Guidelines on Urinary Incontinence

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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.

These Guidelines from the European Association of Urology (EAU) Working Panel on Urinary Incontinence are written by urologists primarily for urologists, though we recognise that they 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 EAU Panel knew that they would find little evidence for some issues and a lot of evidence for others. This difference, to some extent, reflects the greater funding available for industry-sponsored trials of drugs, the results of which are required for licensing in Europe and the USA. The less stringent regulatory requirements for the introduction of new devices or surgical techniques means that there are far fewer high-quality studies regarding these interventions. Although the lack of high-quality evidence means that judgements about the worth of interventions are prone to bias, the Panel took the view that clinicians still require some guidance concerning clinical practice. In these circumstances, we have summarised the available evidence and made recommendations based on expert opinion, with uncertainty reflected by a lower grade of recommendation.

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 health care professionals such as elderly care physicians is recommended.

1.1 Methodology

The current Guidelines provide:

- A clear clinical pathway (algorithm) for common clinical problems. This can provide the basis for thinking through a patient's management and also for planning and designing clinical services.
- A brief but 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.

*1.1.1 **PICO questions***

The 'PICO' (Population, Intervention, Comparison, Outcome) framework was used to develop a series of clinical questions that would provide the basis of presentation of the guidelines (4,5). There are four elements to each clinical question:

- population
- intervention
- comparison
- outcome.

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

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

In this third edition of these new EAU Guidelines for Urinary Incontinence, the Panel has focused largely on the management of a 'standard' patient. The Panel has referred in places to patients with 'complicated incontinence', by which we mean patients with associated morbidity, a history of previous pelvic surgery, surgery for UI, radiotherapy and women with associated genitourinary prolapse. This third edition does not review the prevention of UI and the management of fistula is introduced as an appendix. These issues will be fully addressed using our standard methodology in future editions.

*1.1.2 **Search strategies***

A number of significant narrative reviews, systematic reviews and guidance documents have been produced within the last few years. The Panel agreed that the literature searches carried out by these reviews would be accepted as valid. Thus, for each PICO question, a search was carried out with a start date that was the same as the cut-off date for the search associated with the most recent systematic review for the PICO topic. This pragmatic selection approach, while being a compromise and open to criticism, made the task of searching the literature for such a large subject area possible within the available resources. For each section, the latest cut-off date for the relevant search is indicated. Thus, for each PICO, a subsequent literature search was carried out (confined to Medline and Embase and to English language articles), which produced an initial list of abstracts. The abstracts were each assessed by two Panel members, who selected the studies relevant to the PICO question, and the full text for these was retrieved (Table 1).

Table 1: Initial list of abstracts

Chapter	*Latest 'cut-off' date for search*
Assessment and diagnosis	28 June 2012 - PROMS & Questionnaires: 20 April 2013
Conservative therapy	28 June 2012 - Containment: 10 July 2013
Drug therapy	28 June 2012 - Anticholinergic load: 29 April 2013 - Mirabegron: 25 September 2013
Surgical therapy	9 July 2012 - POP & OAB: 29 April 2013 - Prolapse reduction stress test: 16 May 2013 - Urethral diverticulum: 7 May 2013

Each PICO was then assigned to a Panel member, who read the papers and extracted the evidence for incorporation into standardised evidence tables. From 2012 onwards we have used a purpose designed web based application in which original papers are downloaded and appraised online according to a standardised format which is based on SIGN. The web application is progressively populated with evidence appraisals which can be displayed in tabular format showing summaries of data quality as well as summaries of outcomes.

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

The quality of evidence for each PICO is commented on in the text, aiming to synthesise the important clinical messages from the available literature and is presented as a series of levels of evidence summaries in the EAU format (Table 2).

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

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

It must be emphasised that clinical guidelines present the best evidence available to the Panel at the time of writing. There remains a need for ongoing re-evaluation of the current guidelines by the Panel. However, following guideline recommendations will not necessarily result in the best outcomes for patients. Guidelines can never replace clinical expertise when making treatment decisions for individual patients; they aim to focus

decisions by addressing key clinical questions, and provide a strong basis for management decisions. Clinical decisions must also take into account the patient's personal values, preferences and specific circumstances.

1.1.3 Level of evidence and grade of recommendation

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

Table 2: Level of evidence (LE)*

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

**Modified from Sackett et al. (6)*

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

Alternatively, an absence of high-level evidence does not necessarily preclude a Grade A recommendation; if there is overwhelming clinical experience and consensus to support a high-level recommendation, then a Grade A recommendation can be given. In addition, there may be exceptional situations in which corroborating studies cannot be performed, perhaps for ethical or other reasons. In this case, unequivocal recommendations are considered helpful for the clinician. Whenever this occurs, it has been clearly indicated in the text with an asterisk, as 'upgraded based on Panel consensus'. The quality of the underlying scientific evidence is a very important factor, but it has to be balanced against benefits and burdens, personal values and preferences when a grade is assigned (7-9).

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

Table 3: Grade of recommendation (GR)*

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

**Modified from Sackett et al. (6)*

1.2 Publication history

The complete update in 2009 was largely a synthesis of guidance by the International Consultation on Urological Diseases (ICUD) and the National Institute for Health and Clinical Evidence (NICE), as was the 2010 edition. In 2011, an addendum was added on the use of drugs, now incorporated in the full text under Chapter 4. The 2012 edition was completely rewritten using new methodology and based on new searches up to July 2011 and those carried out for ICUD and NICE documents. The 2012 edition was updated with new searches up to September 2012 for the 2013 edition.

In this 2014 edition additional searches were done for Patient Reported Outcome Measures (PROMS), urethral diverticulum, containment, prolapse reduction stress test, anticholinergic load, and mirabegron.

The 2013 edition Appendix on mixed urinary incontinence has been incorporated into the main text. The 2013 edition Appendix on Elderly has been removed entirely as it contained only information that already appears in the main text. A separate Appendix is provided on fistula derived from the ICUD 2013 but the contained evidence has not yet been assessed according to our methodology (see Appendix A).

A quick reference guide, presenting the main findings of the Urinary Incontinence Guidelines, is also available, as well as two scientific publications in the journal of the EAU, *European Urology* (10,11). All texts can be viewed and downloaded for personal use at the society website:
http://www.uroweb.org/guidelines/online-guidelines/.

This document was peer-reviewed prior to publication.

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1.4 Use in different healthcare settings and by healthcare professionals

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

1.5 Terminology

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

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

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

2. ASSESSMENT AND DIAGNOSIS

2.1 History and physical examination

Taking a careful clinical history is fundamental to the clinical process. Despite the lack of formal evidence, there is universal agreement that taking a history should be the first step in the assessment of anyone with UI. The history should include details of the type, timing and severity of 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, or cause it.

Similarly, there is little evidence 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 can be assessed digitally.

2.2 Patient questionnaires

Questionnaires may be symptom scores, symptom questionnaires, scales, indexes, patient-reported outcome measures (PROMS) or health-related quality of life (HRQoL) measures. HRQoL questionnaires can be divided into generic (e.g. SF-36) or condition-specific (e.g. Incontinence Impact Questionnaire, the King's Health Questionnaire, OAB-q). Questionnaires are widely used to record patients' symptoms in a standardised way, including their severity and impact, and have been used to monitor the condition over time, e.g. in the context of changes related to treatment. During the last 10 years, many questionnaires have been developed and researched, including ones specifically designed for lower urinary tract symptoms (LUTS), POP, faecal incontinence and both condition-specific and generic quality of life (QoL).

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 4th International Consultation on Incontinence in 2008 (1) and updated in the 5th International Consultation on Incontinence in 2012 (2).

*2.2.1 **Questions***

- 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?
- In patients with UI can the use of Questionnaires/PROMS differentiate between stress, urgency and mixed incontinence, and does this differentiation impact on quality of life after treatment?

2.2.2 ***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 greatly limits the extent to which results and conclusions from these studies can be applied in adults with UI. There is low-level evidence that questionnaires may be more sensitive to change than a bladder diary (3).

Randomised crossover studies (3,4) suggested that web-based questionnaires may be acceptable to patients as well as paper versions and another randomized crossover study suggested that postal questionnaires were better than interview-assisted questionnaire (5).

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

The 5th ICUD review evaluated a full range of existing questionnaires in relation to validity, reliability, responsiveness to change and categorised them as A B or C depending on whether all three, two or one (respectively) of these attributes has been studied and reported.

These instruments can be classified according to their purpose and include the following.

	Category A	Category B	Category C
Symptom measures and health related QOL measures	ICIQ-UI Short Form, ICIQ-FLUTS, IIQ and IIQ-7, I-QOL (ICIQ-Uqol), ISS, KHQ, LIS (?-interview), N-QoL, OAB-q SF, OAB-q (ICIQ-OABqol), PFDI and PFDI-20, PFIQ and PFIQ-7, PRAFAB, UISS;	Contilife, EPIQ, IOQ, YIPS;	ISI, ISQ, UIHI
Measure of patient satisfaction (patient's measure of treatment satisfaction)	BSW, OAB-S, OAB-SAT-q, TBS		EPI, GPI, PSQ
Goal attainment scales			SAGA
Screening tools (used to identify patients with UI)	B-SAQ, OAB-SS, OAB-V8, 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

ICIQ = International Consultation on Incontinence Modular Questionnaire
ICIQ-FLUTS = ICIQ-Female Lower Urinary Tract Symptoms
IIQ (IIQ-7) = Incontinence Impact Questionnaire (short form)
I-QOL (ICIQ-Uqol) = Urinary Incontinence-Specific Quality of Life Instrument
ISS = Incontinence Symptom Severity Index
KHQ = King's Health Questionnaire
LIS = Leicester Impact Scale
N-QoL = Nocturia Quality of Life Questionnaires
OAB-q (ICIQ-OABqol) = Overactive Bladder Questionnaire
PFDI (PFDI-20) = Pelvic Floor Distress Inventory (short form)
PFIQ (PFIQ-7) = Pelvic Floor Impact Questionnaire (short form)
PRAFAB = Protection, Amount, Frequency, Adjustment, Body image)
UISS = Urinary Incontinence Severity Score
BSW = Benefit, Satisfaction with treatment and Willingness
OAB-S = Overactive Bladder Satisfaction measure
OAB-SAT-q = OAB Satisfaction questionnaire
TBS = Treatment Benefit Scale
B-SAQ = Bladder Self-Assessment Questionnaire
OAB-SS = Overactive Bladder Symptom Score

OAB-v8 = OAB Awareness Tool
OAB-v3 = OAB short form
QUID = Questionnaire for Urinary Incontinence Diagnosis
PPBC = Patient Perception of Bladder Condition
UDI (UDI-6) = Urogenital Distress Inventory (-6)
LUSQ = Leicester Urinary Symptom Questionnaire
PGI-I and PGI-S = Patient Global Impression of Severity and Improvement
IUSS = Indevus Urgency Severity
U-IIQ = Urge Incontinence Impact Questionnaire
UU Scale = 10-item Scale to Measure Urinary Urgency
U-UDI = Urge-Urogenital distress inventory
Contlife® = Quality of Life Assessment Questionnaire Concerning Urinary Incontinence
EPIQ - Epidemiology of Prolapse and Incontinence Questionnaire
IOQ = Incontinence Outcome Questionnaire
YIPS = York Incontinence Perceptions Scale
ISQ = Incontinence Stress Index
USP = Urinary Symptom Profile
PFBQ = Pelvic Floor Bother Questionnaire
SSI and SII = Symptom Severity Index and Symptom Impact Index for Stress Incontinence in women
PPIUS = Patient's Perception of Intensity of Urgency Scale
SUIQ = Stress/Urge Incontinence Questionnaire
UPScore = Urgency Perception Score
UPScale = Urgency Perception Scale
UQ = Urgency Questionnaire
USIQ-QOL = Urgency Severity & Intensity Questionnaire: Symptom Severity
USIQ-S = Urgency Severity & Intensity Questionnaire: Quality of Life
USS = Urinary Sensation Scale
FSFI = Female Sexual Function Index
ICIQ-VS = International Consultation on Incontinence Questionnaire - Vaginal Symptoms
PISQ = Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire
SQoL-F = Sexual Quality of Life - Female
ISI = Incontinence Severity Index
UIHI = Urinary Incontinence Handicap Inventory
SAGA = Self-Assessment Goal Achievement Questionnaire
3IQ = Three Incontinence Questions Questionnaire
CLSS = Core Lower Urinary Tract Symptom Score
MESA = Medial Epidemiological and Social Aspects of Aging Questionnaire
PUF = patient symptom scale (Pelvic Pain, Urgency and Frequency)
PMSES = Broome Pelvic Muscle Exercise Self-Efficacy Scale
POSQ = Primary OAB Symptom Questionnaire
UI-4 = Urinary Incontinence -4 Questionnaire

There are specific questionnaires for older people such as the Urge Impact Scale - URIS (Category B), and for caregivers - the Overactive Bladder Family Impact - OAB-FIM *Category B).

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

Evidence summary	**LE**
Validated condition specific symptom scores assist in the screening for, and categorisation of UI.	3
Validated symptom scores measure the bothersomeness 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*

*2.2.3 **Research priorities***

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

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2.3 Voiding diaries

Measurement of the frequency and severity of LUTS is an important step in the evaluation and management of lower urinary tract dysfunction, including UI. Voiding diaries are a semi-objective method of quantifying symptoms, such as frequency of urinary incontinence 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 as a semi-objective measure of treatment outcome.
In patients with severe UI, a voiding diary is unlikely to accurately report total urine output and so the functional bladder capacity measured by voided volume will be lower than total bladder capacity.

*2.3.1 **Questions***

In adults with UI, what are the reliability, diagnostic accuracy and predictive value of a voiding diary compared to patient history or symptom score?
How does the accuracy of a computerised voiding diary compare to a paper diary?

*2.3.2 **Evidence***

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

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

Several studies have compared patients' preference for, and the accuracy of, electronic and paper voiding diaries in voiding dysfunction (3-7). Several studies have compared shorter (3 or 5 days) and longer diary durations (7 days) (8-13). The choice of diary duration appears to be based upon the possible behavioural therapeutic effect of keeping a diary rather than on better validity or reliability.

Two studies have demonstrated the reproducibility of voiding diaries in both men and women (8,13). Further studies have demonstrated variability of diary data within a 24-hour period and compared voided volumes recorded in diaries with those recorded on uroflowmetry (14,15). Other studies have investigated the correlation between data obtained from voiding diaries and standard symptom evaluation (16-19).

One study investigated the effect of diary duration on the observed outcome of treatment of LUTS (20). Another study found that keeping a voiding diary had a therapeutic benefit (21).

In conclusion, Voiding diaries generally give reliable data on lower urinary tract function. There remains a lack of consensus on diary duration and how well diary data correlate with some symptoms.

Evidence summary	LE
Voiding diaries of 3-7 days duration are a reliable tool for the objective measurement of mean voided volume, daytime 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 to complete a voiding diary to evaluate co-existing storage and voiding dysfunction in patients with urinary incontinence.	A
Use a diary duration of between 3 and 7 days.	B

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2.4 Urinalysis and urinary tract infection

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

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

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

It is generally agreed that dipstick urinalysis of a mid-stream urine specimen provides sufficient screening information for UTI in both men and women with UI. Microscopy and other tests may be necessary to confirm any abnormalities identified on dipstick analysis.

*2.4.1 **Questions***

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

*2.4.2 **Evidence***

In both men and women with UI, the diagnosis of a UTI by positive leucocytes or nitrites using urine culture as the reference standard had a low sensitivity and very high specificity (3,4). A negative urine dipstick test in patients with UI therefore excludes a UTI with a high degree of certainty. There is a consensus that urinalysis should be a standard part of the basic evaluation of UI, irrespective of sex, age or aetiology.

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

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

** Recommendation based on expert opinion*

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2.5 Post-voiding residual volume

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

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

2.5.1 ***Question***

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

2.5.2 ***Evidence***

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

Several studies have evaluated PVR in different subjects and patient cohorts (7-17). In peri- and postmenopausal women without significant LUTS or pelvic organ symptoms, 95% of women had a PVR < 100 mL (9).
A comparison of women with and without LUTS suggested that symptomatic women had a higher incidence of elevated PVR (11). In women with UUI, a PVR > 100 mL was found in 10% of cases (16). Other research has found that a high PVR is associated with POP, voiding symptoms and an absence of SUI (8,12,14,15).

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 (16). Overall, women with symptoms of lower urinary tract or pelvic floor dysfunction and POP have a higher rate of elevated PVR compared to asymptomatic subjects.

There is evidence to suggest that elevated PVR should be particularly looked for in patients with voiding symptoms (18-21), but there is no evidence to define a threshold between normal and abnormal PVR values. Expert opinion has therefore been used to produce definitions of elevated PVR values (22-25), There is a lack of evidence to support the routine measurement of PVR in patients with UI (26-30).

Evidence summary	**LE**
US provides an accurate estimate of post-voiding residual.	1b
Lower urinary tract dysfunction is associated with a higher rate of post-voiding residual compared to	
asymptomatic subjects.	2
Elevated post-voiding residual is not a risk factor for poor outcome from treatment of SUI.	2

Recommendations	GR
Use ultrasound to measure post-voiding residual.	A
Measure post-voiding residual in patients with urinary incontinence who have voiding dysfunction.	B
Measure post-voiding residual when assessing patients with complicated urinary incontinence.	C
Post-voiding residual should be monitored in patients receiving treatments that may cause or worsen voiding dysfunction.	B
Consider the presence of voiding dysfunction in patients whose post-voiding residual is persistently above 100 mL.	A*

** Recommendation based on expert opinion*

*2.5.3 **Research priority***

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

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2.6 Urodynamics

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

Multichannel cystometry, ambulatory monitoring and video-urodynamics aim to observe the effects on intravesical and intra-abdominal pressures while reproducing a patient's symptoms. Bladder filling may be artificial or physiological and voiding is prompted. Any incontinence observed may be categorised as urodynamic SUI, detrusor overactivity (DO) incontinence, a mixture of SUI/DO incontinence, or, rarely, urethral relaxation incontinence. A test may fail to reproduce a patient's symptoms because of poor diagnostic accuracy or because the symptoms are not directly attributable to an urodynamically measurable phenomenon.

