EAU Guidelines on

Urinary Incontinence in Adults

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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 and the population studied. However, there is universal agreement about the importance of the problem in terms of human suffering and economic cost.

1.1 Aim and objectives

These Guidelines from the European Association of Urology (EAU) Working Panel on Urinary Incontinence are written by a multidisciplinary group, primarily for urologists, and are likely to be referred to by other professional groups. They aim to provide sensible and practical evidence-based guidance on the clinical problem of UI rather than an exhaustive narrative review. Such a review is already available from the International Consultation on Incontinence [1], and so the EAU Guidelines do not describe 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, or in children, as this is covered by complementary EAU Guidelines [2, 3].

The elderly

The Panel decided to include a separate but complimentary set of recommendations referring to the elderly population within each section. Older people with UI deserve special consideration for a number of reasons. Physiological changes with natural ageing mean that all types of UI become more common with increasing age. Urinary incontinence commonly co-exists with other comorbid conditions, reduced mobility, and impaired cognition and may require specific interventions, such as assisted toileting.

For the elderly person expectations of assessment and treatment may need to be modified to fit in with specific circumstances, needs, and preferences, while taking into account any loss of capacity for consent. When the urologist is dealing with a frail elderly patient with urinary incontinence, collaboration with other healthcare professionals such as elderly care physicians is recommended.

It must be emphasised that clinical guidelines present the best evidence available to the experts. However, following guideline recommendations will not necessarily result in the best outcome. Guidelines can never replace clinical expertise when making treatment decisions for individual patients, but rather help to focus decisions - also taking personal values and preferences/individual circumstances of patients into account.

1.2 Panel composition

The EAU Urinary Incontinence Panel consists of a multidisciplinary group of experts, including urologists, a gynaecologist and a physiotherapist. All experts involved in the production of this document have submitted potential conflict of interest statements which can be viewed on the EAU website: http://www.uroweb.org/guideline/urinary-incontinence.

1.3 Available publications

A quick reference document (Pocket Guidelines) is available, both in print and in a number of versions for mobile devices. These are abridged versions which may require consultation together with the full text versions. Two scientific publications in the journal European Urology are also available [4, 5]. All documents are accessible through the EAU website: http://www.uroweb.org/guideline/urinary-incontinence.

1.4 Publication history

The EAU published the first Urinary Incontinence Guidelines in 2001 with updates in 2012, 2013, 2014 and 2015. For this 2016 print updates were made to:

- 4.1 Conservative Management;
- 4.2.8 Oestrogen;
- 4.3.6.1 Bladder wall injection of botulinum toxin A.

2. METHODS

2.1 Introduction

For the 2016 Urinary Incontinence Guidelines, new and relevant evidence has been identified, collated and appraised through a structured assessment of the literature.

References used in this text are assessed according to their level of evidence (LE) and Guidelines are given a grade of recommendation (GR), according to a classification system modified from the Oxford Centre for Evidence-Based Medicine Levels of Evidence [6]. Additional methodology information can be found in the general Methodology section of this print, and online at the EAU website: http://www.uroweb.org/guideline/. A list of Associations endorsing the EAU Guidelines can also be viewed online at the above address.

The current Guidelines provide:

- A clear 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 authoritative summary of the current state of evidence on clinical topics, complete with references to the original sources.
- 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 high-quality evidence.

In this edition the Panel has continued to focus, 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. An appendix is included on non-obstetric genitourinary fistulae. The subject of prevention of urinary incontinence has not been addressed. A systematic review on nocturnal incontinence found no studies on the topic. We are of the opinion nocturnal incontinence should be considered in future research studies.

2.2 Review

This document was subjected to peer review prior to publication in 2015. The decision for re-review is made based on the extent of the revision. A major revision resulting in significant changes to the clinical recommendations presented in the text will warrant re-review.

2.3 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;

- **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.
- **Do not** perform (i.e. 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.

3. DIAGNOSTIC EVALUATION

3.1 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 UI, associated voiding and other urinary symptoms. The history should allow UI to be categorised into stress urinary incontinence (SUI), urgency urinary incontinence (UUI) or mixed urinary incontinence (MUI). It should also identify patients who need rapid referral to an appropriate specialist. These include patients with associated pain, haematuria, a history of recurrent urinary tract infection (UTI), pelvic surgery (particularly prostate surgery) or radiotherapy, constant leakage suggesting a fistula, voiding difficulty or suspected neurological disease. In women, 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 other ill health and for the details of current medications, as these may impact on symptoms of UI.

Similarly, there is little evidence from clinical trials that carrying out a clinical examination improves care, but wide consensus suggests that it remains an essential part of assessment of people with UI. It should include abdominal examination, to detect an enlarged bladder or other abdominal mass, and perineal and digital examination of the rectum (prostate) and/or vagina. Examination of the perineum in women includes an assessment of oestrogen status and a careful assessment of any associated pelvic organ prolapse (POP). A cough test may reveal SUI if the bladder is sufficiently full and pelvic floor contraction together with urethral mobility can be assessed digitally.

3.2 Patient questionnaires

This section includes symptom scores, symptom questionnaires, scales, indexes, patient reported outcome measures (PROMs) and health-related quality of life (HRQoL) measures. The latter include generic or condition specific measures. Questionnaires should have been validated for the language in which they are being used, and, if used for outcome evaluation, must have been shown to be sensitive to change. The methodology for questionnaire development was reviewed in the 5th International Consultation on Incontinence in 2012 [7].

*3.2.1 **Questions***

- In patients with UI, can the use of Questionnaires/PROMS differentiate between stress, urgency and mixed incontinence, and does this differentiation impact on QoL after treatment?
- In adults with UI, does assessment using either urinary symptom or QoL questionnaires improve 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?

*3.2.2 **Evidence***

Although many studies have investigated the validity and reliability of urinary symptom questionnaires and PROMs most have taken place in adults without UI. This limits the extent to which results and conclusions from these studies can be applied in adults with UI. Some questionnaires (QUID, 3IQ) have potential to discriminate UI types in women [8, 9]. In men ICIQ-UI-SF score does not differentiate UI types [10]. Some are responsive to change and may be used to measure outcomes, though evidence on their sensitivity is inconsistent [11-13].

No evidence was found to indicate whether use of QoL or condition specific questionnaires have an impact on outcome of treatment.

Table 1 shows a summary of the ICUD review, 2012, with recent additions. Criteria on which questionnaires are assessed include validity, reliability and responsiveness to change.

Table 1: Summary of the ICUD review 2012*.

	Category A (all 3 criteria fulfilled)**	Category B (2 criteria fulfilled)**	Category C (only 1 criterion fulfilled)**
Symptom measures and health related QOL measures	ICIQ-UI Short Form, ICIQFLUTS,ICIQ-MLUTS IIQ and IIQ-7, I-QOL (ICIQ-Uqol), ISS, KHQ, LIS (interview), N-QoL, OAB-q SF, OAB-q (ICIQOABqol), PFDI and PFDI-20, PFIQ and PFIQ-7, PRAFAB, UISS	Contilife, EPIQ, LUTS tool IOQ,YIPS	ABSST ISI, ISQ, UIHI, UIQ
Measure of patient satisfaction (patient's measure of treatment satisfaction)	BSW, OAB-S, OABSAT-q, TBS	PPQ	EPI, GPI, PSQ
Goal attainment scales		SAGA	
Screening tools (used to identify patients with UI)	B-SAQ, OAB-SS, OABV8, OAB-V3, QUID	ISQ, USP	3IQ, CLSS, MESA, PUF
Patient symptom scale			
Assessment of symptom bother and overall bother	PPBC, UDI or UDI-6, LUSQ, PGI-I and PGI-S	PFBQ, SSI and SII	PMSES, POSQ, UI-4
Assessment of the impact of urgency	IUSS, U-IIQ, UU Scale, U-UDI	PPIUS, SUIQ, UPScore, UPScale, UQ, USIQ-QOL, USIQ-S, USS	
Questionnaires to assess sexual function and urinary symptoms		FSFI, ICIQ-VS, PISQ, SQoL-F	SFQ
Treatment adherence Measures		MASRI	

** For all abbreviations please see the 2016 Abbreviations List in Appendix A.*
*** Criteria on which questionnaires are assessed include validity, reliability and responsiveness to change.*

To date, there is no one questionnaire that fulfils all requirements for assessment of people with UI. Clinicians must evaluate the tools which exist, for use alone or in combination, for assessment and monitoring of treatment outcome [14].

The questionnaires can be found on the following websites: www.iciq.net, www.proqolid.org, www.mapi-institute.com, www.pfizerpatientreportedoutcomes.com, www.ncbi.nlm.nih.gov.

Summary of evidence	LE
Validated condition specific symptom scores assist in the screening for, and categorisation of UI.	3
Validated symptom scores measure the severity of UI.	3
Both condition specific and general health status questionnaires measure current health status, and change following treatment.	3

Recommendation	GR
Use a validated and appropriate questionnaire when standardised assessment is required.	B*

** Recommendation based on expert opinion.*

3.3 Voiding diaries

Measurement of the frequency and severity of LUTS is an important step in the evaluation and management of lower urinary tract (LUT) dysfunction, including UI. Voiding diaries are a semi-objective method of quantifying symptoms, such as frequency of UI 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.

Discrepancy between diary recordings and the patient rating of symptoms, e.g. frequency or UI, can be useful in patient counselling. 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. In patients with severe UI, a voiding diary is unlikely to accurately report 24-hour urine output and so voided volume may be lower than total bladder capacity.

*3.3.1 **Questions***

- In adults with UI, what is the reliability, diagnostic accuracy and predictive value of a voiding diary compared to patient history or symptom score?

*3.3.2 **Evidence***

Two articles have suggested a consensus has been reached in the terminology used in voiding [15, 16]. However the terms micturition diary, frequency voiding chart and voiding diary, have been used interchangeably for many years and include information on fluid intake, times of voiding, voided volumes, incontinence episodes, pad usage, degree of urgency and degree of UI recorded for at least 24 hours. When reviewing the evidence all possible terminology has been included.

Two studies have demonstrated the reproducibility of voiding diaries in both men and women [17, 18]. Further studies have demonstrated variability of diary data within a 24-hour period and compared voided volumes recorded in diaries with those recorded by uroflowmetry [19, 20]. Another study found that keeping a voiding diary had a therapeutic benefit [21].

A number of observational studies have demonstrated a close correlation between data obtained from voiding diaries and standard symptom evaluation [22-25].

Summary of evidence	**LE**
Voiding diaries of 3-7 days duration are a reliable tool for the objective measurement of mean voided volume, day time and night time frequency and incontinence episode frequency.	2b
Voiding diaries are sensitive to change and are a reliable measure of outcome.	2b

Recommendations	**GR**
Ask patients with urinary incontinence to complete a voiding diary.	A
Use a diary duration of between 3 and 7 days.	B

3.4 Urinalysis and urinary tract infection

Reagent strip ('dipstick') urinalysis may indicate urinary tract infection (UTI), proteinuria, haematuria or glycosuria requiring further assessment. Refer to the Urological Infections Guideline for diagnosis and treatment of UTI [26].

*3.4.1 **Questions***

- In adults with UI, what is the diagnostic accuracy of urinalysis to detect UTI?
- In adults with UI does treatment of UTI or asymptomatic bacteriuria cure or improve UI compared to no treatment?

*3.4.2 **Evidence***

Urinalysis negative for nitrite and leucocyte esterase reliably excludes UTI in people with UI [27] and should be included, with urine culture when necessary, in the evaluation of all patients with UI. Urinary incontinence may occur during symptomatic UTI [28] and existing UI may worsen during UTI [29]. The rate and severity of UI was unchanged after eradication of asymptomatic bacteriuria in nursing home residents [30].

Summary of evidence	**LE**
Urinalysis negative for nitrite and leucocyte esterase reliably excludes UTI.	1
UI may be a symptom during UTI.	3
The presence of a symptomatic UTI worsens symptoms of UI.	3
Elderly nursing home patients with UI do not benefit from treatment of asymptomatic bacteriuria.	2

Recommendations	GR
Preform urinalysis as a part of the initial assessment of a patient with urinary incontinence.	A*
If a symptomatic urinary tract infection is present with urinary incontinence, reassess the patient after treatment.	A*
Do not routinely treat asymptomatic bacteriuria in elderly patients to improve urinary incontinence.	B

** Recommendation based on expert opinion.*

3.5 Post-voiding residual volume

Post-voiding residual (PVR) volume 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 UTI, upper urinary tract (UUT) 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 in patients with UI is uncertain, partly because of the lack of a standard definition of an abnormal PVR volume.

*3.5.1 **Question***

In adults with UI, what is the value of measuring PVR?

*3.5.2 **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 [31-36] have led to the consensus that US measurement of PVR is preferable to catheterisation.

In peri- and postmenopausal women without significant LUTS or pelvic organ symptoms, 95% of women had a PVR < 100 mL [37]. In women with UUI, a PVR > 100 mL was found in 10% of cases [38]. Other research has found that a high PVR is associated with POP, voiding symptoms and an absence of SUI [37, 39-41].

In women with SUI, the mean PVR was 39 mL measured by catheterisation and 63 mL measured by US, with 16% of women having a PVR > 100 mL [38].

Summary of evidence	LE
Lower urinary tract symptoms coexisting with UI are associated with a higher rate of PVR compared to asymptomatic subjects.	2

Recommendations	GR
When measuring post void residual urine volume, use ultrasound.	A
Measure post-voiding residual in patients with urinary incontinence who have voiding symptoms.	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, including surgery for stress urinary incontinence.	A*

** Recommendation based on expert opinion.*

3.6 Urodynamics

Urodynamic testing is widely used as an adjunct to clinical diagnosis, in the belief that it may help to provide or confirm diagnosis, predict treatment outcome, or facilitate discussion during counselling For all these reasons, urodynamics is often performed prior to invasive treatment for UI. These Guidelines will focus on invasive tests, including multichannel cystometry, ambulatory monitoring and video-urodynamics, and different tests of urethral function, such as urethral pressure profilometry, Valsalva leak point pressure estimation and retrograde urethral resistance measurement.

*3.6.1 **Question***

In adults with UI, what is the reproducibility, diagnostic accuracy and predictive value of urodynamic testing?

*3.6.2 **Evidence***

3.6.2.1 Variability

In common with most physiological tests there is variability in urodynamics results. Numerous small studies of

multichannel cystometry have been done over many years in differing populations. Whilst in healthy women the same session repeatability has been shown to be poor [42], in those with incontinence it may be acceptable [43]. Measurement of urethral closure pressure (MUCP) correlates poorly with incontinence severity [44] and there is conflicting evidence about its reproducibility [45, 46]. One method of recording MUCP cannot be compared meaningfully to another [47].

Valsalva leak point pressures are not standardised and there is minimal evidence about reproducibility. Valsalva leak point pressure did not reliably assess incontinence severity in a cohort of women selected for surgical treatment of SUI [48]. The predictive value of the tests, regarding the outcome of treatment, remains unclear.

No studies on the reproducibility of ambulatory monitoring were found.

3.6.2.2 Diagnostic accuracy

The diagnostic accuracy of urodynamics is assessed in terms of its correlation with clinical diagnosis of UI and incontinence severity. The problem is that clinical diagnosis and urodynamic findings often do not correlate [49, 50], and normal healthy people may have urodynamic abnormalities.

The diagnostic accuracy of urethral pressure profilometry [44] and 'Urethral Retro resistance' is generally poor [51]. Urethral reflectometry may have greater diagnostic accuracy but its clinical role remains unclear [52].

Ambulatory urodynamics may detect unexpected physiological variance from normal more often than conventional cystometry, but the clinical relevance of this is uncertain [53, 54].

3.6.2.3 Does urodynamics influence the outcome of conservative therapy?

A Cochrane review of seven RCTs showed that use of urodynamic tests increased the likelihood of prescribing drugs or avoiding surgery. However, there was no evidence that this influence on decision making altered the clinical outcome of treatment [55]. Subanalysis of an RCT comparing fesoterodine to placebo [56, 57] showed no predictive value for treatment response, by the urodynamic diagnosis of DO.

3.6.2.4 Does urodynamics influence the outcome of surgery for urinary incontinence?

A high quality RCT (n = 630) compared office evaluation alone to office evaluation and urodynamics in women with clinical demonstrable SUI about to undergo surgery for SUI. Whilst urodynamics changed the clinical diagnosis in 56% of women [58] there was no difference in levels of UI or any secondary outcome at 12 months follow-up after surgery [59]. Another similar study was closed with only 59 women [60] after finding no difference in outcome. It was then redesigned so that patients in whom urodymanics were discordant with clinical assessment (n = 109) were randomly allocated to receive either immediate surgery or individually tailored therapy based on urodynamics. In this trial, performing immediate surgery irrespective of the result of urodynamics did not result in inferior outcomes [61].

In observational studies there is no consistent correlation between the result of urethral function tests and subsequent success or failure of SUI surgery [23, 25, 26, 62]. The same is true for a secondary analysis of an RCT [63].

Augmentation cystoplasty is only performed in patients with a urodynamic diagnosis of DO so no statement can be made about predictive value for this group [57].

The Panel recognise that it may be valuable to use urodynamic test results to choose the optimum surgical procedure but at the time of this review there is inconsistent evidence to show any predictive value that would support this approach.

3.6.2.5 Does urodynamics help to predict complications of surgery for UI?

There have been no RCTs designed to answer this question.

The presence of pre-operative DO has been associated with post-operative UUI, but did not predict overall treatment failure following mid-urethral sling [63] or following sling surgery or colposuspension.

Whilst low pre-operative flow rate has been shown to correlate with post-operative voiding dysfunction [64, 65], post hoc analysis of two high quality surgical trials showed that no pre-operative urodynamic parameter had the ability to predict post-operative voiding dysfunction in a selected population of women with low preoperative PVR [66, 67].

3.6.2.6 Does urodynamics influence the outcome of treatment for post-prostatectomy urinary incontinence in men?

There are no RCTs examining the clinical usefulness of urodynamics in post-prostatectomy UI. Whilst urodynamics will distinguish causes of incontinence, its ability to predict outcome of surgery for incontinence for these men is uncertain [68, 69].

