankiewicz K, et al. The clinical effectiveness of retropubic (IVS-02) and transobturator (IVS-04) midurethral slings: randomized trial. Eur Urol 2009 Jul;56(1):24-30.
http://www.ncbi.nlm.nih.gov/pubmed/19285788
47. Rinne K, Laurikainen E, Kivelä A, et al. A randomized trial comparing TVT with TVT-O: 12-month results. Int Urogynecol J Pelvic Floor Dysfunct 2008 Aug;19(8):1049-54.
http://www.ncbi.nlm.nih.gov/pubmed/18373046
48. Tcherniakovsky M, Fernandes CE, Bezerra CA, et al. Comparative results of two techniques to treat stress urinary incontinence: synthetic transobturator and aponeurotic slings. Int Urogynecol J Pelvic Floor Dysfunct 2009 Aug;20(8):961-6.
http://www.ncbi.nlm.nih.gov/pubmed/19582386
49. Wang W, Zhu L, Lang J. Transobturator tape procedure versus tension-free vaginal tape for treatment of stress urinary incontinence. Int J Gynaecol Obstet 2009 Feb;104(2):113-6.
http://www.ncbi.nlm.nih.gov/pubmed/18957269
50. Ogah J, Cody JD, Rogerson L. Minimally invasive synthetic suburethral sling operations for stress urinary incontinence in women. Cochrane Database Syst Rev 2009;(4):CD006375.
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD006375.pub2/abstract
51. Latthe PM, Singh P, Foon R, et al. Two routes of transobturator tape procedures in stress urinary incontinence: a meta-analysis with direct and indirect comparison of randomized trials. BJU Int 2010 Jul;106(1):68-76.
http://www.ncbi.nlm.nih.gov/pubmed/19912182
52. Ogah J, Cody JD, Rogerson L. Minimally invasive synthetic suburethral sling operations for urinary incontinence in women. Cochrane Database Syst Rev 2009 Oct 7;(4):CD006375.
http://www.ncbi.nlm.nih.gov/pubmed/19821363
53. Novara G, Artibani W, Barber MD, et al. Updated systematic review and meta-analysis of the comparative data on colposuspensions, pubovaginal slings, and midurethral tapes in the surgical treatment of female stress urinary incontinence. Eur Urol 2010 Aug;58(2):218-38.
http://www.ncbi.nlm.nih.gov/pubmed/20434257
54. Dmochowski RR, et al; Female Stress Urinary Incontinence Update Panel of the American Urological Association Education and Research, Whetter LE. Update of AUA guideline on the surgical management of female stress urinary incontinence. J Urol 2010 May;183(5):1906-14.
http://www.ncbi.nlm.nih.gov/pubmed/20303102
55. Schulz JA,Chan MC, Farrel SA, et al; Sub-Committee on Urogynaecology. Midurethral minimally invasive sling procedures for stress urinary incontinence. J Obstet Gynaecol Can 2008 Aug;30(8): 728-40. [English, French]
http://www.ncbi.nlm.nih.gov/pubmed/18786297
56. Urinary incontinence: the management of urinary incontinence in women. Clinical guidelines CG40. National Institute for Health and Clinical Excellence, October 2006.
http://publications.nice.org.uk/CG40

5.1.3 ***Single-incision slings***

There is continued innovation to reduce the invasiveness of procedures for SUI. Single-incision mid-urethral slings have been introduced on the basis of providing mid-urethral support, using a variety of modifications to a short macroporous polypropylene tape. These modifications allow the tape to be fixed to the retropubic tissues, endopelvic fascia or obturator fascia, while avoiding the troublesome complications of obturator nerve

injury or passage through the gracilis muscle or skin of the inner thigh, or through the retropubic space. These procedures are usually performed as day cases under local anaesthesia.

5.1.3.1 Questions

- In women with SUI, do 'single-incision' slings cure UI or improve QoL, or cause adverse outcomes?
- How does a 'single-incision' sling compare to other surgical treatments for SUI?

5.1.3.2 Evidence

Although there have been many studies published on single-incision devices, it should be noted that there are significant differences in design between devices and it may be misleading to make general statements about them as a class of operations.

One systematic review has been published (1), which included RCTs and quasi-RCTs, comparing single-incision slings to either retropubic or transobturator mid-urethral slings. The literature search included non-English trials and unpublished studies. A further systematic review is currently being undertaken by the Cochrane centre (2).

The nine RCTs in the current Cochrane review included 758 participants, who were followed up for a mean of 9.5 months. There was poor reporting of allocation concealment, as well as poorly reported randomisation, resulting in a high risk of bias. One centre provided several of the studies. Seven studies included only patients with tension-free vaginal tape secure (TVTS). The remaining two studies include only patients with a Miniarc® device.

Meta-analysis showed that the outcome of single-incision sling insertion was consistently worse compared with mid-urethral slings in terms of patient-reported cure of UI. Single-incision techniques had a shorter operating time, lower blood loss and and lower pain levels compared to a standard mid-urethral sling. One RCT found no difference in effectiveness between two different methods of insertion of the TVTS® device with 12 months' follow-up (3). One RCT designed to compare the TVTS device to a standard retropubic mid-urethral sling in 280 women found a significantly lower objective cure at 2 months for TVTS and a higher complication rate and was terminated early (4). Another RCT (5) compared the TVTS device to a standard transobturator mid-urethal sling but was underpowered to show a statistical difference between the techniques. A small, three-treatment arm, phase II RCT compared standard transobturator mid-urethral sling to TVTS and Miniarc® devices [6]. The results suggested that cure rates were lower for TVT but no statistical analysis was presented.

A more recent RCT comparing the TVTS device to standard transobturator mid-urethral sling, not included in the Cochrane review, demonstrated a lower objective cure rate and lower pain levels for the TVTS device [7].

Another recent non-randomised study compared the TVTS to the Curemesh® device showed no difference in outcomes at a minimum of 15.5 months (8). Similarly, a quasi-RCT comparing a standard transobturator mid-urethral sling to a Contasure® device found no difference in cure of UI or adverse events (9).

There are a number of case series with a minimum of 12 months' follow-up, including five series using the Miniarc device (10-15), two series using the TVTS device (11,16) and one series using the Minitape® device (17). The 12-month outcomes range from 52% objective cure to 92% subjective cure. Results from one study reporting outcome at 2 years found that only 10% of included participants remained cured (17). One study reported a 24% rate of de-novo urgency but generally there were few reported adverse effects (11).

There are no RCTs relating to the Solyx® device. There is one retrospective review of 63 women with short-term follow-up (18), and one report of 12 months' follow-up of the Ophira® device 176 women (19). These studies did not report outcomes of interest for these Guidelines.

Evidence summary	**LE**
Single-incision mid-urethral slings are effective in curing SUI in women in the short term.	1b
Operation times for insertion of single-incision mid-urethral slings are shorter than for standard retropubic slings.	1b
Blood loss and immediate post-operative pain are lower for insertion of single-incision slings compared with standard mid-urethral slings.	1b
Single-incisions slings are less effective than other mid-urethral slings at medium-term follow-up*.	1b

There is no evidence that other adverse outcomes from surgery are more or less likely with single-incision slings than with standard mid-urethral slings.	1b

**NB: Most evidence on single-incision slings comes from studies using the tension-free vaginal tape secure (TVTS) device.*

5.1.3.3 References

1. Abdel-Fattah M, Ford JA, Lim CP, et al. Single-incision mini-slings versus standard midurethral slings in surgical management of female stress urinary incontinence: a meta-analysis of effectiveness and complications. Eur Urol 2011 Sep;60(3):468-80. http://www.ncbi.nlm.nih.gov/pubmed/21621321
2. Jeffery ST, De Jong P, Abdool Z, et al. Single-incision sling operations for urinary incontinence in women (Protocol). Cochrane Database Syst Rev 2010;(9):CD008709. http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD008709/pdf
3. Kim JJ, Lee YS, Lee KS. Randomized comparative study of the U- and H-type approaches of the TVT-Secur procedure for the treatment of female stress urinary incontinence: one-year follow-up. Korean J Urol 2010 Apr;51(4):250-6. http://www.ncbi.nlm.nih.gov/pubmed/20428427
4. Andrada Hamer M, Larsson PG, Teleman P, et al. Short-term results of a prospective randomized evaluator blinded multicenter study comparing TVT and TVT-Secur. Int Urogynecol J 2011 Jul;22(7):781-7. http://www.ncbi.nlm.nih.gov/pubmed/21499755
5. Jeong MY, Kim SJ, Kim HS, et al. Comparison of efficacy and satisfaction between the TVT-SECUR(R) and MONARC(R) procedures for the treatment of female stress urinary incontinence. Korean J Urol 2010 Nov;51(11):767-71. http://www.ncbi.nlm.nih.gov/pubmed/21165197
6. Oliveira R, Botelho F, Silva P, et al. Exploratory study assessing efficacy and complications of TVT-O, TVT-Secur, and Mini-Arc: results at 12-month follow-up. Eur Urol 2011 Jun;59(6):940-4. http://www.ncbi.nlm.nih.gov/pubmed/21277076
7. Hinoul P, Vervest HA, den Boon J, et al. A randomized, controlled trial comparing an innovative single incision sling with an established transobturator sling to treat female stress urinary incontinence. J Urol 2011 Apr;185(4):1356-62. http://www.ncbi.nlm.nih.gov/pubmed/21334682
8. Joo YM, Choe JH, Seo JT. One-year surgical outcomes and quality of life after minimally invasive sling procedures for the treatment of female stress urinary incontinence: TVT SECUR(R) vs. CureMesh(R). Korean J Urol 2010 May;51(5):337-43. http://www.ncbi.nlm.nih.gov/pubmed/20495697
9. Amat I, Tardiu L, Martinez FE, et al. Contasure-Needleless compared with transobturator-TVT for the treatment of stress urinary incontinence. Int Urogynecol J 2011 Jul;22(7):827-33. http://www.ncbi.nlm.nih.gov/pubmed/21365331
10. Gauruder-Burmester A, Popken G. The MiniArc sling system in the treatment of female stress urinary incontinence. Int Braz J Urol 2009 May-Jun;35(3):334-41; author reply 341-3. http://www.ncbi.nlm.nih.gov/pubmed/19538769
11. Krofta L, Feyereisl J, Velebil P, et al. TVT-S for surgical treatment of stress urinary incontinence: prospective trial, 1-year follow-up. Int Urogynecol J 2010 Jul;21(7):779-85. http://www.ncbi.nlm.nih.gov/pubmed/20358177
12. Deole N, Kaufmann A, Arunkalaivanan A. Evaluation of safety and efficacy of single-incision mid-urethral short tape procedure (MiniArc tape) for stress urinary incontinence under local anaesthesia. Int Urogynecol J 2011 Mar;22(3):335-9. http://www.ncbi.nlm.nih.gov/pubmed/20938645
13. Kennelly MJ, Moore R, Nguyen JN, et al. Prospective evaluation of a single incision sling for stress urinary incontinence. J Urol 2010 Aug;184(2):604-9. http://www.ncbi.nlm.nih.gov/pubmed/20639024
14. Moore RD, Mitchell GK, Miklos JR. Single-center retrospective study of the technique, safety, and 12-month efficacy of the MiniArc single-incision sling: a new minimally invasive procedure for treatment of female SUI. Surg Technol Int 2009;18:175-81. http://www.ncbi.nlm.nih.gov/pubmed/19585431
15. Pickens RB, Klein FA, Mobley JD 3rd, et al. Single incision mid-urethral sling for treatment of female stress urinary incontinence. Urology 2011 Feb;77(2):321-4. http://www.ncbi.nlm.nih.gov/pubmed/21167559

16. Meschia M, Barbacini P, Ambrogi V, et al. TVT-secur: a minimally invasive procedure for the treatment of primary stress urinary incontinence. One year data from a multi-centre prospective trial. Int Urogynecol J Pelvic Floor Dysfunct 2009 Mar;20(3):313-7. http://www.ncbi.nlm.nih.gov/pubmed/19037575
17. North CE, Hilton P, Ali-Ross NS, et al. A 2-year observational study to determine the efficacy of a novel single incision sling procedure (Minitape) for female stress urinary incontinence. BJOG 2010 Feb;117(3):356-60. http://www.ncbi.nlm.nih.gov/pubmed/20015305
18. Serels S, Douso M, Short G. Preliminary findings with the Solyx single-incision sling system in female stress urinary incontinence. Int Urogynecol J 2010 May;21(5):557-61. http://www.ncbi.nlm.nih.gov/pubmed/20024648
19. Palma P, Riccetto C, Bronzatto E, et al. Efficacy of Ophira mini sling system for stress urinary incontinence: midterm follow up of 176 patients in a multicenter international clinical trial. Scientific Programme, 41st Annual Meeting of the International Continence Society (ICS), 29 August-2 September 2011, Glasgow, UK. Neurourol Urodyn Aug 2011;30(6):830-1,abstract no. 22. http://www.icsoffice.org/Abstracts/Publish/106/000022.pdf

5.1.4 ***Adjustable sling***

Voiding dysfunction is an adverse effect of anti-incontinence procedures and may require further intervention such as clean intermittent self-catheterisation. One possible cause is overcorrection of the anatomical deformity by the sling. Adjustable slings seek to overcome this problem because they enable the tension of the newly implanted sling to be increased or decreased, either during or shortly after the operation. An adjustable sling aims to optimise the balance between correcting the SUI, while allowing normal voiding to continue. However, this concept has not been adequately tested. There is still no evidence to show that being able to adjust the tension of a sling has a beneficial effect on outcome.

5.1.4.1 Questions

- In women with SUI, does an adjustable sling cure SUI and improve QoL or does it cause adverse outcome(s)?
- How does an adjustable sling compare to other surgical treatments for SUI?

5.1.4.2 Evidence

There are no RCTs investigating outcome of adjustable sling insertion for women with SUI. There is limited data from cohort studies on adjustable tension slings with variable selection criteria and outcome definition. Few studies include sufficient numbers of patients or have a long enough follow-up to provide useful evidence. The available devices have differing designs, making it difficult to use existing data to make general conclusions about adjustable slings as a class of procedure. Three adjustable sling devices were reviewed: Remeex®, Safyre®, Ajust®. The latter is an adjustable single-incision sling.

Remeex®

Two cohort studies included a total of 155 patients and had more than 22 months' follow-up (1,2). The results showed that at least 86% of women had objective cure of SUI, with re-adjustment of the device required in up to 16% of women.

Saffyre®

Two cohort studies included a total of 208 patients with a minimum of 12 months follow-up (3,4). The reported cure rate was up to 92% with adverse effects of late vaginal erosion in 8% and dyspareunia in 11% (3).

Ajust®

A single cohort study reported an 80% success rate (patient's global impression of improvement) in 90 women after 12 months of follow-up.