Urodynamic testing is widely used as an adjunct to clinical diagnosis, to direct decisions about treatment and to provide prognostic information. When clinical diagnosis is difficult because of an unclear history or inconclusive examination, urodynamics may provide the only 'diagnosis' available. Although it is unlikely that carrying out a test, in itself, would alter the outcome of treatment, it remains possible that the test results would influence treatment decisions to such an extent that better outcomes are achieved. This has been the rationale for using urodynamics prior to surgery.

2.6.1 ***Question***

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

2.6.2 ***Evidence***

2.6.2.1 Repeatability

Although a recent study has suggested that test retest variability is acceptable (1), many older studies have shown a variability of up to 15% in different urodynamic parameters (2-9). No published studies on the reliability of ambulatory monitoring were found.

Various techniques are used to measure urethral profilometry. Individual techniques are generally reliable in terms of repeatability, but results may vary between different techniques, so that one type of test cannot be compared meaningfully to another (10-12).

The measurement of abdominal or Valsalva leak point pressures has not been standardised. It has not been possible to correlate consistently any method of measuring Valsalva leak point pressure with either UI severity or other measures of urethral function (13-18).

Studies of technical accuracy have included adults with LUTS, with or without UI. The studies used different equipment and lacked standardised techniques (19,20). As with all physiological investigation, results have shown a wide range of variability. Inter-rater and intra-rater reliability of video-urodynamics for the severity and type of SUI is good (21).

2.6.2.2 Diagnostic accuracy

The diagnostic accuracy of urodynamics cannot be measured against a 'gold standard'. Instead, the types of dysfunction identified by urodynamics are often correlated with clinical findings and clinical history. Ambulatory urodynamics may detect unexpected physiological variance from normal, more often than conventional cystometry, but the clinical relevance of this is uncertain (22,23).

The diagnostic accuracy of Leak Point Pressure, Urethral Pressure Profile and Urethral Retroresistance and Urethral Reflectometry (URR) is generally poor (24).

Detrusor overactivity may be found in asymptomatic patients, while normal cystometry is found in patients who are symptomatic. There have been many studies of variable quality investigating the relationship between UI symptoms and subsequent urodynamic findings. For their UK-based guidance, NICE reviewed 11 studies (25), which investigated the relationship between clinical diagnosis and urodynamic findings and the diagnostic accuracy of urodynamic measurement, specifically in females. We found that no new evidence has been published since the NICE search in 2005 up until September 2012.

There is a consensus that urodynamic tests should aim to reproduce the patient's symptoms and should be performed with attention to technical and methodological detail. In clinical practice, urodynamic testing (cystometry) may help to provide, or confirm, a diagnosis, predict treatment outcome, or facilitate discussion during a consultation. It is unlikely that any test, in itself, would alter the outcome of treatment. However, it is possible that the way test results influence treatment choices may have an impact on this. For all these reasons, urodynamics is often performed prior to invasive treatment for UI.

2.6.2.3 Does urodynamics influence the outcome of conservative therapy

A recent Cochrane review included seven RCTs that examined the question of whether urodynamics influences therapy for UI including conservative therapy. The review showed that urodynamic tests influenced clinical decision making; (increased likelihood of using drugs in two trials or to avoid surgery in three trials. However, there was not enough evidence to suggest that this altered the clinical outcome of treatment (26). Subanalysis of a RCT comparing fesoterodine to placebo, and another dose finding study of botulinum toxin (27) showed no predictive value, in terms of drug response, for the urodynamic diagnosis of DO (28).

2.6.2.4 Does urodynamics influence the outcome of surgery for SUI?

Post-hoc analysis of surgical RCTs has shown the risk of failure of SUI surgery is higher in women who have worse leakage or urodynamically demonstrable SUI (29).

One Two high quality RCTs compared office evaluation alone to office evaluation and urodynamics in women with clinical demonstrable SUI about to undergo surgery for SUI. There was no difference in levels of UI or any secondary outcome at 12 months' follow-up (30,31).

Various studies have examined the relationship between measures of poor urethral function, i.e. low maximal urethral closure pressure, low Valsalva leak point pressure, and subsequent failure of surgery. Some studies found a correlation between low urethral pressures and surgical failure, while other studies did not (32-35). A correlation, in itself, was not necessarily predictive.

2.6.2.5 Does urodynamics help to predict complications of surgery?

There have been no RCTs. A large number of case series, or post-hoc analyses of larger studies, have examined the relationship between urodynamic parameters and complications of surgery for SUI. A low Qmax or low voiding pressure were not consistently associated with postoperative voiding difficulty (36-43).

The presence of pre-operative DO has more consistently been associated with development of postoperative UUI. Post-hoc analysis of an RCT comparing the autologous fascial sling to Burch colposuspension showed inferior outcomes for women who suffered pre-operative urgency (44). However pre-operative urodynamics had failed to predict this outcome (45). Other case series, however, have shown there is a consistent association of poor outcomes with pre-operative DO, although the predictive value was not calculated (46,47).

2.6.2.6 Does urodynamics influence the outcome of surgery for DO?

No studies were found on the relationship between urodynamic testing and subsequent surgical outcome for DO. However, most studies reporting surgical outcomes for DO have included only patients with urodynamically proven DO or DO incontinence. Higher-pressure DO appears to be consistently associated with surgical failure and persistent or de novo urgency. As with other suggested 'predictors', the predictive value has not often been formally calculated (32,48,49). Pre-operative urgency was resolved in some patients (50,51).

2.6.2.7 Does urodynamics influence the outcome of treatment for post-prostatectomy UI in men?

There are no RCTs examining the clinical usefulness of urodynamics in post-prostatectomy UI. However, many case series have demonstrated the ability of urodynamics to distinguish between different causes of UI (52-54). The ability of urodynamic testing to predict surgical outcome for post-prostatectomy UI is inconsistent (55,56).

Evidence summary	LE
Most urodynamic parameters show a high random immediate and short-term test-retest variability of up to 15% in the same subject.	2
Test-retest variability creates an overlap between 'normal' and 'abnormal' populations, which may make it more difficult to categorise urodynamic findings in a particular individual.	2
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
Preliminary urodynamics in women with uncomplicated, clinically demonstrable SUI does not improve the outcome of surgery for SUI.	1b
There is conflicting low-level evidence that urodynamic tests of urethral function predict outcome of surgery for SUI in women.	3
There is consistent low-level evidence that pre-operative DO predicts poorer outcomes of mid-urethral sling surgery in women.	3
There is limited evidence for whether preliminary urodynamics predicts the outcomes of treatment for UI in men.	4

Recommendations	GR
(NB: These refer only to neurologically intact adults with urinary incontinence)	
Clinicians carrying out urodynamics in patients with urinary incontinence should: • Ensure that the test replicates the patient's symptoms. • Interpret results in context of the clinical problem. • Check recordings for quality control. • Remember there may be physiological variability within the same individual.	C
Advise patients that the results of urodynamics may be useful in discussing treatment options, although there is limited evidence that performing urodynamics will predict the outcome of treatment for urinary incontinence.	C
Do not routinely carry out urodynamics when offering conservative treatment for urinary incontinence.	B
Perform urodynamics if the findings may change the choice of invasive treatment.	B
Do not use urethral pressure profilometry or Leak Point pressures to grade severity of incontinence or predict the outcome of treatment.	C
Urodynamic practitioners should adhere to the standards laid out in the ICS document "Good Urodynamic Practice" (57).	C

*2.6.3 **Research priority***

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

*2.6.4 **References***

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2.7 Pad testing

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

*2.7.1 **Question***

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

*2.7.2 **Evidence***

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

A few studies have tried to use pad testing to predict the outcome of treatment for UI with inconsistent results (12-14). Currently, pad tests are mostly used as objective outcomes in clinical trials. However, pad tests may be helpful in daily clinical practice, and most guidelines already include the use of pad testing to evaluate treatment outcome (15,16). There is good evidence to show that repeat pad testing can detect change following treatment for UI (17-19).

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

Recommendations	**GR**
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

*2.7.3 **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?

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2.8 Imaging

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

Ultrasound and magnetic resonance imaging (MRI) have replaced X-ray imaging, as both procedures are safer and can provide both qualitative and quantitative data on the kidneys, bladder neck and pelvic floor. Ultrasound is preferred to MRI because of its ability to produce three-dimensional and four-dimensional (dynamic) images at lower cost and wider availability. The current lack of knowledge about the pathophysiology of UI makes it difficult to carry out research in the imaging of UI. Studies on lower urinary tract imaging in patients with UI often include an evaluation of surgical outcomes, making design and conduct of these trials challenging.

2.8.1 ***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?

2.8.2 ***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 (1). In addition, the generalised increase in urethral mobility after childbirth does not appear to be associated with de novo SUI (2).

There is a general consensus that MRI provides good global pelvic floor assessment, including POP, defecatory function and integrity of the pelvic floor support (3). However, there is a large variation in MRI interpretation between observers (4) 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 (5). In addition, the position of mid-urethral slings with respect to the pubis has been associated with the cure of UI (6).

Several imaging studies have investigated the relationship between sphincter volume and function in women (7) and between sphincter volume and surgery outcome in men and women (8,9). Imaging of urethral anastomosis following radical prostatectomy has been used to investigate continence status (10). 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 clinical benefit.

Detrusor wall thickness

As OAB has been linked to detrusor overactivity, it has been hypothesised that frequent detrusor contractions may increase detrusor wall thickness (DWT) and, bladder wall thickness (BWT). However, it has not demonstrated if the routine use of these parameters improves management of people with OAB. Bladder wall thickness and DWT measurement are operator dependent and may be influenced by the degree of bladder filling (11), route used for scanning (12), type of ultrasound probes and image resolution (13). One study noted that a BWT of > 5 mm is typically found in women with OAB and that antimuscarinic treatment reduced BWT (14). However, this study did not include a group of healthy women. Serati et al concluded that only a BWT ≥ 6.5 mm offers a very high probability of a diagnosis of DO (15). Khun et al in a study of 123 women found that BWT was significantly higher in those with DO or BOO than in those with SUI (16), whilst two other studies found that DWT was similar in women with and without OAB (17,18).

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

Recommendations	**GR**
Do not routinely carry out imaging of the upper or lower urinary tract as part of the assessment of urinary incontinence.	A
Do not include bladder (detrusor) wall thickness measurement in the routine assessment of urinary incontinence.	C

2.8.3 ***Research priority***

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

2.8.4 ***References***

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3. CONSERVATIVE MANAGEMENT

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

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

It is sometimes necessary to advise use of containment devices, usually pads, whilst individuals are trying options of conservative treatment for UI, although it is important not to consider containment as a treatment in itself. People with UI who lack motivation to trial treatments, or in whom active treatment is impossible, may require long-term usage of containment devices.

3.1 Simple clinical interventions

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

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

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

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

3.1.1.1 Question

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

3.1.1.2 Evidence

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

Evidence summary	LE
Improved diabetic control does not improve UI.	3

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*3.1.2 **Adjustment of medication***

Although UI is listed as an adverse effect of many drugs in many drug compendiums, e.g. *British National Formulary*, 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 (1). There is also a risk that stopping or altering medication may result in more harm than benefit.

3.1.2.1 Question

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

3.1.2.2 Evidence

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

Several case series have suggested a link between drugs with a CNS site of action and UI (2). A secondary analysis of a large observational database of elderly Italians found a higher risk of UI among those taking benzodiazepines. In addition, a retrospective analysis of a large Dutch database of dispensed prescriptions found that patients started on a selective serotonin re-uptake inhibitor were more likely to require a subsequent prescription of antimuscarinic drugs or absorbent urinary pads, suggesting the development of UI (4). Although one would expect that diuretic therapy would increase UI in the same way as polyuria, limited evidence in men suggests that this is not the case (2).

Oestrogenic drugs including conjugated equine oestrogens, oestradiol, tibolone and raloxifene, are used as hormone replacement therapy (HRT) for women with natural or therapeutic menopause. 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 (5-8). In a single RCT use of raloxifene was not associated with development or worsening of UI (9). Three small RCTs using oral oestriol or oestradiol as HRT for vulvovaginal atrophy suggested that UI symptoms were improved although the evidence was unclear (1,10,11).

Evidence summary	LE
Alpha-blockers used to treat hypertension in women may cause or exacerbate UI, and stopping them may relieve UI.	3
Individuals taking drugs acting on the CNS may experience UI as a side effect.	3
Diuretics in elderly patients does not cause or worsen UI.	3
Systemic hormone replacement therapy using conjugate equine estrogens in previously continent women increases the risk of developing UI and worsens pre-existing UI.	1a

Recommendations	GR
Take a drug history from all patients with urinary incontinence.	A
For women taking oral conjugated equine oestrogen as hormone replacement therapy who develop or worsen UI, suggest discussion of alternative hormone replacement therapies with the relevant clinician.	A
Advise women who are taking systemic oestradiol who suffer from UI, that stopping the oestradiol is unlikely to improve their incontinence.	A
Review any new medication associated with the development or worsening of urinary incontinence.	C

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*3.1.3 **Constipation***

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

3.1.3.1 Question

Does treatment for constipation improve UI?

3.1.3.2 Evidence

One RCT found that a multimodal intervention in elderly patients, involving assisted toileting, fluid intake, etc, reduced the occurrence of UI and constipation, while behavioural therapy appeared to improve both (1).

An observational study comparing women with UI and women with POP to controls found that a history of constipation was associated with both prolapse and UI (2). Two, large, cross-sectional population-based studies (3,4) and two longitudinal studies (5,6) showed that constipation was a risk factor for LUTS.

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

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

Recommendation	**GR**
For adults with urinary incontinence, treat co-existing constipation.	C

3.1.3.3 Research priority

Does the normalisation of bowel habit improve urinary UI in patients who are constipated?

3.1.3.4 References

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3.1.4 ***Containment***

Containment is important for people with urinary incontinence when active treatment does not cure the problem, or when it is not available or not possible. Absorbent pads are most frequently used and vary in design according to sex of user, degree of incontinence and degree of dependency. Dermatitis related to pad use for incontinence can be reduced by active skin care regimens (1). Alternatives to pads are indwelling or intermittent catheterisation, external collection devices and penile clamps for men; and intravaginal devices for women. It should be noted that studies of catheter use are not specific to patients with non-neurogenic UI. Detailed literature summaries can be found in the current ICUD monograph (2) and in European Association of Urological Nurses guidance documents (3-5). A useful resource for health care professionals and patients can be found at URL: http://www.continenceproductadvisor.org/.

3.1.4.1 Question

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

3.1.4.2 Evidence

One RCT involving elderly women in care compared management with pads to indwelling urethral catheter found no difference in dependency level or skin integrity score at six months (6). Overall, 90% of those randomised to catheter changed to pads and 20% of pad users changed to catheter. Bacteriuria and antibiotic treatment for UTI were more common in catheter users. Use of an external sheath was compared with indwelling catheterisation over 30 days in a RCT involving elderly men resident in hospital (7). There were no differences in bacteriuria or symptomatic UTI but the sheath was more comfortable. A short-term 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 (8).

3.1.4.3 Question

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

3.1.4.4 Evidence

Qualitative studies show that for women with UI, pad use is a crucial part of self-management (9,10). 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 (11). For men with light UI a randomised crossover trial found that a leaf-shaped type of pad was preferred to rectangular pads (12). A series of three crossover RCTs examined performance of different pad designs for differing populations (13). For women with light UI disposable insert pads 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.

3.1.4.5 Question

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

3.1.4.6 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 (14). A systematic review of non-randomised studies found no differences in any UTI outcome or for upper urinary tract changes between use of suprapubic or urethral catheter drainage, but patients with suprapubic catheters were less likely to have urethral complications (15). For people using intermittent catheterisation, a Cochrane review found no evidence that one type of catheter or regimen of catheterisation was better than another (16). A Cochrane review summarised five trials comparing washout policies in adults with indwelling urinary catheters and found inconsistent evidence of benefit (17).

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 (18).

A randomised crossover study comparing six different brands of self-adhesive one-piece external collection sheath devices found that men preferred sheaths without an applicator and one brand received significantly better ratings then the others (19). An industry-funded crossover RCT found one type of self-adhesive one-piece penile sheath was better than another but the relevant difference in technology was not stated (20).

3.1.4.7 Question

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

3.1.4.8 Evidence

A crossover RCT in 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 (21).

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 intraurethral devices and that there was no difference in control of UI between intravaginal and intraurethral devices (22). There was no difference in outcome at 12 months in women with SUI between vaginal pessary alone; PFMT alone; and vaginal pessary + PFMT though vaginal pessary was inferior to PFMT at three months for bother from UI. Three further cohort studies found that use of a vaginal pessary reduced incontinence episodes

compared to no treatment (23-25). A qualitative study found that women valued pessary use but required adjustment of personal attitudes and continued support and training from healthcare professionals (26).

Evidence summary	LE
Pads with greater absorbency are more effective.	1b
Hinge-type penile clamps control SUI in men.	2a
Vaginal devices control SUI in women.	2a
Vaginal devices are no better than PFMT for women with SUI.	2a
A sheath-type external collection device for men is better than pads for improvement in incontinence-related QoL.	2a

Recommendations	GR
Ensure that adults with UI 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 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

** Based on expert opinion*

3.1.4.9 Research Priority

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

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3.2 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.