Summary of evidence	**LE**
Most urodynamic parameters show variability within the same session and over time, and this limits their clinical usefulness.	3
Different techniques of measuring urethral function may have good test-retest reliability, but do not consistently correlate to other urodynamic tests or to the severity of UI.	3
There is limited evidence that ambulatory urodynamics is more sensitive than conventional urodynamics for diagnosing SUI or DO.	2
There may be inconsistency between history and urodynamic results.	3
Preliminary urodynamics can influence the choice of treatment for UI, but does not affect the outcome of conservative therapy or drug therapy for SUI.	1a
Preoperative urodynamics in women with uncomplicated, clinically demonstrable SUI does not improve the outcome of surgery for SUI.	1b
There is no consistent correlation between the result of urethral function tests and subsequent success or failure of SUI surgery.	3
There is no consistent evidence that pre-operative DO is associated with surgical failure of mid-urethral sling in women.	3
The presence of preoperative DO may be associated with persistence of urgency postoperatively	3
There is no evidence that urodynamics predicts the outcomes of treatment for post-prostatectomy incontinence in men.	4

Recommendations ***(NB: Concerning only neurologically intact adults with urinary incontinence)***	**GR**
Clinicians carrying out urodynamics in patients with urinary incontinence should: • Ensure that the test replicates the patient's symptoms. • Interpret results in the 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 predict the outcome of treatment for uncomplicated urinary incontinence.	C
Do not routinely carry out urodynamics when offering treatment for uncomplicated urinary incontinence.	B
Perform urodynamics if the findings may change the choice of invasive treatment.	B
Do not use urethral pressure profilometry or leak point pressure to grade severity of incontinence or predict the outcome of treatment.	C
Urodynamic practitioners should adhere to standards defined by the International Continence Society.	C

3.6.3 ***Research priority***

Does any individual urodynamic test, or combination of tests, influence the choice of treatments or prediction of treatment outcome for UI?

3.7 Pad testing

Measurement of urine loss using an absorbent pad worn over a set period of time or during a protocol of physical exercise can be used to quantify the presence and severity of UI, as well as a patient's response to treatment.

3.7.1 ***Question***

- In adults with UI, what is the reliability, diagnostic accuracy and predictive value of pad testing?
- In adults with UI is one type of pad test better than another?

3.7.2 ***Evidence***

The clinical usefulness of pad tests for people with UI has been assessed in two systematic reviews [70, 71].

A 1-hour pad test using a standardised exercise protocol and a diagnostic threshold of 1.4 g shows good specificity but lower sensitivity for symptoms of SUI and MUI. A 24-hour pad test using a threshold of 4.4 g is more reproducible but is difficult to standardise with variation according to activity level [72]. Pad test with a specific short graded exercise protocol also has diagnostic value but a negative test should be repeated or the degree of provocation increased [73]. The usefulness of pad tests in quantifying severity and predicting outcome of treatment is uncertain [70, 74] although early post-operative testing may predict future continence in men after prostatectomy [75]. Pad test is responsive to change following successful treatment [76]. There is no evidence that one type of pad test is superior to another.

Summary of evidence	**LE**
A pad test can diagnose UI accurately.	2
Standardisation of bladder volume and degree of provocation improves reproducibility.	2
24 hours is sufficient duration for home-based testing balancing diagnostic accuracy and adherence.	2
Change in leaked urine volume on pad tests can be used to measure treatment outcome.	2

Recommendations	**GR**
Have a standardised duration and activity protocol for pad test.	B
Use a pad test when quantification of urinary incontinence is required.	C
Use repeat pad test after treatment if an objective outcome measure is required.	C

*3.7.3 **Research priority***

- Do the results of pad testing influence the choice of treatments or the prediction of the outcome of treatment for UI?
- Does the amount of physical activity influence the outcome of 24-hour pad testing leading to overestimation of the severity of incontinence?

3.8 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 anatomy and function, between conditions of the central nervous system (CNS) or of the lower urinary tract (LUT) and UI, and to investigate the relationship between LUT and pelvic floor imaging and treatment outcome.

US and magnetic resonance imaging (MRI) have largely replaced X-ray imaging. Ultrasound is preferred to MRI because of its ability to produce three-dimensional and four-dimensional (dynamic) images at lower cost and wider availability. Studies on LUT imaging in patients with UI often include an evaluation of surgical outcomes, making design and conduct of these trials challenging.

*3.8.1 **Questions***

In adults with UI:

- What is the reliability and accuracy of imaging in the diagnosis of UI?
- Do the results of imaging influence the choice of treatment for UI?
- Do the results of imaging help predict outcome of treatment for UI?
- Do the results of imaging help evaluate outcome of treatments for UI?

*3.8.2 **Evidence***

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 [77]. In addition, the generalised increase in urethral mobility after childbirth does not appear to be associated with *de novo* SUI [78].

There is a general consensus that MRI provides good global pelvic floor assessment, including POP, defecatory function and integrity of the pelvic floor support [79]. However, there is a large variation in MRI interpretation between observers [80] and little evidence to support its clinical usefulness in the management of UI.

Studies have assessed the use of imaging to assess the mechanism of mid-urethral sling insertion for SUI. One study suggested that mid-urethral sling placement decreased mobility of the mid-urethra but not mobility of the bladder neck [81]. Following midurethral sling, a wider gap between symphysis and sling (assessed by imaging) has been shown to correlate with a lower chance of cure of SUI [82].

Several imaging studies have investigated the relationship between sphincter volume and function in women [83] and between sphincter volume and surgery outcome in men and women [84, 85]. In patients undergoing radical prostatectomy, longer membranous urethra before and after surgery was associated with a higher rate of continence [86]. However, no imaging test has been shown to predict the outcome of treatment for UI. Imaging of the pelvic floor can identify levator ani detachment and hiatus size, although there is little evidence of a relationship to clinical benefit after treatment of UI.

Detrusor wall thickness

As overactive bladder syndrome (OAB) has been linked to detrusor overactivity, it has been hypothesised that frequent detrusor contractions may increase detrusor/bladder wall thickness (DWT/BWT). However, there is no evidence that BWT/DWT imaging improves management of OAB in practice. No consensus exists as to the relationship between OAB and increased BWT/DWT [87].

Summary of evidence	**LE**
Imaging can reliably be used to measure bladder neck and urethral mobility, although there is no evidence of clinical benefit for patients with UI.	2b
There is no consistent evidence that bladder (detrusor) wall thickness measurement is useful in the management of UI.	3

Recommendation	**GR**
Do not routinely carry out imaging of the upper or lower urinary tract as part of the assessment of urinary incontinence.	A

*3.8.3 **Research priority***

More research is needed into the relationship between sling position, as determined by imaging, and surgical outcome.

4. DISEASE MANAGEMENT

4.1 Conservative management

In clinical practice, it is the convention that non-surgical therapies are tried first because they usually carry the least risk of harm. They are often used in combination which makes it difficult to determine which components are effective. Containment devices play an important role, especially for individuals who prefer to avoid the risks of interventional treatments, or in whom active treatment is impossible for any reason.

*4.1.1 **Simple clinical interventions***

4.1.1.1 Underlying disease/cognitive impairment

Urinary incontinence, especially in the elderly has been associated with multiple comorbid conditions including

- cardiac failure
- chronic renal failure
- diabetes
- chronic obstructive pulmonary disease
- neurological disease including stroke and multiple sclerosis
- general cognitive impairment
- sleep disturbances, e.g. sleep apnoea
- depression
- metabolic syndrome

It is possible that improvement of associated 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 alteration in an underlying disease has affected a patient's UI.

4.1.1.1.1 Question

In adults with UI, does improving an associated condition improve UI compared to no correction of that condition?

4.1.1.1.2 Evidence

There is compelling evidence that the prevalence of UI in women with type 2 diabetes is higher. One study showed no correlation between earlier intensive treatment of type 1 diabetes mellitus and the prevalence of UI in later life vs. conventional treatment [88].

Summary of evidence	LE
There is a lack of evidence that improving any associated condition improves UI.	3

Recommendation	GR
Patients with UI who have associated conditions, should have appropriate treatment for those conditions in line with good medical practice.	A*

** Recommendation based on expert opinion.*

4.1.1.2 Adjustment of other (non-incontinence) medication

Although UI is listed as an adverse effect of many drugs in drug compendia, this mainly results from 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. In most cases, it is therefore not possible to be sure that a drug causes UI.

In patients with existing UI, particularly the elderly, it may be difficult or impossible to distinguish between the effects of medication, comorbidity or ageing on UI. Although changing drug regimens for underlying disease may be considered as a possible early intervention for UI, there is very little evidence of benefit [49]. There is also a risk that stopping or altering medication may result in more harm than benefit.

4.1.1.2.1 Question

In adults with UI, does adjustment of other (non-incontinence) medication improve UI compared to no change in treatment?

4.1.1.2.2 Evidence

Structured literature review failed to identify any studies addressing whether adjustment of specific medications could alter existing symptoms of UI. Also there is little evidence relating to the occurrence or worsening of UI in relation to prescription of any specific drugs.

Summary of evidence	LE
There is very little evidence that alteration of non-incontinence medication can cure or improve symptoms of urinary incontinence.	3

Recommendations	GR
Take a drug history from all patients with urinary incontinence.	A
Review any new medication associated with the development or worsening of urinary incontinence.	C

4.1.1.3 Constipation

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

4.1.1.3.1 Question

Does treatment for constipation improve UI?

4.1.1.4 Evidence

Two, large, cross-sectional population-based studies [89, 90] and two longitudinal studies [91, 92] showed that constipation was a risk factor for LUTS. An observational study comparing women with UI and women with pelvic organ prolapse (POP) to controls found that a history of constipation was associated with both prolapse

and UI [93]. 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 [94].

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

Summary of evidence	**LE**
There is a consistent association between a history of constipation and the development of UI and pelvic organ prolapse.	3
There is no consistent evidence in adults, that treatment of constipation alone improves UI.	4

Recommendation	**GR**
Adults with urinary incontinence who also suffer from constipation should be given advice about bowel management in line with good medical practice.	C

4.1.1.4.1 Research priority
Does the normalisation of bowel habit improve UI in patients who are constipated?

4.1.1.5 Containment
Containment is important for people with UI when active treatment does not cure the problem, or when it is not available or not possible. Some individuals may prefer to choose containment rather than undergo active treatment with its associated risks. This includes the use of absorbent pads, urinary catheters, external collection devices, penile clamps for men and intravaginal devices for women. Studies of catheter use are not specific to patients with non-neurogenic UI. Detailed literature summaries can be found in the current ICUD monograph [1] and in European Association of Urological Nurses guidance documents [95-97]. A useful resource for health care professionals and patients can be found at: www.continenceproductadvisor.org

4.1.1.5.1 Question
For adults with UI, is one type of containment device better than another?

4.1.1.5.2 Evidence
One RCT involving elderly women in care comparing management with pads to indwelling urethral catheter found no difference in dependency level or skin integrity score at six months [98]. Use of an external sheath was compared with indwelling catheterisation over 30 days in an RCT involving elderly men resident in hospital [99], there were no differences in bacteriuria or symptomatic UTI but the sheath was more comfortable. A short-term (2 weeks) crossover RCT in men with UI found that disease specific QoL was better when using an external sheath and more men preferred it, compared to pads [100].

4.1.1.5.3 Question
For men or women with UI is one type of pad better than another?

4.1.1.5.4 Evidence
A systematic review of six RCTs comparing different types of pads found that pads filled with superabsorbent material were better than standard pads, whilst evidence that disposable pads were better than washable pads was inconsistent [101]. For men with light UI a randomised crossover trial found that a leaf-shaped type of pad was preferred to rectangular pads [102]. A series of three crossover RCTs examined performance of different pad designs for differing populations [103]. For women with light UI, disposable insert pads (within washable pouch pants) were most effective. In adults with moderate/severe incontinence, disposable pull-up pants were more effective for women, whilst for men disposable diapers were more effective during the day and washable diapers at night.

4.1.1.5.5 Question
For men or women with UI is one type of catheter or external collection device better than another?

4.1.1.5.6 Evidence
A Cochrane review summarised three RCTs comparing different types of long-term indwelling catheters and

found no evidence that one catheter material or type of catheter was superior to another [104]. A systematic review of non-randomised studies found no differences in UTI outcome or UUT changes between use of suprapubic or urethral catheter drainage however, patients with suprapubic catheters were less likely to have urethral complications [105]. For people using intermittent catheterisation, a Cochrane review found no evidence that one type of catheter or regimen of catheterisation was better than another [106]. However, there is recent evidence from a narrative review suggesting that in certain populations using single use catheters may reduce urethral trauma and UTI [107]. A Cochrane review summarising five trials comparing washout policies in adults with indwelling urinary catheters found inconsistent evidence of benefit [108].

A further Cochrane review summarising eight trials testing whether antibiotic prophylaxis was beneficial for adults using intermittent or indwelling catheterisation found it reduced incidence of symptomatic UTI but possible harms were not assessed [109].

4.1.1.5.7 Question

For men and women with UI, are external pressure devices more effective than standard treatment and is one device better than another?

4.1.1.5.8 Evidence

A crossover RCT in 12 men with post-prostatectomy incontinence found a hinge-type penile clamp to be more effective than circular clamps for control of UI and was preferred by participants although it reduced penile blood flow [110].

A Cochrane review summarised seven trials comparing mechanical devices in women with UI finding limited evidence that SUI was reduced by intravaginal devices, no evidence on the effectiveness of intra-urethral devices and that there was no difference in control of UI between intravaginal and intra-urethral devices [111]. There was no difference in outcome at 12 months in women with SUI between vaginal pessary alone; PFMT alone; and vaginal pessary + PFMT, although vaginal pessary was inferior to PFMT at three months for bother from UI.

Summary of evidence	**LE**
Pads are effective in containing urine.	1b
Hinge-type penile clamps are more effective than circular clamps to control SUI in men.	2a
Vaginal devices may improve SUI in women in selective groups.	2a

Recommendations	**GR**
Ensure that adults with urinary incontinence and/or their carers are informed regarding available treatment options before deciding on containment alone.	A*
Suggest use of disposable insert pads for women and men with light urinary incontinence.	A*
In collaboration with other healthcare professionals with expertise in urinary incontinence help adults with moderate/severe urinary incontinence to select the individually best containment regimen considering pads, external devices and catheters, and balancing benefits and harms.	A*
Choice of pad from the wide variety of different absorbent materials and designs available should be made with consideration of the individual patient's circumstance, degree of incontinence and preference.	B

** Recommendation based on expert opinion.*

4.1.1.5.9 Research priority

To develop methods for assessing the best method of containment for individual adults with UI.

*4.1.2 **Lifestyle interventions***

Examples of lifestyle factors that may be associated with incontinence include obesity, smoking, level of physical activity and diet. Modification of these factors may improve UI.

4.1.2.1 Caffeine reduction

Many drinks contain caffeine, particularly tea, coffee and cola. Anecdotal evidence of urinary symptoms being aggravated by excessive caffeine intake has focused attention on whether caffeine reduction may improve UI. However, a cross-sectional population survey found no statistical association between caffeine intake and UI [112]. Lack of knowledge about caffeine content of different drinks has made the role of caffeine reduction in alleviating UI difficult to assess.

4.1.2.1.1 Question

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

4.1.2.1.2 Evidence

Four studies were found on the effect of caffeine reduction on UI [113-116]. They were of moderate quality and the results were inconsistent. The studies were mainly in women, so results can only be cautiously generalised to men [114, 115]. One RCT showed that reducing caffeine intake as an adjunct to behavioural therapy resulted in reduced urgency but not reduced UI compared to behavioural therapy alone [114]. Another RCT found that reducing caffeine had no benefit for UI [115]. A further interventional study in the elderly showed borderline significance for the benefit of reducing caffeine intake on UI [116]. In a large prospective cohort study there was no evidence that caffeine reduction reduced the risk of progression of UI over 2 years [117].

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

4.1.2.2 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.

4.1.2.2.1 Question

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

4.1.2.2.2 Evidence

The association between exercise and UI is unclear. Four studies [112, 118-120] in differing populations concluded that strenuous physical exercise increases the risk of SUI during periods of physical activity. There is also consistent evidence that physically active females and elite athletes experience higher levels of SUI than control populations [121-126]. On the other hand, the presence of UI may prevent women from taking exercise [127]. There is no evidence that strenuous exercise predisposes athletes to the development of SUI later in life [128]. 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 [129, 130].

The elderly

Three RCTs in the elderly confirmed that exercise, as a component of a multidimensional regime including PFMT and weight loss, was effective in improving UI in women. It is not clear which component of such a scheme is most important [94, 131, 132].

Summary of evidence	**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
Moderate exercise is associated with lower rates of UI in middle-aged or older women.	2b

4.1.2.3 Fluid intake

Modification of fluid intake, particularly restriction, is a strategy commonly used by people with UI to relieve symptoms. Advice on fluid intake given by healthcare professionals should be based on 24-hour fluid intake and urine output measurements. Form a general health point of view it should be advised that fluid intake should be sufficient to avoid thirst and that low or high 24-hour urine output should be investigated.

4.1.2.3.1 Question

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

4.1.2.3.2 Evidence

The few RCTs [115, 133, 134] provide inconsistent evidence. In most studies, the instructions for fluid intake were individualised and it is difficult to assess participant adherence to protocol. All available studies were in women. A recent RCT [134] showed that a reduction in fluid intake by 25% improved symptoms in patients with OAB but not UI. Personalised fluid advice compared to generic advice made no difference to continence outcomes in people receiving antimuscarinics for OAB, according to an RCT comparing drug therapy alone to drug therapy with behavioural advice [135].

Summary of evidence	LE
There is conflicting evidence on whether fluid modification improves UI.	2

4.1.2.4 Obesity and weight loss

Being overweight or obese has been identified as a risk factor for UI in many epidemiological studies [136, 137]. There is evidence that the prevalence of both UUI and SUI increases proportionately with rising body mass index [138]. The proportion of patients who undergo surgery for incontinence who are overweight or obese is higher than that of the general population. [139].

4.1.2.4.1 Question

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

4.1.2.4.2 Evidence

All the available evidence relates to women. Three systematic reviews plus 2 large RCTs concluded that weight loss was beneficial in improving UI [136, 137, 140]. Five further RCTs reported a similar beneficial effect on incontinence following surgical weight reduction programmes [141-144].

Two large studies in women with diabetes, for whom weight loss was the main lifestyle intervention showed UI did not improve but there was a lower subsequent incidence of UI among those who lost weight [141, 145]. There have been other cohort studies and case-control studies suggesting similar effects, including surgery for the morbidly obese [146-150].

Summary of evidence	LE
Obesity is a risk factor for UI in women.	1b
Non-surgical weight loss in overweight and obese women improves UI.	1a
Surgical weight loss improves UI in obese women.	1b
Weight loss in obese women improves UI.	1b
Weight loss in obese adults with diabetes mellitus reduces the risk of developing UI.	1b

4.1.2.5 Smoking

Smoking cessation is now a generalised public health measure and has been shown to be associated with urgency frequency and UI [112] [151].

4.1.2.5.1 Question

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

4.1.2.5.2 Evidence

The effect of smoking cessation on UI was described as uncertain in a Cochrane review [152].

Summary of evidence	LE
There is no evidence that smoking cessation will improve the symptoms of UI.	4

4.1.2.6 Recommendations for lifestyle interventions

Recommendations	GR
Encourage obese women with urinary incontinence to lose weight and maintain weight loss.	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 in line with good medical practice.	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.	A

4.1.2.7 Research priority

Which lifestyle modifications are effective for the cure or sustained improvement of UI?