Evidence summary	**LE**
Adjustable mid-urethral synthetic sling devices may be effective for cure or improvement of SUI in women.	3
There is no evidence that adjustable slings are superior to standard mid-urethral slings.	4

5.1.4.3 References

1. Giberti C, Gallo F, Cortese P, et al. The suburethral tension adjustable sling (REMEEX system) in the treatment of female urinary incontinence due to 'true' intrinsic sphincter deficiency: results after 5 years of mean follow-up. BJU Int 2011 Oct;108(7):1140-4. http://www.ncbi.nlm.nih.gov/pubmed/21554527
2. Errando C, Rodriguez-Escovar F, Gutierrez C, et al. A re-adjustable sling for female recurrent stress incontinence and sphincteric deficiency: outcomes and complications in 125 patients using the Remeex sling system. Neurourol Urodyn 2010 Nov;29(8):1429-32. http://www.ncbi.nlm.nih.gov/pubmed/20127837
3. Kuschel S, Schuessler B. Results on function and safety of the Safyre-t, a hybrid transobturator vaginal sling for the treatment of stress urinary incontinence. Neurourol Urodyn 2008;27(5):403-6. http://www.ncbi.nlm.nih.gov/pubmed/17985372
4. Palma PC, Riccetto CL, Dambros M, et al. [SAFYRE. A new concept for adjustable minimally invasive sling for female urinary stress incontinence]. Actas Urol Esp 2004 Nov-Dec;28(10):749-55. [Spanish] http://www.ncbi.nlm.nih.gov/pubmed/15666517

5.1.5 ***Bulking agents***

Injection of a bulking agent into the submucosal tissues of the urethra is thought to increase the coaptation of the urethral walls, in turn leading to increased urethral resistance and improved continence. Whether this is achieved through causing obstruction or improving the mucosa-to-mucosa sealing is unknown. The recommended site of injection varies with the bulking agent, and numerous materials have been developed for this use over 20 years (see below). They are injected transurethrally or paraurethrally under urethroscopic control, or alternatively using a purpose-made device (implacer), which reliably positions the needle-tip under local anaesthetic at the required position in the urethral wall.

5.1.5.1 Question

In women with SUI, does injection of a urethral bulking agent cure SUI or improve QoL, or cause adverse outcomes?

5.1.5.2 Evidence

There is one Cochrane systematic review (1), which reported on 12 RCTs or quasi-RCTs of injectable agents. In general, the trials were only of moderate quality and small, and many of them had been reported in abstract form. Wide confidence intervals meant a meta-analysis was not possible. Since the Cochrane review, two further RCTs have been reported (2,3).

Each injectable product has been the subject of many case series. Short-term efficacy in reducing the symptoms of SUI has been demonstrated for all materials used. In 2006, NICE published an extensive review of these case series (4). These case series have added very little to the evidence provided by RCTs. There has been only one placebo-controlled RCT, in which an autologous fat injection was compared with the placebo of a saline injection.

Polytetrafluoroethylene (Polytef)

There are no RCTs available. NICE 2006 (4) did not recommend this treatment because of the high incidence of adverse events.

Glutaraldehyde cross-linked bovine collagen (Contigen)

Most evidence from RCTs of the efficacy of collagen comes from six trials, in which collagen has been used as a comparator to an experimental synthetic product (see below). This implies that collagen has been regarded as the 'gold standard' bulking agent. In one RCT, collagen was compared to open surgery (5).

Autologous fat

One study found no difference in efficacy between autologous fat and saline injection (22% vs. 20% improvement at 3 months, respectively) (6). Due to a fatality from fat embolism, NICE 2006 (4) and the Cochrane Review (1) made a strong recommendation that this treatment should not be used.

Silicon particles (Macroplastique™)

Silicon particles have been compared to collagen in two RCTs, only one of which has been published as a full article (7). No significant difference in efficacy was found.

Carbon beads (Durasphere™)
Carbon beads have been compared to collagen in two RCTs (3,8). Although one study lacked appropriate statistical power, the other was a good-quality study (n = 235), with 12 months' follow-up, that showed no difference in efficacy.

Calcium hydroxylapatite (CaHA) (Coaptite™)
A study with small sample size comparing collagen to hydroxylapatite found the failure rate was significantly higher at 6 months for collagen (6/18 vs. 3/22, respectively) (9).

Ethylene vinyl alcohol copolymer (EVOH) (Uryx™)
There is one RCT (n = 210), comparing ethylene copolymer to collagen, which demonstrated similar efficacy at 6 months' follow-up (10).

Porcine dermal implant (Permacol™)
There is one very small RCT comparing porcine dermis to silicon particles. There was no significant difference in failure rates between the two procedures at 6 months' follow-up (11).

Hydrogel cross-linked with polyacrilamide (BulkamidTM)
No RCT data are available. There is a single multicentre case series of 135 women, which reported 66% success rate with 35% participants requiring re-injection (12).

Non-animal stabilised hyaluronic acid/dextranomer (NASHA/Dx) (Zuidex™)
There is one RCT, comparing dextranomer (placed in mid-urethra) to collagen injection (at the bladder neck). At 12 months, results were inferior in women given dextranomer (13).

Stem cells
Early reports of dose-ranging studies (14) suggest that stem cell injection is a safe procedure in the short term. However, its efficacy (compared to its bulking effect) has yet to be established.

Comparison with open surgery
Two RCTs studies compared collagen injection to conventional surgery for SUI (autologous sling vs. silicon particles and collagen vs. assorted procedures). The studies reported greater efficacy but higher complication rates for open surgery. In comparison, collagen injections showed inferior efficacy but equivalent levels of satisfaction and fewer serious complications (5,15).

Another trial found that a periurethral route of injection can carry a higher risk of urinary retention compared to a transurethral injection (16). A recent small RCT found no difference in efficacy between a mid-urethral and bladder neck injection of collagen (2).

Evidence summary	**LE**
Periurethral injection of bulking agent may provide short-term improvement in symptoms (3 months), but not cure, in women with SUI.	2a
Repeat injections to achieve therapeutic effect are very common.	2a
Bulking agents are less effective than colposuspension or autologous sling for cure of SUI.	2a
Adverse effect rates are lower compared to open surgery.	2a
There is no evidence that one type of bulking agent is better than another type.	1b
Periurethral route of injection may be associated with a higher risk of urinary retention compared to transurethral route.	2 b

Recommendations for surgery for uncomplicated stress urinary incontinence in women	**GR**
Offer the mid-urethral sling to women with uncomplicated stress urinary incontinence as the preferred surgical intervention whenever available.	A
Offer colposuspension (open or laparoscopic) or autologous fascial sling to women with stress urinary incontinence if mid-urethral sling cannot be considered.	A
Warn women who are being offered a retropubic insertion synthetic sling about the relatively higher risk of peri-operative complications compared to transobturator insertion.	A

Warn women who are being offered transobturator insertion of mid-urethral sling about the higher risk of pain and dyspareunia in the longer term.	A
Warn women undergoing autologous fascial sling that there is a high risk of voiding difficulty and the need to perform clean intermittent self-catheterisation; ensure they are willing and able to do so.	A
Do a cystoscopy as part of retropubic insertion of a mid-urethral sling, or if difficulty is encountered during transobturator sling insertion, or if there is a significant cystocoele.	C
Women being offered a single-incision sling device for which an evidence base exists, should be warned that short-term efficacy is inferior to standard mid-urethral slings and that long-term efficacy remains uncertain.	C
Only offer single-incision sling devices, for which there is no level 1 evidence base, as part of a structured research programme.	A
Only offer adjustable mid-urethral sling as a primary surgical treatment for stress urinary incontinence as part of a structured research programme.	C
Do not offer bulking agents to women who are seeking a permanent cure for stress urinary incontinence.	A

5.1.5.3 References

1. Keegan PE, Atiemo K, Cody J, et al. Periurethral injection therapy for urinary incontinence in women. Cochrane Database Syst Rev 2007 Jul 18;(3):CD003881. http://www.ncbi.nlm.nih.gov/pubmed/17636740
2. Kuhn A, Stadlmayr W, Lengsfeld D, et al. Where should bulking agents for female urodynamic stress incontinence be injected? Int Urogynecol J Pelvic Floor Dysfunct 2008 Jun;19(6):817-21. http://www.ncbi.nlm.nih.gov/pubmed/18157642
3. Lighter D, Calvosa C, Andersen R, et al. A new injectable bulking agent for treatment of stress urinary incontinence: results of a multicenter, randomized, controlled, double-blind study of Durasphere. Urology 2001 Jul;58(1):12-5. http://www.ncbi.nlm.nih.gov/pubmed/11445471
4. Urinary incontinence: the management of urinary incontinence in women. Clinical guidelines CG40. National Institute for Health and Clinical Excellence, October 2006. http://guidance.nice.org.uk/CG40
5. Corcos J, Collet JP, Shapiro S, et al. Multicenter randomized clinical trial comparing surgery and collagen injections for treatment of female stress urinary incontinence. Urology 2005 May;65(5): 898-904. http://www.ncbi.nlm.nih.gov/pubmed/15882720
6. Lee PE, Kung RC, Drutz HP. Periurethral autologous fat injection as treatment for female stress urinary incontinence: a randomized double-blind controlled trial. J Urol 2001 Jan;165(1):153-8. http://www.ncbi.nlm.nih.gov/pubmed/11125386
7. Ghoniem G, Corcos J, Comiter C, et al. Cross-linked polydimethylsiloxane injection for female stress urinary incontinence: results of a multicenter, randomized, controlled, single-blind study. J Urol 2009 Jan;181(1):204-10. http://www.ncbi.nlm.nih.gov/pubmed/19013613
8. Andersen RC. Long-term follow-up comparison of durasphere and contigen in the treatment of stress urinary incontinence. J Low Genit Tract Dis 2002 Oct;6(4):239-43. http://www.ncbi.nlm.nih.gov/pubmed/17051030
9. Dmochowski R, Appell R, Klimberg I, et al. Initial clinical results from coaptite injection for stress urinary incontinence comparative clinical study. Proceedings of the International Continence Society 32nd Annual Meeting. Heidelburg, Germany, 28-30 August 2002. Neurourol Urodyn 2002;21(4): 275-442, abstract 282. http://www.icsoffice.org/Abstracts/Publish/40/000282.pdf
10. Dmochowski R, Herschorn S, Corcos J, et al. Multicenter randomized controlled study to evaluate uryxo urethral bulking agent in treating female stress urinary incontinence. Proceedings of the International Continence Society 32nd Annual Meeting. Heidelburg, Germany, 28-30 August 2002. Neurourol Urodyn 2002;21(4):275-442, abstract 285. http://www.icsoffice.org/Abstracts/Publish/40/000285.pdf
11. Bano F, Barrington JW, Dyer F. Comparison between porcine dermal implant (Permacol TM) and silicone injection (Macroplastique) for urodynamic stress incontinence. Int Urogynecol J Pelvic Floor Dysfunct 2005 Mar-Apr;16(2):147-50; discussion 150. http://www.ncbi.nlm.nih.gov/pubmed/15378234

12. Lose G, Sorensen HC, Axelsen SM, et al. An open multicenter study of polyacrylamide hydrogel (Bulkamid®) for female stress and mixed urinary incontinence. Int Urogynecol J 2010 Dec;21(12): 1471-7.
http://www.ncbi.nlm.nih.gov/pubmed/20645077
13. Lightner DJ, Fox J, Klingele C. Cystoscopic injections of dextranomer hyaluronic acid into proximal urethra for urethral incompetence: efficacy and adverse outcomes. Urology 2010 Jun;75(6):1310-4.
http://www.ncbi.nlm.nih.gov/pubmed/20299087
14. Carr L, Herschorn S, Birch C, et al. Autologous muscle-derived cells as a therapy for stress urinary incontinence: a randomized, blinded, multi-dose study. J Urol 2009 Apr 28;181(4 Suppl):546, abstract 1526.
http://download.journals.elsevierhealth.com/pdfs/journals/0022-5347/PIIS0022534709615408.pdf
15. Maher CF, O'Reilly BA, Dwyer PL, et al. Pubovaginal sling versus transurethral Macroplastique for stress urinary incontinence and intrinsic sphincter deficiency: a prospective randomised controlled trial. BJOG 2005 Jun;112(6):797-801.
http://www.ncbi.nlm.nih.gov/pubmed/15924540
16. Schulz JA, Nager CW, Stanton SL, et al. Bulking agents for stress urinary incontinence: short-term results and complications in a randomized comparison of periurethral and transurethral injections. Int Urogynecol J Pelvic Floor Dysfunct 2004 Jul-Aug;15(4):261-5.
http://www.ncbi.nlm.nih.gov/pubmed/15517671

5.2 Complicated SUI in women

This section will address surgical treatment for women who have had previous surgery for SUI, which has failed, or those women who have undergone previous radiotherapy affecting the vaginal or urethral tissues. Neurological lower urinary tract dysfunction is not considered because it is reviewed by the EAU Guidelines on Neurogenic Lower Urinary Tract Dysfunction (1). Women with associated genitourinary prolapse will be included in the next edition of these Guidelines in 2013.

*5.2.1 **Failed surgery***

The reported failure rates from any operation for SUI vary widely from 5-80%, depending on how failure was defined. Even using a very strict definition, this means that at least hundreds of the many thousands of women undergoing primary surgery for SUI will require further surgery for recurrent symptoms. A primary operation may fail from the start or may occur some years after the original procedure. There may be persistent or recurrent SUI, or the development of de-novo UUI or voiding difficulty. Expert opinion therefore considers careful urodynamic evaluation to be an essential part of the work-up of these patients.

However, the underlying reasons for failure are poorly understood. Consequently, which operation to offer women with failed previous surgery for UI is usually driven by individual clinician opinion about the mechanisms of failure, familiarity with certain procedures, and experience in personal series. Most surgeons believe the results of any operation will be inferior to the same operation used as a primary procedure and will warn their patients of this.

The Panel have limited their literature search to the surgical management of recurrent SUI. It is presumed that the management of de-novo UUI will follow the pathway recommended for the management of primary UUI and DO, starting with conservative management. The Panel has not addressed the management of voiding difficulty because this does not require further treatment for incontinence.

5.2.1.1 Question

In women who have recurrent SUI following previous corrective surgery, what is the best surgical treatment?

5.2.1.2 Evidence

Most data on surgery for SUI are for primary surgery. When secondary procedures are included, it is unusual for the outcomes to be separately reported. Even if they are, the numbers of patients are usually too small to allow meaningful comparisons.

The 4th International Consultation on Incontinence included a review of this topic up until 2008, and the subject has also been reviewed by Ashok and Wang (1). Cochrane reviews of individual operative techniques have not included a separate evaluation of outcomes in women undergoing second-line surgery. However, there is a current protocol advising on this issue (2). A further literature review up until October 2011 has been carried out since that time by the EAU Panel with the following findings.

Three RCTs were found. Two of the trials compared Burch colposuspension to a biological sling in recurrent SUI (3,4). There was no difference in efficacy between the procedures, but the complication rates were higher for slings. Another small RCT (abstract only) compared retropubic mid-urethral sling to laparoscopic colposuspension in women with recurrent SUI and reported similar short-term cure rates and adverse events (5).

Post-hoc analysis of high-quality RCTs comparing one surgical procedure to another reported higher failure rates for SUI and higher rates for adverse effects in women who had had previous surgery for SUI. There was no difference in these rates between the compared procedures (4,6-8). A history of prior surgery for UI was not an independent predictor of failure at 2 years in women undergoing open colposuspension or autologous fascial sling (4).

One large non-randomised cohort study suggested that cure rates after more than two previous operations were 0% for open colposuspension and 38% for autologous sling (9).

Several cohort studies have reported outcomes for retropubic mid-urethral synthetic sling specifically for primary and secondary cases. There is conflicting evidence on the effectiveness of second-line retropubic sling insertion, with some series showing equivalent outcomes for primary and secondary cases (10-12) and other series showing inferior outcomes for secondary surgery (13,14). Other confounding variables make meaningful conclusions difficult. There appears to be no evidence supporting the concept that the original mid-urethral sling should be removed.

Many small case series report satisfactory outcomes for repeat procedures of many types, but this evidence is not suitable to generate guidance.