*3.2.1 **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 (1). Lack of knowledge about caffeine content of different drinks has made the role of caffeine reduction in alleviating UI difficult to assess.

3.2.1.1 Question

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

3.2.1.2 Evidence

Four studies were found on the effect of caffeine reduction on UI (2-5). They were of moderate quality and the results were inconsistent. The studies were mainly in women, so results can only be cautiously generalised to men (3,4). One RCT showed that reducing caffeine intake as an adjunct to BT resulted in reduced urgency but not reduced UI compared to BT alone (3). Another RCT found that reducing caffeine had no benefit for UI (4). A further interventional study in the elderly showed borderline significance for the benefit of reducing caffeine intake on UI (5). In a large prospective cohort study there was no evidence that caffeine reduction reduced the risk of progression of urinary incontinence over 2 years (6).

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

3.2.1.3 References

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3.2.2 ***Physical exercise***

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

3.2.2.1 Question

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

3.2.2.2 Evidence

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

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 (15-17).

Evidence summary	LE
Female athletes may experience UI during intense physical activity but not during common activities.	3
Strenuous physical activity does not predispose to UI for women later in life.	3
Moderate exercise is associated with lower rates of UI in middle-aged or older women.	2b

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3.2.3 ***Fluid intake***

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

3.2.3.1 Question

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

3.2.3.2 Evidence

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

Two RCTs of limited quality due to high drop-out rates and small sample size (1,2) produced conflicting results regarding recommendations for fluid intake. One study found that increased fluid intake improved symptoms, while the other study, which was limited to patients with DO, found that decreased fluid intake improved QoL. A more recent RCT (3) showed that a reduction in fluid intake by 25% improved symptoms in patients with OAB but not UI. An observational study also addressed fluid intake as part of a behavioural regime (4). 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 (5).

Evidence summary	**LE**
There is conflicting evidence on whether fluid modification changes symptoms of UI and QoL.	2

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3.2.4 ***Obesity and weight loss***

Obesity has been identified as a risk factor for UI in many epidemiological studies (1,2). There is evidence that the prevalence of both UUI and SUI increases proportionately with rising body mass index. A significant proportion of patients who undergo surgery for incontinence are overweight or obese.

3.2.4.1 Question

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

3.2.4.2 Evidence

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

Two systematic reviews plus 1 large RCT concluded that weight loss was beneficial in improving symptoms of UI (4-6). Five further RCTs reported a similar beneficial effect on incontinence following surgical weight reduction programmes (7-11).

Two large studies in diabetic women, 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 (7,12). There have been other cohort studies and case-control studies suggesting similar effects, including surgery for the morbidly obese (6,13-19). For example, in a longitudinal cohort study, a weight loss of 5-10% was associated with a significant reduction in UI measured by pad test (20).

Evidence summary	**LE**
Obesity is a risk factor for UI in women.	1b
Weight loss (> 5%) in obese women improves UI.	1b
Weight loss in obese adults with diabetes mellitus reduces the risk of developing UI.	1b

3.2.4.3 References

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*3.2.5 **Smoking***

Smoking cessation is now a generalised public health measure. Smoking, especially if > 20 cigarettes per day, is considered to intensify UI.

3.2.5.1 Question

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

3.2.5.2 Evidence

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

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

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

*3.2.6 **Recommendations for lifestyle interventions***

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

3.2.7 ***Research priority***

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

3.2.8 ***References***

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3.3 Behavioural and Physical therapies

Terminology relating to behavioural and physical therapies remains confusing because of the wide variety of ways in which treatment regimes and combinations of treatments have been delivered in different studies (1). The terms are used here to encompass all those treatments which require a form of self-motivated personal retraining by the patient and also includes those 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.

Treatment programmes are designed to gradually increase a person's control over bladder function, reduce urgency and to reduce episodes of UI, and increase a person's self-confidence. This can take months to achieve and may not persist long-term unless the programme is maintained.

The detail of delivery is likely to depend on differences in healthcare systems as much as proven efficacy. The variation in these packages of care make any comparison between studies increasingly difficult and it is unusual to find trials that have evaluated only a single component.

3.3.1 ***Bladder Training***

The patient is instructed on bladder function and fluid intake, including caffeine restriction and bowel habits. Patients may be asked to void according to a fixed voiding schedule. Alternatively, patients may be encouraged to follow a schedule established by their own bladder diary/voiding chart (habit training). 'Timed voiding' is voiding initiated by the patient, while 'prompted voiding' is voiding initiated by the caregiver. Timed and habit voiding are recommended to patients who can void independently.

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

3.3.1.1 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?

3.3.1.2 Evidence

There have been three systematic reviews covering the effect of BT compared to standard care (2-4). Two RCTs, which compared BT with no intervention, found that UI was improved, but not cured, by timed bladder voiding at intervals of between 2.5 and 4 hours (5,6). However, it is unclear whether these findings also applied to specific groups of individuals with UI. However, another two RCTs reported inconsistent findings regarding treatment adherence (7).

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

Studies have shown that the addition of BT to antimuscarinic therapy provides no added benefit for an mprovement in UI (8,9,13). However, BT combined with antimuscarinic therapy does provide a greater benefit in reducing urinary frequency and nocturia (13,14). Bladder training does not improve an individual's capacity to discontinue drug therapy and maintain improvement of UUI (8). However, the addition of BT to antimuscarinic drugs may increase patient satisfaction with pharmacological treatment (15), including for patients previously dissatisfied with the antimuscarinic treatment (16).

Bladder training combined with PFMT is better than standard care for controlling UI in elderly women living in institutions (16,17). However, BT alone is inferior to a high-intensity programme of PFMT to improve SUI in elderly women (18). 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 2 RCTs (4).

Evidence summary	**LE**
Behavioural interventions are 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 have other benefits.	1b
Bladder training is better than pessary alone.	1b

For recommendations see section 3.3.7

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

Pelvic floor muscle training is used to improve function of the pelvic floor. This increases urethral closure pressure and stabilises the urethra, preventing downward movement during moments of increased activity. There is some evidence that improving pelvic floor function may inhibit bladder contraction in patients with OAB (19).

Traditionally, following vaginal examination and pelvic floor assessment by a trained professional, patients are taught to contract their pelvic floor muscles, and to repeat these exercises a number of times every day. This training can be delivered in many ways, including women teaching themselves (e.g. using an information leaflet), group training in classes, or intensive one-to one supervision from a trained physical therapist.

Pelvic floor muscle training 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. Additional techniques, such as kinesitherapy proprioception training (20) and trunk stabilisation (21) have been proposed, but the benefits, and the extent to which they vary from one another as interventions, are unclear.

3.3.2.1 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?

3.3.2.2 Evidence

Although there have been many randomised trials of PFMT, the trials vary widely in terms of quality, mode of delivery, intensity and duration of treatment, and the details of contractions and repetitions. In a recent UK Health Technology Appraisal (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 (2). 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 (4).

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

This question has been addressed by several systematic reviews (2,4,22), 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 (23). 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 (24).

Numerous systematic reviews have addressed the question of whether the effects of PFMT and BT are additive (2,4,25). 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 (4,25).

Comparison of PFMT to other treatments was extensively reviewed by both AHRQ and the 2010 UK HTA (2,4), 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.

3.3.2.4 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 (18,26,27).

3.3.2.5 PFMT and Radical prostatectomy

A Cochrane review concluded that there was no benefit at 12 months post-surgery for men who received postoperative PFMT for the treatment of post-prostatectomy urinary incontinence (PPI) and that the benefits of conservative treatment of PPI remain uncertain (28). There have been further RCTs which leave uncertainty about whether or not PFMT leads to earlier recovery of continence (29-33). Two additional RCTs have shown that written instructions alone offer similar levels of improvement to supervised PFMT (34,35). One RCT found that PFMT was helpful in men who had been incontinent for years after radical prostatectomy, and who had had no previous therapy (36).

Evidence summary	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 years' follow-up.	2
PFMT for post-prostatectomy UI	**LE**
PFMT does not cure UI in men post prostatectomy.	1b
There is conflicting evidence as to whether PFMT speeds the recovery of continence following radical prostatectomy.	1b
There is conflicting evidence on whether the addition of bladder training, electrical stimulation or biofeedback increases the effectiveness of PFMT alone.	2
There is no evidence that pre-operative PFMT prevents UI following radical prostatectomy though it may lead to earlier recovery of continence.	2

For recommendations see section 3.3.7

*3.3.3 **Scheduled voiding***

The term scheduled voiding implies that carers, rather than the patient, initiate the decision to void and this applies largely to patients who are in an assisted care setting. Prompted voiding is the giving of positive reinforcement for requesting toileting assistance, either spontaneously or following verbal prompts from a caregiver. Two systematic reviews including 9 RCTs examined the effectiveness of prompted voiding in elderly people with UI in assisted care settings (37,38). All RCTs showed a positive effect on continence outcomes of prompted voiding in comparison to standard care using intervals of 1, 2, or 3 hours (38).

Both reviews included five RCTs that consistently showed that the behaviour modification programme known as 'Functional Incidental Training (FIT)' (which included prompted voiding) improved continence in addition to activities of daily living (ADL). The review by Flanagan et al (38) also included another two RCTs that showed no added clinical benefit for incontinence from oxybutinin or oestrogen combined with prompted voiding.

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 (39).

Evidence summary	LE
Prompted voiding, either alone or as part of a behavioural modification programme, improves continence in elderly, care-dependent people.	1b
The inclusion of prompted voiding in behavioural modification programmes improves continence in elderly, care-dependent people.	1b

For recommendations see section 3.3.7

*3.3.4 **Electrical stimulation (surface electrodes)***

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

Electrical stimulation (ES) 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, UUI, urgency/frequency syndromes 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.

3.3.4.1 Question

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

3.3.4.2 Evidence

Most evidence on ES refers to women with SUI. The topic has been included in two health technology appraisals (2,4) and three systematic reviews (3,40,41).

The reviews include analysis of 15 trials and use different comparison methods, but conflict 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.

A systematic review reported two RCTs in which ES had been compared to oxybutynin in patients with UUI, showing similar efficacy (42).

A Cochrane review of ES in men with UI (6 RCTs) concluded that, in the short-term, there was limited evidence of ES augmenting effectiveness of PFMT and there was better improvement of incontinence than with sham stimulation (43).

Evidence summary	**LE**
In adults with UI, there is inconsistent evidence whether ES is effective in improving UI compared to sham treatment or adds any benefit to PFMT alone.	1
The comparative benefit of electrical stimulation and antimuscarinic therapy, for improvement of patients with UUI, remains uncertain.	1

For recommendations see section 3.3.7

3.3.5 ***Magnetic stimulation***

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

3.3.5.1 Question

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

3.3.5.2 Evidence

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

Three RCTs induced magnetic stimulation in women with UI, using a coil placed over the sacral foramina. Two were poor-quality RCTs, with a short follow-up and an inconclusive effect in SUI and UUI or OAB (40,41,44,45). The third better-quality RCT observed no improvement in UUI or OAB after a longer 12-week follow-up and did not recommend treatment with magnetic stimulation (46).

A portable device (Pulsegen) was compared in two RCTs to sham treatment in women with UI. Inconclusive effects were obtained. Both trials were poor quality with a short follow-up (47,48).

In adult women with SUI, an RCT using the NeoControl chair found no improvement (49). A cohort study for 6 weeks, but with a follow-up of 2 years, showed a moderate improvement in UI measured by pad test (50) while another cohort study found no improvement (51). A further poor-quality RCT using the NeoControl chair also found no benefit in women with UUI or OAB (52). No clinical benefits were reported when magnetic stimulation using the NeoControl chair was also compared to functional electrical stimulation with surface electrodes (53) or to conventional PFMT (54).

The negative or inconclusive effects obtained from the reviewed literature were considered to be consistent and generally applicable to adult women with SUI or UUI. There was a lack of evidence in men with UI.

Evidence summary	LE
Magnetic stimulation does not cure or improve UI.	2a
There are no reports of adverse events for magnetic stimulation.	1b

For recommendations see section 3.3.7

*3.3.6 **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.

Commonly, the PTNS is stimulated percutaneously with a fine, 34-G, needle, which is inserted just above the medial aspect of the ankle (equivalent to the SP6 acupuncture point) (P-PTNS). Transcutaneous stimulation is also available (T-PTNS) though there remain uncertainties about the extent to which surface stimulation is capable of direct nerve stimulation. Treatment cycles typically consist of 12-weekly treatments of 30 minutes.

3.3.6.1 Question

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

3.3.6.2 Evidence

P-PTNS

The reviewed studies included two RCTs of PTNS against sham treatment (55,56) and one comparing PTNS to tolterodine in patients with UUI (57). 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 antimuscarinic 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.

In patients who initially respond to PTNS, the improvement is maintained in some patients at 2 years with continued treatment (approximately monthly) (58).

T-PTNS

A small RCT compared transcutaneous PTNS plus standard treatment (PFMT and BT) with PFMT and BT alone in older women (59). Women in the T-TPNS group were more likely to achieve Improvement at the end of therapy.

Evidence summary	LE
P-PTNS appears effective for improvement of UUI, in women who have had no benefit from antimuscarinic medication.	2b
P-PTNS is no more effective than 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

3.3.7 *Recommendations for behavioural and physical therapies*

Recommendations	GR
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
Consider using biofeedback as an adjunct in women with stress urinary incontinence.	A
Offer instruction on PFMT to men undergoing radical prostatectomy to speed recovery of incontinence.	B
Offer bladder training as a first-line therapy to adults with urgency urinary incontinence or mixed urinary incontinence.	A
Offer timed voiding to adults with incontinence, who are cognitively impaired.	A
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 UI.	B
Do not offer magnetic stimulation for the treatment of incontinence or overactive bladder in adult women.	B
Do not offer PTNS to women or men who are seeking a cure for urgency urinary incontinence.	A
Offer, if available, P-PTNS as an option for improvement of urgency urinary incontinence in women, but not men, who have not benefitted from antimuscarinic medication.	B
Support other healthcare professionals in use of rehabilitation programmes including prompted voiding for care of 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

3.3.8 *Research priorities*

- What is the comparative effectiveness of different regimens for PFMT?
- What is the long-term durability of PFMT?
- What is the most effective method of delivering PFMT?
- What is the effectiveness of augmenting PFMT by the addition of electrical stimulation or vaginal cones in patients with either SUI or UUI?

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3.4 Conservative therapy in mixed urinary incontinence

About one-third of women with UI have mixed urinary incontinence (MUI) with symptoms of both stress UI (SUI) and urgency UI (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.

*3.4.1 **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?

*3.4.2 **Evidence***

No specific systematic reviews were found that addressed the above question. However, a Cochrane report on pelvic floor muscle training (PFMT) (1) concluded that training was less likely to result in a cure in patients with MUI than in patients with pure SUI, though it is not clear from the report how this conclusion was reached.

A small RCT in MUI patients compared intravaginal electrical stimulation to PFMT. No difference was seen in outcome (2).

A small RCT (n = 71) compared delivery of PFMT, with or without an instructive audiotape. It showed equal efficacy for different types of UI (3).

An RCT in 121 women with SUI, UUI or MUI compared transvaginal electrical stimulation with sham stimulation and was found to be equally effective in UUI as in MUI (4).

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 (5).

Evidence summary	**LE**
Pelvic floor muscle training appears less effective for mixed UI than for SUI alone.	2
Electrical stimulation is equally effective for mixed UI and SUI.	1b

*3.4.3 **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 less satisfactory than for stress urinary incontinence alone.	B

*3.4.4 **References***

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4. DRUG TREATMENT

4.1 Antimuscarinic drugs

Antimuscarinic drugs (also commonly referred to as anticholinergic drugs) are currently the mainstay of treatment for UUI. Antimuscarinic agents differ in their pharmacological profiles, e.g. muscarinic receptor affinity and other modes of action, in their pharmacokinetic properties, e.g. lipid solubility and half-life, and in their formulation, e.g. immediate release (IR), extended release (ER) or transdermal.

The evaluation of cure or improvement of UI using oxybutynin and tolterodine IR formulations is made harder by the lack of a standard definition of improvement and the failure to use cure as a primary outcome. Meta-analysis of the published evidence is therefore not always possible.

In general, systematic reviews note that the overall treatment effect of drugs is usually small, while the treatment effect of other conservative therapies is large.

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

The 2012 edition of these Guidelines separated out IR antimuscarinics from ER and once-daily preparations. The 2012 AHRQ review did a detailed evaluation of all antimuscarinic drugs up to December 30th 2011, but did not review IR preparations separately.

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

4.1.1.1 Question

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

4.1.1.2 Evidence

Five systematic reviews of individual antimuscarinic drugs versus placebo were reviewed by the Guidelines Panel for this section (1-5). As well as the studies included in these reviews, the Panel have examined studies published since these reviews up until September 2012. Most studies included patients with OAB, with a mean age of 55-60 years. Because most patients in the studies were women, the results can be generalised to women, but not to men. The reported rates for improvement or cure of UUI were only for short-term treatment (up to 12 weeks). The evidence reviewed was consistent, indicating that ER and IR formulations of antimuscarinics offer clinically significant short-term cure and improvement rates for UUI.

The Guidelines Panel considered that the most important outcome for this section was the cure of UI, and that the risk of adverse events was best represented by withdrawal from a trial because of adverse events. Table 4 shows a summary of the findings from the most recent systematic review (5). In summary, every drug where this data was available shows superiority compared to placebo in achieving UI, but the absolute effect is small.