4.1.3 ***Behavioural and Physical therapies***

Terminology relating to behavioural and physical therapies remains confusing because of the wide variety of ways in which treatment regimens and combinations of treatments have been delivered in different studies [153]. The terms are used to encompass all treatments which require a form of self-motivated personal retraining by the patient and also include techniques which are used to augment this effect.

Approaches include bladder training (BT) and pelvic floor muscle training (PFMT), but terms such as bladder drill, bladder discipline and bladder re-education and behaviour modification are also used. Almost always in clinical practice, these will be introduced as part of a package of care including lifestyle changes, patient education and possibly some cognitive therapy as well. The extent to which individual therapists motivate, supervise and monitor these interventions is likely to vary but it is recognised that these influences are important components of the whole treatment package.

4.1.3.1 Prompted voiding

The term prompted voiding implies that carers, rather than the patient, initiate the decision to void and this applies largely to an assisted care setting.

Two systematic reviews (9 RCTs) [154, 155] confirmed a positive effect on continence outcomes for prompted voiding in comparison to standard care [155].

Timed voiding is defined as fixed, pre-determined, time intervals between toileting, applicable for those with or without cognitive impairment. A Cochrane review of timed voiding reviewed two RCTs finding inconsistent improvement in continence compared with standard care in cognitively impaired adults [156].

4.1.3.2 Bladder Training

Bladder training (also referred to in the past as bladder drill, bladder discipline, bladder re-education, bladder re-training): A program of patient education along with a scheduled voiding regimen with gradually adjusted voiding intervals. Specific goals are to correct faulty habit patterns of frequent urination, improve control over bladder urgency, prolong voiding intervals, increase bladder capacity, reduce incontinent episodes and restore patient confidence in controlling bladder function.

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.

4.1.3.2.1 Questions

In adults with UI:

- 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?
- Does BT as an adjunct to other conservative treatments cure or improve UI?
- Are the benefits of BT durable in the longer term?
- Are there any patient groups for whom BT is more effective?

4.1.3.2.2 Evidence

There have been three systematic reviews on the effect of BT compared to standard care [49, 152, 157] confirming that BT is more effective than no treatment in improving UUI. The addition of BT to anticholinergic therapy did not improve UI compared to antimuscarinics alone but it did improve frequency and nocturia [158].

This review identified 7 RCTs in which BT was compared to drug therapy alone and showed only a benefit for oxybutynin in cure and improvement of UI (RAI 2012).

BT alone is inferior to a high-intensity programme of PFMT to improve SUI in elderly women [159]. Bladder training 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. Biofeedback combined with BT increased continence rates and improved MUI in two RCTs [157].

Summary of evidence	LE
Bladder training is effective for improvement of UI in women.	1b
The effectiveness of bladder training diminishes after the treatment has ceased.	2
The comparative benefit of bladder training and drugs for the improvement of UUI remains uncertain.	2
The combination of bladder training with antimuscarinic drugs does not result in greater improvement of UI but may improve frequency and nocturia.	1b
Bladder training is better than pessary alone.	1b
Prompted voiding, either alone or as part of a behavioural modification programme, improves continence in elderly, care-dependent people.	1b

For recommendations see section 4.1.3.5.

4.1.3.3 Pelvic floor muscle training (PFMT)

Pelvic floor muscle training is used to improve function of the pelvic floor, improving urethral stability. There is some evidence that improving pelvic floor function may inhibit bladder contraction in patients with OAB [160]. 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 (using visual, tactile or auditory stimuli), surface electrical stimulation or vaginal cones.

4.1.3.3.1 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?

4.1.3.3.2 Evidence

In a recent UK Health Technology Appraisal (HTA), the role of PFMT in the care of women with SUI was analysed in direct comparisons of treatments and a mixed treatment comparison model, which compared different 'packages' of care [152]. 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 may provide more accurate estimates of effect. Where relevant, the Technology Appraisal has influenced the evidence and recommendations in these Guidelines. The Agency for Healthcare Research and Quality (AHRQ) review of nonsurgical treatment of UI in adult women also included indirect comparison methods as well as conventional meta-analysis [157].

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

This question has been addressed by several systematic reviews [152, 157, 161], all report inconsistency between studies because of poor reporting of technique and different outcome measures. Meta-analysis showed that PFMT was effective for cure or improvement of incontinence, and improvement in QoL. The effect applies in women with SUI, UUI and MUI though the effect in MUI is lower than in women with pure SUI. A Cochrane review comparing different approaches to delivery of PFMT (21 RCTs) concluded that increased intensity of delivery of the therapy improves response and that there is no consistent difference between group therapy and individualised treatment sessions [162]. No other consistent differences between techniques were found.

With regard to the durability of PFMT, another RCT reported 15-year follow-up outcomes of an earlier RCT, showing that long-term adherence to treatment was poor and half of patients had progressed to surgery [163]. Numerous systematic reviews have addressed the question of whether the effects of PFMT and BT are additive [152, 157, 164]. These reviews are confounded by differences in patient selection and have arrived at conflicting conclusions leaving uncertainty about the extent to which one treatment may augment the other. Similarly, there remains uncertainty about the additional value of biofeedback with systematic reviews reaching differing conclusions [157, 164].

Comparison of PFMT to other treatments was extensively reviewed by both AHRQ and the 2010 UK HTA [152, 157], which considered additional non-randomised data as part of a mixed treatment comparison. The UK HTA resulted in a number of different findings from those based solely on direct comparisons. In conclusion, the HTA, using a revised methodology, supported the general principle that greater efficacy was achieved by adding together different types of treatment and by increasing intensity.

Efficacy of PFMT in childbearing women
Two systematic reviews [165, 166] reviewed RCTs in pregnant or postpartum women, which included PFMT in one arm of the trial. Treatment of UI with PFMT in the postpartum period increased the chances of continence at 12 months' postpartum.

4.1.3.3.4 PFMT in the elderly
The effect of PFMT in women with SUI does not seem to decrease with increased age: in trials with older women with SUI it appeared both primary and secondary outcome measures were comparable to those in trials focused on younger women [131, 159, 167].

4.1.3.3.5 PFMT and Radical prostatectomy
A 2015 Cochrane review 2015 concluded that there was no overall benefit at 12 months post-surgery for men who received post-operative PFMT for the treatment of post-prostatectomy urinary incontinence (PPI) and that the benefits of conservative treatment of PPI remain uncertain [168]. A meta-analysis within this review showed that a greater proportion of men were dry from between 3 and 12 months suggesting that PFMT may speed recovery of continence. A subsequent study adds to this evidence [169].

Two additional RCTs have shown that written instructions alone offer similar levels of improvement to supervised PFMT [170, 171]. One RCT found that PFMT was helpful in men who had been incontinent for at least one year after prostatectomy, and who had had no previous therapy [172].

One RCT compared PFMT to no treatment in men undergoing TURP. There was no demonstrable difference in the incidence of post-operative incontinence up to 12 months [173].

Summary of evidence	**LE**
PFMT for Women with UI	
PFMT is better than no treatment for improving UI and QoL in women with SUI and MUI.	1
Higher-intensity, supervised treatment regimes, and the addition of biofeedback, confer greater benefit in women receiving PFMT.	1
Short-term benefits of intensive PFMT are not maintained at 15-year follow-up.	2
PFMT commencing in the early postpartum period improves UI in women for up to 12 months.	1
PFMT for post-prostatectomy UI	
PFMT appears to speed the recovery of continence following radical prostatectomy.	1b
PFMT does not cure UI in men post radical prostatectomy or transurethral prostatectomy.	1b
There is conflicting evidence on whether the addition of bladder training, electrical stimulation or biofeedback increases the effectiveness of PFMT alone.	2
Pre-operative PFMT does not confer additional benefit to men undergoing radical prostatectomy.	1b

For recommendations see section 4.1.3.5.

4.1.3.3.6 Electrical stimulation
The details and methods of delivery of electrical stimulation vary considerably.

Electrical stimulation (ES) of the pelvic floor 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. Electrical stimulation is also used in patients with OAB and UUI, for detrusor inhibition. It has been suggested that ES probably targets the pelvic floor directly in SUI and the detrusor muscle or pelvic floor muscle or afferent innervation in UUI.

4.1.3.3.7 Question
In adults with UI, does treatment with ES improve or cure symptoms of UI or QoL compared to no/sham treatment or antimuscarinics?

4.1.3.3.8 Evidence
Most evidence on ES refers to women with SUI. The topic has been included in two health technology appraisals [152, 157] and three systematic reviews [49, 174, 175].

The reviews include analysis of 15 trials and use different comparison methods, but differ in their assessment of whether ES is more effective than sham stimulation and whether ES adds to the benefit of PFMT alone. Studies were considered to be of generally low quality, with a variety of stimulation parameters, treatment regimens and outcome parameters [168].

A sub-analyses in a systematic review on one small low quality RCT in which ES had been compared to oxybutynin and PFMT in patients with UI, showed no difference in incontinence outcomes [176].

A Cochrane review of ES in men with UI (6 RCTs) concluded that, in the short-term, there was some evidence that electrical stimulation enhanced the effect of PFMT in the short term but not after six months. ES was also more effective than sham stimulation at six, but not 12 months. There were, however, more adverse effects (pain or discomfort) with electrical stimulation. [177].

Electromagnetic stimulation has been promoted as treatment for UI but weak evidence of the short term and long term effects has been found in systematic reviews [178, 179].

Summary of evidence	**LE**
In adults with UI, ES may improve UI compared to sham treatment and antimuscarinics.	2
ES may add benefit to PFMT in the short term.	2

For recommendations see section 4.1.3.5.

4.1.3.4 Posterior 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. Stimulation is done percutaneously with a fine, 34-G, needle, inserted just above the medial aspect of the ankle (P-PTNS). Transcutaneous stimulation is also available (T-PTNS). Treatment cycles typically consist of 12 weekly treatments of 30 minutes.

4.1.3.4.1 Question

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

4.1.3.4.2 Evidence

P-PTNS

The reviewed studies included two 12-week RCTs of PTNS against sham treatment [180, 181] one comparing PTNS to tolterodine, and a 3-year extension trial utilising a maintenance protocol in patients with UUI [182, 183]. The results of studies of PTNS in women with refractory UUI are consistent. Considered together, these results suggest that PTNS improves UUI in women who have had no benefit from anti-muscarinic therapy or who are not able to tolerate these drugs. However, there is no evidence that PTNS cures UUI in women. In addition, PTNS is no more effective than tolterodine for improvement of UUI in women. In men there is insufficient evidence to make a conclusion about efficacy.

T-PTNS

A small RCT compared transcutaneous PTNS plus standard treatment (PFMT and BT) with PFMT and BT alone in older women [184]. Women in the T-TPNS group were more likely to achieve Improvement at the end of therapy.

Summary of evidence	**LE**
P-PTNS appears effective for improvement of UUI in women who have had no benefit from antimuscarinic medication.	2b
A maintenance programme of P-PTNS has been shown to be effective up to 3 years.	1b
P-PTNS has comparable effectiveness to tolterodine for improvement of UUI in women.	1b
No serious adverse events have been reported for P-PTNS in UUI.	3
There is limited evidence for effectiveness of T-PTNS.	2a
There is no evidence that P-PTNS cures UI.	2b

4.1.3.5 *Recommendations for behavioural and physical therapies*

Recommendations	GR
Offer bladder training as a first-line therapy to adults with urgency urinary incontinence or mixed urinary incontinence.	A
Offer prompted voiding for adults with incontinence, who are cognitively impaired.	A
Offer supervised intensive PFMT, lasting at least 3 months, as a first-line therapy to women with stress urinary incontinence or mixed urinary incontinence.	A
PFMT programmes should be as intensive as possible.	A
Offer PFMT to elderly women with urinary incontinence.	B
Offer PFMT to post-natal women with urinary incontinence.	A
Consider using biofeedback as an adjunct in women with stress urinary incontinence.	A
Offer PFMT to men undergoing radical prostatectomy to speed recovery of incontinence.	B
Do not offer electrical stimulation with surface electrodes (skin, vaginal, anal) alone for the treatment of stress urinary incontinence.	A
Consider offering electrical stimulation as an adjunct to behavioural therapy in patients with urgency urinary incontinence.	B
Do not offer magnetic stimulation for the treatment of incontinence or overactive bladder in adult women.	B
Offer, if available, P-PTNS as an option for improvement of urgency urinary incontinence in women who have not benefitted from antimuscarinic medication.	B
Support other healthcare professionals in use of rehabilitation programmes including prompted voiding for elderly care-dependent people with urinary incontinence.	A

PFMT = pelvic floor muscle training; P-PTNS = percutaneous posterior tibial nerve stimulation; T-PTNS = transcutaneous posterior tibial nerve stimulation.

4.1.4 ***Conservative therapy in mixed urinary incontinence***

About one-third of women with UI have MUI with symptoms of both SUI and UUI, and this becomes more common with increasing age. In terms of evidence base, many studies include patients with MUI, but it is rare for these studies to provide a separate analysis of patients with MUI.

4.1.4.1 *Question*

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

4.1.4.2 *Evidence*

No specific systematic reviews were found that addressed the above question. However, a Cochrane report on pelvic floor muscle training (PFMT) [183] 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 small RCT (n = 71) compared delivery of PFMT, with or without an instructive audiotape. It showed equal efficacy for different types of UI [185].

Following a RCT of PFMT, 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 [186].

Summary of evidence	LE
Pelvic floor muscle training appears less effective for MUI than for SUI alone.	2
Electrical stimulation is equally effective for MUI and SUI.	1b

4.1.4.3 *Recommendations conservative therapy in mixed urinary incontinence*

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 lower than for stress urinary incontinence alone.	B

4.2 Pharmacological management

4.2.1 ***Antimuscarinic drugs***

Antimuscarinic (anticholinergic) drugs are currently the mainstay of treatment for UUI. They 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.

The evaluation of cure or improvement of UI is made harder by the lack of a standard definition of improvement and the failure to use cure as a primary outcome. In general, systematic reviews note that the overall treatment effect of drugs is usually small but larger than placebo.

Dry mouth is the commonest side effect, though constipation, blurred vision, fatigue and cognitive dysfunction may occur [157].

The immediate release (IR) formulation of oxybutynin is the archetype drug in the treatment of UUI. Oxybutynin IR provides maximum dosage flexibility, including an off-label 'on-demand' use. Immediate-release drugs have a greater risk of side effects than extended release (ER) formulations because of differing pharmacokinetics. A transdermal delivery system (TDS) and gel developed for oxybutynin gives a further alternative formulation.

4.2.1.1 Question

In adults with UUI, are antimuscarinic drugs better than placebo for improvement or cure of UUI and for the risk of adverse effects?

4.2.1.2 Evidence

Five systematic reviews of individual antimuscarinic drugs vs. placebo were reviewed for this section [157, 187-190] as well as studies published since these reviews up until September 2013. Most studies included patients with a mean age of 55-60 years. Both female and male subjects were included in different studies but results cannot be generalised across sexes. Only short-term rates for improvement or cure of UUI are reported. The evidence reviewed was consistent, indicating that ER and IR formulations of antimuscarinics offer clinically significant short-term cure and improvement rates for UUI compared to placebo.

Cure of UI was deemed to be the most important outcome measure. Risk of adverse events was best represented by withdrawal from a trial because of adverse events although this does not reflect practice. Table 2 shows a summary of the findings from the most recent systematic review [157]. In summary, every drug where cure of UI was available shows superiority compared to placebo in achieving UI, but the absolute size of effect is small.

Table 2. Summary of cure rates and discontinuation rates of antimuscarinic drugs from RCTs which reported these outcomes [157]

Drug	No. of studies	Patients	Relative risk of curing UI (95% CI)	Number needed to treat to achieve one cure of UI (95% CI)
Cure of incontinence				
Fesoterodine	2	2465	1.3 (1.1-1.5)	8 (5-17)
Oxybutynin (includes IR)	4	992	1.7 (1.3-2.1)	9 (6-16)
Propiverine (includes IR)	2	691	1.4 (1.2-1.7)	6 (4-12)
Solifenacin	5	6304	1.5 (1.4-1.6)	9 (6-17)
Tolterodine (includes IR)	4	3404	1.2 (1.1-1.4)	12 (8-25)
Trospium (includes IR)	4	2677	1.7 (1.5-2.0)	9 (7-12)
Discontinuation due to adverse events				
			Relative risk of discontinuation (95% CI)	**NNT of one discontinuation (95% CI)**
Darifenacin	7	3138	1.2 (0.8-1.8)	
Fesoterodine	4	4433	2.0 (1.3-3.1)	33 (18-102)
Oxybutynin (includes IR)	5	1483	1.7 (1.1-2.5)	16 (8-86)
Propiverine (includes IR)	2	1401	2.6 (1.4-5)	29 (16-27)
Solifenacin	7	9080	1.3 (1.1-1.7)	78 (39-823)
Tolterodine (includes IR)	10	4466	1.0 (0.6-1.7)	
Trospium (includes IR)	6	3936	1.5 (1.1-1.9)	56 (30-228)

Darifenacin
The cure rates for darifenacin were not included in the AHRQ review. Continence rates were 29-33% for darifenacin compared to 17-18% for placebo [157].

Transcutaneous oxybutynin
Transdermal oxybutynin has shown a significant improvement in the number of incontinence episodes and micturitions per day vs. placebo and other oral formulations but incontinence was not reported as an outcome [157].

Oxybutynin topical gel was superior to placebo for improvement of UUI with a higher proportion of participants being cured [157].

Summary of evidence	**LE**
All formulations of fesoterodine, oxybutynin, propiverine, solifenacin, tolterodine, darifenacin and trospium, provide a significantly better rate of cure or improvement of UUI compared to placebo.	1a
All formulations of fesoterodine, oxybutynin, propiverine, solifenacin, tolterodine, darifenacin and trospium, result in higher rates of side effects compared to placebo.	1b

*4.2.2 **Comparison of antimuscarinic agents***
Head-to-head comparison trials of the efficacy and side effects of different antimuscarinic agents are of interest for decision making in practice.

4.2.2.1 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?

4.2.2.2 Evidence
There are over 40 RCTs and five systematic reviews [157, 176, 187, 189, 191]. Nearly all the primary studies were industry sponsored. Upward dose titration is often included in the protocol for the experimental arm, but not for the comparator arm.

In general, these studies have been designed for regulatory approval. They have short treatment durations (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. The clinical utility of these trials in real life practice in questionable. Most trials were of low or moderate quality [189].

The 2012 Agency for Healthcare Research and Quality (AHRQ) review included a specific section addressing comparisons of antimuscarinic drugs (Table 3).