A systematic review of older trials of open surgery for SUI suggests that the longer-term outcomes of repeat open colposuspension may be worse than those seen with autologous fascial slings (15). Successful results have been reported from mid-urethral slings after various types of primary surgery, while good outcomes are reported for both repeat retropubic mid-urethral sling and for 'tightening' of existing mid-urethral slings, but data were limited to small case series only.

Finally, clinical guidelines have been developed by the Society of Obstetricians and Gynaecologists of Canada, based on a literature review and expert opinion. Unfortunately, the methodology and the rationale for grading decisions were not clear (16).

Evidence summary	**LE**
The risk of treatment failure from surgery for SUI is higher in women who have had prior surgery for incontinence or prolapse.	1b
Open colposuspension and autologous fascial sling appear to be as effective for first-time repeat surgery as for primary surgery.	1b
The mid-urethral sling is less effective as a second-line procedure than for primary surgery.	2

5.2.1.3 Research priority on failed SUI surgery

There is a need for well-structured research trials to compare surgical procedures in women who have had previous failed surgery for SUI.

5.2.1.4 References

1. Ashok K, Wang A. Recurrent urinary stress incontinence: an overview. J Obstet Gynaecol Res 2010 Jun;36(3):467-73. http://www.ncbi.nlm.nih.gov/pubmed/20598022
2. Bakali E, Buckley BS, Hilton P, et al. Treatment of recurrent stress urinary incontinence after failed minimally invasive synthetic suburethral tape surgery in women (Protocol). Cochrane Database Syst Rev 2011;(10):CD009407. http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD009407/abstract
3. Enzelsberger H, Helmer H, Schatten C. Comparison of Burch and lyodura sling procedures for repair of unsuccessful incontinence surgery. Obstet Gynecol 1996 Aug;88(2):251-6. http://www.ncbi.nlm.nih.gov/pubmed/8692511

4. Richter HE, Diokno A, Kenton K, et al. Predictors of treatment failure 24 months after surgery for stress urinary incontinence. J Urol 2008 Mar;179(3):1024-30. http://www.ncbi.nlm.nih.gov/pubmed/18206917
5. Maher C, Qatawneh A, Baessler K, et al. Laparoscopic colposuspension or tension-free vaginal tape for recurrent stress urinary incontinence and/or urethral sphincter deficiency-a randomised controlled trial. Joint Meeting of the International Continence Society and the International UroGynecological Associations, 34rd Annual Meeting, Paris, France, 25th-27th August 2004. Neurourol Urodyn 2004;23(5/6):433-4. http://www.icsoffice.org/Abstracts/Publish/42/000025.pdf
6. Richter HE, Litman H, Lukacz E, et al. Baseline predictors of one year treatment failure of retropubic and transobturator midurethral sling procedures for stress urinary incontinence. [Abstract]. Female Pelvic Medicine & Reconstructive Surgery 2010 Sep/Oct;16 (5) supplement 2:S62. http://journals.lww.com/jpelvicsurgery/toc/2010/09002
7. Richter HE, Litman HJ, Lukacs ES, et al. Demographic and clinical predictors of treatment failure one year after midurethral sling surgery. Obstet Gynecol 2011 Apr;117(4):913-21. http://www.ncbi.nlm.nih.gov/pubmed/21422865
8. Abdel-Fattah M, Ramsay I, Pringle S, et al. Evaluation of transobturator tension-free vaginal tapes in management of women with recurrent stress urinary incontinence. Urology 2011 May;77(5):1070-5. http://www.ncbi.nlm.nih.gov/pubmed/21414653
9. Amaye-Obu FA, Drutz HP. Surgical management of recurrent stress urinary incontinence: a 12-year experience. Am J Obstet Gynecol 1999 Dec;181(6):1296-307; discussion 1307-9. http://www.ncbi.nlm.nih.gov/pubmed/10601904
10. Rezapour M, Ulmsten U. Tension-free vaginal tape (TVT) in women with mixed urinary incontinence-a long-term follow-up. Int Urogynecol J Pelvic Floor Dysfunct 2001;12 Suppl 2:S15-18. http://www.ncbi.nlm.nih.gov/pubmed/11450974
11. Rardin CR, Kohli N, Rosenblatt PL, et al. Tension-free vaginal tape: outcomes among women with primary versus recurrent stress urinary incontinence. Obstet Gynecol 2002 Nov;100(5 Pt 1):893-7. http://www.ncbi.nlm.nih.gov/pubmed/12423849
12. Koops SE, Bisseling TM, van Brummen HJ, et al. What determines a successful tension-free vaginal tape? A prospective multicenter cohort study: results from The Netherlands TVT database. Am J Obstet Gynecol 2006 Jan;194(1):65-74. http://www.ncbi.nlm.nih.gov/pubmed/16389011
13. Stav K, Dwyer PL, Rosamilia A, et al. Repeat synthetic mid urethral sling procedure for women with recurrent stress urinary incontinence. J Urol 2010 Jan;183(1):241-6. http://www.ncbi.nlm.nih.gov/pubmed/19913831
14. Lee KS, Doo CK, Han Dh, et al. Outcomes following repeat mid urethral synthetic sling after failure of the initial sling procedure: rediscovery of the tension-free vaginal tape procedure. J Urol 2007 Oct;178(4 Pt 1):1370-4; discussion 1374. http://www.ncbi.nlm.nih.gov/pubmed/17706716
15. Jarvis GJ. Surgery for genuine stress incontinence. Br J Obstet Gynaecol 1994 May;101(5):371-4. http://www.ncbi.nlm.nih.gov/pubmed/8018606
16. Lovatsis D, Easton W, Wilkie D. Guidelines for the evaluation and treatment of recurrent urinary incontinence following pelvic floor surgery. J Obstet Gynaecol Can 2010 Sep;32(9):893-904. [English, French] http://www.ncbi.nlm.nih.gov/pubmed/21050525

5.2.2 ***External compression devices***

Some of the earliest techniques for treating SUI simply applied intra-corporeal compression external to the urethra. External compression devices are still widely used in the treatment of recurrent SUI after the failure of previous surgery. They are also commonly used in women with neurological LUTD, in whom there is thought to be profound intrinsic failure of the sphincter mechanism, characterised by very low leak point pressures or low urethral closure pressures.

There are two intracorporeal external urethral compression devices available. They are the adjustable compression therapy (ACT) device and the artificial urinary sphincter (AUS). Using ultrasound or fluoroscopic guidance, the ACT device is inserted by placement of two inflatable spherical balloons on either side of the bladder neck. Each volume of each balloon can be adjusted through a subcutaneous port placed within the labia majora. More recently, an adjustable artificial urinary sphincter (Flowsecure) has been introduced. It has the added benefit of 'conditional occlusion', enabling it to respond to rapid changes in intra-abdominal pressure.

5.2.2.1 Question

- In women with SUI, does insertion of an external compressive device cure SUI, improve QoL or cause adverse outcomes?
- How do external compression devices compare to other surgical treatments for SUI?

5.2.2.2 Evidence

The major advantage of artificial sphincters over other anti-incontinence procedures is the perceived ability of women to be able to void normally. However, voiding dysfunction is a known side effect, with a lack of data making it difficult to assess its importance. Because of significant differences in design between devices and in selection criteria between case series, results obtained with specific devices cannot be extrapolated generally to the use of adjustable devices. A recent consensus report has standardised the terminology used for reporting complications arising from implantation of materials into the pelvic floor region (1).

Artificial urinary sphincter

The 2011 Cochrane review on AUS (2) applies only to men with post-prostatectomy incontinence. A previous review of mechanical devices concluded that there was insufficient evidence to support the use of artificial sphincters in women (3).

There are no RCTs regarding the AUS in women. There are a few case series in women, including four series (n = 611), with study populations ranging from 45 to 215 patients and follow-up ranging from 1 month to 25 years (4-7). Case series have been confounded by varying selection criteria, especially the proportion of women who have neurological dysfunction or who have had previous surgery. Most patients achieved an improvement in SUI, with reported subjective cures in 59-88% of patients. However, common side effects included mechanical failure requiring revision (up to 42% at 10 years) and explantation (5.9-15%). In a retrospective series of 215 women followed up for a mean of 6 years, the risk factors for failure were older age, previous Burch colposuspension and pelvic radiotherapy (6). Peri-operative injury to the urethra, bladder or rectum was also a high-risk factor for explantation (4).

Early reports of laparoscopically implanted AUS do not have sufficient patient populations and/or sufficient follow-up to be able to draw any conclusions (8,9).

Adjustable compression device

There are no RCTs on use of the ACT device. There are four case series (n = 349), with follow-up ranging from 5 to 84 months (11-14). An improvement in UI outcomes was reported, ranging from 47% objective cure to 100% subjective improvement. However, most patients required adjustment to achieve continence and 21% required explantation.

Evidence summary	**LE**
Implantation of an artificial sphincter may achieve continence in women with complicated SUI.	3
Implantation of the ACT device may improve complicated UI.	3
Failure and device explantation are common adverse effects of both the artificial sphincter and the adjustable compression device.	3
Explantation is more frequent in older women and among those who have had previous Burch colposuspension or pelvic radiotherapy.	3

Recommendations for surgery for complicated stress urinary incontinence in women	**GR**
The choice of surgery for recurrent stress urinary incontinence should be based on careful evaluation of the individual patient.	C
Women should be warned that the outcome of second-line surgical procedures is likely to be inferior to first-line treatment, both in terms of reduced benefit and increased risk of harm.	C
Offer implantation of AUS or ACT as an option for women with complicated stress urinary incontinence if they are available and appropriate monitoring of outcome is in place.	C
Warn women receiving AUS or ACT that there is a high risk of mechanical failure or a need for explantation.	C

AUS = Artificial Urinary Sphincter; ACT = Adjustable Compression Therapy.

5.2.2.3 References

1. Haylen BT, Freeman RM, Swift SE, et al. An International Urogynecological Association (IUGA)/ International Continence Society (ICS) joint terminology and classification of the complications related directly to the insertion of prostheses (meshes, implants, tapes) and grafts in female pelvic floor surgery. Neurourol Urodyn 2011 Jan;30(1):2-12. http://www.ncbi.nlm.nih.gov/pubmed/21181958
2. Silva LA, Andriolo RB, Atallah AN, et al. Surgery for stress urinary incontinence due to presumed sphincter deficiency after prostate surgery. Cochrane Database Syst Rev 2011 Apr 13;(4):CD008306. http://www.ncbi.nlm.nih.gov/pubmed/21491408
3. Shaikh S, Ong EK, Glavind K, et al. Mechanical devices for urinary incontinence in women. Cochrane Database Syst Rev 2006 Jul 19;(3):CD001756. http://www.ncbi.nlm.nih.gov/pubmed/16855977
4. Costa P, Mottet N, Rabut B, et al. The use of an artificial urinary sphincter in women with type III incontinence and a negative Marshall test. J Urol 2001 Apr;165(4):1172-6. http://www.ncbi.nlm.nih.gov/pubmed/11257664
5. Heitz M, Olianas R, Schreiter F. [Therapy of female urinary incontinence with the AMS 800 artificial sphincter. Indications, outcome, complications and risk factors]. Urologe A 1997 Sep;36(5):426-31. [German] http://www.ncbi.nlm.nih.gov/pubmed/9424794
6. Vayleux B, Rigaud J, Luyckx F, et al. Female urinary incontinence and artificial urinary sphincter: study of efficacy and risk factors for failure and complications. Eur Urol 2011 Jun;59(6):1048-53. http://www.ncbi.nlm.nih.gov/pubmed/21420781
7. Chung E, Cartmill RA. 25-year experience in the outcome of artificial urinary sphincter in the treatment of female urinary incontinence. BJU Int 2010 Dec;106(11):1664-7. http://www.ncbi.nlm.nih.gov/pubmed/20500509
8. Mandron E, Bryckaert PE, Papatsoris AG. Laparoscopic artificial urinary sphincter implantation for female genuine stress urinary incontinence: technique and 4-year experience in 25 patients. BJU Int 2010 Oct;106(8):1194-8; discussion 1198. http://www.ncbi.nlm.nih.gov/pubmed/20132197
9. Roupret M, Misrai V, Vaessen C, et al. Laparoscopic approach for artificial urinary sphincter implantation in women with intrinsic sphincter deficiency incontinence: a single-centre preliminary experience. Eur Urol 2010 Mar;57(3):499-504. http://www.ncbi.nlm.nih.gov/pubmed/19346059
10. Lee R, Te AE, Kaplan SA, et al. Temporal trends in adoption of and indications for the artificial urinary sphincter. J Urol 2009 Jun;181(6):2622-7. http://www.ncbi.nlm.nih.gov/pubmed/19375102
11. Aboseif SR, Franke EI, Nash SD, et al. The adjustable continence therapy system for recurrent female stress urinary incontinence: 1-year results of the North America Clinical Study Group. J Urol 2009 May;181(5):2187-91. http://www.ncbi.nlm.nih.gov/pubmed/19296967
12. Aboseif SR, Sassani P, Franke EI, et al. Treatment of moderate to severe female stress urinary incontinence with the adjustable continence therapy (ACT) device after failed surgical repair. World J Urol 2011 Apr;29(2):249-53. http://www.ncbi.nlm.nih.gov/pubmed/20959993
13. Kocjancic E, Crivellaro S, Ranzoni S, et al. Adjustable continence therapy for severe intrinsic sphincter deficiency and recurrent female stress urinary incontinence: long-term experience. J Urol 2010 Sep;184(3):1017-21. http://www.ncbi.nlm.nih.gov/pubmed/20643464
14. Wachter J, Henning A, Reohlich M, et al. Adjustable continence therapy for female urinary incontinence: a minimally invasive option for difficult cases. Urol Int 2008;81(2):160-6. http://www.ncbi.nlm.nih.gov/pubmed/18758213

5.3 Men with SUI

*5.3.1 **Bulking agents in men***

Injection of bulking agents has been used to try and improve the coaptation of a damaged sphincter zone. More recently, more modern compounds have been used to treat female and male SUI, e.g. bovine collagen (Contigen™), cross-linked polyacrylamide hydrogel (Bulkamid™) and dextranomer/hyaluronic acid copolymer (Deflux™), pyrolytic carbon particles (Durasphere™) and polymethylsyloxane (Macroplastique™). Initial reports showed limited efficacy in treating incontinence following radical prostatectomy incontinence (1,2).

5.3.1.1 Question

In men with post-prostatectomy incontinence or SUI, does injection of a urethral bulking agent cure SUI, improve QoL, or cause adverse outcomes?

5.3.1.2 Evidence

Most studies are case series with small sample sizes. Small cohort studies showed a lack of benefit using a number of different materials (3,4) However, polyacrylamide hydrogel resulted in limited improvement in QoL without curing the UI (4). A Cochrane review on the surgical treatment of post-prostatectomy incontinence found only one study that fulfilled the inclusion criteria (5). A prospective, randomised study compared the AUS to silicon particles (Macroplastique™) in 45 patients (1). Eighty-two per cent of patients receiving an AUS were continent compared to 46% of patients receiving silicone particles. In patients with severe incontinence, this difference was significant, but in patients with moderate and mild incontinence, the difference was less.