Table 4. Summary of cure rates and discontinuation rates of antimuscarinic drugs from RCTs which reported these outcomes (5)

Drug	No. of Studies	Patients	Relative risk (95% CI)	Number needed to reat (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				
Darifenacin	7	3138	1.2 (0.8-1.8)	
Fesoterodine	4	4433	2 (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 (0.6-1.7)	
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. Two RCTs compared darifenacin to placebo, comparing cure rates, involving 838 patients (681 women). One study only included patients older than 65 years (6,7). Continence rates were 29-33% for darifenacin compared to 17-18% for placebo.

Transcutaneous oxybutynin

Randomised controlled trials of transdermal oxybutynin versus placebo and other oral formulations have shown a significant improvement in the number of incontinence episodes and micturitions per day but incontinence was not reported as an outcome.

Oxybutynin topical gel was superior to placebo for improvement of UUI with a higher proportion of participants being cured (8,9).

Evidence summary	LE
Oxybutynin IR and transdermal, tolterodine IR, and propiverine IR provide a significantly better rate of cure or improvement of UI compared to placebo.	1a
Trospium IR provides a significantly better reduction in incontinence episodes than placebo.	1a
ER or once daily formulations of antimuscarinic agents are effective for improvement and cure of UUI.	1b
ER or once daily formulations of antimuscarinic agents result in higher rates of dry mouth compared to placebo.	1b

For recommendations on antimuscarinic drugs see page 63.

4.1.1.3 References

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4.2 Comparison of antimuscarinic agents

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

4.2.1 ***Question***

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

4.2.2 ***Evidence***

There is a considerable body of evidence covering this question, comprising over 40 RCTs and five systematic reviews (1-5). Nearly all the primary studies have been funded and sponsored by the manufacturer of the newer drug under evaluation, which forms the experimental arm of the RCT. It was noted that upward dose titration is often included in the protocol for the experimental arm, but not for the comparator arm.

In general, these studies have been designed for regulatory approval. They have short treatment durations of typically 12 weeks and a primary outcome of a change in OAB symptoms rather than a cure of, or an improvement in, UUI, which were generally analysed as secondary outcomes. It is therefore difficult to use the results from these trials in daily clinical practice to select the best first-line drug or second-line alternative following the failure of initial treatment. A quality assessment carried out as part of one systematic review (3) found that all the trials were of low or moderate quality.

The 2012 AHRQ review included a specific section addressing comparisons of antimuscarinic drugs. Table 5 shows the results of these comparisons.

Table 5: Comparison of antimuscarinic drugs as reviewed in the 2012 AHRQ review (3)

Experimental drug versus standard drug	No. of studies	Patients	Relative risk (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			
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)

There was no evidence that any one antimuscarinic agent improved QoL more than another agent (3). Dry mouth is the most prevalent and most studied adverse effect of antimuscarinic agents. Good evidence indicates that, in general, ER formulations of short-acting drugs and longer-acting drugs are associated with lower rates of dry mouth than IR preparations (3,4). 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 (3,4). Overall, oxybutynin ER has higher rates of dry mouth than tolterodine ER, but generally oxybutynin did not have higher rates for moderate or severe dry mouth. Transdermal oxybutynin was associated with a lower rate of dry mouth than oxybutynin IR and tolterodine ER, but had an overall higher rate of withdrawal due to an adverse skin reaction (3). Solifenacin, 10 mg daily, had higher rates of dry mouth than tolterodine ER (3). Fesoterodine, 8 mg daily, had a higher rate of dry mouth than tolterodine, 4 mg daily (6,7). In general, discontinuation rates were similar for each treatment arm in comparative RCTs, irrespective of differences in the occurrence of dry mouth.

Evidence summary	LE
There is no consistent evidence that one antimuscarinic drug is superior to an alternative antimuscarinic drug for cure or improvement of UUI.	1a
The ER formulation of oxybutynin is superior to the ER and IR formulations of tolterodine for improvement of UUI.	1b
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 and once-daily formulations of antimuscarinic drugs are generally associated with lower rates of dry mouth than IR preparations, although discontinuation rates are similar.	1b
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

For recommendations on antimuscarinic drugs see page 58.

4.2.3 ***References***

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4.3 Antimuscarinic drugs versus non-drug treatment

The choice of drug versus non-drug treatment of UUI is an important question for many clinicians especially in low resource countries.

4.3.1 ***Question***

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

4.3.2 ***Evidence***

There is a large body of evidence comparing non-drug and drug treatment, including more than 100 RCTs and several, recently published, high-quality reviews (1-5). Most of these studies were not funded by the pharmaceutical industry, whose main focus is on drug treatment rather than on conservative treatment. The subject has also been considered by a Cochrane review (6).

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

The HTA included a comparison between procedural and pharmaceutical treatments, including one RCT that showed a substantial benefit for sacral neuromodulation compared with medical therapy (7).

In men with storage LUTS, one RCT compared oxybutynin to behavioural therapy, finding no difference in efficacy (8). Another RCT showed that adding BT to solifenacin in women with OAB conferred no additional benefit in terms of continence (9).

Two older small RCTs (10,11), reported a similar improvement in subjective parameters with either transcutaneous electrical nerve stimulation or Stoller afferent nerve stimulation. However, only oxybutynin-treated patients showed significant improvements in objective urodynamic parameters (capacity). The oxybutynin-treated group had more side effects. Two studies compared antimuscarinics to ES finding no difference in UI outcomes (12). One underpowered RCT found that the addition of P-PTNS to tolterodine ER improved UI and QoL (13).

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

IR = immediate release; ER = extended release.

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

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4.4 Antimuscarinic agents: adherence and persistence

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

4.4.1 ***Question***

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

4.4.2 ***Evidence***

Thirteen papers have been published on adherence/persistence to antimuscarinic medication in everyday clinical practice (1-13). Ten papers used established pharmaco-epidemiological parameters (2,4,6-13), including: two recent open-label extensions of RCTs of fesoterodine 8 mg showing adherence rates at 2 years from 49-84%, depending on populations (14,15).

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

One study was in an open-label extension population (3). One study used only self-reports of patients and did not follow patients from the start of treatment (5). Most of the data was not derived from RCTs, but from pharmacy refill records. Pharmacy records are likely to overestimate adherence and persistence, because it is often not clear whether patients have been monitored from the start of treatment or whether monitoring (for the purpose of the study) was started in patients already taking the drug for some time and therefore defined as persistent users.

The main drugs studied in adherence/persistence trials were oxybutynin IR and ER and tolterodine IR and ER. These reviews demonstrated high non-persistence rates for tolterodine at 12 months, and particularly high rates (68-95%) for oxybutynin (7-10,13).

Five articles reported 'median days to discontinuation' as between < 30 days and 50 days (7,9,10,12,13), with one study reporting 273 days in a military health system (which provided patients with free medication) (9).

Only one RCT (3) included solifenacin, darifenacin and trospium. The only open-label extension study included in the review also studied solifenacin, darifenacin and trospium. However, determining adherence/persistence in an open-label extension population is not the preferred methodology, as these patients will not have been monitored from the start of treatment and are therefore self-selected as persistent patients.

Several of the RCT trials tried to identify the factors associated with a lower, or low, adherence or persistence of antimuscarinic agents (4,6,9,10). These were identified in order of importance as:

- low level of efficacy (41.3%)
- adverse events (22.4%)
- cost (18.7%), as most adherence measures were higher in populations, which did not pay for medication, e.g. patients with health insurance (9).

Other reasons for poor adherence included:

- IR versus ER formulations
- age, with persistence lower among younger adults
- unrealistic expectations of treatment
- gender distribution, because adherence/persistence was better in studies that include relatively more female patients
- ethnic group because African-Americans and other minorities were more likely to discontinue or switch treatment
- effectiveness of treatment because in Campbell et al. only 52% were somewhat satisfied to very satisfied with treatment (6).

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

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

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4.5 Antimuscarinic agents, the elderly and cognition

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

Muscarinic receptors exist throughout the body and are involved in many physiological processes. The specificity of a drug for one or another receptor and the degree of penetration into the CNS through the blood-brain barrier may have an impact on cognitive function. In recent years, the effects of antimuscarinic agents on cognition have been studied in more detail.

4.5.1 ***Question***

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

4.5.2 ***Evidence***

There have been two systematic reviews of antimuscarinic agents in elderly patients (1,2). One review was confined to evidence on nursing home residents with UUI (2). A community-based cohort study on the burden of antimuscarinic drugs in an elderly population (n = 372) found a high incidence of cognitive dysfunction (3). Other systematic reviews have included sections on the efficacy and safety of antimuscarinics in elderly patients (4,5).

A systematic review in 2012 included nine studies in which the cognitive impact of antimuscarinics was tested, but the evidence was found to be inconclusive (6).

There have been very few trials specifically investigating the cognitive changes that might occur with the use of antimuscarinic agents. Most trials have been done in healthy volunteers of different age groups and only for a short period (varying from a single dose to 12 weeks). Other publications describe post-hoc analyses of other trials or reviewed only a number of selected publications. In general, these trials have measured CNS side effects in a non-specific way that does not allow the impact on cognition to be considered in a particular patient population (7,8).

Studies on antimuscarinic effects have been done in elderly persons (9), and in people with dementia with UUI (10). There have been no specific studies in vulnerable patient populations who are likely to have cognitive dysfunction and might suffer deterioration of their cognitive function due to using antimuscarinic medication.

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

4.5.2.1 Oxybutynin

There is evidence from older trials that oxybutynin IR may cause or worsen cognitive dysfunction in adults (7,9,11). However, a more recent comparison of solifenacin to oxybutynin IR showed no difference in cognitive dysfunction between these two drugs when measured over a short time period (12).

A crossover RCT in elderly volunteers given oxybutynin IR reported increased cognitive dysfunction. A short-term safety RCT of oxybutynin ER in elderly women with cognitive dysfunction observed no increase in delirium (13), but secondary analysis revealed no change in incontinence so the relevance of this study is difficult to interpret (14). Two studies in the elderly demonstrated additional benefit from oxybutynin IR combined with scheduled voiding versus scheduled voiding alone. Another study found no differences between oxybutynin ER and IR in elderly patients, although the study did not reach its recruitment target (15).

A large observational study (n = 3536) suggested that more rapid functional deterioration might result from the combined use of cholinesterase inhibitors with antimuscarinic agents in elderly patients with cognitive dysfunction (16). However, the nature of the interaction with cholinesterase inhibitors is unclear. No general conclusions can be made, but caution is advised in prescribing these combinations.

4.5.2.2 Solifenacin

One pooled analysis from several RCTs (17) has shown that solifenacin improves UI and does not increase cognitive impairment in the elderly. Another RCT found no age-related differences in the pharmacokinetics of solifenacin between elderly, middle-aged or younger patients. One post-marketing surveillance study reported more frequent adverse events in subjects over 80 years old. Another study on healthy elderly volunteers showed no cognitive effect (11). In a subanalysis of a large trial, solifenacin 5-10 mg appeared effective for

improvement in symptoms and QoL in people aged older than 75 years who had not responded to tolterodine (18). Another sub analysis of patients with mild cognitive impairment, over 65 in an RCT comparing solifenacin to oxybutynin IR showed no difference in efficacy between age groups and a lower incidence of most side effects for solifenacin (12,19).

4.5.2.3 Tolterodine

Pooled data from RCTs showed no change in efficacy or side effects related to age, but reported a higher discontinuation rate for both tolterodine and placebo in elderly patients (7). Two RCTs of tolterodine specifically designed in the elderly found that tolterodine showed a similar efficacy and side effect profile, as in younger patients (20-23). Post-hoc analysis from other RCTs has shown little effect on cognition. One non-randomised comparison showed lower rates of depression amongst elderly participants treated with tolterodine ER compared to oxybutynin IR (24).

4.5.2.4 Darifenacin

Two RCTs carried out specifically in the elderly population (one RCT in patients with UUI and the other RCT in volunteers) concluded that darifenacin was effective and the risk of cognitive change, measured as memory scanning tests, were no different to placebo (25,26). Another comparison between darifenacin and oxybutynin ER in elderly subjects concluded that the two agents had a similar efficacy, but that cognitive function was more often affected in patients receiving oxybutynin ER (9).

4.5.2.5 Trospium chloride

Trospium is a quaternary amine compound that does not cross the blood-brain barrier in healthy individuals, so theoretically is less likely to have an impact on cognitive function compared to other antimuscarinic agents. Two (EEG) studies in healthy volunteers showed no effect from trospium whilst tolterodine caused occasional changes and oxybutynin caused consistent changes (27,28). No published evidence was found regarding the comparative efficacy and side effect profiles of trospium in the elderly compared with younger patients. Even recent studies have not stratified results according to different age groups. However, there is some evidence that trospium does not impair cognitive function (10,29) and that it is effective compared to placebo in this group (30).

4.5.2.6 Fesoterodine

There is no evidence comparing the efficacy and side effects of fesoterodine in elderly and younger patients. Two separate pooled analyses of the same two RCTs of fesoterodine, and another similar pooled analysis of two other phase 3 trials in the elderly, confirmed the efficacy of the 8 mg but not the 4 mg dose in over-75 year olds (31). Adherence was lower in the over-75 year-old group but the effect on mental status was not reported (32-34). A small RCT in healthy older subjects compared cognitive function with fesoterodine and placebo, finding no difference between the two groups (35).

4.5.2.7 Duloxetine in the elderly

Although RCTs comparing duloxetine to placebo included women up to the age of 85, none included stratification according to age so it is impossible to say whether this drug has a similar effect in the elderly as younger women. There is no evidence of a differential effect of Duloxetine according to age.

4.5.2.8 Mirabegron

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

4.5.2.9 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. The community-based studies of the prevalence of antimuscarinic side effects in this age group may be the most helpful (3).

When starting anticholinergic medication in patients at risk of worsening cognitive function, it has been suggested that mental function is assessed objectively and monitored to detect any significant changes during treatment (36). However, there remains no consensus on the best mental function test to use as they may lack sensitivity to detect early decline or the responsiveness to detect changes (16,31).

4.5.2.10 Anticholinergic load

A wide range of medications are considered to have anticholinergic side effects and physicians who care for the elderly are concerned about the cumulative effects that these drugs may have on cognitive function

4.5.2.11 Question

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

4.5.2.12 Evidence

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

It is difficult to obtain a definitive list of drugs with definite or possible anticholinergic effects. One scale is available from the systematic review by Boustani 2008 (37) which is the Anticholinergic Cognitive Burden Scale (ACB) (http://www.indydiscoverynetwork.org/AnticholinergicCognitiveBurdenScale.html). Much of the research evidence available on this topic derives from a single department in Indiana who developed this scale.

There are two systematic reviews both of which include largely retrospective cohort studies, with over 8000 patients in total. There was a consistent association between long-term anticholinergic use and cognitive dysfunction (38). A review of 3690 older people showed that those who are receiving three or more drugs with potential anticholinergic effects have an increased risk of cognitive dysfunction (39).

Longitudinal studies in older people over 2 to 4 years have found increased rate of decline in cognitive function for patients receiving definite anticholinergics (OR; 1.68) and those receiving possible anticholinergics (OR; 1.56) (40,41).

Evidence summary	**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
There is inconsistent evidence as to whether oxybutynin IR may worsen cognitive function.	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

Additional recommendations for antimuscarinic drugs in the elderly	**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
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
Check mental function in patients on antimuscarinic medication if they are at risk of cognitive dysfunction.	C

4.5.3 ***Research priority***

- 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?

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4.6 Adrenergic drugs for UI

Previous trials of adrenergic drugs have focused on the effect of alpha-adrenoceptors in increasing the closure pressure of the urethral continence mechanism in women as a means of improving SUI. More recently, research has focused on beta-adrenoceptor stimulation as a means of increasing detrusor relaxation and therefore improving urine storage in people with overactive bladder and UUI.

A Cochrane review updated to 2010 (1) found 22 trials of adrenergic drugs for the treatment of women with predominant SUI in comparison to placebo or PFMT. Eleven of these trials involved phenylpropanolamine, which has since been 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 and the review is therefore currently categorised as stable. At present, these drugs are not licensed for use in UI and are not part of the standard treatment algorithm.

Mirabegron is a beta 3 agonist available from 2013. Beta 3 adrenoceptors are largely expressed in the smooth muscle cells of the detrusor and their stimulation induces detrusor relaxation.

Three RCTs and one pooled analysis have shown that mirabegron at doses of 25, 50 and 100 mg, results in significantly greater reduction in incontinence episodes and micturition frequency/24 hrs than placebo, with no difference in the rate of adverse events (2-5). The placebo dry rates in most of these trials are unusually high at between 35-40%, and the cure rates on average are between 43 and 50%. In all trials the statistically significant difference is consistent only for improvement and not cure of UI.

Another large multi-centre RCT of mirabegron 50 and 100 mg, and tolterodine ER 4 mg vs. placebo showed significant improvement in UIfor mirabegron vs. placebo. Use of 100 mg gave no additional benefit compared to 50 mg. Rates of dry mouth were significantly lower compared to tolterodine, and no different than placebo (6).

RCTs have specifically addressed the comparative risk of QTc prolongation (7) and raised intraocular pressure (8) and showed no diference from placebo up to 100 mg dose. There is no significant difference in rate of side effects at different doses of Mirabegron (9)

An RCT assessing the effect of mirabegron on urodynamic parameters (max flow rate and detrusor pressure at max flow) in men with combined BOO and OAB concluded that mirabegron (50 or 100 mg) did not adversely affect voiding urodynamic parameters compared to placebo(10).

A post-hoc analysis of an RCT assessed effect of mirabegron on work productivity and activity impairment and found that mirabegron treated patients experienced a significant reduction in total activity impairment vs. placebo (12.3% vs. 6.1%) (11).