Table 3: Comparison of antimuscarinic drugs as reviewed in the 2012 AHRQ review [157]

Experimental drug vs. standard drug	**No. of studies**	**Patients**	**Relative risk of curing UI (95% CI)**
Efficacy			
Fesoterodine vs. tolterodine ER (continence)	2	3312	1.1 (1.04-1.16)
Oxybutynin ER vs. tolterodine ER (improvement)	3	947	1.11 (0.94-1.31)
Solifenacin vs. tolterodine ER	1	1177	1.2 (1.08-1.34)
Trospium vs. oxybutynin	1	357	1.1 (1.04-1.16)
Discontinuation due to adverse events			
			Relative risk of discontinuation (95% CI)
Solifenacin vs. tolterodine ER	3	2755	1.28 (0.86-1.91)
Trospium vs. oxybutynin	2	2015	0.75 (0.52 -1.1)
Fesoterodine vs. tolterodine	4	4440	1.54 (1.21-1.97)

No antimuscarinic agent improved QoL more than another agent [189]. Dry mouth is the most prevalent adverse effect. Good evidence indicates that, in general, higher doses of any drug are likely to be associated with higher rates of adverse events. Also, ER formulations of short-acting drugs, and longer-acting drugs are generally associated with lower rates of dry mouth than IR preparations [189, 191]. 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 [189, 191]. Overall, oxybutynin ER has higher rates of dry mouth than tolterodine ER, although the incidence of moderate or severe dry mouth were similar. Transdermal oxybutynin had 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 [189]. Solifenacin, 10 mg daily, had higher rates of dry mouth than tolterodine ER [189]. Fesoterodine, 8 mg daily, had a higher rate of dry mouth than tolterodine, 4 mg daily [192, 193]. In general, similar discontinuation rates were observed, irrespective of differences in the occurrence of dry mouth.*

**Doses have been given were the evidence relates to a specific dose level typically from trials with a dose escalation element.*

Summary of evidence	**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
Solifenacin is more effective than tolterodine IR for improvement of UUI.	1b
Fesoterodine, 8 mg daily, is more effective than tolterodine ER, 4 mg daily, for cure and improvement of UUI, but with a higher risk of side effects.	1b
ER formulations and once-daily antimuscarinic drugs are generally associated with lower rates of dry mouth than IR preparations, although trial discontinuation rates are similar.	1b
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 **Antimuscarinic drugs vs. non-drug treatment***

The choice of drug vs. non-drug treatment of UUI is an important question.

4.2.3.1 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?

4.2.3.2 Evidence

More than 100 RCTs and high-quality reviews are available [158, 176, 189, 190, 194, 195]. Most of these studies were independent.

A US HTA [176] found that trials were of a low- or moderate-quality. The main focus of the review was to compare the different drugs used to treat UUI. In one study, multicomponent behavioural modification produced significantly greater reductions in incontinence episodes compared to oxybutynin and higher patient satisfaction for behavioural vs. drug treatment. One RCT showed a substantial benefit for sacral neuromodulation compared with medical therapy [196]. In men with storage LUTS no difference in efficacy was found between oxybutynin and behavioural therapy [197]. The combination of BT and solifenacin in women with OAB conferred no additional benefit in terms of continence [198].

Two small RCTs [199, 200], reported a similar improvement in subjective parameters with either transcutaneous electrical nerve stimulation or T-PTNS. However, only oxybutynin treated patients showed significant improvements in objective urodynamic parameters (bladder capacity). The oxybutynin-treated group had more side effects. One study compared tolterodine ER to transvaginal/anal electrical stimulation without differences in UI outcomes [201]. One small RCT found that the addition of P-PTNS to tolterodine ER improved UI and QoL [202].

Summary of evidence	LE
There is no consistent evidence to show superiority of drug therapy over behavioural therapy for treatment of UUI.	1b
Behavioural treatment has higher patient satisfaction than drug treatment.	1b
There is no consistent evidence to show superiority of drug therapy over PFMT for treatment of UUI.	1b

4.2.3.3 Recommendations for antimuscarinic drugs

Recommendations	GR
Offer IR or ER formulations of antimuscarinic drugs 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

IR = immediate release; ER = extended release.

*4.2.4 **Antimuscarinic agents: adherence and persistence***

Most studies on antimuscarinic medication are short term (12 weeks). Adherence in clinical trials is considered to be much higher than in practice.

4.2.4.1 Question

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

4.2.4.2 Evidence

This topic has been reviewed for the development of these Guidelines [203]. Two recent open-label extensions of RCTs of fesoterodine 8 mg showed adherence rates at 2 years of 49-84% [204, 205]. The main drugs studied were oxybutynin and tolterodine IR and ER. Non-persistence rates were high for tolterodine at 12 months, and particularly high (68-95%) for oxybutynin.

Five articles reported 'median days to discontinuation' as between < 30 days and 50 days [206-210]. In a military health system where free medication was provided the median time to discontinuation extended to 273 days [207].

Data on adherence/persistence from open-label extension populations are questionable as these patients are self-selected to be compliant. Data from pharmacy databases is included in this section.

Several of the RCT trials tried to identify the factors associated with low/lower, adherence or persistence of antimuscarinics. These were identified as:

- low level of efficacy (41.3%);
- adverse events (22.4%);
- cost (18.7%), higher adherence rates were observed when drugs were provided at no cost to the patient [207].

Other reasons for poor adherence included:

- IR vs. ER formulations;
- age (lower persistence among younger adults);
- unrealistic expectations of treatment;
- gender distribution (better adherence/persistence in female patients);
- ethnic group (African-Americans and other minorities more likely to discontinue or switch treatment).

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

Summary of evidence	LE
Most patients will stop antimuscarinic agents within the first 3 months because of lack of efficacy, adverse events and/or cost.	2

*4.2.5 **Antimuscarinic agents, the elderly and cognition***

Limited trials have been conducted in elderly people with UI. Issues include the multifactorial aetiology of UI in the elderly, comorbidities such as cognitive impairment, the effect of co-medications and the risk of adverse events.

The effects of antimuscarinic agents on cognition have been studied in more detail.

4.2.5.1 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?

4.2.5.2 Evidence

Two systematic reviews are available [211, 212]. A community-based cohort study found a high incidence of cognitive dysfunction [213]. Other systematic reviews have included sections on the efficacy and safety of antimuscarinics in elderly patients [157, 189]. A systematic review in 2012 found inconclusive evidence as to the impact of antimuscarinics on cognition [214].

Very few trials specifically investigated the cognitive changes associated with antimuscarinic agents. In general, these trials have measured CNS side effects in a non-specific way therefore, the impact of antimuscarinic agents on specific patient cohorts is poorly understood [215, 216]. There are studies on antimuscarinic effects in elderly persons [217], and in people with dementia with UUI [218].

4.2.5.2.1 Oxybutynin

There is evidence that oxybutynin IR may cause/worsen cognitive dysfunction in adults [215, 217, 219-223]. Recent evidence has emerged from a prospective cohort study showing cumulative cognitive deterioration associated with prolonged use of antimuscarinic medication including oxybutynin [224].

More rapid functional deterioration might result from the combined use of cholinesterase inhibitors with antimuscarinic agents in elderly patients with cognitive dysfunction [225].

4.2.5.2.2 Solifenacin

One pooled analysis [226] has shown that solifenacin does not increase cognitive impairment in the elderly. No age-related differences in the pharmacokinetics of solifenacin in different age groups was found although more frequent adverse events in subjects over 80 years of age were observed. No cognitive effect on healthy elderly volunteers was shown [223]. In a subanalysis of a large trial, solifenacin 5-10 mg improved symptoms and QoL in people ≥75 years who had not responded to tolterodine [227]. In patients with mild cognitive impairment, over 65 years, solifenacin showed no difference in efficacy between age groups and a lower incidence of most side effects compared to oxybutynin IR [222, 228].

4.2.5.2.3 Tolterodine

No change in efficacy or side effects related to age have been reported, although a higher discontinuation rate was found for both tolterodine and placebo in elderly patients [215]. Two RCTs in the elderly found a similar efficacy and side-effect profile to younger patients [229-232]. Post-hoc analysis has shown little effect on cognition. One non-randomised comparison showed lower rates of depression in elderly participants treated with tolterodine ER compared to oxybutynin IR [233].

4.2.5.2.4 Darifenacin

Two RCTs in the elderly population (one in patients with UUI and the other in volunteers) concluded that darifenacin was effective with no risk of cognitive change, measured as memory scanning tests, compared to placebo [234, 235]. Another study on 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 the oxybutynin ER arm [217].

4.2.5.2.5 Trospium chloride

Trospium is not supposed to cross the blood-brain barrier in healthy individuals. Two (EEG) studies in healthy volunteers showed no effect from trospium whilst tolterodine caused occasional changes and oxybutynin caused consistent changes [236, 237]. No evidence as to the comparative efficacy and side effect profiles of trospium in different age groups in available. However, there is some evidence that trospium does not impair cognitive function [218, 238] and that it is effective compared to placebo in the elderly [239].

4.2.5.2.6 Fesoterodine

There is no evidence comparing the efficacy and side effects of fesoterodine in elderly and younger patients. Pooled analyses of the RCTs of fesoterodine confirmed the efficacy of the 8 mg but not the 4 mg dose in over-75-year olds [240]. Adherence was lower in the over-75 year-old group but the effect on mental status was not reported [204, 241, 242]. No difference between fesoterodine and placebo on cognitive function was reported in healthy older patients [243].

4.2.5.2.7 Duloxetine in the elderly

RCTs comparing duloxetine and placebo included women up to 85 years, but no age stratification of the results is available.

4.2.5.2.8 Mirabegron

No trials of mirabegron have yet been reported in the elderly population with UI.

4.2.5.2.9 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. Community-based studies of the prevalence of antimuscarinic side effects may be the most helpful [213].

When starting anticholinergics in elderly patients, mental function should be assessed objectively and monitored [244]. No consensus exists as to the best mental function test to detect changes in cognition [225, 240].

4.2.5.2.10 Anticholinergic load

A number of medications have anticholinergic effects and their cumulative effects on cognition should be considered [245].

4.2.5.2.11 Question

In older people suffering from UI what is the effect of anticholinergic burden (defined by anticholinergic cognitive burden scale, ACB) on cognitive function?

4.2.5.2.12 Evidence

There were no studies specifically in older people with UI, but evidence was available from observational cohort studies relating to the risk in a general population of older people.

Lists of drugs with anticholinergic properties are available from two sources [245, 246].

Two systematic reviews of largely retrospective cohort studies, showed a consistent association between long-term anticholinergic use and cognitive dysfunction [247, 248].

Longitudinal studies in older people over two to four years have found increased rate of decline in cognitive function for patients on definite and possible anticholinergics [249, 250].

Summary of evidence	**LE**
All antimuscarinic drugs are effective in elderly patients.	1b
In older people, the cognitive impact of drugs which have anticholinergic effects is cumulative and increases with length of exposure.	3
Oxybutynin may worsen cognitive function in elderly patients.	2
Solifenacin, darifenacin and fesoterodine have been shown not to cause increased cognitive dysfunction in elderly people.	1b
There is no evidence as to whether tolterodine and trospium chloride affect cognitive function.	3

4.2.5.2.13 Additional recommendations for antimuscarinic drugs in the elderly

Recommendations	GR
In older people being treated for urinary incontinence, every effort should be made to employ non-pharmacological treatments first.	C
Use antimuscarinic drugs with caution in elderly patients who are at risk of, or have, cognitive dysfunction.	B
Do not use oxybutynin in elderly patients who are at risk of cognitive dysfunction.	A*
In older people who are being prescribed antimuscarinic drugs for control of urinary incontinence, consider modifications to other medications to help reduce anticholinergic load.	C

**Recommendation based on expert opinion.*

4.2.5.3 Research priorities

- All drug trials should report cure rates for urinary incontinence based on a bladder diary.
- What is the relative incidence of cognitive side effects of antimuscarinic drugs?

*4.2.6 **Mirabegron***

Mirabegron is the first clinically available beta 3 agonist, available from 2013. Beta 3 adrenoceptors are the predominant beta receptors expressed in the smooth muscle cells of the detrusor and their stimulation is thought to induce detrusor relaxation.

Mirabegron has undergone evaluation in industry-sponsored phase 2 and phase 3 trials. Two systematic reviews of all currently reported studies assessing the clinical effectiveness of mirabegron [251, 252] reported that mirabegron at doses of 25, 50 and 100 mg, results in significantly greater reduction in incontinence episodes, urgency episodes and micturition frequency/24 hrs than placebo, with no difference in the rate of common adverse events [251]. The placebo dry rates in most of these trials are between 35-40%, and 43 and 50% for mirabegron. In all trials the statistically significant difference is consistent only for improvement but not for cure of UI. Similar improvement in frequency of incontinence episodes and micturitions/24 hrs was found in people who had previously tried and those who had not previously tried antimuscarinic agents.

The most common treatment adverse events in the mirabegron groups were hypertension (7.3%), nasopharyngitis (3.4%) and UTI (3%) [251].

In a 12-month, active-controlled RCT of mirabegron 50/100 mg vs. tolterdine ER 4 mg, the improvement in efficacy seen at 12 weeks was sustained at 12-month evaluation in all groups. The reported dry rates at 12 months were 43%, 45% and 45% for mirabegron 50 mg, 100 mg and tolterodine 4 mg respectively [253].

No risk of QTc prolongation on electrocardiogram [254] and raised intraocular pressure [255] were observed up to 100 mg dose, however patients with uncontrolled hypertension or cardiac arrhythmia were excluded from these trials. There is no significant difference in rate of side effects at different doses of mirabegron [253].

Evaluation of urodynamic parameters in men with combined BOO and OAB concluded that mirabegron (50 or 100 mg) did not adversely affect voiding urodynamic parameters compared to placebo [256].

Equivalent adherence was observed for tolterodine and mirabegron at 12 months (5.5% and 3.6%), although the incidence of dry mouth was significantly higher in the tolterodine group [253]. In mirabegron treated patients, improvement in objective outcome measures correlates directly with clinically relevant PROMs (OAB-q and PPBC) [257, 258].

Summary of evidence	LE
Mirabegron is better than placebo for improvement of UUI symptoms.	1a
There is no evidence that mirabegron is better than placebo for curing incontinence.	1b
Mirabegron is no more effective than tolterodine.	1b
Adrenergic-mediated side effects of mirabegron appear mild and not clinically significant in a trial setting.	1a
Discontinuation rates from mirabegron are similar to tolterodine in a trial setting.	1b

Recommendation	GR
Offer mirabegron to people with urgency urinary incontinence, but inform patients receiving mirabegron that the possible long-term side effects remain uncertain.	B

*4.2.7 **Drugs for stress urinary incontinence***

Trials have focused on the effect of alpha-adrenoceptors in increasing the closure urethral pressure in women as a means of improving SUI.

A Cochrane review [259] found 22 trials of adrenergic drugs in women with predominant SUI in comparison to placebo or PFMT. Eleven of these trials involved phenylpropanolamine (withdrawn in some countries because of an increased risk of haemorrhagic stroke). The review found weak evidence that these drugs are better than placebo at improving UI in women. Comparative trials with PFMT gave inconsistent results. No new trials were published between 2007 and 2010. At present, these drugs are not licensed for use in UI.

Duloxetine inhibits the presynaptic re-uptake of neurotransmitters, serotonin (5-HT) and norepinephrine (NE). 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.

4.2.7.1 Questions

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

4.2.7.2 Evidence

Duloxetine was evaluated as a treatment for female SUI or MUI in two systematic reviews [190, 259] of 10 RCTs, and one subsequent RCT. The typical dose of duloxetine was 80 mg daily, with dose escalation up to 120 mg daily allowed in one study, 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.

Improvement in UI compared to placebo was observed with no clear differences between SUI and MUI. One study reported cure for UI in about 10% of patients. An improvement in I-QoL was not found in the study using IQoL as a primary endpoint. In a further study comparing duloxetine, 80 mg daily, with PFMT alone, PFMT + duloxetine, and placebo [260], 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.

Two open-label studies with a follow-up of 1 year or more evaluated the long-term effect of duloxetine in controlling SUI, however both had high discontinuation rates [261, 262].

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 [263]. Episodes of UUI were also significantly reduced by duloxetine.

One study [264] compared PFMT + duloxetine vs. 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.

All studies had a high patient withdrawal rate of about 20-40% in short-term studies and up to 90% in long-term studies. Cause of the high withdrawal rate included lack of efficacy and high incidence of adverse events, including nausea and vomiting (40% or more of patients), dry mouth, constipation, dizziness, insomnia, somnolence and fatigue.

Summary of evidence	LE
Duloxetine does not cure UI.	1a
Duloxetine, 80 mg daily improves SUI and MUI in women.	1a
Duloxetine causes significant gastrointestinal and CNS side effects leading to a high rate of treatment discontinuation.	1a
Duloxetine 80 mg daily, can improve SUI in men.	1b
Duloxetine 80 mg - 120 mg daily can improve UUI in women.	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.	B*
Duloxetine should be initiated using dose titration because of high adverse effect rates.	A

** Downgraded based on expert opinion.*

*4.2.8 **Oestrogen***

Oestrogenic drugs including conjugated equine oestrogens, oestradiol, tibolone and raloxifene, are used as hormone replacement therapy (HRT) for women with natural or therapeutic menopause.

Oestrogen treatment for UI has been tested using oral, transdermal and vaginal routes of administration. Available evidence suggests that vaginal oestrogen treatment with oestradiol and oestriol is not associated with the increased risk of thromboembolism, endometrial hypertrophy, and breast cancer seen with systemic administration [265-267]. Vaginal (local) treatment is primarily used to treat symptoms of vaginal atrophy in postmenopausal women.

4.2.8.1 Questions

- In women with UI, does vaginal (local) oestrogen cure or improve UI compared to no treatment or other active treatment?
- In women with UI, does oral (systemic) oestrogen cure or improve UI compared to no treatment?

4.2.8.2 Evidence

Vaginal oestrogens

A recent Cochrane systematic review looked at the use of oestrogen therapy in postmenopausal women [265] given local oestrogen therapy. There is also a more recent narrative review of oestrogen therapy in urogenital diseases [268]. No new RCTs have been published up to September 2012. The Cochrane review (search date June 2012) found that vaginal oestrogen treatment improved symptoms of UI in the short term [265]. The review found small, low quality trials comparing vaginal oestrogen treatment with phenylpropanolamine, PFMT, electrical stimulation and its use as an adjunct to surgery for SUI . Local oestrogen was less likely to improve UI than PFMT but no differences in UI outcomes were observed for the other comparisons. A single trial of local oestrogen therapy comparing a ring device to pessaries found no difference in UI outcomes although more women preferred the ring device. No adverse effects of vaginal administration of oestradiol for vulvovaginal atrophy over 2 years was seen in one trial [269].

Vaginal oestrogen therapy can be given as conjugated equine oestrogen, oestriol or oestradiol in vaginal pessaries, vaginal rings or creams. Current data do not allow differentiation among the various types of oestrogens or delivery methods. The ideal treatment duration and the long-term effects are uncertain. One RCT compared oestradiol ring pessary with treatment with oxybutynin ER showing no difference in outcomes [270].