Evidence summary	**LE**
There is no evidence that bulking agents cure post-prostatectomy incontinence.	2a
There is weak evidence that bulking agents can offer temporary improvement in QoL in men with post-prostatectomy incontinence.	3
There is no evidence that one bulking agent is superior to another.	3

5.3.1.3 References

1. Imamoglu MA, Tuygun C, Bakirtas H, et al. The comparison of artificial urinary sphincter implantation and endourethral macroplastique injection for the treatment of postprostatectomy incontinence. Eur Urol 2005 Feb;47(2):209-13. http://www.ncbi.nlm.nih.gov/pubmed/15661416
2. Secin FP, Martínez-Salamanca JI, Eilber KS. [Limited efficacy of permanent injectable agents in the treatment of stress urinary incontinence after radical prostatectomy]. Arch Esp Urol 2005 Jun;58(5):431-6. [Spanish] http://www.ncbi.nlm.nih.gov/pubmed/16078785
3. Werther M, Seibold J, Amend B, et al. Stress urinary incontinence after radical prostatectomy: long term effects of endoscopic injection with dextranomer/hyaluronic acid copolymer. 39th Annual Meeting of the International Continence Society, San Francisco, USA. 29 September to 3 October. Neurourol Urodyn 2009;28(7):567-935, abstract no. 643. http://www.icsoffice.org/Abstracts/Publish/47/000643.pdf
4. Mantovani F, Maruccia S, Cozzi G, et al. Bulkamide hydrogel: limits of a new bulking agent in the mini-invasive therapy of incontinence after prostatectomy. 34th Congress SIUD, 17-19 2010, Verona, Italy. Neurourol Urodyn 2010 Jun;29(S2):95. http://onlinelibrary.wiley.com/doi/10.1002/nau.20930/pdf
5. Silva LA, Andriolo RB, Atallah AN, et al. Surgery for stress urinary incontinence due to presumed sphincter deficiency after prostate surgery. Cochrane Database Syst Rev 2011 Apr 13;(4):CD008306. http://www.ncbi.nlm.nih.gov/pubmed/21491408

5.3.2 ***Fixed male sling***

As well as external compression devices and bulking agents, slings have been introduced to treat post-prostatectomy incontinence. Fixed slings are positioned under the urethra and fixed by a retropubic or transobturator approach. The tension is adjusted during the surgery and cannot be re-adjusted post-operatively.

For the restoration of continence by these male slings, two concepts are now being proposed:

- continence restoration by urethral compression (InVance®, TOMS , Argus®)
- continence restoration by repositioning the bulb of urethra (AdVance) (1).

In principle, the AUS can be used for all degrees of post-prostatectomy incontinence, while male slings are advocated for mild-to-moderate incontinence. However, the definitions of mild and moderate incontinence are not clear. The definition of cure, used in most studies, was no pad use or one security pad per 24 hours. Some authors used a stricter criterion of less than 2 g urine loss in a 24-hour pad test (2).

5.3.2.1 Question

In men with post-prostatectomy SUI, does insertion of a fixed suburethral sling cure SUI, improve QoL, or cause adverse outcomes?

5.3.2.2 Evidence

Concerning the surgical treatment of post-prostatectomy incontinence, three recent literature reviews are available (3-5). There are a large number of uncontrolled case series concerning men implanted with several types of slings (6-14).

For the repositioning sling (AdVance), the benefit after a mean follow-up of 3 years has been published on 136 patients (15). Data were available on at least 614 patients with a mean follow-up of between 3 months and 3 years (2,12,15-21). Subjective cure rates for the device vary between 8.6% and 73.7%, with a mean of 49.5%. Radiotherapy was a negative prognostic factor (13,21). Post-operative voiding dysfunction occurred in 5.7-1.3%, while erosions and chronic pain were uncommon (0-0.4%). The overall failure rate was about 20%.

For the compression sling (InVance), 5-year data were available on 27 patients, 3-year data were available on 45 patients, and 1-year data were available on an additional 177 patients (22,23-27) The cure rate for this device varied between 36% and 62.7%, with a mean of 51.8% (22,23,25,26). Radiotherapy was a negative prognostic factor. Infection occurred in 3.2-15%, while de-novo urgency was reported in 2.3-11.9% of patients. The overall failure rate was about 20%.

Evidence summary	**LE**
There is limited short-term evidence that fixed male slings cure post-prostatectomy incontinence in patients with mild-to-moderate incontinence.	3
Men with severe incontinence, previous radiotherapy or urethral stricture surgery have poor outcomes from fixed male slings.	3
There is no evidence that one type of male sling is better than another.	3

5.3.2.3 References

1. Zeif HJ, Almallah Z. The male sling for post-radical prostatectomy urinary incontinence: urethral compression versus urethral relocation or what is next? Br J Med Surg Urol 2010;3(4):134-143. http://www.sciencedirect.com/science/article/pii/S1875974210000248
2. Cornel EB, Elzevier HW, Putter H. Can advance transobturator sling suspension cure male urinary postoperative stress incontinence? J Urol 2010 Apr;183(4):1459-63. http://www.ncbi.nlm.nih.gov/pubmed/20172561
3. Bauer RM, Gozzi C, Hubner W, et al. Contemporary management of postprostatectomy incontinence. Eur Urol 2011 Jun;59(6):985-96. http://www.ncbi.nlm.nih.gov/pubmed/21458914
4. Abrams P, Andersson KE, Birder L, et al. Fourth International Consultation on Incontinence Recommendations of the International Scientific Committee: evaluation and treatment of urinary incontinence, pelvic organ prolapse, and fecal incontinence. Neurourol Urodyn 2010;29(1):213-40. http://www.ncbi.nlm.nih.gov/pubmed/20025020
5. Herschorn S, Bruschini H, Comiter C, et al. Surgical treatment of stress incontinence in men. Neurourol Urodyn 2010;29(1):179-90. http://www.ncbi.nlm.nih.gov/pubmed/20025026
6. Bauer R, Mayer M, May F, et al. Complications of the AdVance transobturator male sling in the treatment of male stress urinary incontinence. Urology 2010 Jun;75(6):1494-8. http://www.ncbi.nlm.nih.gov/pubmed/20156654
7. Bauer RM, Mayer ME, Gratzke C, et al. Prospective evaluation of the functional sling suspension for male postprostatectomy stress urinary incontinence: results after 1 year. Eur Urol 2009 Dec;56(6): 928-33. http://www.ncbi.nlm.nih.gov/pubmed/19660850
8. Bauer R, Mayer M, Buchner A, et al. Surgical treatment of male stress incontinence after radical prostatectomy and its impact on quality of life. [Abstract] Urology 2009 Oct;74 (Supplement 4A):S119
9. Bauer R, Fullhase C, Stief C, et al. AdVance sling: the 'repositioning test', the most important tool for preoperative evaluation. Urology 2010 Sep;76(3 Suppl 1):S4, abstract no. POD-1.09. http://www.siu-urology.org/userfiles/files/URL 1.pdf
10. Bauer RM, Mayer ME, May F, et al. Complications of the AdVance transobturator male sling in the treatment of male stress urinary incontinence. Urology 2010 Jun;75(6):1494-8. http://www.ncbi.nlm.nih.gov/pubmed/20156654

11. Bauer R, Fullhase C, Becker A, et al. Mid-term results of the functional transobturator sling suspension for male post-prostatectomy stress urinary incontinence. Urology 2010 Sep;76(3 Suppl 1):S1-2; abstract no. POD-1.03.
http://www.siu-urology.org/userfiles/files/URL 1.pdf
12. Bauer RM, Soljanik I, Fullhase C, et al. Mid-term results for the retroluminar transobturator sling suspension for stress urinary incontinence after prostatectomy. BJU Int 2011 Jul;108(1):94-8.
http://www.ncbi.nlm.nih.gov/pubmed/20883489
13. Bauer RM, Soljanik I, Fullhase C, et al. Results of the AdVance transobturator male sling after radical prostatectomy and adjuvant radiotherapy. Urology 2011 Feb;77(2):474-9.
http://www.ncbi.nlm.nih.gov/pubmed/21167563
14. Bauer R, Gozzi C, Becker A, et al. Urodynamic findings after AdVance sling implantation. AUA 2011 Annual Scientific Meeting, May 14-19, 2011, Washington DC. Abstract 2159.
http://www.aua2011.org/abstracts/abstracts.cfm
15. Cornu J-N, Sebe P, Ciofu C, et al. Mid-term evaluation of the transobturator male sling for post-prostatectomy incontinence: focus on prognostic factors. BJU Int 2011 Jul;108(2):236-40.
http://www.ncbi.nlm.nih.gov/pubmed/20955265
16. Gill BC, Swartz MA, Klein JB, et al. Patient perceived effectiveness of a new male sling as treatment for post-prostatectomy incontinence. J Urol 2010 Jan;183(1):247-52.
http://www.ncbi.nlm.nih.gov/pubmed/19913826
17. Gill B, Li H, Nowacki A, et al. Durability of subjective outcomes of the Advance sling: initial insights. Society for Urodynamics and Female Urology, 2011 Winter Meeting, March 1-5 2011, Phoenix, Arizona, USA. Neururol Urodyn 2011 Feb:30(2):204-79. [Abstract no. 13]
http://onlinelibrary.wiley.com/doi/10.1002/nau.21058/full
18. Bertoloni R, Amenta M, Olivo G, et al. The retrourethral trans-obturator sling is an effective and attractive treatment option for male stress urinary incontinence resulting from radical prostatectomy (RP) after 1 year of implantation. Abstracts of the 20th Annual Meeting of the Italian Society of Uro-oncology (SIUrO), Rome, June 23-25, 2010. Anticancer Res 2011;30(4):1389, abstract no. 26.
http://www.iiar-anticancer.org/openAR/journals/index.php/anticancer/article/view/205
19. Hegele A, Frohme C, Olbert P, et al. Long term results after AdVance® male sling procedure in male stress urinary incontinence (SUI). 25th Anniversary EAU Congress, 16-20 April 2009, Barcelona, Spain. Eur Urol Suppl 2010;9(2):102, abstract no. 233.
http://www.uroweb.org/events/abstracts-online/?AID=26295
20. Rehder P, Mitterberger MJ, Pichler R, et al. The 1 year outcome of the transobturator retroluminal repositioning sling in the treatment of male stress urinary incontinence. BJU Int 2010 Dec;106(11):1668-72.
http://www.ncbi.nlm.nih.gov/pubmed/20518761
21. Rehder P, Pichler R, Schachtner L, et al. Two year outcome of the transobturator retroluminal repositioning sling in the treatment of male stress urinary incontinence. 26th Annual EAU Congress, 18-22 March 2011, Vienna, Austria. Eur Urol Suppl 2011;10(2):309, abstract no. 994.
http://www.uroweb.org/events/abstracts-online/?AID=34202
22. Carmel M, Hage B, Hanna S, et al. Long-term efficacy of the bone-anchored male sling for moderate and severe stress urinary incontinence. BJU Int 2010 Oct;106(7):1012-6.
http://www.ncbi.nlm.nih.gov/pubmed/20201839
23. Guimaraes M, Oliveira R, Resende A, et al. The bone-anchored perineal male sling for post-prostatectomy incontinence: results up to 5 years of follow-up. Urology 2010 Sep;76 (Suppl 3A):S2, abstract no. POD-1.04
http://www.siu-urology.org/userfiles/files/URL 1.pdf
24. Lynch W. Treatment parameters for the bone anchored male perineal sling. [Abstract UP-1.188] Urology 2009 Oct;74 (Supplement 4A):S229-S230.
http://www.goldjournal.net/search/results
25. Giberti C, Gallo F, Schenone M, et al. The bone-anchor sub-urethral sling for the treatment of iatrogenic male incontinence: subjective and objective assessment after 41 months of mean follow-up. World J Urol 2008 Apr;26(2):173-8.
http://www.ncbi.nlm.nih.gov/pubmed/17982750
26. Giberti C, Gallo F, Schenone M, et al. The bone anchor suburethral synthetic sling for iatrogenic male incontinence: critical evaluation at a mean 3-year followup. J Urol 2009 May;181(5):2204-8.
http://www.ncbi.nlm.nih.gov/pubmed/19296976
27. Comiter CV. The male perineal sling: intermediate-term results. Neurourol Urodyn 2005;24(7):648-53.
http://www.ncbi.nlm.nih.gov/pubmed/16167352

5.3.3 *Adjustable slings in males*

Adjustability in male sling surgery attempts to adjust the tension of the sling post-operatively. Two main systems are used in men:

- The Remeex® system consists of tension wires, which are adjusted using a type of screwdriver that temporarily comes out of the suprapubic wound. Once the ideal tension is achieved, it is easy to dislodge the screwdriver and close the wound. It is possible to repeat the procedure later during secondary surgery.
- The Argus® system consists of a silicone cushion, which is placed under the urethra and tensioned by two silicone arms, positioned either retropubically or in a transobturator fashion. Re-adjustment is usually carried out several months after the initial implant, by tightening or loosening the tensioning arms during a second surgical intervention.

5.3.3.1 *Question*

In men with post-prostatectomy incontinence or SUI, does insertion of an adjustable suburethral sling cure SUI, improve QoL, or cause adverse outcomes?

5.3.3.2 *Evidence*

There are no prospective RCTs comparing adjustable male slings to any other procedure. Most studies consist of prospective or retrospective case series, with variable follow-up and different definitions of success. Some have been published only as conference abstracts.

Remeex® system

For the Remeex® system, only two abstracts, with conflicting findings, have been published. One study followed 19 patients for nearly 7 years and reported 70% success (1), with no explants, infections or erosions. The second study followed 14 patients for 25 months. Only 36% of patients were satisfied and multiple re-adjustments were needed. Mechanical failure was reported in 21% (2).

Argus® system

Data on the Argus® system have been reported for 404 men, but only four series have reported on more than 50 patients (3-6), with the longest follow-up being 2.4 years. Success rates varied between 17% and 91.6%, with a mean of 57.6% predominantly reporting a subjective cure. The number of implants requiring re-adjustment was reported as between 22.9% and 41.5% (5,7,8). Infection of the device occurred in 5.4-8% (3,6,9). Erosions were reported in 5-10% (9,10). Urethral perforations occurred in 2.7-16% (3,4,6). Pain at the implant site was usually only temporary, but chronic pain has been reported (4,8,10,11). These complications resulted in explantation rates of 10-15% (5,8).

Evidence summary	**LE**
There is limited evidence that adjustable male slings are effective at curing SUI in men.	3
There is limited evidence that early explantation rates are high.	3
There is no evidence that adjustability of the male sling offers additional benefit over other types of sling.	3

5.3.3.3 *References*

1. Sousa A. Long term follow-up of the male remeex system for the surgical treatment of male incontinence. ICS/IUGA 2010 Scientific Meeting, 23-27 Aug 2010, Toronto, Canada. Abstract no. 136. https://www.icsoffice.org/Abstracts/Publish/105/000136.pdf
2. Kim JH, Kim JC, Seo JT. Long term follow-up of readjustable urethral sling procedure (Remeex System®) for male stress urinary incontinence. [Abstract 11] Society for Urodynamics and Female Urology, 2011 Winter Meeting, March 1-5, 2011, Arizona Biltmore Hotel, Phoenix, Arizona. Neurourology Urodyn 2011; 30:204-279. http://onlinelibrary.wiley.com/doi/10.1002/nau.21058/pdf
3. Bochove-Overgaauw D, Hoefnagels J, Schrier B. The Argus (adjustable sling for treatment of all degrees of male stress urinary incontinence: retrospective evaluation of efficacy and complications after a minimal follow-up of 14 months. [Abstract] http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed9&NEWS=N&AN=70272834.