A sub-group analysis of a large RCT population assessed the efficacy of mirabegron in patients who were treatment naïve and those who had undergone prior antimuscarinic therapy for OAB (stratified by reason for discontinuation). They reported similar improvements in frequency of incontinence episodes and micturitions/24 hrs in all the groups (12).

In an RCT with 12 months of follow up adherence to tolterodine and mirabegron was equivalent (9). There is good evidence that improvement in objective outcome measures correlates directly with clinically relevant PROMs (OAB-q and PPBC) (13,14).

Evidence summary	LE
Mirabegron is effective for the cure or improvement of UUI.	1a
Adrenergic-mediated side effects of mirabegron appear mild and not clinically significant in a trial setting.	1a

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

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4.7 Duloxetine

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

*4.7.1 **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?

*4.7.2 **Evidence***

Duloxetine was evaluated as a treatment for female SUI or MUI in two systematic reviews (1,2) including 10 RCTs (3-12) and one subsequent RCT (5). The typical dose of duloxetine was 80 mg daily, with dose escalation up to 120 mg daily allowed in one study (4), over a period of 8-12 weeks. One RCT extended the observation period up to 36 weeks and used the Incontinence Quality of Life (I-QoL) score as a primary outcome (7).

The studies provided reasonably consistent results demonstrating improvement in UI compared to placebo. There were no clear differences between SUI and MUI. One study reported cure for UI in about 10% of patients (3). An improvement in I-QoL was not found in the study using I-QoL as a primary endpoint (7). A further study compared duloxetine, 80 mg daily, with PFMT alone, PFMT + duloxetine, and placebo (13). Duloxetine reduced leakage compared to PFMT or no treatment. Global improvement and QoL were better for combined therapy than no treatment. There was no significant difference between PFMT and no treatment.

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

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

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

In general, all studies had a high patient withdrawal rate of about 20-40% of patients in short-term studies and up to 90% in long-term studies. The high withdrawal rate was caused by a combination of a lack of efficacy and a high incidence of adverse events, including nausea and vomiting (40% or more of patients), dry mouth, constipation, dizziness, insomnia, somnolence and fatigue.

Evidence summary	**LE**
Duloxetine does not cure 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*

4.7.3 ***References***

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4.8 Oestrogen

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 (1-3). Vaginal (local) treatment is primarily used to treat symptoms of vaginal atrophy in postmenopausal women.

*4.8.1 **Questions***

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

*4.8.2 **Evidence***

For women with SUI the results of three trials using oral conjugated equine estrogens, estradiol, or estrone showed no improvement (4-6). Two placebo-controlled trials using sub-cutaneous estradiol or oral estriol showed no benefit for improvement of UI (7).

A Cochrane review (search date June 2012) including data from four low quality trials found that vaginal oestrogen treatment improved symptoms of UI in the short-term (1). The review found single, 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. The review included a single trial of local oestrogen therapy comparing a ring device to pessaries which found no difference in UI outcomes although more women preferred the ring device.

A single trial showed no adverse effects of vaginal administration of estradiol for vulvovaginal atrophy over 2 years (8).

A recent Cochrane systematic review including 33 trials looked at the use of oestrogen therapy in postmenopausal women (1) given local oestrogen therapy. There is also a more recent narrative review of oestrogen therapy in urogenital diseases (9). However, since the Cochrane review, no new RCTs have been published up to September 2012.

Vaginal oestrogen therapy can be given as conjugated equine, oestriol or oestradiol in vaginal pessaries, vaginal rings or creams. Besides improving vaginal atrophy (10), vaginal oestrogen therapy reduces UI and frequency and urgency in OAB (1). There is no consistent evidence for cure of incontinence in women with SUI. Current data do not allow differentiation among the various types of oestrogens or delivery methods. Moreover, the ideal duration of this type of therapy and the long-term effects are uncertain. One RCT compared oestradiol ring pessary with treatment with oxybutynin ER showing no difference in outcomes (11).

Evidence summary	**LE**
Vaginal oestrogen therapy improves UI for post-menopausal women.	1b
Oral oestrogen therapy does not improve UI.	1a
Vaginal oestrogen therapy in post-menopausal women may improve or cure UUI.	1a
There is no consistent evidence that vaginal oestrogen therapy cures SUI.	2
The ideal duration of therapy and best delivery method are unknown.	4
There is no evidence available on the neoadjuvant or adjuvant use of local oestrogens at the time of surgery for UI.	1a
There is no evidence that oestrogen therapy by non-vaginal route confers any improvement in UI.	1a

Recommendations	GR
Offer post-menopausal women with urinary incontinence vaginal oestrogen therapy particularly if other symptoms of vulvovaginal atrophy are present.	A
Do not offer oral (systemic) oestrogen replacement therapy as treatment for urinary incontinence.	A
Offer vaginal oestrogen therapy to post-menopausal women with urinary incontinence, and vaginal atrophy.	A
Vaginal oestrogen therapy should be long-term and in an appropriate dose.	C

4.8.3 ***References***

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4.9 Desmopressin

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

4.9.1 ***Questions***

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

4.9.2 ***Evidence***

4.9.2.1 Improvement of incontinence

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

4.9.2.2 Monitoring for hyponatraemia

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

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

Recommendations	**GR**
Offer desmopressin to patients requiring occasional short-term relief from urinary incontinence 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

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4.10 Drug treatment in Mixed urinary incontinence

4.10.1 ***Question***

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

4.10.2 ***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. These results show that the efficacy of tolterodine for UUI was not altered by the presence of SUI (1). In another study, secondary analysis showed that tolterodine (n = 1380) was equally effective in reducing urgency and UUI symptoms, regardless of whether there was associated SUI (2). Similar results were found for solifenacin (3,4).

Duloxetine

In one RCT, involving 588 women, subjects were stratified into either stress-predominant, urgency-predominant or balanced MUI groups and randomised to receive duloxetine or placebo. Duloxetine was effective for improvement of incontinence and QoL in all subgroups (5).

Duloxetine was found to have equal efficacy for SUI and MUI in an RCT (n = 553) following secondary analysis of respective subpopulations (6).

Evidence summary	LE
Limited evidence suggests that antimuscarinic drugs are effective for improvement of 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 MUI unresponsive to other conservative treatments and who are not seeking cure.	B

4.10.3 ***References***

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5. SURGICAL TREATMENT

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

Some generic principles apply to good surgical practice. Any operation for UI should be preceded by a discussion with the patient and/or carers, about the purpose of the operation, the likely benefits and possible risks. It is also important to explain when there are alternative approaches, even if these procedures are not available locally.

The number of procedures that is recommended for surgeons to perform to be adequate for maintenance of expertise seems to be more related to the prevalence of that operation rather than its difficulty. For instance, this threshold number is likely to be higher for mid-urethral slings than for orthotopic bladder replacement, despite the obvious relative complexity of the latter. We have therefore avoided such statements but expert opinion would support the centralisation of infrequently performed or technically complex procedures into centres where experience and expertise can then grow rapidly. In line with the recommendations from NICE (1) 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.

Some newer surgical interventions can be very costly and the availability of devices varies from one healthcare system to another. We have tried to recognise this in the recommendations by suggesting that procedures should be offered 'when available'.

The section considers surgical options for the following situations:

- Women with uncomplicated SUI. This means no history of previous surgery, no neurological LUTD, no bothersome genitourinary prolapse, and not considering further pregnancy.
- Women with complicated SUI. Neurogenic LUTD is reviewed in the EAU Guidelines on Neurogenic Lower Urinary Tract Dysfunction (2).
- Associated genitourinary prolapse has been included in these Guidelines in terms of treating the 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.

It is inevitable that very few studies will be found which compare a surgical treatment to sham operation (the surgical equivalent of placebo control) since this is both hard to justify and usually impossible to blind to surgeon or patient. Consequently most evidence for surgery derives either from large cohort studies or from trials that compare an experimental technique to an established, gold standard, procedure.

New devices, and modifications to existing procedures, are emerging all the time. Some of these are introduced into the market, and to clinical practice, on the basis of very little clinical evidence. It is impossible, in the context of a guideline, to recognise every permutation of design that might be considered important by those who introduce it. The Panel has tried to acknowledge emerging techniques as they think appropriate and have made a strong recommendation (section 5.1.5.2) that new devices are only used as part of a structured research programme.

Risk Factors for outcome of SUI surgery

Much has been written about risk factors for the outcome of surgery for SUI but in general there is a lack of high quality evidence addressing this question. Factors that have been considered in detail include older age, obesity, concurrent illness, levels of physical activity, the performance of concomitant gynaecological surgery, the presence of coexistent symptoms of urgency incontinence. These subjects have been extensively reviewed by the ICUD report 2013 (3). Certainly when multiple factors coexist, experts agree that the risks of surgery increase, but it is difficult to establish clear and consistent correlations between any individual factor in different trials

5.1 Women with uncomplicated SUI

5.1.1 ***Open and laparoscopic surgery for SUI***

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

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

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

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

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

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

5.1.1.1 Question

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

5.1.1.2 Evidence

Four systematic reviews were found, which covered the subject of open surgery for SUI, including 46 RCTs (2,4-6), but no RCTs comparing any operation to a sham procedure.

Open colposuspension

The Cochrane review (7) included 46 trials (4738 women) having open colposuspension. In most of these trials, open colposuspension was used as the comparator to an experimental procedure. Consequently, for this review we have only considered the absolute effect of colposuspension, but have not reviewed all of these comparisons. No additional trials have been reported since this review.

Within the first year, complete continence rates of approximately 85-90% were achieved for open colposuspension, while failure rates for 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%).

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

Open colposuspension was compared with conservative treatment in one small study (8). One trial compared open colposuspension with antimuscarinic treatment, while another compared it with periurethral injection of bulking agents. Colposuspension resulted in superior outcomes, but had significantly higher rates of adverse events.

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

Anterior colporrhaphy

Anterior colporrhaphy is now considered an obsolete operation for UI. In a Cochrane review (3), 10 trials compared anterior colporrhaphy (385 women) with colposuspension (627 women). The failure rate for 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 (5,9) described 26 RCTs, including 2284 women undergoing autologous sling procedure in comparison to other operations. The trials did not identify those women undergoing repeat surgery for recurrent UI. No further studies have been reported.

There were seven trials of autologous fascial sling versus colposuspension. Except for one very high-quality study (10), 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 versus mid-urethral synthetic slings, the procedures showed similar efficacy. However, use of the synthetic sling resulted in shorter operating times and lower rates of complications, including voiding difficulty. Six trials compared autologous fascial slings with other materials of different origins, with results favouring traditional autologous fascial slings. There were no trials that compared traditional suburethral slings with anterior colporrhaphy, laparoscopic retropubic colposuspension or the artificial urinary sphincter device.

Laparoscopic colposuspension

The Cochrane review (4) 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 5.1.2.

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

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5.1.2 ***Mid-urethral slings***

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

with a relatively large pore size (macroporous). Mid-urethral slings are now the most frequently used surgical intervention in Europe for women with SUI. Surgical procedures are rarely compared to sham treatment or no treatment in clinical trials, but one RCT did compare tension-free vaginal tape surgery and no treatment for the management of stress urinary incontinence in elderly women (2).

5.1.2.1 Questions

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

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

5.1.2.2 Evidence

For the 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 (3-16). 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%) (3,8,10-16). 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 (3,7,17). 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) (5,6,8,18,19).

A single, randomised trial, comparing the mid-urethral sling (transobturator) with open colposuspension, reporting similar rates of patient-reported and clinician-reported cure and no evidence of differential harms (20). In all the trials, operative time and duration of hospital stay was shorter for women randomised to insertion of the mid-urethral synthetic sling.

Transobturator route versus retropubic route

The EAU Panel meta-analysis identified thirty-four 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) (21). Voiding dysfunction was less common (4%) following transobturator insertion compared to retropubic insertion (7%), as was the risk of bladder perforation (0.3%) or urethral perforation (5%). Similarly, the risks of de novo urgency and vaginal perforation were 6% and 1.7%, respectively. Chronic perineal pain at 12 months after surgery was reported by 21 trials and meta-analysis showed a higher rate in women undergoing transobturator insertion (7%) compared to retropubic insertion (3%).

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

A Cochrane systematic review and meta-analysis found that the skin-to-vagina direction (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 (22). 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 (23). These differences in adverse effects were not found in the Cochrane review, which only used the limited amount of direct head-to-head comparative data and found no differences in effectiveness or adverse effects (22).

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 (24) were consistent with those of the Cochrane systematic review (22), 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 (25) and the difference may result from the Panel's decision to only consider trial data with at least 12 months of follow-up. The cure rates at 12 months in our meta-analysis for

mid-urethral sling were similar to those calculated in the meta-analysis for the American Urological Association guidelines (26). In addition, our results and recommendations are consistent with those of the Society of Obstetricians and Gynaecologists of Canada (27) and those of NICE in the UK (28).

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 (29). One recent RCT (30) and another cohort study (31) have shown that overall sexual activity improves after sling surgery, although the cohort study also recorded a small group (6/79) who became sexually inactive. A further small RCT comparing sling techniques showed no difference between pre- and postoperative sexual function nor between any of the techniques used (32).

SUI surgery in the elderly
There are no RCTs comparing surgical treatment in older versus 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 (33). An RCT assessing risk factors for the failure of TVT versus 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 (34). In a subanalysis of the SISTER 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 postoperative normal voiding (35).

Another RCT comparing immediate TVT versus no surgery (delayed TVT) in older women, confirmed efficacy of surgery in terms of QOL and satisfaction, but with higher complication rates (2).

A cohort study of 256 women undergoing inside-out transobturator tape reported similar efficacy in older versus younger women, but found a higher risk of de novo urgency in older patients (36).

Evidence summary	**LE**
Compared to colposuspension, the retropubic insertion of a mid-urethral synthetic sling gives equivalent patient-reported cure of SUI at 12 months.	1a
Compared to colposuspension, the transobturator insertion of a mid-urethral synthetic sling gives equivalent patient-reported outcome at 12 months.	2
Mid-urethral synthetic sling inserted by either the transobturator or retropubic route gives equivalent patient-reported outcome at 12 months.	1a
The skin-to-vagina (top down) direction of retropubic insertion of mid-urethral sling is less effective than a vagina-to-skin (bottom up) direction.	1a
Mid-urethral sling insertion is associated with a lower rate of a new symptom of urgency, and voiding dysfunction, compared to colposuspension.	1a
The retropubic route of insertion is associated with a higher intra-operative risk of bladder perforation and a higher rate of voiding dysfunction than the transobturator route.	1a
The transobturator route of insertion is associated with a higher risk of chronic pain at 12 months than the retropubic route.	1a
The skin-to-vagina direction of both retropubic and transobturator insertion is associated with a higher risk of postoperative voiding dysfunction.	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 postoperative sexual dysfunction differs between mid-urethral sling procedures.	3

5.1.2.3 References

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*5.1.3 **Single-incision slings***

There is continued innovation to reduce the invasiveness of procedures for SUI. Single-incision mid-urethral slings have been introduced on the basis of providing mid-urethral support, using a variety of modifications to a short macroporous polypropylene tape. These modifications allow the tape to be fixed to the retropubic tissues, endopelvic fascia or obturator fascia, while avoiding the troublesome complications of obturator nerve injury or passage through the gracilis muscle or skin of the inner thigh, or through the retropubic space. Fixation methods, and the degree of adjustability vary from one technique to another. These procedures are usually performed as day cases under local anaesthesia.

5.1.3.1 Questions

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

5.1.3.2 Evidence

Although there have been many studies published on single-incision devices, it should be noted that there are significant differences in 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.

Three systematic reviews have compared single incision slings to retropubic or transobturator tapes (1-3). Two of these meta-analyses included trials of the TVT Secur device (2,3), for which results were inferior and this device has been withdrawn from the market. It has been recognised that there was a problem with the fixation method of the TVT Secur device and that other designs have been modified to eliminate this problem. The Cochrane review of 32 RCTs involving 3427 women (search cut-off date September 2012) concluded that TVT-Secur should no longer be used for the treatment of stress incontinence in women (3). There was evidence to suggest single-incision slings are quicker to perform and cause less postoperative 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 (2) and a reanalysis of the Cochrane review data by our 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.

Evidence summary	**LE**
Self-fixing single-incision slings are as effective as conventional mid-urethral slings in improving SUI in women at up to 18 months.	1b
Operation times for insertion of single-incision mid-urethral slings are shorter than for standard retropubic slings.	1b
Blood loss and immediate postoperative pain are lower for insertion of single-incision slings compared with conventional mid-urethral slings.	1b
TVT Secur is less effective than conventional mid-urethral slings at medium-term follow-up*.	1b
There is no evidence that other adverse outcomes from surgery are more or less likely with single-incision slings than with conventional mid-urethral slings.	1b

**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.*

5.1.3.3 References

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5.1.4 ***Adjustable sling***

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

5.1.4.1 Questions

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

5.1.4.2 Evidence

There are no RCTs investigating outcome of adjustable sling insertion for women with SUI. There 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. Three adjustable sling devices were reviewed: Remeex®, Safyre®, Ajust®. The latter is an adjustable single-incision sling.

Remeex®

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

Saffyre®

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

A non-randomised comparison of adjustable tape and transobturator tape in a single centre suggested fewer obstructive voiding symptoms in women receiving an adjustable tape though objective voiding parameters were no different (5).

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

5.1.4.3 References

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5.1.5 ***Bulking agents***

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

5.1.5.1 Question

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

5.1.5.2 Evidence

There have been two Cochrane systematic reviews (1,2) and one independent SR (3), which reported on 12 RCTs or quasi-RCTs of injectable agents. In general, the trials were only of moderate quality and small and many of them had been reported in abstract form. Wide confidence intervals meant a meta-analysis was not possible. Since the Cochrane review, two further RCTs have been reported (4,5).