Systemic oestrogens

Studies of HRT with non-urogenital primary outcomes have looked for change in urinary continence in secondary analyses. Large trials using conjugated equine oestrogens showed a higher rate of development or worsening of UI compared to placebo [271-274]. In a single RCT use of raloxifene was not associated with development or worsening of UI [275]. Three small RCTs using oral oestriol or oestradiol as HRT for vulvovaginal atrophy suggested that UI symptoms were improved although the evidence was unclear [49, 276, 277].

Summary of evidence	LE
Vaginal oestrogen therapy improves UI for post-menopausal women in the short term.	1b
There is no consistent evidence that vaginal oestrogen therapy cures SUI.	2
There is no evidence that one method of vaginal delivery is better than another.	4
Neoadjuvant or adjuvant use of local oestrogens are ineffective as an adjunct to surgery for UI.	2
Systemic hormone replacement therapy using conjugate equine oestrogens in previously continent women increases the risk of developing UI and worsens pre-existing UI.	1a

Recommendations	GR
Offer post-menopausal women with urinary incontinence vaginal oestrogen therapy particularly if other symptoms of vulvovaginal atrophy are present.	A
Vaginal oestrogen therapy should be long-term and in an appropriate dose.	C
For women taking oral conjugated equine oestrogen as hormone replacement therapy who develop or experience worsening urinary incontinence, discuss alternative hormone replacement therapies.	A
Advise women who are taking systemic oestradiol who suffer from urinary incontinence, that stopping the oestradiol is unlikely to improve their incontinence.	A

*4.2.9 **Desmopressin***

Desmopressin is a synthetic analogue of vasopressin (also known as antidiuretic hormone). 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.

4.2.9.1 Questions

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

4.2.9.2 Evidence

4.2.9.2.1 Improvement of incontinence

Few studies have examined the use of desmopressin exclusively for the treatment of UI. No evidence was found that demonstrated any effect on nocturnal incontinence. Two RCTs have compared desmopressin to placebo with daytime UI as an outcome measure. Improved continence was shown during the first 4 hours after taking desmopressin in women [278]. The continuous use of desmopressin improved frequency and urgency, but did not improve UI in men and women with OAB [279]. There is no evidence reporting desmopressin cure rates for UI and no evidence that compares desmopressin with other non-drug treatments for UI.

4.2.9.2.2 Monitoring for hyponatraemia

The use of desmopressin carries a risk of developing hyponatraemia (please refer to the EAU Guidelines on Male LUTS).

Summary of evidence	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 daytime urinary incontinence and inform them that this drug is not licensed for this indication.	B
Do not use desmopressin for long-term control of urinary incontinence.	A

*4.2.10 **Drug treatment in mixed urinary incontinence***

4.2.10.1 Question

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

4.2.10.2 Evidence

Many RCTs include patients with MUI with predominant symptoms of either SUI or UUI but few report outcomes separately for those with MUI compared to pure SUI or UUI groups.

Tolterodine

In an RCT of 854 women with MUI, tolterodine ER was effective for improvement of UUI, but not SUI suggesting that the efficacy of tolterodine for UUI was not altered by the presence of SUI [280]. In another study (n = 1380) tolterodine was equally effective in reducing urgency and UUI symptoms, regardless of whether there was associated SUI [281]. Similar results were found for solifenacin [282, 283].

Duloxetine

In one RCT of duloxetine vs. placebo in 588 women, subjects were stratified into either stress-predominant, urgency-predominant or balanced MUI groups. Duloxetine was effective for improvement of incontinence and QoL in all subgroups [284].

Duloxetine was found to have equal efficacy for SUI and MUI in an RCT (n = 553) following secondary analysis of respective subpopulations [285].

Summary of evidence	LE
Limited evidence suggests that antimuscarinic drugs are effective for improvement of the UUI component in patients with MUI.	2
Duloxetine is effective for improvement of both SUI and UUI in patients with MUI.	1b

Recommendations	GR
Treat the most bothersome symptom first in patients with mixed urinary incontinence.	C
Offer antimuscarinic drugs to patients with urgency-predominant mixed urinary incontinence.	A*
Consider duloxetine for patients with mixed urinary incontinence unresponsive to other conservative treatments and who are not seeking cure.	B

**Recommendation based on expert opinion.*

4.3 Surgical management

In line with the recommendations from the UK National Institute for Healthcare and Clinical Excellence (NICE) [58] the Panel agreed that surgeons and centres performing surgery should:

- be properly trained in each procedure;
- not be trained by someone who is not surgically qualified;
- perform sufficient numbers of a procedure to maintain expertise of him/herself and the surgical team;
- be able to offer alternative surgical treatments;
- be able to deal with the complications of surgery;
- provide suitable arrangements for follow-up long-term if necessary.

This section considers surgical options for the following situations:

- Women with uncomplicated SUI. This means no history of previous surgery, no neurogenic LUT dysfunction, no bothersome genitourinary prolapse, and women not considering further pregnancy.
- Women with complicated SUI. Neurogenic LUTD is reviewed in the EAU Guidelines on Neurogenic Lower Urinary Tract Dysfunction [286].
- Associated genitourinary prolapse has been included in these Guidelines in terms of treating incontinence, but no attempt has been made to comment on treatment of prolapse itself.
- Men with SUI, mainly in men with post-prostatectomy incontinence without neurological disease affecting the lower urinary tract.
- Patients with refractory DO incontinence.

Although the outcome of surgical 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 Panel has tried to acknowledge emerging techniques as they think appropriate and have made a strong recommendation (section 4.3.1.5.2) that new devices are only used as part of a structured research programme.

*4.3.1 **Women with uncomplicated stress urinary incontinence***

4.3.1.1 Mid-urethral slings

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.

4.3.1.1.1 Questions

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

- 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?

4.3.1.1.2 Evidence

For the purpose of these Guidelines, 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 [287-297]. 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%) [290-297]. 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 [76, 289]. 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) [288, 290, 298-300].

Transobturator route vs. retropubic route

The EAU Panel meta-analysis identified 34 RCTs (5786 women) comparing 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) [4]. 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%). 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 showed a higher rate in women undergoing transobturator insertion (7%) compared to retropubic insertion (3%).

Insertion using a skin-to-vagina direction vs. a vagina-to-skin direction

A Cochrane systematic review and meta-analysis found that the skin-to-vagina direction (top - down) for retropubic insertion of mid-urethral slings was less effective than the vagina-to-skin (bottom - up) direction and was associated with higher rates of voiding dysfunction, bladder perforation and vaginal erosion [301]. 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 [302].

4.3.1.2 Adjustability

4.3.1.2.1 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?

4.3.1.2.2 Evidence

There are no RCTs investigating outcome of adjustable sling insertion for women with SUI. There are 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.

4.3.1.3 Single-incision slings

4.3.1.3.1 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?

4.3.1.3.2 Evidence

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

withdrawn from the market (eg TVT Secur, Minitape), and yet evidence relating to these may be included in current meta-analyses. There was evidence to suggest single-incision slings are quicker to perform and cause less post-operative thigh pain, but there was no difference in the rate of chronic pain. There was not enough evidence to conclude any difference between single-incision slings in direct comparisons.

The most recent meta-analysis [303] and a re-analysis of the Cochrane review data by the Panel (excluding TVT Secur data) have demonstrated that there was no difference in efficacy between available single incision devices and conventional mid-urethral slings. However, not all single incision devices have been subjected to RCT evaluation and it may be unsafe to assume that they are collectively technically similar devices.

Generalisability of evidence to adult women with SUI
Analysis of the population studied in trials included 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 POP, or a history of previous surgery for SUI. The results of the EAU Panel meta-analysis [4] were consistent with those of the Cochrane systematic review [301], except that in the EAU Panel meta-analysis the objective cure rates appeared slightly higher for retropubic (88%) compared to transobturator insertion (84%). The EAU Panel finding is consistent with an additional systematic review and meta-analysis [304] and the difference may result from the Panel's decision to only consider trial data with at least 12 months of follow-up.

Sexual function after mid-urethral tape surgery
A systematic review concluded there was a lack of RCTs addressing the effects of incontinence surgery on sexual function but noting a reduction in coital incontinence [305]. One recent RCT [306] and another cohort study [307] have shown that overall sexual activity improves after sling surgery.

SUI surgery in the elderly
There are no RCTs comparing surgical treatment in older vs. younger women, although subgroup analyses of some RCTs have included a comparison of older with younger cohorts. Definitions of elderly vary from one study to another so no attempt was made to define the term here. Instead, the Panel attempted to identify those studies which have addressed age difference as an important variable.

An RCT of 537 women comparing retropubic to transobturator tape, showed that increasing age was an independent risk factor for failure of surgery over the age of 50 [308]. An RCT assessing risk factors for the failure of TVT vs. transobturator tension-free vaginal tape (TVT-O) in 162 women found that age is a specific risk factor (adjusted OR 1.7 per decade) for recurrence at 1 year [309]. In a subanalysis of a trial cohort of 655 women at 2 years' follow-up, it was shown that elderly women were more likely to have a positive stress test at follow-up (OR 3.7, 95% CI 1.7-7.97), are less likely to report objective or subjective improvement in stress and urgency UI, and are more likely to undergo retreatment for SUI (OR 3.9, 95% CI 1.3-11.48). There was no difference in time to post-operative normal voiding [310].

Another RCT comparing immediate TVT vs. no surgery (delayed TVT) in older women, confirmed efficacy of surgery in terms of QOL and satisfaction, but with higher complication rates [311].

A cohort study of 256 women undergoing inside-out transobturator tape reported similar efficacy in older vs. younger women, but found a higher risk of de novo urgency in older patients [312].

Summary of evidence	LE
Compared to colposuspension, the retropubic insertion of a mid-urethral synthetic sling provides equivalent patient-reported cure of SUI at 5 years.	1a
Mid-urethral synthetic sling inserted by either the transobturator or retropubic route provides equivalent patient-reported outcome at 12 months.	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 pain and vaginal erosion and extrusion 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
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
The comparative efficacy of single-incision slings against conventional mid-urethral slings is uncertain.	1c
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 conventional mid-urethral slings.	1b
There is no evidence that other adverse outcomes from surgery are more or less likely with single incision slings than with conventional mid-urethral slings.	1b
Older women benefit from surgical treatment for UI.	1
The risk of failure from surgical repair of SUI, or suffering adverse events, appears to increase with age.	2
There is no evidence that any surgical procedure has greater efficacy or safety in older women than another procedure.	4
In women undergoing surgery for SUI, coital incontinence is likely to improve.	3
Overall, sexual function is unlikely to deteriorate following SUI surgery.	3
There is no consistent evidence that the risk of post-operative sexual dysfunction differs between midurethral sling procedures.	3

NB: Most evidence on single-incision slings is from studies using the tension-free vaginal tape secure (TVTS) device and although this device is no longer available, many women still have the device in place.

4.3.1.4 Open and laparoscopic surgery for stress urinary incontinence

Open colposuspension was previously considered the gold standard surgical intervention for SUI, and was used as the comparator in RCTs of newer, less invasive, surgical techniques. These include laparoscopic techniques, which have enabled colposuspension to be performed with a minimally invasive approach.

4.3.1.4.1 Question

In women with SUI, what is the effectiveness of open and laparoscopic surgery, compared to other surgical procedures, measured in terms of cure or improvement of incontinence or QoL, or the risk of adverse events?

4.3.1.4.2 Evidence

Four systematic reviews were found, which covered the subject of open surgery for SUI, including 46 RCTs [286, 313-315], but no RCTs comparing any operation to a sham procedure were identified.

Open colposuspension

The Cochrane review [316] included 46 trials in which 4738 women had 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 UI were 17% up to 5 years and 21% over 5 years. The re-operation rate for UI was 2%. Colposuspension was associated with a higher rate of development, at 5 years, of enterocoele/vault/cervical prolapse (42%) and rectocele (49%) compared to tension-free vaginal tape (TVT) (23% and 32%, respectively). The rate of cystocoele was similar in colposuspension (37%) and with TVT (41%).

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

Anterior colporrhaphy
Anterior colporrhaphy is now considered an obsolete operation for UI. In a Cochrane review [330], 10 trials compared anterior colporrhaphy (385 women) with colposuspension (627 women). The failure rate for UI 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 [314, 317] described 26 RCTs, including 2284 women undergoing autologous sling procedure in comparison to other operations.

There were seven trials of autologous fascial sling vs. colposuspension. Except for one very high-quality study [48] showing superiority of fascial sling, 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 cure rate 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 vs. 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.

Post-hoc analysis of an RCT comparing the autologous fascial sling to Burch colposuspension showed inferior outcomes for women who suffered pre-operative urgency [310].

Laparoscopic colposuspension
The Cochrane review [313] 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 mid-uretheral 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-urethral sling. Comparisons of colposuspension to mid-uretheral sling are covered in section 4.3.1.1.

Summary of evidence	**LE**
Autologous fascial sling is more effective than colposuspension for improvement of SUI .	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

4.3.1.5 Bulking agents

4.3.1.5.1 Question

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

4.3.1.5.2 Evidence

There have been two Cochrane systematic reviews [318, 319] and one independent systematic review [320], which reported on 12 RCTs or quasi-RCTs of injectable agents. In general, the trials were only of moderate quality and small with many of them had being reported only in abstract form. Wide confidence intervals meant a meta-analysis was not possible. Since the Cochrane review, two further RCTs have been reported [321, 322].

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 [323]. 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.

Comparison with open surgery
Two RCTs 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 [49, 324].

Another trial found that a peri-urethral route of injection can carry a higher risk of urinary retention compared to a transurethral injection [325]. A recent small RCT found no difference in efficacy between mid-urethral and bladder neck injection of collagen [321].

Summary of evidence	**LE**
Peri-urethral 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 often required.	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
Transperineal route of injection may be associated with a higher risk of urinary retention compared to the transurethral route.	2b

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
Warn women who are being offered a retropubic insertion of mid-urethral 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 who are being offered a single-incision sling that long-term efficacy remains uncertain.	A
Do a cystourethroscopy as part of the insertion of a mid-urethral sling.	C
Offer colposuspension (open or laparoscopic) or autologous fascial sling for women with stress urinary incontinence if mid-urethral sling cannot be considered.	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.	C
Inform older women with stress urinary incontinence about the increased risks associated with surgery, including the lower probability of success.	B
Inform women that any vaginal surgery may have an impact on sexual function.	B
Only offer new 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.	A*
Do not offer bulking agents to women who are seeking a permanent cure for stress urinary incontinence.	A*

** Recommendation based on expert opinion.*

*4.3.2 **Complicated stress urinary incontinence 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. Neurogenic LUT dysfunction is reviewed by the EAU Guidelines on Neurogenic Lower Urinary Tract Dysfunction [286]. Women with associated genitourinary prolapse are included in this edition (see section 4.3.3).

4.3.2.1 Colposuspension or sling following failed surgery

There may be persistent or recurrent SUI, or the development of de novo UUI. This means that careful evaluation including urodynamics becomes an essential part of the work-up of these patients.

4.3.2.1.1 Question

In women who have had failed surgery for SUI, what is the effectiveness of any second-line operation, compared to any other second-line operation, in terms of cure or improvement of UI, QoL or adverse events?

4.3.2.1.2 Evidence

Most of the data on surgery for SUI refer to primary operations. Even when secondary procedures have been included, it is unusual for the outcomes in this subgroup to be separately reported. When they are, the numbers of patients is usually too small to allow meaningful comparisons.

The 4th International Consultation on Incontinence includes a review of this topic [326] up till 2008 and the subject has also been reviewed by Ashok [327] and Lovatsis *et al.* [328]. A further literature review has been carried out since that time by the Panel.

Cochrane reviews of individual operative techniques have not included separate evaluation of outcomes in women undergoing second-line surgery. However, there is a current protocol to address this issue [329]. Only one RCT was found (abstract only) comparing TVT to laparoscopic colposuspension in women with recurrent SUI. This small study found similar cure rates and adverse events in the short-term for both procedures [300].

Post-hoc subgroup analysis of high-quality RCTs comparing one procedure to another have shown conflicting evidence of relative effectiveness [74, 310, 330, 331]. One large non-randomised comparative series suggested that cure rates after more than two previous operations were 0% for open colposuspension and 38% for fascial sling [332].

Several cohort studies have reported outcomes for TVT specifically for primary and secondary cases. Evidence on the effectiveness of second-line retropubic tapes conflicts with some series showing equivalent outcomes for primary and secondary cases [333, 334], whilst other research has shown inferior outcomes for secondary surgery [335, 336]. Other confounding variables make meaningful conclusions difficult.

Systematic review of older trials of open surgery for SUI suggest that the longer term outcomes of redo open colposuspension may be poor compared to autologous fascial slings [337]. Successful results have been reported from mid-urethral slings after various types of primary surgery, while good outcomes are reported for both repeat TVT and for 'tightening' of TVT, but data are limited to small case series only.

Summary of evidence	**LE**
There is conflicting evidence whether prior surgery for stress incontinence or prolapse results in inferior outcomes from repeat operations for SUI.	2
Most procedures will be less effective when used as a second-line procedure than when used for primary surgery.	2
In women who have had more than two procedures for SUI, the results of open colposuspension are inferior to autologous fascial sling.	2

4.3.2.2 External compression devices

External compression devices are still widely used in the treatment of recurrent SUI after the failure of previous surgery and if there is thought to be profound intrinsic failure of the sphincter mechanism, characterised by very low leak point pressures or low urethral closure pressures. This should be confirmed by urodynamic evaluation.

The two intracorporeal external urethral compression devices available 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. The 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.

4.3.2.2.1 Questions

- 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?

4.3.2.2.2 Evidence

The major advantage of AUS over other anti-incontinence procedures is the perceived ability to be able to void normally [111]. 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 [16].

Artificial urinary sphincter (AUS)

A previous review of mechanical devices concluded that there was insufficient evidence to support the use of AUS in women [338].

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 [339-342]. 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%. 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 [342]. Peri-operative injury to the urethra, bladder or rectum was also a high-risk factor for explantation [340].

A newly introduced artificial sphincter using an adjustable balloon capacity through a self-sealing port, and stress responsive design, has been introduced to clinical use. A series of 100 patients reported 28% explantation at 4 years but the device has undergone redesign and more up-to-date evidence is awaited [343]. Early reports of laparoscopically implanted AUS do not have sufficient patient populations and/or sufficient follow-up to be able to draw any conclusions [344, 345].

Adjustable compression device (ACT)

There are four case series (n = 349), with follow-up ranging from 5 to 84 months [346-349]. Reported outcome ranged from 47% objective cure to 100% subjective improvement. However, most patients required adjustment to achieve continence and 21% required explantation.

