Guidelines on Urinary Incontinence

M.G. Lucas (chair), D. Bedretdinova, J.L.H.R. Bosch, F. Burkhard, F. Cruz, A.K. Nambiar, D.J.M.K. de Ridder, A. Tubaro, R.S. Pickard

European Association of Urology

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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 for urologists, and 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, as this is covered by complementary EAU Guidelines (2).

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, with uncertainty reflected by a lower grade of recommendation.

1.1 Methodology

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

- A clear clinical pathway (algorithm) for common clinical problems. This can provide the basis for thinking through a patient's management and also for planning and designing clinical services.
- A brief but 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 (3,4). 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 second 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 second edition does not review the prevention of UI, or the management of fistula, but these issues will be fully addressed 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
Conservative therapy	28 June 2012
Drug therapy	28 June 2012
Surgical therapy	9 July 2012

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

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 expert 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 outcome. Guidelines can never replace clinical expertise when making treatment decisions for individual patients; they aim to focus decisions. Clinical decisions must also take into account the patient's personal values, preferences and specific circumstances.

*1.1.3 **Level of evidence and grade of recommendation***

References used in the text have been assessed according to their level of scientific evidence (Table 2), which is a modification of the system used by the Oxford Centre for Evidence Based Medicine (CEBM). A similar modification has been used for 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. (5)*

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

Alternatively, an absence of high-level evidence does not necessarily preclude a Grade A recommendation; if there is overwhelming clinical experience and consensus to support a high-level recommendation, 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 (6-8).

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

Table 3: Grade of recommendation (GR)*

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. (5).*

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 also partly based on guidance from the ICUD and NICE, but new searches were conducted from June 2008 to 2011; these have now been updated with new searches up to September 2012.

Two separate addenda are provided on mixed urinary incontinence (MUI) and management of UI in the elderly (*see* Appendices A and B). We expect to update these Guidelines annually.

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* (9,10). 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.

1.3 References

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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 treatment, e.g. physiotherapy, may also not be a urologist. For this reason, some healthcare professionals may find that the Guidelines do not explain a particular topic in enough detail for their needs, e.g. delivery modalities for pelvic floor muscle training (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 the UI to be categorised into stress urinary incontinence (SUI), urge urinary incontinence (UUI) or mixed urinary incontinence (MUI). It should also identify patients who need rapid referral to a specialist. These include patients with associated pain, haematuria, a history of recurrent urinary tract infections (UTIs), pelvic surgery (particularly prostate surgery) or radiotherapy, constant leakage suggesting a fistula, voiding difficulty or suspected neurological disease. 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, condition-specific patient-reported outcome measures (PROMS) or generic health-related quality of life (HRQoL) measures. 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 all measures that are used for outcome evaluation must have been shown to be sensitive to change. Many questionnaires have been developed by commercial organisations; there is a risk that the way such questionnaires are developed could produce questionnaires sensitive to small changes of little clinical importance. The methodology for their development was reviewed in the 4th International Consultation on Incontinence in 2008 (1).

*2.2.1 **Questions***

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

*2.2.2 **Evidence***

Although many studies have investigated the validity and reliability of questionnaires and PROMs, most have taken place in adults without UI. This greatly limits the extent to which results and conclusions from these studies can be applied in adults with UI. There is low-level evidence that questionnaires may be more sensitive to change than a bladder diary. A randomised crossover study (2) suggested that web-based questionnaires may be more acceptable to patients than paper versions (3).