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 (6). These case series have added very little to the evidence provided by RCTs. There has been only one placebo-controlled RCT, in which an autologous fat injection was compared with the placebo of a saline injection.

Polytetrafluoroethylene (Polytef)

There are no RCTs available. NICE 2013 (7) did not recommend this treatment because of the high incidence of adverse events.

Glutaraldehyde cross-linked bovine collagen (Contigen)

Most evidence from RCTs of the efficacy of collagen comes from six trials, in which collagen has been used as a comparator to an experimental synthetic product (see below). This implies that collagen has been regarded as the 'gold standard' bulking agent. In one RCT, collagen was compared to open surgery (7).

Autologous fat

One study found no difference in efficacy between autologous fat and saline injection (22% vs. 20% improvement at 3 months, respectively) (8). Due to a fatality from fat embolism, NICE 2006 (6) and the Cochrane Review (2) made a strong recommendation that this treatment should not be used.

Silicon particles (Macroplastique™)

Silicon particles have been compared to collagen in two RCTs, only one of which has been published as a full article (9). No significant difference in efficacy was found.

Carbon beads (Durasphere™)

Carbon beads have been compared to collagen in two RCTs (5,10). Although one study lacked appropriate statistical power, the other was a good-quality study (n = 235), with 12 months' follow-up, that showed no difference in efficacy.

Calcium hydroxylapatite (CaHA) (Coaptite™)
A study with small sample size comparing collagen to hydroxylapatite found the failure rate was significantly higher at 6 months for collagen (6/18 vs. 3/22, respectively) (11).

Ethylene vinyl alcohol copolymer (EVOH) (Uryx™)
There is one RCT (n = 210), comparing ethylene copolymer to collagen, which demonstrated similar efficacy at 6 months' follow-up (12).

Porcine dermal implant (Permacol™)
There is one very small RCT comparing porcine dermis to silicon particles. There was no significant difference in failure rates between the two procedures at 6 months' follow-up (13).

Hydrogel cross-linked with polyacrilamide (Bulkamid™)
No RCT data are available. There is a single multicentre case series of 135 women, which reported 66% success rate with 35% participants requiring re-injection (14).

Non-animal stabilised hyaluronic acid/dextranomer (NASHA/Dx) (Zuidex™)
There is one RCT, comparing dextranomer (placed in mid-urethra) to collagen injection (at the bladder neck). At 12 months, results were inferior in women given dextranomer (15). However, this product has now been withdrawn from the market because of high complication rates.

Stem cells
Early reports of dose-ranging studies (16) suggest that stem cell injection is a safe procedure in the short-term. However, its efficacy (compared to its bulking effect) has yet to be established.

Comparison with open surgery
Two RCTs studies compared collagen injection to conventional surgery for SUI (autologous sling vs. silicon particles and collagen vs. assorted procedures). The studies reported greater efficacy but higher complication rates for open surgery. In comparison, collagen injections showed inferior efficacy but equivalent levels of satisfaction and fewer serious complications (7,17).

Another trial found that a periurethral route of injection can carry a higher risk of urinary retention compared to a transurethral injection (18). A recent small RCT found no difference in efficacy between a mid-urethral and bladder neck injection of collagen (4).

Evidence summary	**LE**
Periurethral injection of bulking agent may provide short-term improvement in symptoms (3 months), but not cure, in women with SUI.	2a
Repeat injections to achieve therapeutic effect are 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 (retropubic, transobturator and self-fixing single incision slings) 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 midurethral 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 cystoscopy as part of retropubic insertion of a mid-urethral sling, or if difficulty is encountered during transobturator sling insertion, or if there is a significant cystocoele.	C
Offer colposuspension (open or laparoscopic) or autologous fascial sling to women with stress urinary incontinence if mid-urethral sling cannot be considered.	A C
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.	
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.	
Women who suffer from multiple risk factors should be warned that they are less likely to have a successful outcome from surgery for stress urinary incontinence.	
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*

5.1.5.3 Research priorities

- What is the influence of surgical skill on the outcome of surgery?
- How does minimally invasive first-line surgery compare to conservative treatment in treatment of women with SUI?
- How do single-incision slings compare to standard operations in treatment of women with SUI?
- What is the effect of varying tension of a mid-urethral sling on cure or improvement of SUI?

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5.2 Complicated SUI in women

This section will address surgical treatment for women who have had previous surgery for SUI, which has failed, or those women who have undergone previous radiotherapy affecting the vaginal or urethral tissues. Neurological lower urinary tract dysfunction is not considered because it is reviewed by the EAU Guidelines on Neurogenic Lower Urinary Tract Dysfunction (1). Women with associated genitourinary prolapse are included in this edition (see section 5.3).

*5.2.1 **Colposuspension or sling following failed surgery***

The reported failure rates from any operation for SUI vary widely from 5-80%, depending on how failure has been defined. Even with a very tight definition this implies that, of the many thousands of women undergoing primary surgery for SUI, there will be hundreds who later require further surgery for recurrent symptoms. A primary operation may fail from the start or in other cases occur years after the original procedure. 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.

However, the underlying reasons for failure are poorly understood. Consequently, the decision on which operation to offer in the secondary setting is usually driven by individual opinion about these mechanisms, familiarity with certain procedures, and experience in personal series. Most surgeons believe that the results of any operation will be inferior to the same operation used as a primary procedure, and will warn their patients accordingly.

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

5.2.1.1 Question

In women who have 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?

5.2.1.2 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 (2) up till 2008 and the subject has also been reviewed by Ashok (3) and Lovatsis et al. (4). 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 (5).
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 (6).

Post-hoc subgroup analysis of high-quality RCTs comparing one procedure to another have shown conflicting evidence of relative effectiveness (7-10).

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 (11).

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 (12,13), whilst other research has shown inferior outcomes for secondary surgery (14,15). Other confounding variables make meaningful conclusions difficult.

There are numerous small case series reporting satisfactory outcomes for redo procedures of many types, but this evidence is difficult to interpret in a way that allows conclusions about the best therapeutic approach.

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 (16). 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.

Evidence summary	**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
There is no evidence that any other operation is superior to another in the cure or improvement of SUI in women who have had previous surgery.	3

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5.2.2 ***External compression devices***

Some of the earliest techniques for treating SUI simply applied intra-corporeal compression external to the urethra. External compression devices are still widely used in the treatment of recurrent SUI after the failure of previous surgery. They are also used in women with neurological LUTD, in whom there is thought to be

profound intrinsic failure of the sphincter mechanism, characterised by very low leak point pressures or low urethral closure pressures. This is a common finding following failure of a previous operation for incontinence but should be confirmed by urodynamic evaluation.

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

5.2.2.1 Question

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

5.2.2.2 Evidence

The major advantage of AUS over other anti-incontinence procedures is the perceived ability of women to be able to void normally (1). 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 (2).

Artificial urinary sphincter (AUS)

The 2011 Cochrane review on AUS (3) applies only to men with post-prostatectomy incontinence. A previous review of mechanical devices concluded that there was insufficient evidence to support the use of AUS in women (4).

There are no RCTs regarding the AUS in women. There are a few case series in women, including four series (n = 611), with study populations ranging from 45 to 215 patients and follow-up ranging from 1 month to 25 years (5-8). Case series have been confounded by varying selection criteria, especially the proportion of women who have neurological dysfunction or who have had previous surgery. Most patients achieved an improvement in SUI, with reported subjective cures in 59-88% of patients. However, common side effects included mechanical failure requiring revision (up to 42% at 10 years) and explantation (5.9-15%). In a retrospective series of 215 women followed up for a mean of 6 years, the risk factors for failure were older age, previous Burch colposuspension and pelvic radiotherapy (8). Peri-operative injury to the urethra, bladder or rectum was also a high-risk factor for explantation (6).

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 (9).

Early reports of laparoscopically implanted AUS do not have sufficient patient populations and/or sufficient follow-up to be able to draw any conclusions (10,11).

Adjustable compression device (ACT)

There are no RCTs on use of the ACT device. There are four case series (n = 349), with follow-up ranging from 5 to 84 months (12-15). An improvement in UI outcomes was reported, ranging from 47% objective cure to 100% subjective improvement. However, most patients required adjustment to achieve continence and 21% required explantation.

Evidence summary	**LE**
Implantation of an artificial sphincter 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 for surgery for complicated stress urinary incontinence in women	GR
The choice of surgery for recurrent stress urinary incontinence should be based on careful evaluation of the individual patient including video-urodynamics.	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
Implantation of AUS or ACT for women with complicated stress urinary incontinence should only be offered in expert* centres.	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.

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

5.2.2.3 Research priorities

What is the most effective surgical procedure in women requiring second-line surgery for SUI after failure of a previous operation?

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5.3 Women with both SUI 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 surgical 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.

*5.3.1 **Questions***

1. In women with POP and UI, does combined surgery for POP and SUI reduce the incidence of postoperative UI compared to POP surgery alone?
2. In continent women with POP, does combined surgery for POP and SUI reduce the incidence of postoperative 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 postoperative 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 are the reliability, the diagnostic accuracy and predictive value of a prolapse reduction test to identify patients at risk for denovo SUI following prolapse repair?

5.3.1.1 Evidence

A Cochrane review in 2013 included sixteen trials concerning bladder function after surgery for pelvic organ prolapse (1). In general, after prolapse surgery 434 of 2125 women (20.4%) reported new subjective SUI after prolapse surgery in 16 trials. New voiding dysfunction was reported in 109 of 1209 (9%) women undergoing prolapse surgery in 12 trials.

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

There are two well-designed randomised controlled trials relating to the prevalence of postoperative stress urinary incontinence 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 (2), the other compared vaginal repair with and without a mid-urethral sling (3). 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 (3). This was also the finding of the Cochrane review and meta-analysis.

Two trials addressed postoperative SUI in patients who had had SUI preoperatively. Borstad et al., in a multicenter randomised women with POP and SUI to have a tension-free vaginal tape (TVT) at the time of prolapse repair or 3 months later. Women in the delayed group, who still had SUI at 3 months after the prolapse repair, had a TVT performed (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 (4).

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 (5). 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 postoperatively 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 postoperative 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 post-prolapse 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 (3).

3. *Women with POP and occult SUI*

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

4. *Women with POP and OAB*

There is evidence from 3 case series evaluating patients with concomitant OAB and pelvic organ prolapse assessing incontinence/OAB symptom scores postsurgical 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 (6).

Kummeling assessed the effect of a modified laparosocopic sacrocolpopexy on urodynamic parameters and reported an improvement with no evidence to support a concomitant prophylactic colposuspension (7).
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 OABSS scores post-op (8).

5. *Prolapse reduction stress test*

Data concerning the prolapse reduction stress test (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 (9). 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 (10). In a further study occult SUI only detected by a pessary test in 19% of patients, not by urodynamics, history or clinical examination (11).

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, dispareunia, 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 RCTs were found to investigate which test is best to confirm the clinical suspicion. However, a case series of 27 patients concluded that endoluminal (vaginal or rectal) MRI has better diagnostic accuracy than video cystourethrography VCUG (12). 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 (13). Dwarkasinget al. also reports 100% specificity and sensitivity of MRI in a case series of 60 patients (14). However, in a case series of 41 patients, a study reported 25% discrepancy between MRI and surgical findings (15).

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

Surgical treatment:

No RCTs were found to answer which is the best treatment to a bothersome urethral diverticulum. Surgical removal is the most commonly reported treatment in contemporary cases series. However, recurrence may occur rather frequently in more complex diverticulum. Han et al. found a recurrence rate of 33% in U-shaped and of 60% in circumferential diverticulum within 1 year (16). Ingber et al. found a 10.7% recurrence rate in 122 women undergoing diverticulectomy, with higher risk of recurrence in those with proximal or multiple diverticula or those who had had previous pelvic surgery (17).

SUI may supervene in up to 20% women after diverticulectomy, requiring additional correction (18-21). De novo SUI seems to be more common in proximal and in large size (>30mm) diverticula.

Diverticula may undergo neoplastic alterations (6%) including invasive adenocarcinomas (22).

Evidence summary	**LE**
Women with prolapse + UI	
Surgery for POP + SUI shows a higher rate of cure in the short-term than POP surgery alone.	1a
There is conflicting evidence on the relative benefit of combined surgery long-term.	1b
Combined surgery for POP+SUI carries a higher risk of adverse events.	1b
Continent women with POP	
Are at risk of developing UI postoperatively.	1a
The addition of a prophylactic anti-incontinence procedure reduces the risk of postoperative 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 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
A prolapse reduction stress test can identify occult SUI, however further research is needed to determine its value in predicting occurrence of SUI after POP surgery.	
Women with urethral diverticulum	
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

Recommendations for women requiring surgery for bothersome POP who have symptomatic or unmasked stress urinary incontinence	**GR**
Offer simultaneous surgery for POP 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	**GR**
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
Attempt to unmask occult SUI by a prolapse reduction stress test.	
Symptomatic urethral diverticula should be completely surgically removed.	A*

POP = pelvic organ prolapse.

** based on expert opinion*

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5.4 Men with SUI

*5.4.1 **Bulking agents in men***

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

5.4.1.1 Question

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

5.4.1.2 Evidence

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

Evidence summary	**LE**
There is no evidence that bulking agents cure post-prostatectomy incontinence.	2a
There is weak evidence that bulking agents can offer temporary, 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

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*5.4.2 **Fixed male sling***

As well as external compression devices and bulking agents, slings have been introduced to treat postprostatectomy 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 postoperatively.

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) (1).

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 (2).

5.4.2.1 Question

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

5.4.2.2 Evidence

Concerning the surgical treatment of post-prostatectomy incontinence, three recent literature reviews are available (3-5). There are a large number of uncontrolled case series concerning men implanted with several types of slings (6-13).

For the repositioning sling (AdVance), the benefit after a mean follow-up of 3 years has been published on 136 patients (14). 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 (12,15). Postoperative voiding dysfunction occurred in 5.7-1.3%, while erosions and chronic pain were uncommon (0-0.4%) (2,6,14-20). The overall failure rate was about 20%.

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

Evidence summary	**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

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*5.4.3 **Adjustable slings in males***

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

5.4.3.1 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?

5.4.3.2 Evidence

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

Remeex® system

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

Argus® system

Data on the Argus® system have been reported for 404 men, but only four series have reported on more than 50 patients (3-5), 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% (4,6,7). Infection of the device occurred in 5.4-8% (3,5,7). Erosions were reported in 5-10% (8,9). Urethral perforations occurred in 2.7-16% (3,5). Pain at the implant site was usually only temporary, but chronic pain has been reported (3,7-9). These complications resulted in explantation rates of 10-15% (4,6).

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 for adjustment of cushion volume. Some initial reports show objective cure rates of 60.5% and improvement rates of 23.7% but with the need for up to nine postoperative adjustments (10,11).

Evidence summary	**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

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*5.4.4 **Compression devices in males***

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

There are several recognised complications of AUS implantation, e.g. mechanical dysfunction, urethral constriction by fibrous tissue, erosion and infection. The non-circumferential compression devices consist of two balloons placed close to the vesico-urethral anastomotic site. The balloons can be filled and their volume can be adjusted postoperatively through an intrascrotal port.

5.4.4.1 Question

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

5.4.4.2 Evidence

Artificial urinary sphincter

Although the AUS is considered to be the standard treatment for men with SUI, there are two systematic reviews (2,3) presenting limited evidence, of generally poor quality, except for one RCT comparing with bulking agents (4). More recent case series confirm the previous data (5,6). A continence rate of about 80% can be expected, while this may be lower in men who have undergone pelvic radiotherapy (1).

Trigo Rocha et al. published a prospective cohort study on 40 patients with a mean follow-up of 53 months (7). Pad use was reduced significantly and continence was achieved in 90%, with a significant improvement in QoL. The revision rate was 20%. From all urodynamic parameters, only low bladder compliance had a negative impact on the outcome, although another retrospective study showed that no urodynamic factors adversely altered the outcome of AUS implantation (8).

The penoscrotal approach was introduced to limit the number of incisions and to allow simultaneous implantation of penile and sphincter prostheses. It is uncertain whether this approach alters the outcome (9-11). The transcorporeal technique of placement can be used for repeat surgery but evidence of effectiveness is lacking (12,13).

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 (14-16). Patients who experienced complete continence after AUS implantation had a higher erosion risk (17). One small series reported results of AUS implantation after failure of previous Advance sling, showing no difference in efficacy between secondary and primary implantation (18).

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 (19). A subgroup of radiotherapy patients only had 46% success and a higher percentage of urethral erosions.

A quasi-randomised trial comparing a non-circumferential compression device (ProAct®) with bone-anchored male slings found both types of device resulted in similar improvement of SUI (68% vs. 65%, respectively) (20). Other prospective series have shown similar continence outcomes, but several re-adjustments of the balloon volume were required to achieve cure. Adverse events were frequent, leading to an explantation rate of 11-58% (2,21-25). Although most studies have shown a positive impact on QoL, a questionnaire study showed that 50% of patients were still bothered significantly by persistent incontinence (26).

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 (27).

Other designs of artifical sphincter remain the subject of ongoing evaluation though may have been introduced onto the market, see recommendation at 5.1.5.2.

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

5.4.4.3 Research priorities

What are the comparative indication, efficacy and risk of different operations for post-prostatectomy incontinence?