Summary of evidence	**LE**
Implantation of an artificial sphincter can improve or cure incontinence in women with SUI caused by sphincter insufficiency.	3
Implantation of the ACT device may improve complicated UI.	3
Complications, mechanical failure and device explantation often occur with 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	GR
Management of complicated stress urinary incontinence should only be offered in expert** centres.	A*
The choice of surgery for recurrent stress urinary incontinence should be based on careful evaluation of the individual patient including mutichannel urodynamics and imaging as appropriate.	C
Warn women with recurrent stress urinary incontinence, that the outcome of a surgical procedure, when used as a second-line treatment, is generally inferior to its use as a first-line treatment, both in terms of reduced efficacy and increased risk of complications.	C
Consider secondary synthetic sling, colposuspension or autologous sling as first options for women with complicated stress urinary incontinence.	C
Warn women receiving AUS or ACT that, even in expert centres, there is a high risk of complications, mechanical failure or a need for explantation.	C

AUS = artificial urinary sphincter; ACT = adjustable compression therapy.

** Recommendation based on expert opinion.*

*** Expert centres refers to the comments on surgeon volume in the introduction to the surgical chapter.*

*4.3.3 **Women with both stress urinary incontinence and pelvic organ prolapse***

There is a clear association between the presence of POP and SUI. Although the subject of prolapse is not part of the remit of these Guidelines, the extent to which it impacts on the management of SUI will be addressed. The aim is to assess the options available to women who require surgery for POP and who have associated UI (either symptomatic or after reduction of prolapse), and to assess the value of prophylactic anti-incontinence surgery in women with no evidence of UI.

4.3.3.1 Questions

1. In women with POP and UI, does combined surgery for POP and SUI reduce the incidence of post-operative UI compared to POP surgery alone?
2. In continent women with POP, does combined surgery for POP and SUI reduce the incidence of post-operative de novo UI compared to POP surgery alone?
3. In women with POP and occult SUI, (i.e. seen only on prolapse reduction stress testing/ urodynamics), does combined surgery for POP and SUI reduce the incidence of post-operative UI compared to POP surgery alone?
4. In women with POP and OAB, does surgery for POP improve OAB symptoms?
5. In adults with POP, what is the reliability, the diagnostic accuracy and predictive value of a prolapse reduction test to identify patients at risk from *de novo* SUI following prolapse repair?

4.3.3.2 Evidence

A Cochrane review in 2013 included sixteen trials concerning bladder function after surgery for pelvic organ prolapse [350]. After prolapse surgery 434 of 2125 women (20.4%) reported new subjective SUI, in 16 trials. New voiding dysfunction was reported in 109 of 1209 (9%) women, in 12 trials.

1. In women with POP does combined surgery for POP and SUI reduce the incidence of post-operative UI compared to POP surgery alone?

There are two well-designed RCTs relating to the prevalence of post-operative SUI in women who underwent prolapse surgery with and without an anti-incontinence procedure. Both of these trials involved women with POP who did not complain of symptoms of stress incontinence regardless of objective findings.

One trial compared abdominal sacrocolpopexy with and without Burch colposuspension [351], the other compared vaginal repair with and without a mid-urethral sling [352]. In both trials addition of an anti-incontinence surgery reduced the risk of SUI at 12 months. In one trial there was a higher rate of adverse events reported in the combined surgery group [352]. This was also the finding of the Cochrane review and meta-analysis.

Two trials addressed post-operative SUI in patients who had had SUI preoperatively. Borstad *et al.*, in a multi-center trial randomised women with POP and SUI to have a tension-free vaginal tape (TVT) at the time of prolapse repair or 3 months later, if they still had SUI. (n = 53). One year after surgery there was no difference between the groups regarding continence, however, 44% of the women without initial TVT never required surgery and 29% were dry [353].

In contrast, Costantini *et al.* followed up women with POP and SUI randomised to abdominal POP repair with or without Burch colposuspension, (after a median of 97 months) finding that additional SUI surgery did not

improve outcome [354]. On the contrary, a higher number of patients had de novo storage symptoms when a Burch colposuspension was performed.

In summary, it is difficult to generalise the results of trials using very different procedures to treat both POP and UI. It seems that with a combined procedure the rate of SUI post-operatively is lower. Studies using mid-urethral slings generally have shown more significant differences in UI outcomes with combined procedures than when other types of anti-incontinence procedure have been used. Individual patient characteristics may play the most important role in shaping treatment decisions. It must be taken into account that, although more women may be dry after combined surgery, the risks of repeat surgery, should it become necessary, may outweigh the potential benefits.

2. Continent women with POP

The 2013 Cochrane review included 6 trials showing that post-operative incontinence rates at < 12 months were 19% in the combined surgery group vs. 32% in POP surgery alone. In this group of 438 women undergoing continence surgery at the time of prolapse prevented 62 (14%) women from developing de novo SUI postprolapse surgery. A long-term update of a previously published RCT comparing POP surgery with or without Burch colposuspension in continent women suggested higher UI rates in women undergoing colposuspension [352].

3. Women with POP and occult SUI

The 2013 Cochrane review included five trials addressing this point. Overall, there was a significantly higher rate of post-operative patient-reported SUI with prolapse surgery alone than compared with combined surgery.

4. Women with POP and OAB

There are 3 case series evaluating patients with concomitant OAB and pelvic organ prolapse which assess incontinence/OAB symptom scores post surgical repair. Costantini *et al.* assessed the effect of posterior repair on OAB/DO and reported a 70-75% improvement rate in both parameters along with a 93% anatomic success rate [355]. Kummeling *et al.* assessed the effect of a modified laparosocopic sacrocolpopexy on urodynamic parameters and reported an improvement with no evidence to support a concomitant prophylactic colposuspension [356]. Lee *et al.* assessed the value of pre-op UDS and BOOI in predicting the degree of OAB symptoms post anterior prolapse repair. They reported a significant correlation between low pre-op BOOI and improvement in OAB symptom scores post-op [357].

5. Prolapse reduction stress test (PRST)

Data concerning PRST were made available from the CARE trial where significant differences were noted in the detection of urodynamic stress incontinence with prolapse reduction among the various methods studied, ranging from 6% (pessary) to 30% (speculum). Manual, swab and forceps showed detection rates of 16%, 20% and 21%, respectively [358]. In the study by Duecy about one third of women were diagnosed with occult SUI using a pessary while two thirds were diagnosed with manual reduction of the prolapse [359]. In a further study occult SUI was only detected by a pessary test in 19% of patients, not by urodynamics, history or clinical examination [360].

Summary of evidence	**LE**
Women with prolapse + UI	
Surgery for POP + SUI shows a higher rate of cure of UI in the short term than POP surgery alone	1a
There is conflicting evidence on the relative long term benefit of surgery for POP + SUI vs. POP surgery alone	1b
Combined surgery for POP+SUI carries a higher risk of adverse events.	1b
Continent women with POP	
Are at risk of developing UI post-operatively.	1a
The addition of a prophylactic anti-incontinence procedure reduces the risk of post-operative UI.	1b
The addition of a prophylactic anti-incontinence procedure increases the risk of adverse events.	1b
Women with POP and OAB	
There is some low-level inconsistent evidence to suggest that surgical repair of POP can improve symptoms of OAB.	3
Women with prolapse and occult SUI	
Surgery for POP + occult SUI shows a higher rate of cure of occult SUI in the short-term than POP surgery alone.	1a
Combined surgery for POP + SUI carries a higher risk of adverse events than POP surgery alone.	1b

Recommendations for women requiring surgery for bothersome POP who have symptomatic or unmasked stress urinary incontinence	GR
Offer simultaneous surgery for pelvic organ prolapse and stress urinary incontinence.	A
Warn women of the increased risk of adverse events with combined surgery compared to prolapse surgery alone.	A
Recommendations for women requiring surgery for bothersome POP without symptomatic or unmasked stress urinary incontinence	
Warn women that there is a risk of developing de novo stress urinary incontinence after prolapse surgery.	A
Inform women that the benefit of prophylactic stress urinary incontinence surgery is uncertain.	C
Warn women that the benefit of surgery for stress urinary incontinence may be outweighed by the increased risk of adverse events with combined surgery compared to prolapse surgery alone.	A

*4.3.4 **Urethral diverticulum***

A female urethral diverticulum is a sac-like protrusion made up by the entire urethral wall or only by the urethral mucosa laying between the periurethral tissues and the anterior vaginal wall. Urethral diverticulum give rise to a variety of symptoms that include pain, urgency, frequency, recurrent UTIs, vaginal discharge, dyspareunia, voiding difficulties or urinary incontinence.

1. In a woman with the clinical suspicion of having an urethral diverticulum, what is the best test to confirm the diagnosis?

No robust diagnostic accuracy studies address this question However, a case series of 27 patients concluded that endoluminal (vaginal or rectal) MRI has better diagnostic accuracy than video cystourethrography VCUG [361]. In a case series of 60 subjects Pathi, *et al.* reported that the sensitivity, specificity, positive predictive value and negative predictive value of MRI is 100%, 83%, 92% and 100%, respectively [362]. Dwarkasing *et al.* also reports 100% specificity and sensitivity of MRI in a case series of 60 patients [363]. However, in a case series of 41 patients, a study reported 25% discrepancy between MRI and surgical findings [364].

2. In a woman who has a bothersome urethral diverticulum, what is the relative effectiveness of available surgical treatments?

4.3.4.1 Surgical treatment

No RCTs were found. Surgical removal is the most commonly reported treatment in contemporary cases series. However, recurrence may occur; Han *et al.* found a recurrence rate of 33% in U-shaped and of 60% in circumferential diverticulum within 1 year [365], Ingber *et al.* found a 10.7% recurrence rate in 122 women undergoing diverticulectomy, with a higher risk of recurrence in those with proximal or multiple diverticula or after previous pelvic surgery [366]. SUI may occur in up to 20% of women after diverticulectomy, requiring additional correction [367-370]. De novo SUI seems to be more common in proximal and in large size (> 30 mm) diverticula.

Diverticula may undergo neoplastic alterations (6%) including invasive adenocarcinomas [371].

Summary of evidence	LE
MRI has good sensitivity and specificity for the diagnosis of urethral diverticula, however there is a risk of mis-diagnosis and missing potential intraluminal neoplastic change.	3
Surgical removal of symptomatic urethral diverticula provides good long-term results however, women should be counselled of the risk of recurrence and de novo SUI.	3

Recommendation	GR
Symptomatic urethral diverticula should be completely surgically removed.	A*

** Recommendation based on expert opinion.*

*4.3.5 **Men with stress urinary incontinence***

4.3.5.1 Bulking agents in men

Injection of bulking agents has been used to try and improve the coaptation of a damaged sphincter zone. Initial reports showed limited efficacy in treating incontinence following radical prostatectomy incontinence [372, 373].

4.3.5.1.1 Question

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

4.3.5.1.2 Evidence

Most studies are case series with small sample sizes. Small cohort studies showed a lack of benefit using a number of different materials [374, 375]. However, polyacrylamide hydrogel resulted in limited improvement in QoL without curing the UI [374]. A Cochrane review on the surgical treatment of post-prostatectomy incontinence found only one study that fulfilled the inclusion criteria [376]. A prospective, randomised study compared the AUS to silicon particles (Macroplastique™) in 45 patients. Eighty-two per cent of patients receiving an AUS were continent compared to 46% receiving silicone particles. In patients with severe incontinence, outcome was significantly worse after silicon bulking injection.

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

4.3.5.2 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®, Istop TOMS, Argus®)
- continence restoration by repositioning the bulb of urethra (AdVance) [377].

In principle, the AUS can be used for all degrees of post-prostatectomy incontinence, while male slings are advocated for mild-to-moderate UI. However, the definitions of mild and moderate UI 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 [378].

4.3.5.2.1 Question

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

4.3.5.2.2 Evidence

Concerning the surgical treatment of post-prostatectomy incontinence, three recent literature reviews are available [379-381]. There are a large number of uncontrolled case series concerning men implanted with several types of slings [382, 383].

For the repositioning sling (AdVance), the benefit after a mean follow-up of 3 years has been published on 136 patients [384]. Earlier data were available from other cohort studies, totalling at least 614 patients with a mean follow-up of between 3 months and 3 years. 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 [382]. Post-operative voiding dysfunction occurred in 5.7-1.3%, while erosions and chronic pain were uncommon (0-0.4%) [378, 384-386]. The overall failure rate was about 20%.

The previously available 'InVance®' device has now been removed from the market in some countries.

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

4.3.5.3 Adjustable slings in males

Adjustability in male sling surgery attempts to adjust the tension of the sling post-operatively. Three main systems have been used in men: the Remeex® system, the Argus® system and the ATOMS system.

4.3.5.3.1 Question

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

4.3.5.3.2 Evidence

There are no prospective RCTs. 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, 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% [387].

Argus® system

Data on the Argus® system has been reported for 404 men, but only four series have reported on more than 50 patients [388, 389], 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% [389]. Infection of the device occurred in 5.4- 8% [388]. Erosions were reported in 5-10% [390]. Urethral perforations occurred in 2.7-16% [388]. Pain at the implant site was usually only temporary, but chronic pain has been reported [388, 390]. These complications resulted in explantation rates of 10-15% [389].

The ATOMS system consists of a mesh implant with an integrated adjustable cushion, which uses a titanium port left in the subcutaneous tissue of the lower abdomen or scrotum for adjustment of cushion volume. Initial reports show objective cure rates of 60.5% and improvement rates of 23.7% but with the need for up to nine post-operative adjustments [391, 392].

Summary of evidence	**LE**
There is limited evidence that adjustable male slings can cure or improve 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

4.3.5.4 Compression devices in males

External compression devices can be divided into two types: circumferential and non-circumferential compression of the urethral lumen [379]. The artificial urinary sphincter (AUS) is the standard treatment for moderate-to-severe male SUI. Most data available on the efficacy and adverse effects of AUS implantation are from older retrospective cohort studies with RCTs not performed due to the lack of a comparator. Men considering insertion of an AUS should understand that 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 vesico-urethral anastomotic site. The balloons can be filled and their volume can be adjusted post-operatively through an intra-scrotal port. Men who develop cognitive impairment or lose manual dexterity will have difficulty operating an AUS.

4.3.5.4.1 Question

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

4.3.5.4.2 Evidence

Artificial urinary sphincter

Although the AUS is considered to be the standard treatment for men with SUI, there are two systematic reviews [376, 381] presenting limited evidence, of generally poor quality, except for one RCT comparing AUS

with bulking agents [372]. A continence rate of about 80% can be expected, while this may be lower in men who have undergone pelvic radiotherapy [379].

Trigo Rocha *et al.* published a prospective cohort study on 40 patients with a mean follow-up of 53 months, showing that from all urodynamic parameters only low bladder compliance had a negative impact on the outcome [393]. Another retrospective study showed that no urodynamic factors adversely altered the outcome of AUS implantation [394].

The transcorporeal technique of placement can be used for repeat surgery but evidence of effectiveness is lacking [395]. 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 UI, while the availability of a 3.5 cm cuff may have eliminated the need for a dual cuff [396, 397]. Patients who experienced complete continence after AUS implantation had a higher erosion risk [398]. One small series reported results of AUS implantation after failure of previous Advance sling, showing no difference in efficacy between secondary and primary implantation [399].

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 [400]. 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 that both types of device resulted in similar improvement of SUI (68% vs. 65%, respectively) [401]. Other prospective series have shown that adverse events were frequent, leading to an explantation rate of 11-58% [381, 402-405]. A questionnaire study showed that 50% of patients were still bothered significantly by persistent incontinence [406]. Other designs of artificial sphincter remain the subject of ongoing evaluation though they may have been introduced onto the market.

Summary of evidence	**LE**
There is 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
There are conflicting data on whether previous pelvic radiotherapy affects the outcome of AUS implantation.	3
The usefulness of tandem-cuff placement is uncertain.	3
There is insufficient evidence to state whether one surgical approach for cuff placement is superior to another.	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
The rate of explantation of the AUS because of infection or erosion remains high (up to 24% in some series).	3
Mechanical failure is common with the AUS.	3
Revision and re-implantation of AUS is possible after previous explantation or for mechanical failure.	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 incontinence 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 moderate-to-severe post-prostatectomy incontinence.	B
Implantation of AUS or ACT for men should only be offered in expert centres.	C
Warn men receiving AUS or ACT that, even in expert centres, there is a high risk of complications, mechanical failure or a need for explantation.	C
Do not offer non-circumferential compression device (ProACT®) to men who have had pelvic radiotherapy.	C

AUS = artificial urinary sphincter; ACT = artificial compression device.
** The terms mild and moderate post-prostatectomy incontinence remain undefined.*

*4.3.6 **Surgical interventions for refractory detrusor-overactivity***

4.3.6.1 Bladder wall injection of botulinum toxin A

Onabotulinum toxin A (onabotA; BOTOX®) 100 U dissolved in 10 mL of saline and injected in 20 points of the bladder wall above the trigone (0.5 mL per injection site) is licenced in Europe to treat OAB with persistent or refractory UUI in adults of both gender, despite the small number of males included in the registration trials [407, 408]. Surgeons must realise that other doses of onabotA and other formulations of botulinum toxin A, abobotulinum toxinA and incobotulinum toxin A, are not licensed for use in UUI. Doses for onabotA are not transposable to the other brands of botulinum toxin A. The continued efficacy of repeat injections is the rule but discontinuation rate may be high. The most important adverse events related to onabotA 100 U injection detected in the regulatory trials were UTI and an increase in PVR that may require clean intermittent catheterisation (CIC) [409].

4.3.6.1.1 Question

In adults with UUI, is bladder wall injection of onabotA better than no treatment for cure or improvement?

4.3.6.1.2 Evidence

Following a dose ranging study in which the 100 U of onabotA was established as the ideal dose, two phase III trials randomised (1:1) 1105 OAB incontinent patients whose symptoms were not adequately managed with anticholinergics to receive bladder wall injections of onabotA (100 U) or saline. At baseline the population had on average more than 5 episodes of UUI, around 12 micturitions per day and small PVR. At week 12, in patients treated with onabotA UUI episodes/day were halved and number of micturitions/day reduced by more than two. A total of 22.9% of the patients in the onabotA arm were fully dry, against 6.5% in the saline arm [410].

QoL was substantially improved in the onabotA arm, as shown by the more than 60% of positive responses in the TBS questionnaire at week 12, which was doubled the positive responses in the saline arm. Cohort studies have shown the effectiveness of bladder wall injections of onabotA in the elderly and frail elderly [411], though the success rate might be lower and the PVR (> 150 mL) higher in this group.

The median time to request retreatment in the pooled analysis of the 2 RCTs was 24 weeks [409, 410].