4. Bochove-Overgaauw DM, Schrier BP. An adjustable sling for the treatment of all degrees of male stress urinary incontinence: retrospective evaluation of efficacy and complications after a minimal followup of 14 months. J Urol 2011 Apr;185(4):1363-8. http://www.ncbi.nlm.nih.gov/pubmed/21334683
5. Hubner WA, Gallistl H, Rutkowski M, et al. Adjustable bulbourethral male sling: experience after 101 cases of moderate-to-severe male stress urinary incontinence. BJU Int 2011 Mar;107(5):777-82. http://www.ncbi.nlm.nih.gov/pubmed/20964801
6. Romano S, Hubner W, Trigo Rocha F, et al. Post prostatectomy urinary incontinence treated with Argus T male sling-endurance of the results of a multicentre trial. Scientific Programme, 41st Annual Meeting of the International Continence Society (ICS), Glasgow, UK, 29 August to 2nd September, 2011. Neurourol Urodyn 2011;30(6):787-1206, abstract no. 73. http://www.icsoffice.org/Abstracts/Publish/106/000073.pdf
7. Hind A, Pini G, Viola D, Martino F, et al. Urodynamic and clinical results of an adjustable sling for male urinary incontinence-32 months follow up-ARGUS is effective also in severe cases. 39th Annual Meeting of the International Continence Society, San Francisco, USA. 29 September to 3 October, 2009. Neurourol Urodyn 2009;28(7):567-935, abstract no. 94. http://www.icsoffice.org/Abstracts/Publish/47/000094.pdf
8. Gallistl H, Rutkowski M, Ghawidel C, et al. Argus adjustable bulbourethral male sling-experience after 94 cases [Abstract]. American Urological Association (AUA) Annual Scientific Meeting, San Francisco, USA. May 29 to Jun 3 2010. J Urol 2010 April;183(4);e620. http://download.journals.elsevierhealth.com/pdfs/journals/0022-5347/PIIS0022534710016393.pdf
9. Dalpiaz O, Knopf HJ, Orth S, et al. Mid-term complications after placement of the male adjustable suburethral sling: a single center experience. J Urol 2011 Aug;186(2):604-9. http://www.ncbi.nlm.nih.gov/pubmed/21684559
10. Trigo Rocha F, Gomes C, Brushini H, et al. Adjustable transobturator sling (Argus T) for the treatment of post radical prostatectomy urinary incontinence (PRPUI). 31st Congress of SIU, 16-20 Oct 2011, Berlin, Germany. Urology 2011 Sep;78(Suppl 3A), S161, abstract no. VID-02.05. http://www.siucongress.org/2011/files/VID/VID-02_031-16534.pdf

5.3.4 ***Compressive devices in males***

External compression devices can be divided into two types: circumferential and non-circumferential compression of the urethral lumen (1). The artificial urinary sphincter (AUS) has been used for more than 30 years and is the standard treatment for moderate-to-severe male SUI. Most data available on the efficacy and adverse effects of AUS implantation is from older retrospective cohort studies with RCTs not performed due to the lack of a comparator. Several modifications of the standard single-cuff transperineal technique have been described, including transcorporeal implantation, double-cuff implants and trans-scrotal approaches (2). Men considering insertion of an AUS should understand that they must be able to operate a scrotal pump, requiring adequate dexterity and cognitive function. If the ability of an individual to operate the pump is uncertain, it may not be appropriate to implant an AUS. There are several recognised complications of AUS implantation, e.g. mechanical dysfunction, urethral constriction by fibrous tissue, erosion and infection.

The non-circumferential compression devices consist of two balloons placed close to the anastomotic urethra. The balloons can be filled and their volume can be adjusted post-operatively through an intrascrotal port.

5.3.4.1 Question

In men with post-prostatectomy SUI, does insertion of an external compression device cure SUI, improve QoL, or cause adverse outcomes?

5.3.4.2 Evidence

Artificial urinary sphincter

Although the AUS is considered to be the standard treatment for men with SUI, the quantity and level of evidence is low. There are no well-designed prospective RCTs with most information gained from older case series (2). More recent case series confirm the previous data (3,5). A continence rate of about 80% can be expected, while this may be lower in men who have undergone pelvic radiotherapy (3).

Trigo Rocha et al. published a prospective cohort study on 40 patients with a mean follow-up of 53 months (6). Pad use was reduced significantly and continence was achieved in 90%, with a significant improvement in QoL. The revision rate was 20%. From all urodynamic parameters, only low bladder compliance had a negative impact on the outcome, although another retrospective study showed that no urodynamic factors adversely altered the outcome of AUS implantation (7).

The penoscrotal approach was introduced to limit the number of incisions and to allow simultaneous implantation of penile and sphincter prostheses. It is uncertain whether this approach alters the outcome (8-10). The transcorporeal technique of placement can be used for repeat surgery but evidence of effectiveness is lacking (11,12).

The dual-cuff placement was introduced to treat patients who remained incontinent with a single 4-cm cuff in place. However, it has not improved control of continence, while the availability of a 3.5-cm cuff may have eliminated the need for a dual cuff (13-15). Patients who experienced complete continence after AUS implantation had a higher erosion risk (16).

Non-circumferential compression device (ProAct®)
There have been trials to treat post-prostatectomy SUI by insertion of a device consisting of balloons with adjustable volume external to the proximal bulbar urethra. A prospective cohort study (n = 128) described the functional outcome as 'good' in 68%, while 18% of the devices had to be explanted (17). A subgroup of radiotherapy patients only had 46% success and a higher percentage of urethral erosions.

A quasi-randomised trial comparing a non-circumferential compression device (ProAct®) with bone-anchored male slings found both types of device resulted in similar improvement of SUI (68% vs. 65%, respectively) (18). Other prospective series have shown similar continence outcomes, but several re-adjustments of the balloon volume were required to achieve cure. Adverse events were frequent, leading to an explantation rate of 11-58% (3,19-23). Although most studies have shown a positive impact on QoL, a questionnaire study showed that 50% of patients were still bothered significantly by persistent incontinence (24).

Evidence summary	**LE**
There is limited evidence that primary AUS implantation is effective for cure of SUI in men.	2b
Long-term failure rate for AUS is high although device replacement can be performed.	3
Previous pelvic radiotherapy does not appear to affect the outcome of AUS implantation.	3
Men who develop cognitive impairment or lose manual dexterity are likely to have difficulty operating an AUS.	3
Tandem-cuff placement is not superior to single-cuff placement.	3
The penoscrotal approach and perineal approach appear to give equivalent outcomes.	3
Very limited short-term evidence suggests that the non-circumferential compression device (ProACT®) is effective for treatment of post-prostatectomy SUI.	3
The non-circumferential compression device (ProACT®) is associated with a high failure and complication rate leading to frequent explantation.	3

Recommendations for surgery in men with stress urinary incontinence	**GR**
Only offer bulking agents to men with mild post-prostatectomy incontinence who desire temporary relief of UI symptoms.	C
Do not offer bulking agents to men with severe post-prostatectomy incontinence.	C
Offer fixed slings to men with mild-to-moderate post-prostatectomy incontinence.	B
Warn men that severe incontinence, prior pelvic radiotherapy or urethral stricture surgery, may worsen the outcome of fixed male sling surgery.	C
Offer AUS to men with persistent (more than 6 months) moderate-to-severe post-prostatectomy incontinence that has not responded to conservative management.	B
Warn about the long-term risk of failure and need for revision when counselling men for insertion of AUS.	C
Only offer the non-circumferential compression device (ProACT®) if arrangements for men with post-prostatectomy incontinence if arrangements for monitoring of outcome are in place.	C
Warn men considering a non-circumferential compression device (ProACT®) that there is a high risk of failure and subsequent explantation.	C
Do not offer non-circumferential compression device (ProACT®) to men who have had pelvic radiotherapy.	C

AUS = Artifical urinary sphincter.

5.3.4.3 References

1. Abrams P, Andersson KE, Birder L, et al. Fourth International Consultation on Incontinence Recommendations of the International Scientific Committee: evaluation and treatment of urinary incontinence, pelvic organ prolapse, and fecal incontinence. Neurourol Urodyn 2010;29(1):213-40. http://www.ncbi.nlm.nih.gov/pubmed/20025020
2. Herschorn S, Brushini H, Comiter C, et al. Surgical treatment of urinary incontinence in men. Neurourol Urodyn 2010;29(1):179-90. http://www.ncbi.nlm.nih.gov/pubmed/20025026
3. Sandhu J, Maschino A, Vickers A. The surgical learning curve for artificial urinary sphincter procedures compared to typical surgeon experience. Eur Urol 2011 Dec;60(6):1285-90. http://www.ncbi.nlm.nih.gov/pubmed/21665357
4. Kumar P, Summerton D, Terry T. The artificial urinary sphincter: a contemporary series. Urol 2010;76(3 Suppl 1):S3-S4. [Abstract POD-1.08]
5. Kim SP, Sarmast Z, Daignault S, et al. Long-term durability and functional among patients with artificial urinary sphincters: a 10-year retrospective review from the University of Michigan. J Urol 2008 May;179(5):1912-6. http://www.ncbi.nlm.nih.gov/pubmed/18353376
6. Trigo Rocha F, Gomes CM, Mitre AI, et al. A prospective study evaluating the efficacy of the artificial sphincter AMS 800 for the treatment of postradical prostatectomy urinary incontinence and the correlation between preoperative urodynamic and surgical outcomes. Urology 2008 Jan;71(1):85-9. http://www.ncbi.nlm.nih.gov/pubmed/18242371
7. Lai HH, Hsu EI, Boone TB. Urodynamic testing in evaluation of postradical prostatectomy incontinence before artificial urinary sphincter implantation. Urology 2009;73(6):1264-9. http://www.ncbi.nlm.nih.gov/pubmed/19371935
8. Sotelo TM, Westney OL. Outcomes related to placing an artificial urinary sphincter using a single-incision, transverse-scrotal technique in high-risk patients. BJU Int 2008 May;101(9):1124-7. http://www.ncbi.nlm.nih.gov/pubmed/18399828
9. Henry GD, Graham SM, Cleves MA, et al. Perineal approach for artificial urinary sphincter implantation appears to control male stress incontinence better than the transscrotal approach. J Urol 2008 Apr;179(4):1475-9, discussion 1479. http://www.ncbi.nlm.nih.gov/pubmed/18295275
10. Henry GD, Graham SM, Cornell RJ, et al. A multicenter study on the perineal versus penoscrotal approach for implantation of an artificial urinary sphincter: cuff size and control of male stress urinary incontinence. J Urol 2009 Nov;182(5):2404-9. http://www.ncbi.nlm.nih.gov/pubmed/19762042
11. Aaronson DS, Elliott SP, McAninch JW. Transcorporal artificial urinary sphincter placement for incontinence in high-risk patients after treatment of prostate cancer. Urology 2008 Oct;72(4):825-7. http://www.ncbi.nlm.nih.gov/pubmed/18752838
12. Zafirakis H, Alba F, Shapiro A, et al. Outcomes following transcorporal placement of an artificial urinary sphincter. 39th Annual Meeting of the International Continence Society, San Francisco, USA. 29 September to 3 October, 2009. Neurourol Urodyn 2009;28(7):567-935, abstract no. 90. http://www.icsoffice.org/Abstracts/Publish/47/000090.pdf
13. O'Connor RC, Lyon MB, Guralnick ML, et al. Long-term follow-up of single versus double cuff artificial urinary sphincter insertion for the treatment of severe postprostatectomy stress urinary incontinence. Urology 2008 Jan;71(1):90-3. http://www.ncbi.nlm.nih.gov/pubmed/18242372
14. Zafirakis H, Alba F, Westney OL. Preoperative pad weight and pad number as a predictor of failure of single cuff artificial urinary sphincter. 39th Annual Meeting of the International Continence Society, San Francisco, USA. 29 September to 3 October, 2009. Neurourol Urodyn 2009;38(7):567-935, abstract no. 89. http://www.icsoffice.org/Abstracts/Publish/47/000089.pdf
15. Hudak S, Valadez C, Terlecki R, et al. Impact of 3.5 cm artificial urinary sphincter cuff on primary and revision surgery for male stress urinary incontinence. J Urol 2011 Nov;186(5):1962-6. http://www.ncbi.nlm.nih.gov/pubmed/21944140
16. Smith P, Hudak S, Morey A. Hypercontinence and cuff erosion after artificial sphincter insertion: a comparison of cuff sizes and placement techniques. American Urological Association 2011 Annual Meeting, Washington DC, USA, 14-19 May 2011. Abstract no. 1348. http://www.aua2011.org/abstracts/abstracts.cfm

17. Roupret M, Misra V, Gosseine PN, et al. Management of stress urinary incontinence following prostate surgery with minimally invasive adjustable continence balloon implants: functional results from a single center prospective study. J Urol 2011 Jul;186(1):198-203. http://www.ncbi.nlm.nih.gov/pubmed/21575974
18. Crivellaro S, Singla A, Aggarwal N, et al. Adjustable continence therapy (ProACT) and bone anchored male sling: comparison of two new treatments of post prostatectomy incontinence. Int J Urol. 2008 Oct;15(10):910-4. http://www.ncbi.nlm.nih.gov/pubmed/18761534
19. Hubner WA, Schlarp OM. Treatment of incontinence after prostatectomy using a new minimally invasive device: adjustable continence therapy. BJU Int 2005 Sep;96(4):587-94. http://www.ncbi.nlm.nih.gov/pubmed/16104915
20. Pignot G, Lugagne PM, Yonneau L, et al. Results of minimally invasive adjustable continence balloon device, ProACT, for treatment of male postoperative incontinence: a monocentric experience. European Association of Urology 24th Congress, 17-21 March 2009, Stockholm, Sweden. Eur Urol Suppl 2009 Mar;8(4):335, abstract no. 860. http://www.uroweb.org/events/abstracts-online/?AID=23216
21. Gilling PJ, Bell DF, Wilson LC, et al. An adjustable continence therapy device for treating incontinence after prostatectomy: a minimum 2-year follow-up. BJU Int 2008 Nov;102(10):1426-30, discussion 1430-1. http://www.ncbi.nlm.nih.gov/pubmed/18564132
22. Gregori A, Roman AL, Scieri F, et al. Transrectal ultrasound-guided implantation of the Proact system in patients with postradical prostatectomy stress urinary incontinence: 5 years experience. Eur Urol 2010;57:430-6. http://www.europeanurology-supplement.com/article/S1569-9056(11)60968-8/abstract
23. Martens FM, Lampe MI, Heesakkers JP. ProACT for stress urinary incontinence after radical prostatectomy. Urol Int 2009;82(4):394-8. http://www.ncbi.nlm.nih.gov/pubmed/19506404
24. Kjaer L, Norgaard N, Sonksen J, et al. Adjustable continence balloons-clinical results of a new minimally invasive treatment of male urinary incontinence. European Association of Urology 26th Annual Congress. Eur Urol Suppl 2011;10(2):307, abstract no. 985. http://www.uroweb.org/events/abstracts-online/?id=108&no_cache=1&AID=31776

5.4 Surgical interventions for refractory DO

*5.4.1 **Intravesical injection of botulinum toxin A***

Botulinum toxin (BTX) A injections into the bladder wall are being increasingly used to treat persistent or refractory UUI in adult women, as well as in men despite the lack of high-quality data on BTX in males. Almost all reported studies have used BTX A (1,2). Injection techniques have not been standardised and the various studies differ with reference to the number of injections, the sites of injection and the injection volumes (1,2). Surgeons must realise that there are different products of Botulinum Toxin, onabotulinumtoxina (Botox in Europe) and abobotulinumtoxina (Dysport in Europe) and that the doses are not interchangeable. The effects of repeat injection have not been well studied in patients with UUI. The most important adverse event is an increase in PVR that may require clean intermittent catheterisation (CIC). CIC in turn is associated with an increased risk of UTIs (1,2).