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5.5 Surgical interventions for refractory DO

*5.5.1 **Intravesical injection of botulinumtoxinA***

Botulinum toxin (BTX) injections into the bladder wall are being increasingly used to treat persistent or refractory UUI in adult women, as well as in men despite the lack of high-quality data on BTX in males. Almost all reported studies have used BTX A (1,2). Injection techniques have not been standardised and the various studies differ with reference to the number of injections, the sites of injection and the injection volumes (1,2). Surgeons must realise that there are different products of botulinum toxin, onabotulinumtoxinA (Botox in Europe) abobotulinumtoxinA (Dysport in Europe) and incobotulinum toxin (Xeomin) and that the doses are not interchangeable between the different products. In most European countries only onabotulinum toxin A is licenced for use in OAB.The continued efficacy and risks of repeat injections remain uncertain. The most important adverse events are UTI and an increase in PVR that may require clean intermittent catheterisation (CIC) (1,2).

5.5.1.1 Question

In adults with UUI, is intravesical injection of BTX better than no treatment for cure or improvement?

5.5.1.2 Evidence

Three systematic reviews on the use of BTX have been published (1-3). Only the last review used cure rate as an outcome measure. Two dose ranging RCTs have established that whilst efficacy may increase with higher doses of botulinum toxin, so does the risk of side effects, particularly increased PVR. The established licensed dose of onobotulinum toxinA is 100 units (4,5).

QoL improvement after onabotulinumtoxin administration has been shown to be sustained for 36 weeks (6) and in another study the gains in QoL achieved by increasing the dose, were marginal (7). Successful UUI treatment with onabotulinumtoxinA does not appear to be related to the existence of DO. In a subanalysis a

dose-finding study, no differences were found regardless of the occurrence of DO at baseline (6). Likewise, onabotulinumtoxinA improved UUI in a cohort of 5 male and 27 female patients with OAB and without DO (8).

Other systematic reviews (1,2) showed variation in the number of injections given and dilutions of BTX used, though 20 mL volume given at 20 sites was the most common. The choice of injection site did not appear to impact on efficacy or adverse events. However, two recent small RCTs show conflicting results on whether trigonal injection alters the efficacy of BTX injection; one study having found no difference between including trigonal injection and avoidance of the trigone (9), whilst another study showed superior symptomatic improvement if the trigone was included in the injection protocol (2), though UUI was not specifically evaluated in the latter study.

Cohort studies have shown the effectiveness of botulinum toxin injections in the elderly and frail elderly (10), though 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 (9).

A recent RCT compared onabotulinumtoxinA injection to solifenacin (with dose escalation or switch to trospium possible in the solifenacin group) and showed a similar rates of improvement in UUI over the course of 6 months (11). Patients receiving onabotulinumtoxinA 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.

Evidence summary	**LE**
A single treatment session of intravesical onabotulinumtoxinA (100-300 U) is more effective than placebo at curing UUI and improving UUI and QoL for up to 12 months.	1a
Doses of onabotulinumtoxinA above 100 U are associated with an increased risk of requiring de novo CIC.	1a
Doses of onabotulinumtoxinA above 100 U do not add additional improvement in QoL.	1b
There is no evidence that repeated injections of onabotulinumtoxinA have reduced efficacy.	3
There is a high risk of increased PVR when injecting elderly frail patients.	3
The risk of bacteruria is high following intravesical injection of botulinum toxin but the clinical significance of this remains uncertain.	1b
There is no evidence that one technique of injecting botulinumtoxinA is more efficacious or harmful than another.	1b
OnabotulinumtoxinA 100 U is superior to solifenacin for cure of UUI.	1a
Repeated injections of onabotulinumtoxinA may be associated with a high discontinuation rate.	2

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

UTI = urinary tract infection.

5.5.1.3 Research priorities

- What is the most effective method of injecting botulinum toxin in terms of the site of injection, number of injections, and optimum dilution of the toxin?
- What is the long-term effect of repeated intravesical injection of botulinum toxin?

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*5.5.2 **Sacral nerve stimulation (neuromodulation)***

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

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

5.5.2.1 Question

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

5.5.2.2 Evidence

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

One multicentre RCT involved implantation of half of the participants (5), while the remaining patients formed the control group (delayed implantation) by staying on medical treatment for 6 months. The control group was

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

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

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

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

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

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

Recommendation	**GR**
If available, offer sacral nerve modulation to patients, who have urgency urinary incontinence refractory to conservative therapy.	A

5.5.2.3 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 required.

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*5.5.3 **Cystoplasty/urinary diversion***

5.5.3.1 Augmentation cystoplasty

In augmentation cystoplasty (also known as clam cystoplasty), a detubularised segment of bowel is inserted into the bivalved bladder wall. The aim is to disrupt involuntary detrusor contraction, increase compliance and increase bladder capacity. The segment of bowel most often used is distal ileum, but any bowel segment can be used if it has the appropriate mesenteric length to reach the pelvic cavity without tension. One study did not find any difference between bivalving the bladder in the sagittal plane and bivalving it in the coronal plane (1,2).

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

A number of case series have been reported (2-9), but none within the last 10 years. All these series included a large proportion of patients with neurological bladder dysfunction. The largest case series of bladder augmentation in UUI included 51 women with UUI (3). At an average follow-up of 74.5 months, only 53% were continent and satisfied with the surgery, whereas 25% had occasional leaks and 18% continued to have disabling UUI. It is difficult to extract data on non-neurogenic patients from these case series, but in general the results for patients with idiopathic DO (58%) seemed to be less satisfactory than for patients with neurogenic overactivity (90%).

Adverse effects were common and have been summarised in a review over 5-17 years of more than 267 cases, 61 of whom had non-neurogenic UUI (10). In addition, many patients may require clean intermittent self-catheterisation to obtain adequate bladder emptying (Table 7).

Table 7: 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

5.5.3.2 Detrusor myectomy (bladder auto-augmentation)

Detrusor myectomy aims to increase bladder capacity and reduce storage pressures by incising or excising a portion of the detrusor muscle, to create a bladder mucosal 'bulge' or pseudodiverticulum. It was initially described as an alternative to bladder augmentation in children (11). An additional, non-randomised study (12), which compared bladder augmentation with detrusor myectomy in adult patients with neurogenic and non-neurogenic bladder dysfunction, demonstrated a much lower incidence of short-term complications. However, the poor long-term results caused by fibrosis of the pseudodiverticulum led to the abandonment of this technique in patients with neurogenic dysfunction. A small study of five patients with UUI (13) showed good outcome in all patients at the initial postoperative visit, but clinical and urodynamic failure in four of the five patients at 3 months.

5.5.3.3 Urinary diversion

Urinary diversion remains a reconstructive option for patients, who decline repeated surgery for UI. It is rarely needed in the treatment of non-neurogenic UUI. There are no studies that have specifically examined this technique in the treatment of non-neurogenic UI, although the subject has been reviewed by the Cochrane group (1,14).

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

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

5.5.3.4 References

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5.6 Surgery in patients with mixed urinary incontinence

5.6.1 ***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?

5.6.2 ***Evidence***

Many RCTs include both patients with pure S or UUI and patients with MUI. predominates. 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 versus patients treated with obturator tape alone (1).

Post-hoc analysis of the SISTER trial showed that in women undergoing either autologous fascial sling or Burch colposuspension, the outcomes were poorer for women with a concomitant complaint of pre-operative urgency. This applied to both stress-specific and non-stress incontinence outcomes (2).

A similar post-hoc review of an 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, as assessed objectively, even if surgery had been similar (3). 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 [4]).

Some authors have reported the disappearance of urgency in up to 40% of women after successful SUI surgery for MUI, suggesting that urgency is an accompanying feature of SUI (4-7). It is less clear whether urgency incontinence improves in the same way.

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) (8). One study compared two parallel cohorts of patients undergoing surgery for SUI, with and without DO, and found inferior outcomes in women with MUI (9).

However, in a study of the bulking agent, Bulkamid, similar outcomes were reported in women with pure SUI and MUI (10).

One cohort of 450 women, undergoing mid-urethral sling surgery, had significantly worse outcomes for increased amounts of urgency. In urgency-predominant MUI, the success rate fell to 52% compared to 80% in stress-predominant MUI (11). In a second study in 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 (12).

De novo urgency remains a consistent complication of stress incontinence surgery affecting up to 25% of women (13).

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

Evidence summary	**LE**
Women with MUI are less likely to be cured of their incontinence by SUI surgery than women with SUI alone.	1c
The response of pre-existing urgency symptoms to SUI surgery is unpredictable and symptoms may improve or worsen.	3

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

*5.6.3 **Research priority***

- 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.

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5.7 Surgery for UI in the elderly

There are no RCTs comparing surgical treatment in older versus 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 (1). An RCT assessing risk factors for failure of tension free vaginal tape (TVT) versus 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 (2). 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 postoperative voiding (3).

Another RCT compared immediate TVT versus 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%) (4).

A cohort study of 256 women undergoing inside-out TVT-O reported similar efficacy in older versus younger women but there was a higher risk of de novo urgency in older patients (5).

A case series of 157 elderly (> 70 years) women with OAB given botox for the first time divided them into frail elderly (6), elderly without impaired activities of daily living (7) and those aged 58-70 years old (2). They found a higher rate of post-voiding residual (> 150 mL) in the frail elderly (59.6%) compared to 42.6% and 34.5% in the other groups, respectively (8).

Cohort studies have shown the effectiveness of botulinum toxin injections in the elderly and frail elderly (9,10), 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.

Evidence summary	**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 BTX injection), together with the lower probability of benefit.	B

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APPENDIX A: URINARY FISTULA

A.1 Introduction

Whilst in the developing world, fistulae often result from poor peri-natal care, and the published obstetric series report large numbers of cases, the incidence of non-obstetric fistulae is much lower. In Europe obstetric fistula is very rare and it will not be considered by this guideline.
The epidemiology, aetiology, diagnosis, treatment and prevention have been described in detail during the recent International Consultations on Incontinence (ICI) (1,2). The relevant literature predominantly consists of case series and expert opinion giving a generally low level of evidence.

Non obstetric urinary fistula
The most common causes of vesicovaginal fistula (VVF) are injuries to the urinary tract during hysterectomy for benign conditions (60-75%), followed by hysterectomy for malignant conditions (30%), caesarean section (6%), and obstetric injuries (1%) (3). Urinary tract injury rates vary from 0.1 to 4% during pelvic operations (4,5) with a higher risk in radical hysterectomy (6-8).

Urinary fistulae occur occasionally in association with primary pelvic cancers (9,10) but are more common in patients with malignancy which is treated by radical surgery (especially when there has been prior radiotherapy (up to 52% in one surgical series) and when radiotherapy is used for treatment of recurrent disease. When fistula occurs following radiotherapy for primary treatment, this may be an indication of tumour recurrence. This rule applies as much to ureteric fistulae as to VVF.

A.2 Diagnosis of fistula

Clinical diagnosis
Leakage of stool, urine, or possibly both 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 (5).

The diagnosis of 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 an ureterovaginal and VVF may be useful in some cases (4). Testing the creatinine level in either the extravasated fluid or the accumulated ascites and comparing this to the the serum creatinine levels 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, particular with T2 weighting, also provides optimal diagnostic information regarding fistulae and may be preferred for urinary - intestinal fistulae (10).

A.3 Management of vesicovaginal fistula

A.3.1 ***Conservative management***

Immediate management by urinary catheterisation or diversion
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% (7,9). In general, conservative measures are most likely to be in small fistulae (less than 3mm in diameter).

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 technique applied to the repair of urinary fistulae, the classical saucerisation / partial colpocleisis (6) and the more commonly used dissection and repair in layers or 'flap-splitting' technique (8). 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.

With secondary repair of previously failed VVF surgery, the success rate fell from 81% for first procedures to 65% for those requiring 2 or more procedures (11).
There is only a single randomised trial comparing aspects of surgical technique. Shaker et al. report an RCT comparing trimming of the fistula edge with no trimming (12). Although there was no statistical difference in success rates between the two groups, in those cases where repair was unsuccessful and trimming had been undertaken, the fistula tended to become larger, whereas those where there was no trimming were more likely to be smaller upon recurrence (12).

Laparoscopic
Laparoscopic repair of a VVF was first reported by Nezat et al. in 1994 (13). Fistula repair without cystostomy, guided by transvaginal illumination proved feasible in 4 patients (14). It is possible that there may be both selection and reporting biases that make it difficult to fully evaluate laparoscopic procedures against alternative surgical approaches.

Robotic
The first report of a robot-assisted repair of vesicovaginal fistula was from Melamud et al. in 2005 (15). The reported cure rate is 100% in all series. At this stage, it is not possible to indicate what its place or potential advantages are over alternative approaches.

Fibrin glue
The use of fibrin glue in urological indications was reviewed by Shekarriz and Stoller (16). Overall, the indications for, and optimal patient selection for this approach are not defined.

Adjuvant Techniques in the Repair of VVF: 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.

A.3.3 ***Postoperative management***
Studies of non-obstetric fistula management are not consistent in their description of duration of catheterisation. Most report periods of between seven and 21 days drainage; most typically 10-14 days for surgical fistulae and 14-21 days for radiotherapy-associated fistulae. There is no more than level 3/4 evidence to support any particular practice in these aspects of fistula management.

A.4 Management of radiation fistula
The literature relating to the management of radiotherapy-associated fistula is again limited in quantity and quality.

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 (17).

Because of the wide field abnormality surrounding many radiotherapy-associated fistulae, several authors have suggested that permanent urinary and/or faecal diversion should be seen as the treatment of choice in such cases (18). Others have employed a routine policy of preliminary urinary and faecal diversion, with later undiversion in selected cases. In patients with intractable urinary incontinence from radiation-associated fistula, percutaneous nephrostomy or ureterostomy might be considered (19). 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
The relevant clinical principles are related to prevention, diagnosis, management, and after care (20). 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 intraoperative injury should be performed observing the principles of debridement, adequate blood supply and tension free anastomosis with internal drainage using stents (21). 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.

Repair of such cases should be undertaken by an experienced team and may consist of conservative management with internal or external drainage, endoluminal management using nephrostomy and stenting where available, and early (< 3 months) or delayed (> 6 months) surgical repair when required (22). Surgery should again adhere to the standard principles of tissue repair and safe anastomosis. Functional and anatomical imaging should be used to follow up patients after repair to guard against late deterioration in function of the affected renal unit.

Ureterovaginal fistula

Ureterovaginal fistula occurring in the early postoperative phase predominantly after hysterectomy is the most frequent presentation of upper urinary tract fistula in urological practice. An RCT in 3,141 women undergoing open or laparoscopic gynaecological surgery lasting found that prophylactic insertion of ureteric stents made no difference to the risk of ureteric injury (approx 1%) (23).

A previous cost analysis from the United States perspective suggested stenting was only worthwhile if the risk of injury was > 3.2% (24). If injury does occur, many cases, even those with bilateral injury, can be managed by endoscopic techniques (25).

Where retrograde stenting proves impossible, percutaneous nephrostomy and antegrade stenting might be considered if there is some degree of pelvicalyceal dilatation. Ureteroscopy may also be helpful (26).

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

Introduction

Urethrovaginal fistulae are a rather rare complication of some surgical and medical conditions or treatments. Most of the literature consists of small retrospective series or case reports. There are no randomised prospective trials.

Aetiology

In industrialised countries urethrovaginal fistulae in adults mostly have an iatrogenic aetiology. In feminising genital reconstructions in children with ambiguous genitalia and surgical repairs of cloacal malformations, urethrovaginal fistula can occur as early or late complications (27,28). Also in transsexual adults undergoing female to male reconstruction, urethrovaginal fistulae have been reported (29).

In the surgical treatment of stress incontinence in women with bulking agents or synthetic slings several cases of urethrovaginal fistula have been reported (30). Even conservative treatment of prolapse with pessaries can lead to the formation of fistulae (31). Urethral diverticula and their surgical repair may also lead to urethrovaginal fistula (32). Irradiation complications can also result in the formation of urethrovaginal fistula (33).

A.6.1 ***Diagnosis***

Clinical vaginal examination is often sufficient to diagnose the presence of an urethrovaginal fistula. Urethroscopy and cystoscopy can be performed to assess the extent and location of the fistula. In cases of difficult diagnosis, voiding cystourethrography (VCUG) or ultrasound can be useful (34). 3D MRI or CT scan is becoming utilised more widely (35,36).

A.6.2 ***Surgical repair***

Several techniques for urethrovaginal fistula closure have been described. Depending on the size, localisation and aetiology of the fistula and the amount of tissue loss, urethral reconstruction techniques may be necessary to restore the urethra and to achieve postoperative continence.

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: identifying the fistula, creation of a dissection plane between vaginal wall and urethra, watertight closure of urethral wall, eventual interposition of tissue, and closure of the vaginal wall. 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 (37).

Advancement flaps of vaginal wall can be used to cover the urethral suture line. In some cases more advanced methods are used to close or to protect the urethral closure.

Labial and vaginal flaps and neourethra.
The simplest flap is a vaginal advancement flap.

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 (38,39). The construction of a neo-urethra has mostly been described in traumatic aetiologies. In some cases a transpubic approach has been used (40). 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 postoperatively (41,42).

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 fistula where additional bulking with well vascularised tissue is needed (43). The series of non-obstetrical aetiology are small and all of them are retrospective. There are no prospective data, nor randomised studies (44). The indications for Martius flap in the repair of all types of fistula remain unclear.

Rectus muscle flap
Rectus abdominis muscle flaps have been described by some authors (45,46).

A.6.2.2 Abdominal approach
A retropubic retrourethral technique has been described by Koriatim (47). This approach allows a urethrovesical flap tube to be fashioned to form a continent neourethra.