A recent RCT compared onabotA injection 100 U to solifenacin (with dose escalation or switch to trospium possible in the solifenacin group) and showed similar rates of improvement in UUI over the course of 6 months [412]. However, patients receiving onabotA were more likely to have cure of UUI (27% vs. 13%, p = 0.003), but also had higher rates of urinary retention during the initial 2 months (5% vs. 0%) and of UTIs (33% vs. 13%). Patients taking antimuscarinics were more likely to have dry mouth.

Identification of DO in urodynamics does not influence the outcome of onabotulinum toxin A injections in patients with UUI [413].

Summary of evidence	LE
A single treatment session of onabotulinum toxin A (100 U) injected in the bladder wall is more effective than placebo at curing and improving UUI and QoL.	1a
There is no evidence that repeated injections of onabotulinum toxin A have reduced efficacy.	3
There is a high risk of increased PVR when injecting elderly frail patients.	3
The risk of bacteruria after onabotulinum toxin A (100 U) injection is high but the clinical significance of this remains uncertain.	1b
Onabotulinum toxin A (100 U) is superior to solifenacin for cure of UUI, but rates of improvement were equivalent.	1b

Recommendations	GR
Offer bladder wall injections of onabotulinum toxin A (100 U) to patients with urgency urinary incontinence refractory to antimuscarinic therapy.	A
Warn patients of the limited duration of response, risk of urinary tract infection and the possible prolonged need to self-catheterise (ensure that they are willing and able to do so).	A

4.3.6.2 Sacral nerve stimulation (neuromodulation)

In the first stage of a two-stage implantation, an electrode is placed percutaneously under fluoroscopic control in the sacral foramen alongside a sacral nerve, usually S3. In earlier techniques, a temporary wire electrode was used. More recently, a permanent tined electrode has been used for a longer test phase. Patients, in whom selected symptoms of UUI are reduced by more than 50% during the test phase, are candidates for the full implant, including the pulse generator and reported results only apply to this sub population.

4.3.6.2.1 Question

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

4.3.6.2.2 Evidence

All randomised studies suffer from the limitation that assessors and patients were not blind to the treatment allocation since all recruited subjects had to respond to a test phase before randomisation. A Cochrane review of the literature until March 2008 [414] identified three RCTs that investigated sacral nerve stimulation in patients with refractory UUI.

One study compared implantation to controls who stayed on medical treatment and received delayed implantation at 6 months. Fifty percent of the immediately implanted group had > 90% improvement in UUI at 6 months compared to 1.6% of the control group [196]. The other RCT [415] achieved similar results, although these patients had already been included in the first report [196]. However, Weil *et al.* [431] 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 [416]. After a follow-up duration of between one and three years, approximately 50% of patients with UUI demonstrated > 90% reduction in UI, 25% demonstrated 50-90% improvement, and another 25% demonstrated < 50% improvement. Two case series describing the outcome of sacral nerve neuromodulation, with a mean or median follow-up of at least 4 years [417, 418] reported continued success (> 50% improvement on original symptoms) by about 50 of patients available for follow-up. Cure rates for UUI were 15% [418].

Adverse events occurred in 50% of implanted cases, with surgical revision necessary in 33-41% [417, 418]. In a sub-analysis of the RCT, the outcomes of UUI patients, with or without pre-implant DO, were compared. Similar success rates were found in patients with and without urodynamic DO [419].

Summary of evidence	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, at long-term 50% improvement of UUI is maintained in at least 50% of patients and 15% may remain cured.	3
The use of tined, permanent electrodes in a staged approach results in more patients receiving the final implant than occurs with temporary test stimulation.	4

Recommendation	GR
Offer sacral nerve modulation to patients who have urgency urinary incontinence refractory to antimuscarinic therapy.	A

4.3.6.2.3 Research priority

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

4.3.6.3 Cystoplasty/urinary diversion

4.3.6.3.1 Augmentation cystoplasty

In augmentation cystoplasty (also known as clam cystoplasty), a detubularised segment of bowel is inserted into the bivalved bladder wall. The distal ileum is the bowel segment most often used but any bowel segment can be used if it has the appropriate mesenteric length. One study did not find any difference between bivalving the bladder in the sagittal or in the coronal plane [420, 421].

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.

The largest case series of bladder augmentation in a mixed population of idiopathic and neurogenic UUI included 51 women [422]. 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 seems that the results for patients with idiopathic DO (58%) seemed to be less satisfactory than for patients with neurogenic UUI (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 [423]. In addition, many patients may require clean intermittent self-catheterisation to obtain adequate bladder emptying (Table 4).

Table 4: 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	**Affected patients (%)**
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
Change in bowel symptoms	25

4.3.6.3.2 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 pseudo-diverticulum. It was initially

described as an alternative to bladder augmentation in children [424]. Two case series [425, 426] in adult patients with idiopathic and neurogenic bladder dysfunction, demonstrated poor long-term results caused by fibrosis of the pseudo-diverticulum. This technique is rarely, if ever, used nowadays.

4.3.6.3.3 Urinary diversion

Urinary diversion remains a reconstructive option for patients, who decline repeated surgery for UI. However, there are no studies that have specifically examined this technique in the treatment of non-neurogenic UI [420].

Summary of evidence	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
Detrusor myectomy is ineffective in adults with UI.	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

*4.3.7 **Surgery in patients with mixed urinary incontinence***

4.3.7.1 Question

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

4.3.7.2 Evidence

Many RCTs include both patients with pure SUI or pure UUI and patients with MUI. However, very few RCTs report separate outcomes for MUI and pure UI groups.

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 vs. patients treated with obturator tape alone [427].

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 [310]. A similar post-hoc review of another RCT comparing transobturator and retropubic mid-urethral slings showed that the greater the severity of pre-operative urgency the more likely that treatment would fail [74]. However, an earlier study had found that surgery provided similar outcomes, whether or not urgency was present prior to surgery (this study included only a few patients with urodynamic DO).

Case series tend to show poorer results in patients with MUI compared with those with pure SUI. In a case series of 192 women undergoing mid-urethral sling insertion, overall satisfaction rates were lower for women with mixed symptoms and detrusor overactivity on pre-operative urodynamics compared to those with pure SUI and normal urodynamics (75% vs. 98%, respectively) [428]. A comparison of two parallel cohorts of patients undergoing surgery for SUI, with and without DO, found inferior outcomes in women with MUI [429].

One cohort of 450 women, showed that in urgency-predominant MUI, the success rate fell to 52% compared to 80% in stress-predominant MUI [430]. In a study with 1113 women treated with transvaginal obturator tape, SUI 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 [431].

Overall, the outcome for women with pre-existing urgency incontinence remains uncertain.

Summary of evidence	**LE**
Women with MUI are less likely to be cured of their UI 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

Recommendations	**GR**
Treat the most bothersome symptom first in patients with mixed urinary incontinence.	C
Warn patients with mixed urinary incontinence that surgery is less likely to be successful than surgery in patients with stress urinary incontinence alone.	A
Warn patients with mixed urinary incontinence that one single treatment may not cure UI; it may be necessary to treat other components of the incontinence problem as well as the most bothersome symptom.	A*

** Upgraded following panel consensus.*

4.3.7.3 Research priorities

- Research trials should define accurately what is meant by 'mixed urinary incontinence'.
- 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.

*4.3.8 **Surgery for urinary incontinence in the elderly***

There are no RCTs comparing surgical treatment in older vs. younger women although subgroup analyses of some RCTs have included a comparison of older with younger cohorts.

An RCT of 537 women comparing retropubic to transobturator tape, showed that cure rates decreased and failure increased with each decade over the age of 50 [432]. An RCT assessing risk factors for failure of tension free vaginal tape (TVT) vs. transobturator tension-free vaginal tape (TVT-O) in 162 women found that age is a specific risk factor (adjusted OR 1.7 per decade) for recurrence at 1 year [309]. In a subanalysis of the SISTER trial cohort of 655 women at 2 years of follow-up, it was shown that elderly women were more likely to have a positive stress test at follow-up (OR 3.7, 95% CI 1.7-7.97), are less likely to report objective or subjective improvement in stress and urgency UI, and are more likely to undergo retreatment for SUI (OR 3.9, 95% CI 1.3-11.48). There was no difference in time to normal post-operative voiding [310].

Another RCT compared immediate TVT vs. delayed TVT in older women, confirming significant efficacy for the operated women, but the cohort as a whole suffered higher complication rates, particularly bladder perforation (22%) and urinary retention (13%) [311].

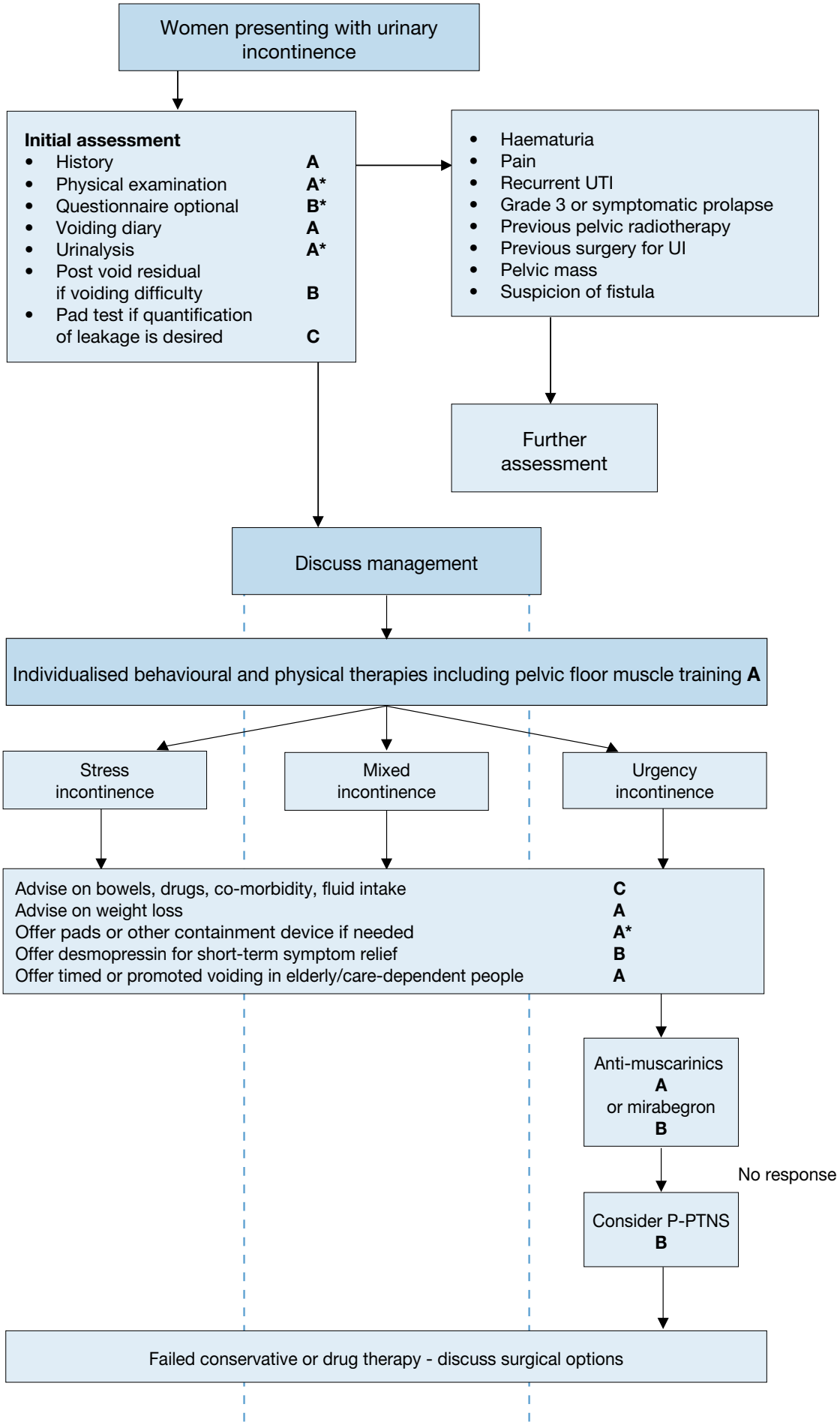
A cohort study of 256 women undergoing inside-out TVT-O reported similar efficacy in older vs. younger women but there was a higher risk of de novo urgency in older patients [312].

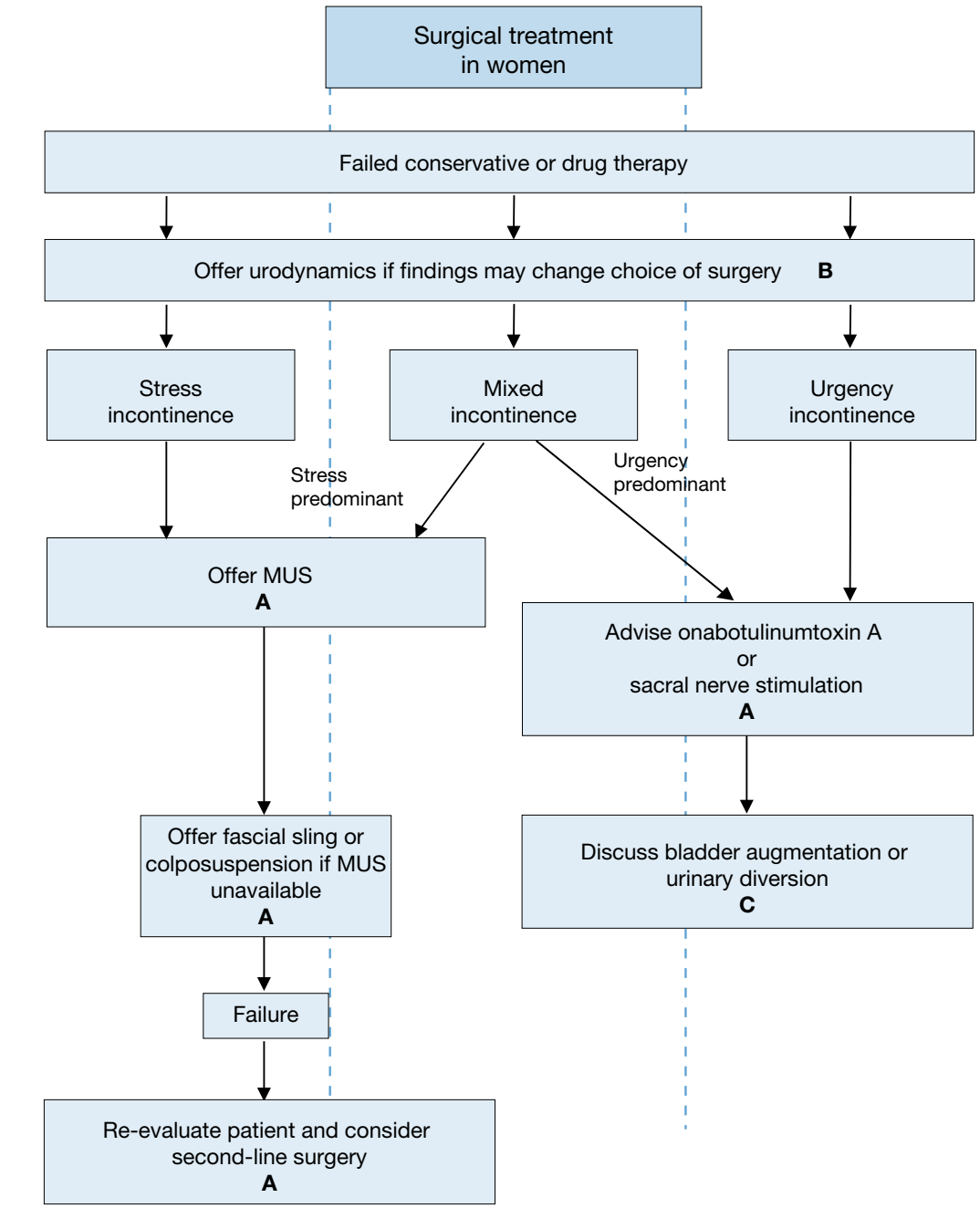
Cohort studies have shown the effectiveness of onabotulinum toxin A injections in the elderly and frail elderly [411, 433], although a comparison of cohort groups suggests that there is a lower success rate in the frail elderly and also a higher rate of increased PVR (> 150 mL) in this group.

Summary of evidence	**LE**
Older women benefit from surgical treatment for incontinence.	1
The risk of failure from surgical repair of SUI, or of suffering adverse events, appears to increase with age.	2
There is no evidence that any surgical procedure has greater efficacy or safety in older women than another procedure.	4

Recommendation	GR
Inform older women with urinary incontinence about the increased risks associated with surgery (including onabotA injection), together with the lower probability of benefit.	B

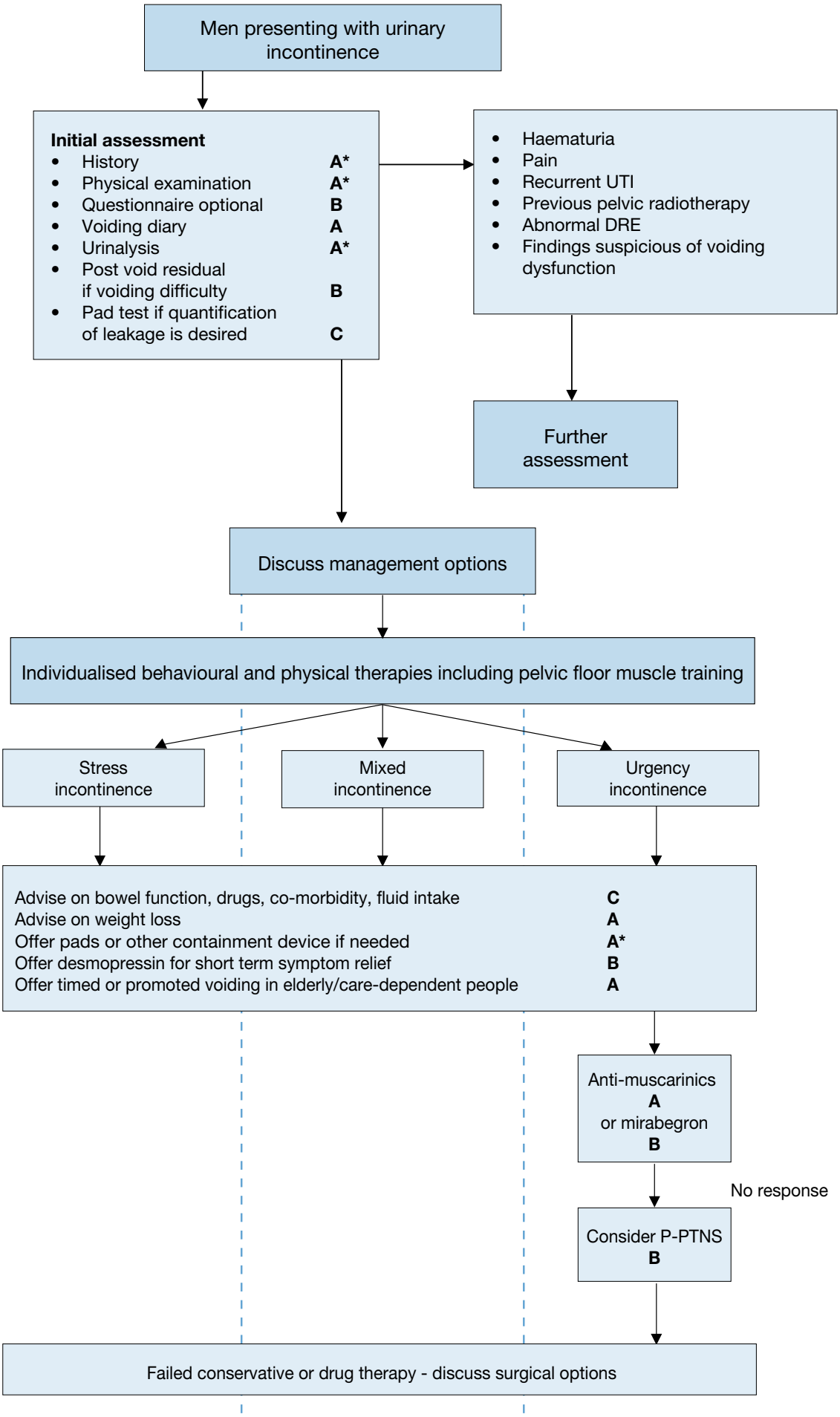
Figure 1: Management and treatment of women presenting with urinary incontinence.