5.4.1.1 Question

In adults with refractory UUI, does botulinum toxin injection in the bladder wall lead to a reduction in the number of incontinence episodes and/or to a higher percentage of continent patients compared to placebo?

5.4.1.2 Evidence

Two systematic reviews on the use of BTX have recently been published (1,2). The Cochrane analysis (1), which included patients with neurogenic or idiopathic DO, reported on RCTs comparing BTX with placebo. (It was not possible to draw conclusions about non-neurogenic incontinence from this review.) Reduction of incontinence episodes favoured BTX over placebo at both 4-6 weeks and 12 weeks. The mean difference in the reduction of incontinence episodes per day was -2.74 (95% CI: -4.47 to -1.01; p = 0.002). The rise in PVR favoured the placebo group, with a mean increase in PVR of 70.2 mL with the BTX. The question of the best injection technique remained largely unanswered. Studies were uniformly small with a maximum of 77 patients in any one study. Up to 66% of patients achieved complete continence, with an effect lasting between 3 and 12 months. The need for CIC was related to how aggressively patients are investigated for PVR. There was some evidence that lower doses produced fewer adverse events in terms of increased PVR and necessity for CIC. The UTI rates are consistently comparable to rates with cystoscopy alone but increase when CIC is required.

The systematic review by Mangera et al. (2) analysed the effect of BTX in adults with idiopathic DO in four RCTs (3-6). These studies (all using Onabotulinum toxin a) all demonstrated significant improvements in adults with idiopathic DO, at doses of 200 U in Brubaker et al. (4), 200/300 U in Flynn et al. (5) and 200 U in Sahai et al. (6). Dmochowski et al. compared a range of doses of BTX (3). These authors reported a change in incontinence episodes per day from baseline, but did not show the original baseline values, so that their results could not be included in the Mangera analysis. Additionally, an abstract from Tincello et al. (7) has recently reported results from the largest RCT of BTX to date. The study of 200 U Botox in 227 patients reported significant improvements in symptoms and QoL parameters versus placebo (7). The analysis of the efficacy data produced similar results to the Cochrane review.

The Cochrane and Mangera et al. reviews (1,2) also showed that the number of injection sites varied from 3 to 40, with 20 being most common, and the injection volume ranged between 3 and 30 mL, with 20 mL being the most common. The choice of injection site did not seem to impact on efficacy or adverse events. A range of 27-43% of patients had a PVR > 200 mL, while 13-44% suffered from UTI (1,2).

The Cochrane and Mangera et al. reviews accounted for all the major RCTs in BTX (1,2). However, cure-dry rates were not used as an outcome measure, and a separate meta-analysis using the original data (3,5-7) and data from a recent paper (8) was performed. Although the Dmochowski study (3) was not included in the analysis for the Mangera review, the EAU Panel have now obtained supplementary data from the authors, including dry rates at 6 and 12 weeks.

The meta-analysis (3,5-8) yielded the following results: the odds ratio (95% CI) of becoming dry with BTX versus placebo are 2.28 (0.95-5.49; p = 0.07) for 50 U, 4.39 (1.91-10.12; p = 0.0005) for 100 U, 4.96 (2.14-11.53; p = 0.0002) for 150 U, 4.34 (2.49-7.59, p < 0.00001) for 200 U and 7.05 (2.68-18.51, p < 0.0001) for 300 U. These results showed that 50 U had inferior efficacy to higher dosages. Although 300 U was the most efficacious dose, it is not a recommended dose because of the high rates of PVR necessitating CIC. A dose of 100-200 U seems to have comparable efficacy in the meta-analysis.

In the Dmochowski study, the cure-dry rate at 12 weeks was 37.0% and 50.9% for 100 U and 200U, respectively. Higher rates of PVR requiring CIC were found with higher doses showing a clear dose-response relationship (3).

Evidence summary	**LE**
A single treatment session of intravesical Onabotulinum toxin A (100-300 U) is more effective than placebo at curing and improving UUI for up to 12 months.	1a
There is no evidence that repeated injections of botulinum toxin A have reduced efficacy.	3
There is a high risk of increased PVR, which is dose dependent and may require intermittent self-catheterisation.	1b
There is a high risk of UTI in those who require intermittent self-catheterisation.	1b
There is no evidence that one technique of injecting botulinum toxin A is more efficacious than another.	1b

Recommendations	**GR**
Offer botulinum toxin A intravesical injections to patients with urgency urinary incontinence refractory to antimuscarinic therapy.	A
Warn patients of the possible need to self-catheterise and the associated risk of urinary tract infection; ensure that they are willing and able to do so.	A
Patients should also be warned of the licensing status of botulinum toxin A, and that the long-term effects remain unknown.	A

5.4.1.3 References

1. Duthie JB, Vincent M, Herbison GP, et al. Botulinum toxin injections for adults with overactive bladder syndrome. Cochrane Database Syst Rev 2011 Dec 7;(12):CD005493. http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD005493.pub3/abstract

2. Mangera A, Andersson KE, Apostolidis A, et al. Contemporary management of lower urinary tract disease with botulinum toxin A: a systematic review of botox (onabotulinumtoxinA) and dysport (abobotulinumtoxinA). Eur Urol 2011 Oct;60(4):784-95. http://www.ncbi.nlm.nih.gov/pubmed/21782318
3. Dmochowski R, Chapple C, Nitti VW, et al. Efficacy and safety of onabotulinumtoxinA for idiopathic overactive bladder: a double-blind, placebo controlled, randomized, dose ranging trial. J Urol 2010 Dec;184(6):2416-22. http://www.ncbi.nlm.nih.gov/pubmed/20952013
4. Brubaker L, Richter HE, Visco A, et al. Refractory idiopathic urge urinary incontinence and botulinum A injection. J Urol 2008 Jul;180(1):217-22. http://www.ncbi.nlm.nih.gov/pubmed/18499184
5. Flynn MK, Amundsen CL, Perevich M, et al. Outcome of a randomized, double-blind, placebo controlled trial of botulinum A toxin for refractory overactive bladder. J Urol 2009 Jun;181(6):2608-15. http://www.ncbi.nlm.nih.gov/pubmed/19375091
6. Sahai A, Khan MS, Dasgupta P. Efficacy of botulinum toxin-A for treating idiopathic detrusor overactivity: results from a single center, randomized, double-blind, placebo controlled trial. J Urol 2007 Jun;177(6):2231-6. http://www.ncbi.nlm.nih.gov/pubmed/17509328
7. Tincello DG, Slack MC, Kenyon S, et al. Botulinum toxin-A for refractory detrusor overactivity in women: a 240 patient randomized placebo controlled trial. Eur Urol Suppl 2011 Mar;10(2):191, abstract no. 581. http://www.europeanurology.com/article/S1569-9056(11)60571-X/abstract
8. Denys P, Le Normand L, Ghout I, et al. Efficacy and safety of low doses of onabotulinumtoxinA for the treatment of refractory idiopathic overactive bladder: a multicentre, double-blind, randomised, placebo-controlled dose-ranging study. Eur Urol 2011 Oct 25. http://www.ncbi.nlm.nih.gov/pubmed/22036776

5.4.1.4. Research priorities

More research is needed to investigate the optimum injection technique and regimen, as well as the long-term effects of intravesical injection of botulinum toxin.

5.4.2 ***Sacral nerve stimulation (neuromodulation)***

Under fluoroscopic control, an electrode is placed percutaneously in the sacral foramen alongside a sacral nerve, usually S3, in the first stage of a two-stage implantation (FS2S). Once it has been shown that the patient can respond, the patient proceeds to the second stage of implantation, in which the electrode is connected by cables under the skin to an implanted, programmable, pulse generator. The generator provides stimulation within established stimulation parameters. In earlier techniques for stimulating the sacral nerve, a temporary test (wire) electrode was placed near the nerve, and then percutaneous nerve evaluation (PNE) and test stimulation, provided by an external pulse generator, was performed. Generally, the PNE lasted for 5-7 days.

More recently, the permanent electrode has been used for a longer test phase, as part of a two-stage procedure. Once the PNE or FS2S has been shown to be successful, the patient proceeds to full implantation with the pulse generator. Patients, in whom selected symptoms of UUI are reduced by more than 50% during the test phase, are candidates for the permanent implant. Schmidt et al. first described the technique of PNE of the S3 sacral nerve (1). The two-stage implant was introduced by Janknegt et al. (2). Spinelli et al. introduced the minimally invasive percutaneous implantation of a tined lead (3).

5.4.2.1 Question

In adults suffering from refractory UUI, what is the clinical effectiveness of sacral nerve neuromodulation compared to alternative treatments?

5.4.2.2 Evidence

A Cochrane review of the literature until March 2008 (4) identified three RCTs that investigated sacral nerve stimulation in patients with refractory UUI. One of these RCTs was only published as an abstract and is not considered here (5,6). The quality of the other two RCTs was poor. No details of method of randomisation or concealment of randomisation were given. Assessors were not blind to the treatment allocation; it was impossible to blind the patients since all had to respond to a PNE before randomisation. In addition, the numbers randomised did not match the numbers in the results in these two studies.

One multicentre RCT involved implantation of half of the participants (5), while the remaining patients formed

the control group (delayed implantation) staying on medical treatment for 6 months. The control group was subsequently offered implantation. Fifty percent of the immediately implanted group had > 90% improvement in UUI at 6 months compared to 1.6% of the control group (5). The other RCT (6) achieved similar results, although these patients had already been included in the first report (5). However, Weil et al. (6) showed that the effect on generic QoL measured by the SF-36, was unclear as it differed between the groups in only one of the eight dimensions.

The results of 17 case series of patients with UUI, who were treated early in the experience with sacral nerve stimulation were reviewed (7). After a follow-up duration of between 1 and 3 years, approximately 50% of patients with UUI, demonstrated > 90% reduction in incontinence, 25% demonstrated 50-90% improvement, and another 25% demonstrated < 50% improvement. Adverse events occurred in 50% of implanted cases, with surgical revision necessary in 33% (7).

In a subanalysis of the RCT, the outcome of UUI patients, with or without pre-implant DO were compared. Similar success rates were found in patients with and without urodynamic DO (8).

There are two case series describing the longer-term outcome of sacral nerve neuromodulation, with a mean or median follow-up of at least 5 years, in patients with refractory UUI (9,10). These studies have reported continued success (> 50% improvement on original symptoms) experienced by 50-63% in those patients available for follow-up. Only one study reported cure rates averaging 15% (10).

Technical modifications have been made, including a change in the anatomical site of the pulse generator, introduction of the tined lead and different test-phase protocols prior to definitive implantation. The lead may also be implanted using a minimally invasive percutaneous procedure (3). The effect of these changes on the outcome of implantation is uncertain.

Evidence summary	**LE**
Sacral nerve neuromodulation is more effective than continuation of failed conservative treatment for cure of UUI, but no sham controls have been used.	1b
In those patients who have been implanted, more than 50% improvement is maintained in at least 50% of patients at 5 years' follow up, and 15% remain cured.	3
One-stage implantation results in more patients receiving the final implant than occurs with prior temporary test stimulation.	4

Recommendations	**GR**
If available, offer patients with urgency urinary incontinence that is refractory to conservative therapy, the opportunity to be treated by sacral nerve neuromodulation before bladder augmentation or urinary diversion is considered.	A

5.4.2.3 Research priority

A RCT comparing a strategy of botulinum toxin injection, repeated as required, against a strategy of test and permanent sacral nerve neuromodulation with an accompanying health economic analysis is required.

5.4.2.4 References

1. Schmidt RA, Senn E, Tanagho EA. Functional evaluation of sacral root integrity. Report of a technique. Urology 1990 May;35(5):388-92. http://www.ncbi.nlm.nih.gov/pubmed/2336766
2. Janknegt RA, Weil EH, Eerdmans PH. Improving neuromodulation technique for refractory voiding dysfunctions: two-stage implant. Urology 1997 Mar;49(3):358-62. http://www.ncbi.nlm.nih.gov/pubmed/9123698
3. Spinelli M, Giardiello G, Gerber M, et al. New sacral neuromodulation lead for percutaneous implantation using local anesthesia: description and first experience. J Urol 2003 Nov;170(5):1905-7. http://www.ncbi.nlm.nih.gov/pubmed/14532804
4. Herbison GP, Arnold EP. Sacral neuromodulation with implanted devices for urinary storage and voiding dysfunction in adults. Cochrane Database Syst Rev 2009 Apr 15;(2):CD004202. http://www.ncbi.nlm.nih.gov/pubmed/19370596

5. Schmidt RA, Jonas U, Oleson KA, et al: Sacral Nerve Stimulation Group. Sacral nerve stimulation for treatment of refractory urinary urge incontinence. J Urol 1999 Aug;162(2):352-7. http://www.ncbi.nlm.nih.gov/pubmed/10411037
6. Weil EH, Ruiz-Cerda JL, Eerdmans PH, et al. Sacral root neuromodulation in the treatment of refractory urinary urge incontinence: a prospective randomized clinical trial. Eur Urol 2000 Feb;37(2):161-71. http://www.ncbi.nlm.nih.gov/pubmed/10705194
7. Brazzelli M, Murray A, Fraser C. Efficacy and safety of sacral nerve stimulation for urinary urge incontinence: a systematic review. J Urol 2006 Mar;175(3 Pt 1):835-41. http://www.ncbi.nlm.nih.gov/pubmed/16469561
8. Groenendijk PM, Lycklama à Nyeholt AA, Heesakkers JP, et al: Sacral Nerve Stimulation Study Group. Urodynamic evaluation of sacral neuromodulation for urge urinary incontinence. BJU Int 2008 Feb;101(3):325-9. http://www.ncbi.nlm.nih.gov/pubmed/18070199
9. van Kerrebroeck PE, van Voskuilen AC, Heesakkers JP, et al. Results of sacral neuromodulation therapy for urinary voiding dysfunction: outcomes of a prospective, worldwide clinical study. J Urol 2007 Nov;178(5):2029-34. http://www.ncbi.nlm.nih.gov/pubmed/17869298
10. Groen J, Blok BF, Bosch JL. Sacral neuromodulation as treatment for refractory idiopathic urge urinary incontinence: 5-year results of a longitudinal study in 60 women. J Urol 2011 Sep;186(3):954-9. http://www.ncbi.nlm.nih.gov/pubmed/21791355

*5.4.3 **Cystoplasty/urinary diversion***

5.4.3.1 Augmentation cystoplasty

In augmentation cystoplasty (also known as clam cystoplasty), a detubularised segment of bowel is inserted into the bivalved bladder wall. The aim is to disrupt involuntary detrusor contraction, increase compliance and increase bladder capacity. The segment of bowel most often used is distal ileum, but any bowel segment can be used if it has the appropriate mesenteric length to reach the pelvic cavity without tension. One study did not find any difference between bivalving the bladder in the sagittal plane and bivalving it in the coronal plane (1).

There are no RCTs comparing bladder augmentation to other treatments for patients with UUI. Most often, bladder augmentation is used to correct neurogenic DO or small-capacity, low-compliant, bladders caused by fibrosis, tuberculosis, radiation or chronic infection.

A number of case series have been reported (1-8), but none within the last 10 years. All these series included a large proportion of patients with neurological bladder dysfunction. The largest case series of bladder augmentation in UUI included 51 women with UUI (2). At an average follow-up of 74.5 months, only 53% were continent and satisfied with the surgery, whereas 25% had occasional leaks and 18% continued to have disabling UUI. It is difficult to extract data on non-neurogenic patients from these case series, but in general the results for patients with idiopathic DO (58%) seemed to be less satisfactory than for patients with neurogenic overactivity (90%).