Evidence Summary	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 postoperatively 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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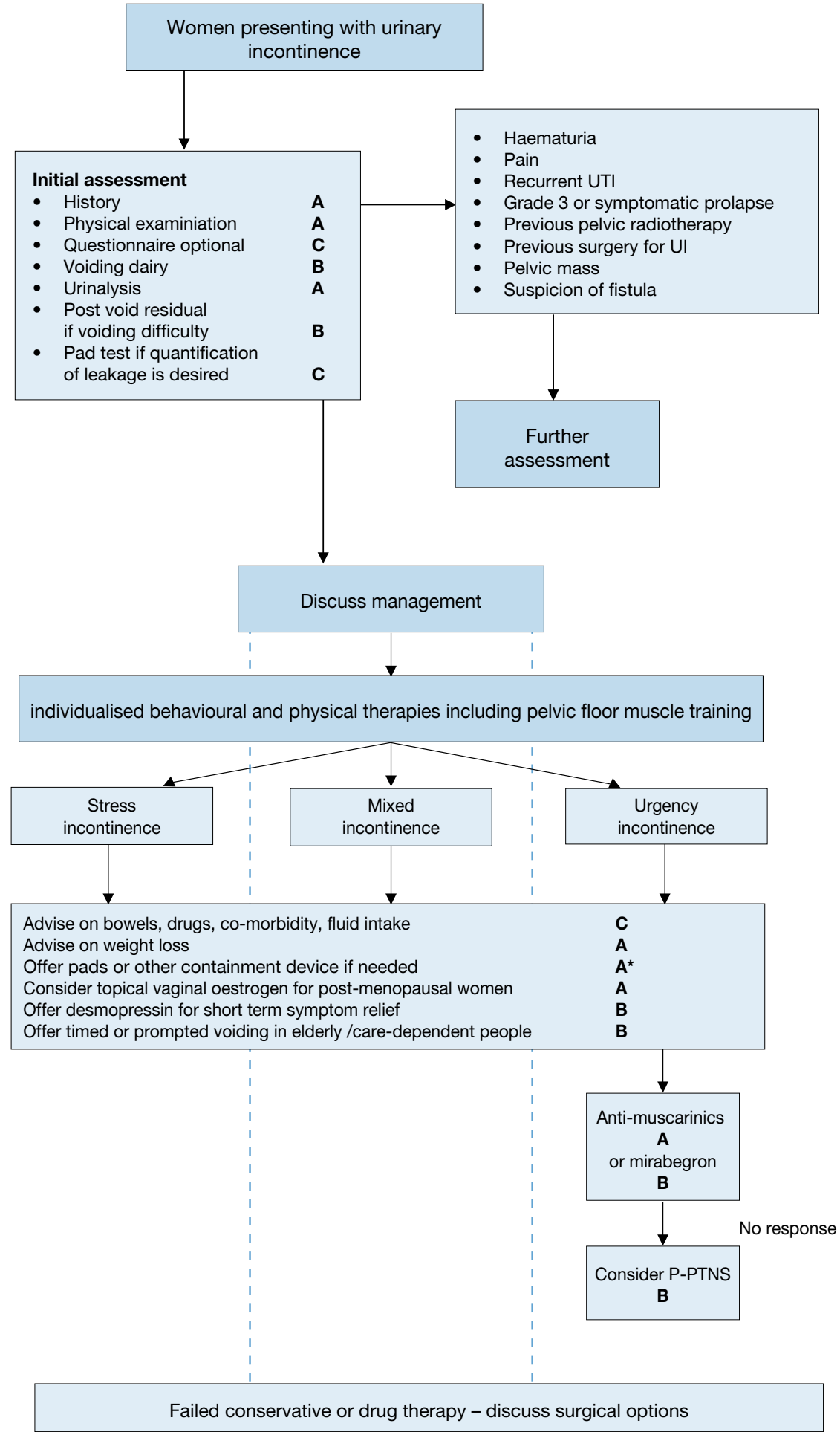
6. ABBREVIATIONS USED IN THE TEXT

This list is not comprehensive for the most common abbreviations.

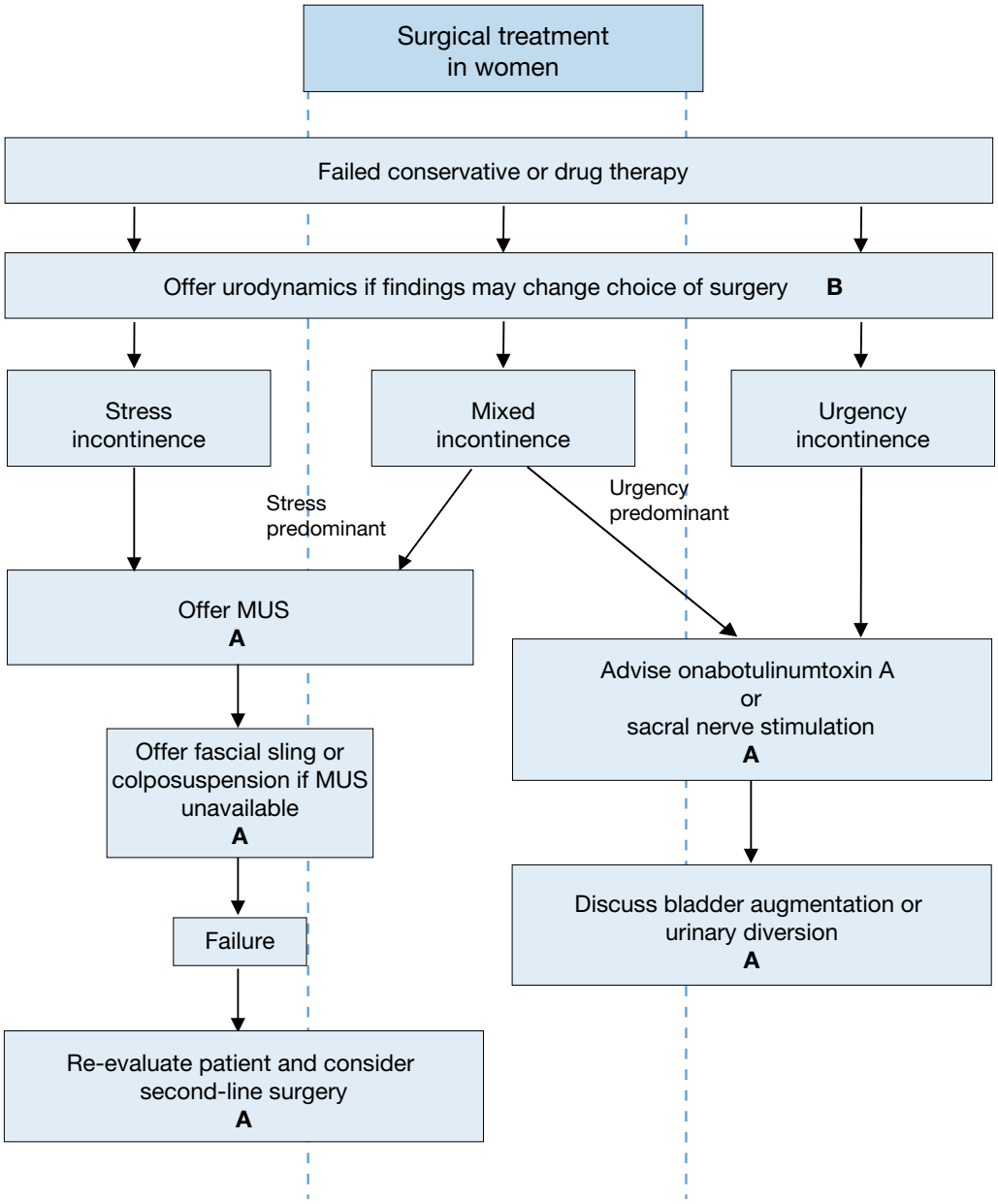
ACT	adjustable compression therapy (device)
ADL	activities of daily living
AHRQ	Agency for Healthcare Research and Quality
AUS	artificial urinary sphincter
BT	bladder training
BTX	botulinum toxin
BWT	bladder wall thickness
CIC	clean intermittent catheterisation
CNS	central nervous system
DO	detrusor overactivity
DWT	detrusor wall thickness
EAU	European Association of Urology
ER	extended release
ES	electrical stimulation
FIT	Functional Incidental Training
FS2S	first stage of two-stage (implantation of sacral neuromodulator)
GR	grade of recommendation
HRQoL	health-related quality of life
I-QoL	Incontinence Quality of Life
IR	Immediate release
LE	level of evidence
LUTS	lower urinary tract symptoms
MPR	medication possession rate (drug adherence)
MRI	magnetic resonance imaging
MUI	mixed urinary incontinence
NICE	National Institute for Health and Clinical Excellence (UK)
OAB	overactive bladder
PFMT	pelvic floor muscle training
PICO	Population, Intervention, Comparison, Outcome
POP	pelvic organ prolapse
POSEI	postoperative stress urinary incontinence
PNE	percutaneous nerve evaluation
PPI	post-prostatectomy urinary incontinence
PROMS	patient-reported outcome measures
PTNS	posterior tibial nerve stimulation
P-PTNS	percutaneous posterior tibial nerve stimulation
T-PTNS	transcutaneous posterior tibial nerve stimulation
PVR	post-voiding residual
Qmax	maximum urinary flow rate
QoL	quality of life
RCT	andomised controlled trial
SIGN	Scottish Intercollegiate Guideline Network
SUI	stress urinary incontinence
TDS	transdermal delivery system
TVT	tension-free vaginal tape
TBT-O	transobturator tension-free vaginal tape
TVTS	tension-free vaginal tape secure
UI	urinary incontinence
URR	Urethral Reflectometry
US	ultrasound
UTI	urinary tract infection
UUI	urgency urinary incontinence

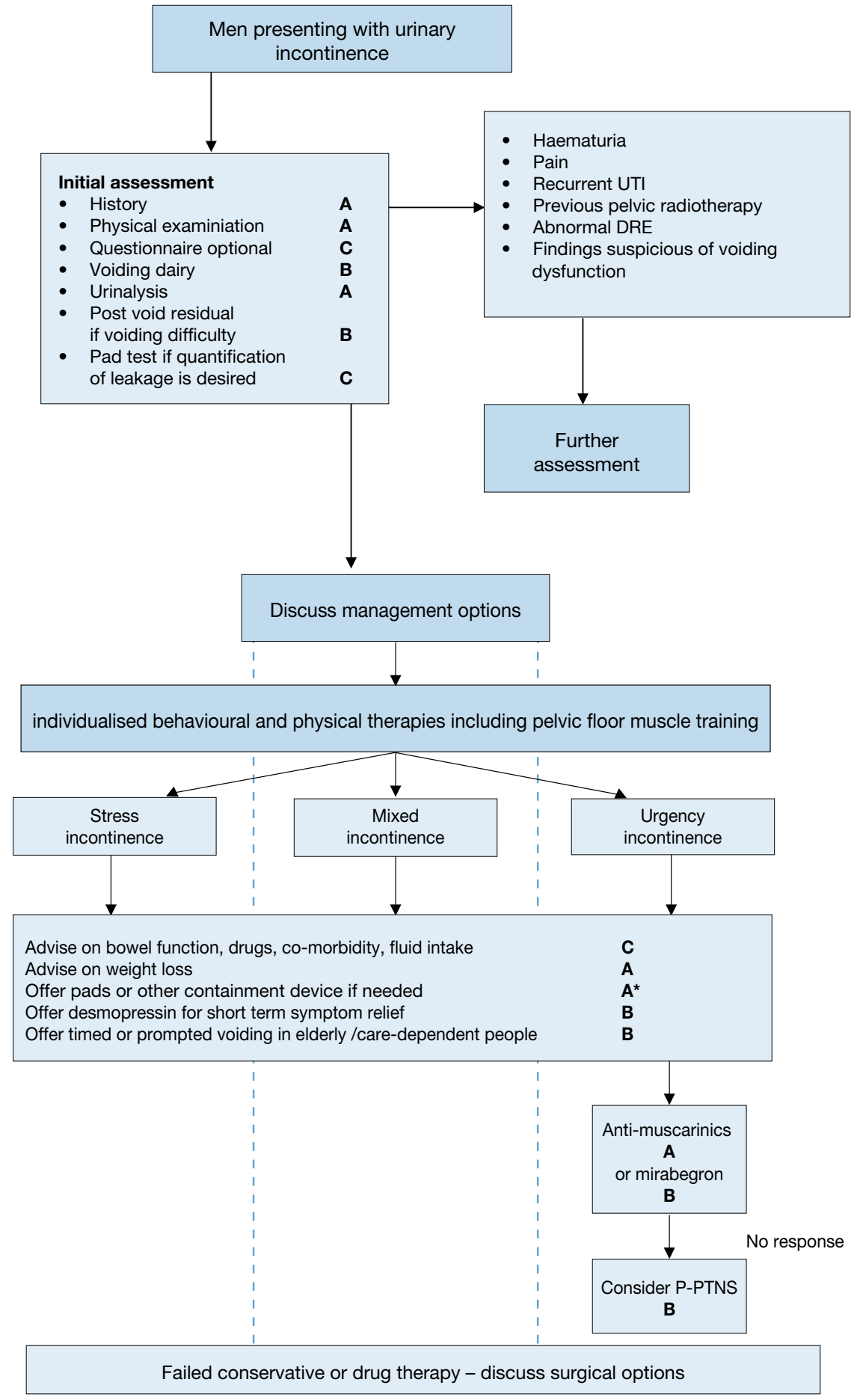
Conflict of interest

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



** Based on expert op opinion*


Surgical treatment in women
Failed conservative or drug therapy
Offer urodynamics if findings may change choice of surgery B
Stress incontinence
Mixed incontinence
Urgency incontinence
Stress predominant
Urgency predominant
Offer MUS A
Offer fascial sling or colposuspension if MUS unavailable A
Failure
Re-evaluate patient and consider second-line surgery A
Advise onabotulinumtoxin A or sacral nerve stimulation A
Discuss bladder augmentation or urinary diversion A



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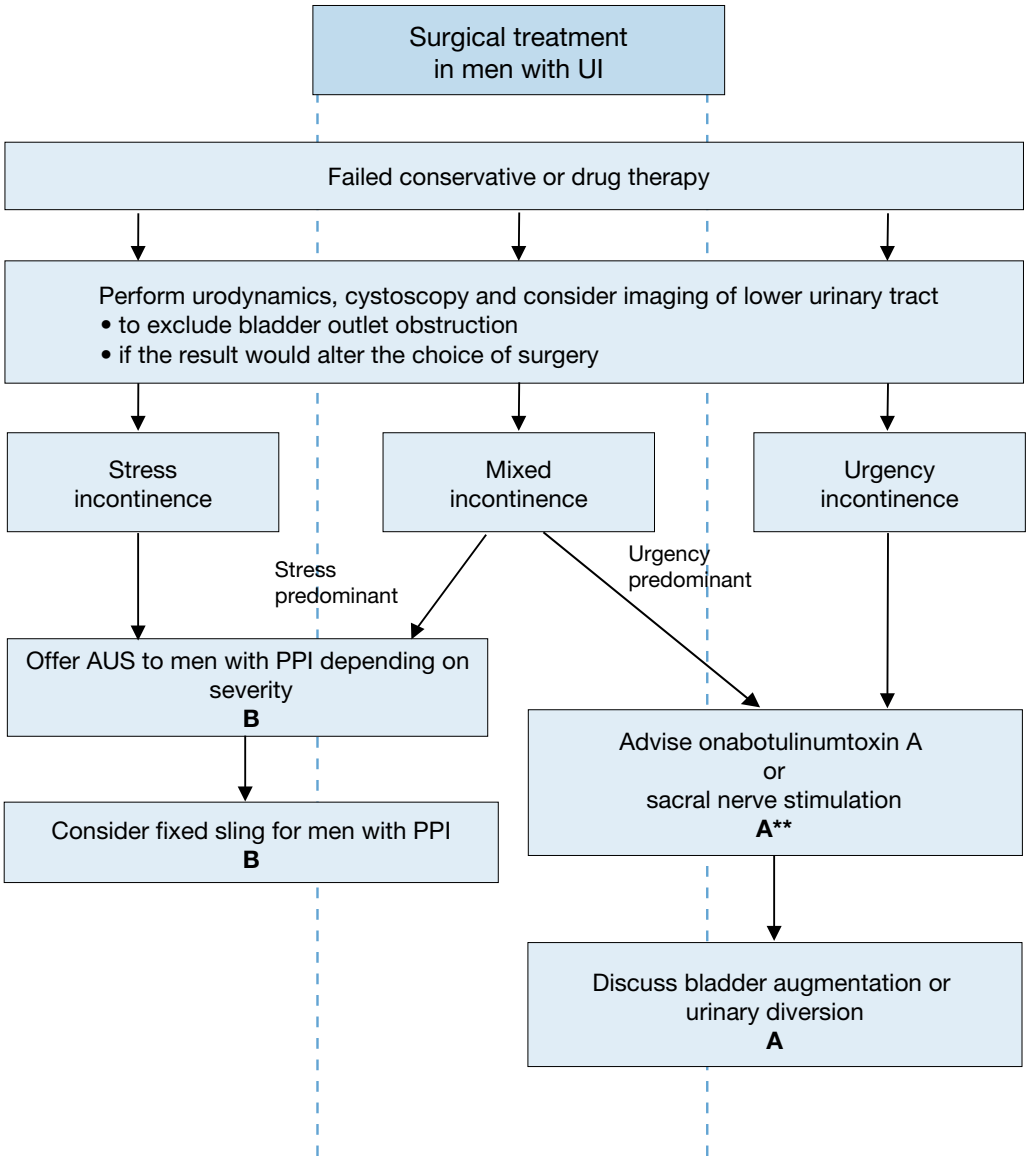

** *Available evidence on onabutulinumtoxinA and sacral nerve stimulation refers mainly to women*