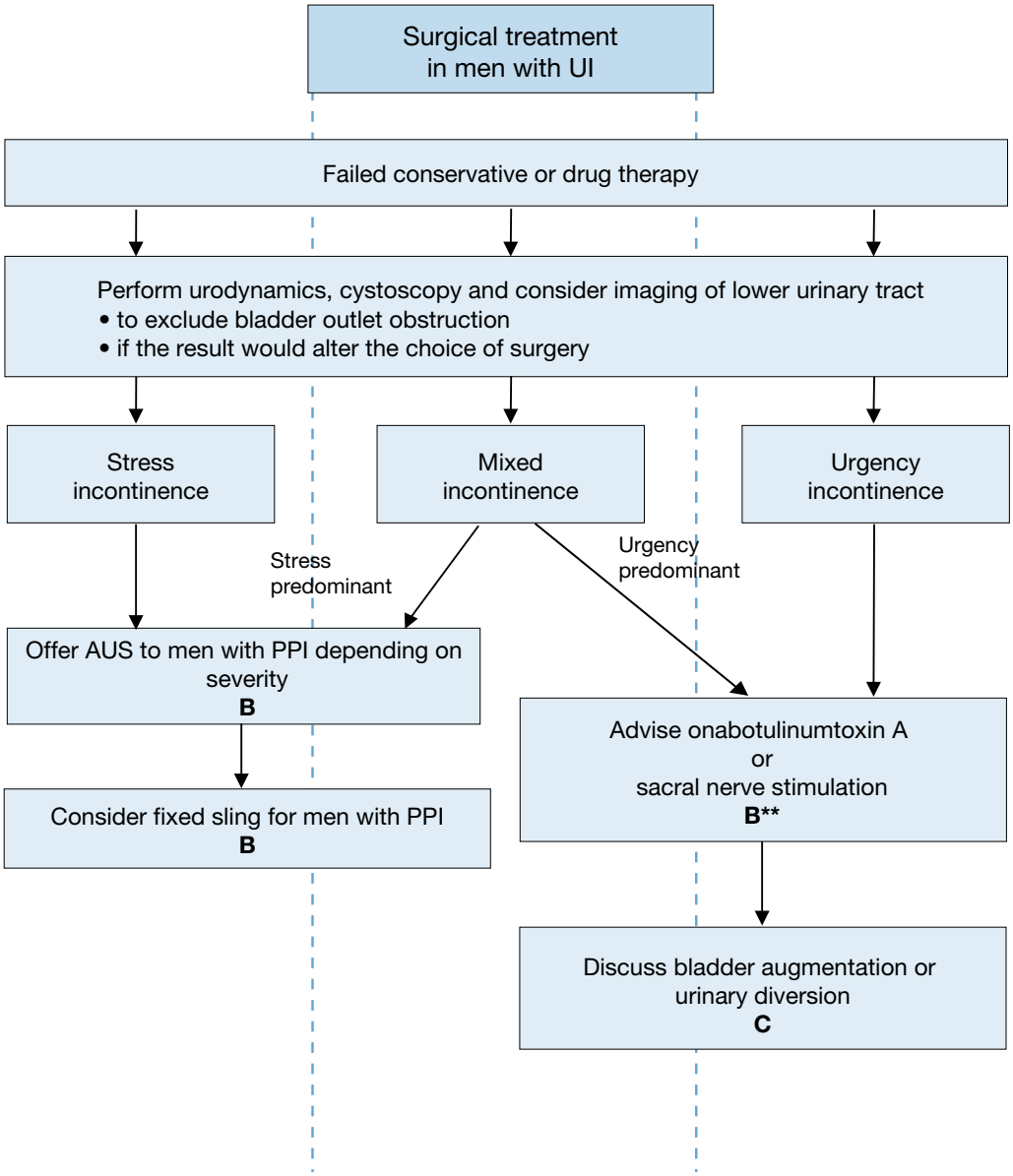




**Based on expert opinion*

Figure 2: Management and treatment of men presenting with urinary incontinence.





** Based on expert opinion*

*** Available evidence on onabutulinumtoxinA and sacral nerve stimulation refers mainly to women.*

APPENDIX A: NON OBSTETRIC URINARY FISTULA

A.1 Introduction

The evidence relating to diagnosis and treatment of urinary fistulae is generally poor and this review inevitably relies largely on numerous case series and other consensus statements. In particular, the epidemiology, aetiology, diagnosis, treatment and prevention of non-obstetric fistulae have been described in detail during the recent International Consultations on Incontinence [434, 435]. Most non-obstetric fistulae are iatrogenic in origin, causes including pelvic surgery (particularly hysterectomy for benign or malignant conditions, caesarean section and obstetric injuries). The risks during pelvic surgery increase relative to the complexity of the resection, the extent of primary disease and when there has been prior radiotherapy (especially for recurrent disease). When a fistula occurs following radiotherapy for primary treatment, this may be an indication of tumour recurrence.

A.2 Diagnosis of fistula

Clinical diagnosis

Leakage of urine is the hallmark sign of a fistula. The leakage is usually painless, may be intermittent if it is position dependent, or may be constant. Unfortunately, intraoperative diagnosis of a GU or GI injury is made in only about half of the cases that result in fistula [436].

The diagnosis of vesicovaginal fistula (VVF) usually requires clinical assessment often in combination with appropriate imaging or laboratory studies. Direct visual inspection, cystoscopy, retrograde bladder filling with a coloured fluid or placement of a tampon into the vagina to identify staining may facilitate the diagnosis of a VVF. A double-dye test to differentiate between a ureterovaginal and VVF may be useful in some cases [437]. Testing the creatinine level in either the extravasated fluid or the accumulated ascites and comparing this to the serum creatinine level will confirm urinary leakage.

Contrast-enhanced CT with late excretory phase reliably diagnoses urinary fistulae and provides information about ureteric integrity and the presence of associated urinoma. Magnetic resonance imaging, in particular with T2 weighting, also provides optimal diagnostic information regarding fistulae and may be preferred for urinary - intestinal fistulae [438].

A.3 Management of vesicovaginal fistula

A.3.1 ***Conservative management***

Before epithelialisation is complete an abnormal communication between viscera will tend to close spontaneously, provided that the natural outflow is unobstructed or if urine is diverted. Combining available data gives an overall spontaneous closure rate of 13% ± 23% (2) though this applies largely to small fistulae [435]. Hence, immediate management should be by urinary catheterisation or diversion.

A.3.2 ***Surgical management***

Timing of surgery

Findings from uncontrolled case series suggest no difference in success rates for early or delayed closure of VVF.

A.3.2.1 Surgical approaches

Vaginal procedures

There are two main types of closure techniques applied to the repair of urinary fistulae, the classical saucerisation/partial colpocleisis [439] and the more commonly used dissection and repair in layers or ‘flapsplitting’ technique [440]. There are no data comparing their outcomes.

Abdominal procedures

Repair by the abdominal route is indicated when high fistulae are fixed in the vault and are inaccessible through the vagina. A transvesical repair has the advantage of being entirely extraperitoneal. A simple transperitoneal repair is used less often although it is favoured by some using the laparoscopic approach. A combined transperitoneal and transvesical procedure is favoured by many urologists and is particularly useful for fistula repair following Caesarean section. There are no randomised studies comparing abdominal and vaginal approaches. Results of secondary and subsequent repairs are not as good as primary repair [441].

A single RCT compared trimming of the fistula edge with no trimming [442]. There was no difference in success rates but failed repairs in trimmed cases ended up with larger recurrences than untrimmed cases, which were smaller.

Laparoscopic and Robotic
Very small series (single figures) have been reported using these techniques, but whilst laparoscopic repair is feasible with and without robotic assistance, it is not possible to compare outcomes with alternative surgical approaches.

Tissue Interposition
Tissue flaps are often added as an additional layer of repair during VVF surgery. Most commonly, such flaps are utilised in the setting of recurrence after a prior attempt at repair, for VVF related to previous radiotherapy (described later), ischemic or obstetrical fistulae, large fistulae, and finally those associated with a difficult or tenuous closure due to poor tissue quality. However, there is no high level evidence that the use of such flaps improves outcomes for either complicated or uncomplicated VVF.

Post-operative management
There is no high level evidence to support any particular practice in post-operative management but most reported series used catheter drainage for at least 10 days and longer periods in radiation associated fistulae. (up to 3 weeks)

A.4 Management of radiation fistula
Modified surgical techniques are often required, and indeed, where the same techniques have been applied to both surgical and post-radiation fistulae, the results from the latter have been consistently poorer [443]. Because of the wide field abnormality surrounding many radiotherapy-associated fistulae, approaches include, on the one hand, permanent urinary and/or faecal diversion [444, 445] or alternatively preliminary urinary and faecal diversion, with later undiversion in selected cases following reconstruction. This may in some cases extend life perhaps inappropriately, and where life expectancy is deemed to be very short, ureteric occlusion might be more appropriate.

A.5 Management of ureteric fistula
General principles
Patients at higher risk of ureteric injury require experienced surgeons who can identify and protect the ureter and its blood supply to prevent injury and also recognise injury promptly when it occurs. Immediate repair of any intra-operative injury should be performed observing the principles of debridement, adequate blood supply and tension free anastomosis with internal drainage using stents [446]. Delayed presentation of upper tract injury should be suspected in patients whose recovery after relevant abdominal or pelvic surgery is slower than expected, if there is any fluid leak, and if there is any unexpected dilatation of the pelvicalyceal system. Whilst there is no evidence to support the use of one surgical approach over another, there is consensus that repair should adhere to the standard principles of tissue repair and safe anastomosis, and be undertaken by an experienced team. Conservative management is possible with internal or external drainage, endoluminal management using nephrostomy and stenting where available, and early (< 2 weeks) or delayed (> 3 months) surgical repair when required [447]. Functional and anatomical imaging should be used to follow up patients after repair to guard against development of ureteric stricture and deterioration in renal function.

Ureterovaginal fistula
Ureterovaginal fistula occurring in the early post-operative phase predominantly after hysterectomy is the most frequent presentation of upper urinary tract fistulae in urological practice. An RCT in 3,141 women undergoing open or laparoscopic gynaecological surgery found that prophylactic insertion of ureteric stents made no difference to the low risk (1%) of ureteric injury [448].

Endoscopic management is sometimes possible [449] by retrograde stenting, percutaneous nephrostomy and antegrade stenting if there is pelvicalyceal dilatation, or ureteroscopic realignment [450].

If endoluminal techniques fail or result in secondary stricture, the abdominal approach to repair is standard and may require end-to-end anastomosis, re-implantation into the bladder using psoas hitch or Boari flap, or replacement with bowel segments with or without reconfiguration.

A.6 Management of urethrovaginal fistula
Aetiology
Whilst they are rare, most urethrovaginal fistulae in adults have an iatrogenic aetiology. Causes include surgical treatment of stress incontinence with bulking agents or synthetic slings, surgery for urethral diverticulum and genital reconstruction in adults. Irradiation and even conservative treatment of prolapse with pessaries can lead to the formation of fistulae.

A.6.1 ***Diagnosis***

Clinical vaginal examination, including the three swab test, is often sufficient to diagnose the presence of a urethrovaginal fistula. Urethroscopy and cystoscopy can be performed to assess the extent and location of the fistulae. In cases of difficult diagnosis, voiding cystourethrography (VCUG) or ultrasound can be useful. 3D MRI or CT scan is becoming utilised more widely to clarify anatomy [451, 452].

A.6.2 ***Surgical repair***

Choice of surgery will depend on the size, localisation and aetiology of the fistula and the amount of tissue loss. Principles of reconstruction include identifying the fistula, creation of a plane between vaginal wall and urethra, watertight closure of urethral wall, eventual interposition of tissue, and closure of the vaginal wall.

A.6.2.1 Vaginal approach

Goodwin described in his series that a vaginal approach yielded a success rate of 70% at first attempt and 92% at second attempt, but that an abdominal approach only leads to a successful closure in 58% of cases. A vaginal approach required less operating time, had less blood loss and a shorter hospitalisation time.

Most authors describe surgical principles that are identical to those of vesicovaginal fistula repair: primary closure rates of 53-95.4% have been described. Pushkar *et al.* described a series of 71 women, treated for urethrovaginal fistula. 90.1% of fistulae were closed at the first vaginal intervention. Additionally, 7.4% were closed during a second vaginal intervention. Despite successful closure, stress incontinence developed in 52%. The stress incontinent patients were treated with synthetic or autologous slings and nearly 60% became dry and an additional 32% improved. Urethral obstruction occurred in 5.6% and was managed by urethral dilation or urethrotomy [453].

Flaps and neourethra.

The simplest flap is a vaginal advancement flap to cover the urethral suture line. Labial tissue can be harvested as a pedicled skin flap. This labial skin can be used as a patch to cover the urethral defect, but can also be used to create a tubular neo-urethra [454, 455]. The construction of a neo-urethra has mostly been described in traumatic aetiologies. In some cases a transpubic approach has been used [456]. The numbers of patients reported are small and there are no data on the long-term outcome of fistula closure and continence rates. The underlying bulbocavernosus tissue can be incorporated in the pedicled flap and probably offers a better vascularisation and more bulking to the repair. This could allow a safer placement of a sling afterwards, in those cases where bothersome stress incontinence would occur post-operatively [457, 458].

Martius flap

While in obstetrical fistula repair it was not found to have any benefit in a large retrospective study in 440 women, the labial bulbocavernosus muscle/fat flap by Martius is still considered by some to be an important adjunctive measure in the treatment of genitourinary fistulae where additional bulking with well vascularised tissue is needed [459]. The series of non-obstetrical aetiology are small and all of them are retrospective. There are no prospective data, nor randomised studies [460]. The indications for Martius flap in the repair of all types of fistulae remain unclear.

Rectus muscle flap

Rectus abdominis muscle flaps have been described by some authors [461, 462].

A.6.2.2 Abdominal approach

A retropubic retrourethral technique has been described by Koriatim [463]. This approach allows a urethrovesical flap tube to be fashioned to form a continent neo-urethra.

Summary of evidence	LE
Spontaneous closure of surgical fistulae does occur, although it is not possible to establish the rate with any certainty.	3
There is no evidence that the timing of repair makes a difference to the chances of successful closure of a fistula.	3
There is no high quality evidence of differing success rates for repair of vesicovaginal fistulae data by vaginal, abdominal, transvesical and transperitoneal approaches.	3
A period of continuous bladder drainage is crucial to successful fistula repair but there is no high level evidence to support one regime over another.	3
A variety of interpositional grafts can be used in either abdominal or vaginal procedures, although there is little evidence to support their use in any specific setting.	3
Post radiation fistula	
Successful repair of irradiated fistulae requires prior urinary diversion and the use of non-irradiated tissues to effect repair.	3
Ureteric fistula	
Prophylactic ureteric stent insertion does not reduce risk of ureteric injury during gynaecological surgery.	2
Antegrade endoluminal distal ureteric occlusion combined with nephrostomy tube diversion often palliates urinary leakage due to malignant fistula in the terminal phase.	4
Urethrovaginal fistula	
Urethrovaginal fistula repair may be complicated by stress incontinence, urethral stricture and urethral shortening necessitating long-term follow-up.	3

Recommendations	GR
General	
Surgeons undertaking complex pelvic surgery should be competent at identifying, preserving and repairing the ureter.	C
Do not routinely use ureteric stents as prophylaxis against injury during routine gynaecological surgery.	B
Suspect ureteric injury or fistula in patients following pelvic surgery if a fluid leak or pelvicalyceal dilatation occurs post-operatively or if drainage fluid contains high levels of creatinine.	C
Suspect uretero-arterial fistula in patients presenting with haematuria with a history of relevant surgery.	C
Use three dimensional imaging techniques to diagnose and localise urinary fistulae.	C
Manage upper urinary tract fistulae by conservative or endoluminal technique where such expertise and facilities exists.	B
Surgical principles	
Surgeons involved in fistula surgery should have appropriate training, skills, and experience to select an appropriate procedure for each patient.	C
Attention should be given as appropriate to skin care, nutrition, rehabilitation, counselling and support prior to and following fistula repair.	C
If a vesicovaginal fistula is diagnosed within six weeks of surgery, consider indwelling catheterisation for a period of up to 12 weeks after the causative event.	C
Tailor the timing of fistula repair to the individual patient and surgeon requirements once any oedema, inflammation, tissue necrosis, or infection, are resolved.	B
Where concurrent ureteric re-implantation or augmentation cystoplasty are required, the abdominal approach is necessary.	C
Ensure that the bladder is continuously drained following fistula repair until healing is confirmed (expert opinion suggests: 10-14 days for simple and/or postsurgical fistulae; 14-21 days for complex and/or post-radiation fistulae).	C
Where urinary and/or faecal diversions are required, avoid using irradiated tissue for repair.	C
Use interposition grafts when repair of radiation associated fistulae is undertaken.	C
In patients with intractable urinary incontinence from radiation-associated fistula, where life expectancy is very short, consider performing ureteric occlusion.	C
Repair persistent ureterovaginal fistula by an abdominal approach using open, laparoscopic or robotic techniques according to availability and competence.	C
Consider palliation by nephrostomy tube diversion and endoluminal distal ureteric occlusion for patients with ureteric fistula associated with advanced pelvic cancer and poor performance status.	C
Urethrovaginal fistulae should preferably be repaired by a vaginal approach.	C

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6. 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 publically accessible through the European Association of Urology website: http://www.uroweb.org/guidelines/. This 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.