Adverse effects were common and have been summarised in a review over 5-17 years of more than 267 cases, 61 of whom had non-neurogenic UUI (9). In addition, many patients may require self CIC to obtain adequate bladder emptying.

.

Table 6: Complications of bladder augmentation

Short-term complications	**Affected patients (%)**
Bowel obstruction	2
Infection	1.5
Thromboembolism	1
Bleeding	0.75
Fistula	0.4
Long-term complications	
Clean intermittent self-catheterisation	38

Urinary tract infection	70% asymptomatic; 20% symptomatic
Urinary tract stones	13
Metabolic disturbance	16
Deterioration in renal function	2
Bladder perforation	0.75

5.4.3.2 Detrusor myectomy (bladder auto-augmentation)

Detrusor myectomy aims to increase bladder capacity and reduce storage pressures by incising or excising a portion of the detrusor muscle, to create a bladder mucosal 'bulge' or pseudodiverticulum. It was initially described as an alternative to bladder augmentation in children (10). An additional, non-randomised study (11), which compared bladder augmentation with detrusor myectomy in adult patients with neurogenic and non-neurogenic bladder dysfunction, demonstrated a much lower incidence of short-term complications. However, the poor long-term results caused by fibrosis of the pseudodiverticulum led to the abandonment of this technique in patients with neurogenic dysfunction. A small study of five patients with UUI (12) showed good outcome in all patients at the initial post-operative visit, but clinical and urodynamic failure in four of the five patients at 3 months.

5.4.3.3 Urinary diversion

Urinary diversion remains a reconstructive option for patients, who decline repeated surgery for UI. It is rarely needed in the treatment of non-neurogenic UUI. There are no studies that have specifically examined this technique in the treatment of non-neurogenic UI, although the subject has been reviewed by the Cochrane group (13).

Evidence summary	**LE**
There is limited evidence on the effectiveness of augmentation cystoplasty and urinary diversion in treatment of idiopathic DO.	3
Augmentation cystoplasty and urinary diversion are associated with high risks of short-term and long-term severe complications.	3
The need to perform clean intermittent self-catheterisation following augmentation cystoplasty is very common.	3
There is no evidence comparing the efficacy or adverse effects of augmentation cystoplasty with urinary diversion.	3
There is no evidence on the long-term effectiveness of detrusor myectomy in adults with idiopathic DO.	3

Recommendations	**GR**
Only offer augmentation cystoplasty to patients with detrusor overactivity incontinence who have failed conservative therapy, in whom the possibility of botulinum toxin and sacral nerve stimulation has been discussed.	C
Warn patients undergoing augmentation cystoplasty of the high risk of having to perform clean intermittent self-catheterisation; ensure they are willing and able to do so.	C
Do not offer detrusor myectomy as a treatment for urinary incontinence.	C
Only offer urinary diversion to patients who have failed less invasive therapies for the treatment of urinary incontinence and who will accept a stoma.	C
Warn patients undergoing augmentation cystoplasty or urinary diversion of the high risk of short-term and long-term complications, and the possible small risk of malignancy.	C
Life-long follow-up is recommended for patients who have undergone augmentation cystoplasty or urinary diversion.	C

5.4.3.4 References

1. Kockelbergh RC, Tan JB, Bates CP, et al. Clam enterocystoplasty in general urological practice. Br J Urol 1991 Jul;68(1):38-41. http://www.ncbi.nlm.nih.gov/pubmed/1873689

2. Awad SA, Al-Zahrani HM, Gajewski JB, et al. Long-term results and complications of augmentation ileocystoplasty for idiopathic urge incontinence in women. Br J Urol 1998 Apr;81(4):569-73. http://www.ncbi.nlm.nih.gov/pubmed/9598629
3. Hasan ST, Marshall C, Robson WA, et al. Clinical outcome and quality of life following enterocystoplasty for idiopathic detrusor instability and neurogenic bladder dysfunction. Br J Urol 1995 Nov;76(5):551-7. http://www.ncbi.nlm.nih.gov/pubmed/8535671
4. Mundy AR, Stephenson TP. “Clam” ileocystoplasty for the treatment of refractory urge incontinence. Br J Urol 1985 Dec;57(6):641-6. http://www.ncbi.nlm.nih.gov/pubmed/4084722
5. Edlund C, Peeker R, Fall M. Clam ileocystoplasty: successful treatment of severe bladder overactivity. Scand J Urol Nephrol 2001 Jun;35(3):190-5. http://www.ncbi.nlm.nih.gov/pubmed/11487070
6. Bramble FJ. The treatment of adult enuresis and urge incontinence by enterocystoplasty. Br J Urol 1982 Dec;54(6):693-6. http://www.ncbi.nlm.nih.gov/pubmed/7150926
7. George VK, Russell GL, Shutt A, et al. Clam ileocystoplasty. Br J Urol 1991 Nov;68(5):487-9. http://www.ncbi.nlm.nih.gov/pubmed/1747723
8. Kelly JD, Keane PF. Long-term results and complications of augmentation ileocystoplasty for idiopathic urge incontinence in women. Br J Urol 1998 Oct;82(4):609-10; comment in Br J Urol 1998 Apr;81(4):569-73. http://www.ncbi.nlm.nih.gov/pubmed/9806210
9. Greenwell TJ, Venn SN, Mundy AR. Augmentation cystoplasty. BJU Int 2001 Oct;88(6):511-25. http://www.ncbi.nlm.nih.gov/pubmed/11678743
10. Cartwright PC, Snow BW. Bladder autoaugmentation: partial detrusor excision to augment the bladder without use of bowel. J Urol 1989 Oct;142(4):1050-3. http://www.ncbi.nlm.nih.gov/pubmed/2795729
11. Leng WW, Blalock HJ, Fredriksson WH, et al. Enterocystoplasty or detrusor myectomy? Comparison of indications and outcomes for bladder augmentation. J Urol 1999 Mar;161(3):758-63. http://www.ncbi.nlm.nih.gov/pubmed/10022679
12. Ter Meulen PH, Heesakkers JP, Janknegt RA. A study on the feasibility of vesicomyotomy in patients with motor urge incontinence. Eur Urol 1997;32(2):166-9. http://www.ncbi.nlm.nih.gov/pubmed/9286647
13. Nabi G, Cody JD, Dublin N, et al. Urinary diversion and bladder reconstruction/replacement using intestinal segments for intractable incontinence or following cystectomy. Cochrane Database Syst Rev 2003;(1): CD003306. http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD003306/abstract

APPENDIX A: MIXED URINARY INCONTINENCE

About one-third of women with UI have mixed incontinence (MUI), rather than pure stress UI (SUI) or urge UI (UUI). In addition, a mixed combination of symptoms becomes more common with increasing age. However, although many studies include patients with MUI, it is rare for these studies to provide a separate analysis of MUI. It is therefore difficult to find evidence specifically related to MUI.

This issue has been addressed by the Panel after the initial work on the preceding chapters had been completed. It was realised that a crucial part of developing the clinical algorithms was to provide advice on how to mange this large group of patients. A decision was therefore made to include a rapid review of this topic, but the iterative process underpinning the Panel's advice on this issue was necessarily shorter and less robust that for the preceding sections, and will be addressed more systematically for future editions.

A limited literature search was carried out from June 2008 for the terms, 'mixed incontinence' and 'mixed urinary incontinence' in PubMed. A separate search was also done for these terms within all known systematic reviews published since 2008 that had already been used for the rest of the guideline.

A.2 Question

In adults with MUI, is the outcome of a certain treatment different to that obtained with the same treatment in patients with either pure SUI or pure UUI?

A.3 Evidence

No specific systematic reviews were found that addressed the above question. Systematic reviews on conservative therapies, drug therapy and surgery were also reviewed for any analyses of specific incontinence categories, but none were found.

However, a Cochrane report on pelvic floor muscle training (1) concluded that training was less likely to result in a cure in patients with MUI than in patients with pure SUI, though it is not clear from the report how this conclusion was reached.

A.3.1 ***RCTs in MUI population, which compare one treatment to another***

An RCT in MUI patients compared intravaginal electrical stimulation to pelvic floor muscle training. No difference was seen in outcome, but this was a small underpowered study (2).

A.3.1.1 Duloxetine

In one RCT, involving 588 women, subjects were stratified into either stress-predominant, urge-predominant or balanced MUI groups and randomised to receive duloxetine or placebo. Duloxetine was effective in reducing episodes of incontinence and improving QoL compared to placebo in all subgroups (3).

A.3.1.2 Transvaginal obturator tape

In an RCT including 96 women with MUI, objective improvement was better for patients treated with transvaginal obturator tape + the Ingelman Sundberg operation versus patients treated with obturator tape alone (4).

A.3.1.3 Tolterodine

In an RCT of 854 women with MUI, tolterodine ER was effective compared to placebo in reducing frequency, urgency and UUI, but not SUI. These results show that the effect of tolterodine was not altered by the presence of SUI (5).

A.3.2 ***RCTs, including a subanalysis of MUI patients within treatment arms and allowing comparison to patients with pure SUI or pure UUI***

Many RCTs include both patients with pure UI (stress or urge) and patients with MUI, in which pure UI predominates. However, very few RCTs report separate outcomes for MUI and pure UI groups.

A small and underpowered RCT (n = 71) compared delivery of pelvic floor muscle training, with or without an instructive audiotape. It showed equal efficacy for different types of UI (6).

An RCT in 121 women with stress, urgency or mixed UI compared transvaginal electrical stimulation with sham stimulation and was found to be equally effective in urgency UI as in mixed UI (7).

A.3.2.1 Drugs

Duloxetine was found to have equal efficacy for Stress UI and Mixed UI in an RCT (n = 553) following

secondary analysis of subpopulations (8). In another study, secondary analysis showed that tolterodine compared to placebo (n = 1380) was equally effective in reducing urgency and urgency UI symptoms, regardless of whether there was associated stress incontinence (9). Similar findings apply to solifenacin (10,11).

A.3.2.2 Surgery

Post-hoc analysis of the SISTER trial showed that in women undergoing either autologous fascial sling or Burch colposuspension, the outcomes were poorer for women with a concomitant complaint of pre-operative urgency. This applied to both stress-specific and non-stress incontinence outcomes(12).

A similar post-hoc review of an RCT comparing transobturator and retropubic midurethral slings showed that the greater the severity of pre-operative urgency the more likely that treatment would fail, as assessed objectively, even if surgery had been similar (13).

However, an earlier study had found that surgery provided similar outcomes, whether or not urgency was present prior to surgery (14). (This study included only a few patients with urodynamic detrusor overactivity.)

A.3.3 ***Large cohort studies, including a separate analysis of patients with MUI***

Following a RCT of pelvic floor muscle training, a review of 88 women available for follow-up at 5 years found that outcomes were less satisfactory in women with MUI than in women with pure SUI (15).

A.3.3.1 Surgery for SUI

Some authors have reported the disappearance of urgency in up to 40% of women after successful SUI surgery for MUI, suggesting that urgency is an accompanying feature of SUI (14,16-18).

In a case series of 192 women undergoing midurethral sling insertion, overall satisfaction rates were lower for women with mixed symptoms and overactive detrusor function according to pre-operative urodynamics compared to those with pure SUI and normal urodynamics (75% vs 98%, respectively) (19). One study compared two parallel cohorts of patients undergoing surgery for SUI, with and without detrusor overactivity, and found inferior outcomes in women with MUI (20).

However, in a study of the bulking agent, Bulkamid, similar outcomes were reported in women with pure SUI and MUI (21).

One cohort of 450 women, undergoing midurethral sling surgery, had significantly worse outcomes for increased amounts of urgency. In urgency-predominant MUI, the success rate fell to 52% compared to 80% in stress-predominant MUI (22). In a second study in 1,113 women treated with transvaginal obturator tape, Stress UI was cured equally in stress-predominant MUI or urgency-predominant MUI. However, women with stress-predominant MUI were found to have significantly better overall outcomes than women with urgency-predominant MUI (23).

A.4 Evidence statements

Evidence summary	**LE**
Pelvic floor muscle training is less effective for mixed UI than for SUI alone.	2
Electrical stimulation is equally effective for mixed UI and SUI.	1b
Antimuscarinic drugs are equally effective in improving symptoms of urgency and urgency UI, in patients with mixed UI as in patients with urgency UI alone.	1a
Duloxetine is equally effective in improving SUI in patients with MUI as in patients with SUI alone.	1a
Women with mixed UI are less likely to be cured of their incontinence, by SUI surgery, than women with SUI alone.	1c
The response of pre-existing urgency symptoms to SUI surgery is unpredictable, and symptoms may improve or worsen.	3

A.5 Recommendations

Recommendations	GR
Treat the most bothersome symptom first in patients with mixed urinary incontinence.	C
Warn patients with mixed urinary incontinence that the chance of success of pelvic floor muscle training is less satisfactory than for stress urinary incontinence alone.	B
Offer antimuscarinic drugs to patients with urge-predominant mixed urinary incontinence.	A
Warn patients with mixed urinary incontinence that surgery is less likely to be successful than surgery in patients with stress urinary incontinence alone.	A

A.6 Research priority

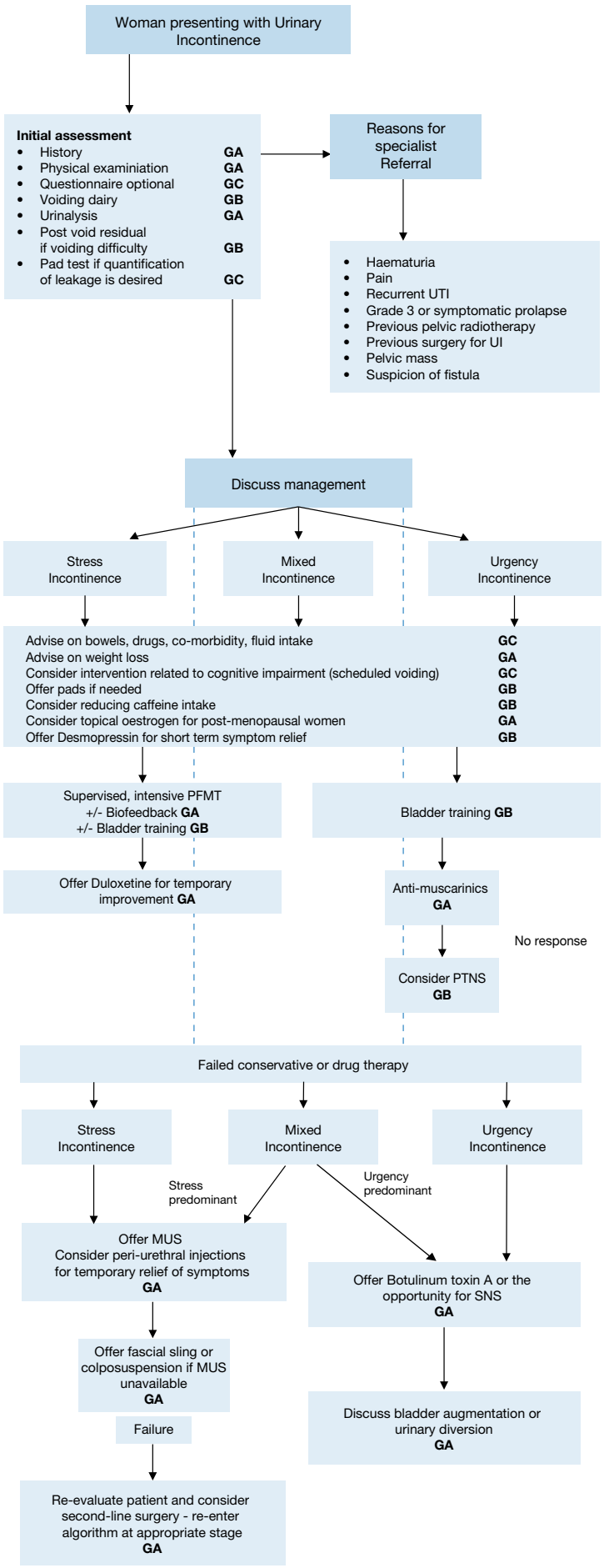
There is a need for well-designed trials comparing treatments in populations with MUI, and in which the type of MUI has been accurately defined.

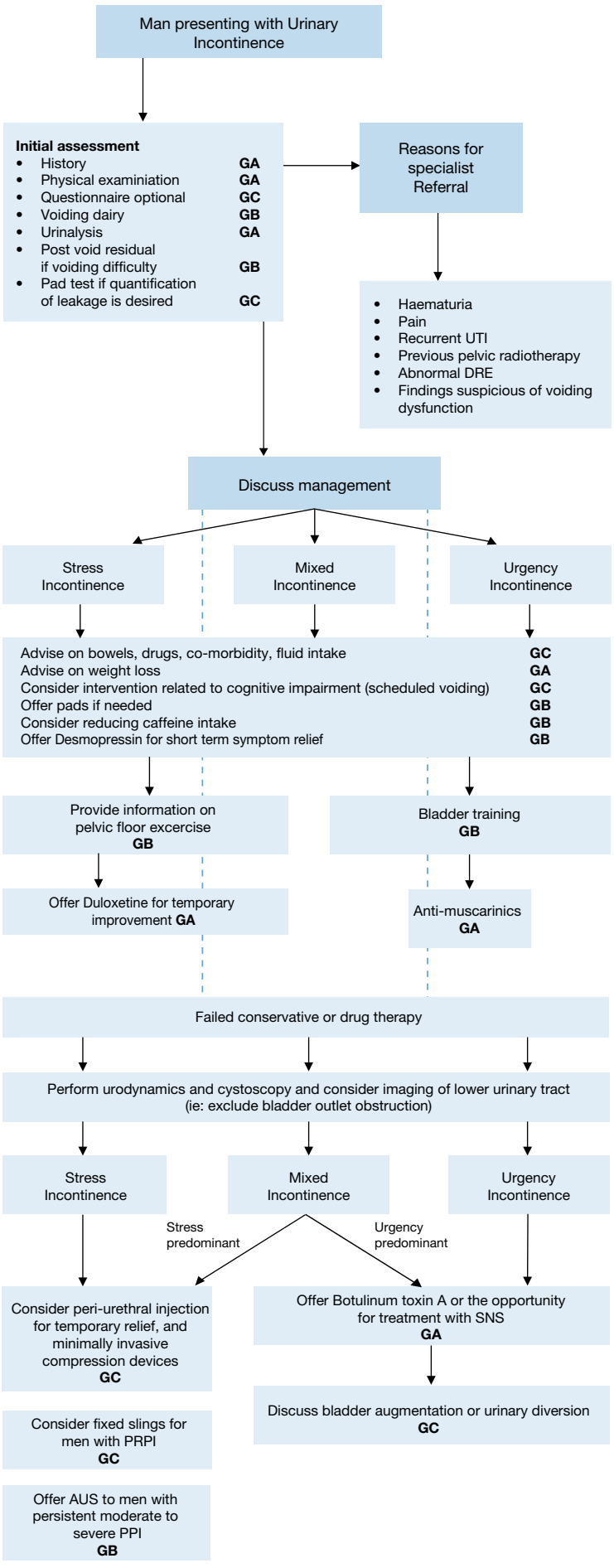
Researchers should be more precise about the definitions of MUI, when evaluating the effects of treatment in this group.

A.7 References

1. Dumoulin C, Hay/Smith J. Pelvic floor muscle training versus no treatment for urinary incontinence in women. A Cochrane systematic review. Eur J Phys Rehabil Med. 2008 Mar;44(1):47-63. http://www.ncbi.nlm.nih.gov/pubmed/18385628
2. Smith JJ 3rd. Intravaginal stimulation randomized trial. J Urol. 1996 Jan;155(1):127-30. http://www.ncbi.nlm.nih.gov/pubmed/7490809
3. Bent AE, Gousse SE, Hendrix SL, et al. Duloxetine compared with placebo for the treatment of women with mixed urinary incontinence. Neurourol Urodyn. 2008;27(3):212-21. http://www.ncbi.nlm.nih.gov/pubmed/17580357
4. Juang CM, Yu KJ, Chou P, et al. Efficacy analysis of trans-obturator tension-free vaginal tape (TVT-O) plus modified Ingelman-Sundberg procedure versus TVT-O alone in the treatment of mixed urinary incontinence: a randomized study. Eur Urol. 2007 Jun;51(6):1671-8; discussion 1679. http://www.ncbi.nlm.nih.gov/pubmed/17254697
5. Khullar V, Hill S, Laval K-U, Schiotz HA, et al. Treatment of urgepredominant mixed urinary incontinence with tolterodine extended release: A randomized, placebo-controlled trial. Urology. 2004 Aug;64(2):269-74; discussion 274-5. http://www.ncbi.nlm.nih.gov/pubmed/15302476
6. Nygaard IE, Kreger KJ, Lepic MM, et al. Efficacy of pelvic floor muscle exercises in women with stress, urge, and mixed urinary incontinence. Am J Obstet Gynecol. 1996 Jan;174(1 Pt 1):120-5. http://www.ncbi.nlm.nih.gov/pubmed/8571994
7. Brubaker L, Benson JT, Bent A, et al. Transvaginal electrical stimulation for female urinary incontinence. Am J Obstet Gynecol. 1997 Sep;177(3):536-40. http://www.ncbi.nlm.nih.gov/pubmed/9322620
8. Bump RC, Norton PA, Zinner NR, et al. Mixed urinary incontinence symptoms: urodynamic findings, incontinence severity, and treatment response. Obstet Gynecol. 2003 Jul;102(1):76-83. http://www.ncbi.nlm.nih.gov/pubmed/12850610
9. Kreder KJ Jr, rubaker L, Mainprize T. Tolterodine is equally effective in patients with mixed incontinence and those with urge incontinence alone. BJU Int. 2003 Sep;92(4):418-21. http://www.ncbi.nlm.nih.gov/pubmed/12930432
10. Staskin DR, Te AE. Short- and long-term efficacy of solifenacin treatment in patients with symptoms of mixed urinary incontinence. BJU Int. 200 6 Jun;97(6):1256-61. http://www.ncbi.nlm.nih.gov/pubmed/16686722
11. Kelleher C, Cardozo L, Kobashi K, et al. Solifenacin: as effective in mixed urinary incontinence as in urge urinary incontinence. Int Urogynecol J Pelvic Floor Dysfunct. 2006 Jun;17(4):382-8. http://www.ncbi.nlm.nih.gov/pubmed/16283422
12. Richter HE, Diokno A, Kenton K, et al. Predictors of treatment failure 24 months after surgery for stress urinary incontinence. J Urol. 2008 Mar;179(3):1024-30. http://www.ncbi.nlm.nih.gov/pubmed/18206917
13. Richter HE, Litman HJ, Lukacz ES, et al. Demographic and Clinical Predictors of Treatment Failure One Year After Midurethral Sling Surgery. Obstetrics and Gynaecology 2011 April;117(4):913-921. http://journals.lww.com/greenjournal/toc/2011/04000

14. Choe JH, Choo MS, Lee KS. The impact of tension-free vaginal tape on overactive bladder symptoms in women with stress urinary incontinence: significance of detrusor overactivity. [see comment]. J Urol. 2008 Jan;179(1):214-9.
http://www.ncbi.nlm.nih.gov/pubmed/18001792
15. Lagro/Janssen T, van Weel C. Long-term effect of treatment of female incontinence in general practice. Br J Gen Pract. 1998 Nov;48(436):1735-8.
http://www.ncbi.nlm.nih.gov/pubmed/10198479
16. Koonings P, Bergman A, Ballard CA. Combined detrusor instability and stress urinary incontinence: where is the primary pathology? Gynecol Obstet Invest. 1988;26(3):250-6.
http://www.ncbi.nlm.nih.gov/pubmed/324089
17. Botros SM, Aramov Y, Goldberg RP, et al. Detrusor overactivity and urge urinary incontinence following midurethral versus bladder sling procedures. Am J Obstet Gynecol. 2005 Dec;193(6):2144-8.
http://www.ncbi.nlm.nih.gov/pubmed/16325631
18. Duckett JR, Tamilselvi A. Effect of tensionfree vaginal tape in women with a urodynamic diagnosis of idiopathic detrusor overactivity and stress incontinence. BJOG. 2006 Jan;113(1):30-3.
http://www.ncbi.nlm.nih.gov/pubmed/16398768
19. Kuo HC. Effect of detrusor function on the therapeutic outcome of a suburethral sling procedure using a polypropylene sling for stress urinary incontinence in women. Scand J Urol Nephrol. 2007;41(2): 138-43.
http://www.ncbi.nlm.nih.gov/pubmed/17454953
20. Colombo M, Zanetta G, Vitobello D, et al. The Burch colposuspension for women with and without detrusor overactivity. Br J Obstet Gynaecol. 1996 Mar;103(3):255-60.
http://www.ncbi.nlm.nih.gov/pubmed/8630311
21. Lose G, SorensenHC, Axelsen SM, et al. An open multicenter study of polyacrylamide hydrogel (Bulkamid®) for female stress and mixed urinary incontinence. Int Urogynecol J. 2010 Dec;21(12):1471-7.
http://www.ncbi.nlm.nih.gov/pubmed/20645077
22. Kulseng-HanssenS, Husby H, Schiotz HA. The tension free vaginal tape operation for women with mixed incontinence: Do preoperative variables predict the outcome? Neurourol Urodyn. 2007;26(1):115-21; discussion 122.
http://www.ncbi.nlm.nih.gov/pubmed/16894616
23. Kulseng-Hanssen S, Husy H, Schiotz HA. Follow-up of TVT operations in 1,113 women with mixed urinary incontinence at 7 and 38 months. Int Urogynecol J Pelvic Floor Dysfunct. 2008 Mar;19(3): 391-6.
http://www.ncbi.nlm.nih.gov/pubmed/17891326


Woman presenting with Urinary Incontinence
Initial assessment
History GA
Physical examiniation GA
Questionnaire optional GC
Voiding dairy GB
Urinalysis GA
Post void residual if voiding difficulty GB
Pad test if quantification of leakage is desired GC
Reasons for specialist Referral
Haematuria
Pain
Recurrent UTI
Grade 3 or symptomatic prolapse
Previous pelvic radiotherapy
Previous surgery for UI
Pelvic mass
Suspicion of fistula
Discuss management
Stress Incontinence
Mixed Incontinence
Urgency Incontinence
Advise on bowels, drugs, co-morbidity, fluid intake GC
Advise on weight loss GA
Consider intervention related to cognitive impairment (scheduled voiding) GC
Offer pads if needed GB
Consider reducing caffeine intake GB
Consider topical oestrogen for post-menopausal women GA
Offer Desmopressin for short term symptom relief GB
Supervised, intensive PFMT +/- Biofeedback GA +/- Bladder training GB
Bladder training GB
Offer Duloxetine for temporary improvement GA
Anti-muscarinics GA
No response
Consider PTNS GB
Failed conservative or drug therapy
Stress Incontinence
Mixed Incontinence
Urgency Incontinence
Stress predominant
Urgency predominant
Offer MUS Consider peri-urethral injections for temporary relief of symptoms GA
Offer Botulinum toxin A or the opportunity for SNS GA
Offer fascial sling or colposuspension if MUS unavailable GA
Failure
Discuss bladder augmentation or urinary diversion GA
Re-evaluate patient and consider second-line surgery - re-enter algorithm at appropriate stage GA


Man presenting with Urinary Incontinence
Initial assessment
History GA
Physical examiniation GA
Questionnaire optional GC
Voiding dairy GB
Urinalysis GA
Post void residual if voiding difficulty GB
Pad test if quantification of leakage is desired GC
Reasons for specialist Referral
Haematuria
Pain
Recurrent UTI
Previous pelvic radiotherapy
Abnormal DRE
Findings suspicious of voiding dysfunction
Discuss management
Stress Incontinence
Mixed Incontinence
Urgency Incontinence
Advise on bowels, drugs, co-morbidity, fluid intake GC
Advise on weight loss GA
Consider intervention related to cognitive impairment (scheduled voiding) GC
Offer pads if needed GB
Consider reducing caffeine intake GB
Offer Desmopressin for short term symptom relief GB
Provide information on pelvic floor excercise GB
Bladder training GB
Offer Duloxetine for temporary improvement GA
Anti-muscarinics GA
Failed conservative or drug therapy
Perform urodynamics and cystoscopy and consider imaging of lower urinary tract (ie: exclude bladder outlet obstruction)
Stress Incontinence
Mixed Incontinence
Urgency Incontinence
Stress predominant
Urgency predominant
Consider peri-urethral injection for temporary relief, and minimally invasive compression devices GC
Consider fixed slings for men with PRPI GC
Offer AUS to men with persistent moderate to severe PPI GB
Offer Botulinum toxin A or the opportunity for treatment with SNS GA
Discuss bladder augmentation or urinary diversion GC

6. ABBREVIATIONS USED IN THE TEXT

This list is not comprehensive for the most common abbreviations.

ACT	adjustable compression therapy (device)
AHRQ	Agency for Healthcare Research and Quality
AUS	artificial urinary sphincter
BT	bladder training
BTX	botulinum toxin
CIC	clean intermittent catheterisation
CNS	central nervous system
DO	detrusor overactivity
EAU	European Association of Urology
ER	extended release
FS2S	first stage of two-stage [implantation of sacral neuromodulator]
GR	grade of recommendation
HRQoL	health-related quality of life
ICI	International Consultation on Incontinence
I-QoL	Incontinence Quality of Life
IR	immediate release
LE	level of evidence
LUTS	lower urinary tract symptoms
MPR	medication possession rate [drug adherence]
MRI	magnetic resonance imaging
MUI	mixed urinary incontinence
NICE	National Institute for Health and Clinical Excellence (UK)
OAB	overactive bladder
PFMT	pelvic floor muscle training
PICO	Population, Intervention, Comparison, Outcome
PNE	percutaneous nerve evaluation
PROMS	patient-reported outcome measures
PTNS	posterior tibial nerve stimulation
PVR	post-voiding residual volume
Q_{max}	maximum urinary flow rate
QoL	quality of life
RCT	randomised controlled trial
RP	radical prostatectomy
SIGN	Scottish Intercollegiate Guideline Network
SUI	stress urinary incontinence
TDS	transdermal delivery system
TVTS	tension-free vaginal tape secure
UI	urinary incontinence
US	ultrasound
UTI	urinary tract infection
UUI	urgency urinary incontinence

Conflict of interest

All members of the Urinary Incontinence Guidelines panel have provided disclosure statements on all relationships that they have and that might be perceived to be a potential source of conflict of interest. This information is kept on file in the European Association of Urology Central Office database. This guidelines document was developed with the financial support of the European Association of Urology. No external sources of funding and support have been involved. The EAU is a non-profit organisation and funding is limited to administrative assistance and travel and meeting expenses. No honoraria or other reimbursements have been provided.