Evidence summary	**LE**
Validated symptom scores may be used to assist in the differential diagnosis of UI.	4
Validated symptom scores may be used to measure the severity of UI.	3
Questionnaires may be used to measure current health status or to suggest change following treatment.	3
The use of either questionnaires or PROMs in the assessment of adults with UI may help predict the outcome of treatment.	2

Recommendation	GR
Use a validated questionnaire when standardised assessment of severity and monitoring of effects of treatment is required, e.g. in trials or registries or for audit purposes.	C

*2.2.3 **Research priorities***

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

*2.2.4 **References***

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2.3 Voiding dairies

Measurement of the frequency and severity of LUTS is an important step in the evaluation and management of lower urinary tract dysfunction, including UI. Voiding diaries are a semi-objective method of quantifying symptoms, such as 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 bladder diary is unlikely to accurately report total urine output and the discrepancy between functional bladder capacity and total bladder capacity may be large.

*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.
- **Bladder 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) (8-14). The choice of diary duration appears to be based upon the possible behavioural therapeutic effect of keeping a diary rather than on validity or reliability.

Two studies have investigated the reproducibility of voiding diaries in both men and women (9,14). Further studies investigated the variability of diary data within a 24-hour period (15) and compared voided volumes recorded in diaries with those recorded on uroflowmetry (16). Other studies have investigated the correlation between data obtained from voided diaries and standard symptom evaluation (17-20).

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

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

Evidence summary	**LE**
Frequency volume charts 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
Frequency volume charts are sensitive to change and are a reliable measure of outcome.	2b

Recommendations	**GR**
Use a frequency volume chart 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 carried out in nursing home residents showed that the severity of UI was unchanged after eradication of bacteriuria (2).

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

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

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

2.4.1 ***Questions***

- In adults with UI, what is the diagnostic accuracy of urinalysis for UTIs?
- What is the benefit 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 part of the initial assessment of a patient with urinary incontinence.	A
In a patient with urinary incontinence, treat a symptomatic urinary tract infection appropriately (see 'EAU Guidelines on Urological Infections' (5)).	A
Do not treat asymptomatic bacteriuria in elderly patients to improve urinary incontinence.	B

*2.4.3 **References***

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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 measurement using catheterisation.

Several studies have evaluated PVR in different subjects and patient cohorts (7-17). In peri- and post-menopausal 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). 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), but unfortunately these differ from one another. 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 in the management 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

*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 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 were 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 (Q_{max}) 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' since all incontinence diagnoses are defined in urodynamic terms. Ambulatory urodynamics may detect unexpected physiological variance from normal, more often than conventional cystometry, but the clinical relevance of this is uncertain (22,23).

Detrusor overactivity may be found in asymptomatic patients, while normal cystometry is found in patients who are clearly symptomatic. There have been many studies of variable quality, investigating the relationship between UI symptoms and subsequent urodynamic findings. For their UK-based guidance, NICE reviewed 11 studies (24), which investigated the relationship between clinical diagnosis and urodynamic findings and the diagnostic accuracy of urodynamic measurement, specifically in females. The Panel found that no new evidence has been published since 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 meta-analysis of 129 studies of diagnostic tests for incontinence, using economic modelling, concluded that urodynamics was not cost-effective in a primary care setting (25).

A recent Cochrane review included seven RCTs that examined the question of whether urodynamics influences the outcome of all therapy for UI. 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 USI (29).

One high-quality RCT 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). Another similar RCT stopped recruitment early and was redesigned, but the outcomes of the second-phase study have not yet been published (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 Q_{max} or low voiding pressure were not consistently associated with post-operative voiding difficulty (36-43).

The presence of pre-operative DO has more consistently been associated with development of post-operative UUI. Post-hoc analysis of an RCT comparing the autologous fascial sling to Burch colposuspension showed inferior outcomes for women who suffered pre-operative urgency (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 alter the outcome of treatment for urinary incontinence.	C
Do not routinely carry out urodynamics when offering conservative treatment for urinary incontinence.	B
Perform urodynamics if the findings may change the choice of invasive treatment.	B
Do not routinely carry out urethral pressure profilometry.	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?

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 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***

- Does 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 particularly challenging.

2.8.1 ***Questions***

- In adults with UI, what is the reliability and accuracy of imaging in the diagnosis of UI?
- In adults do the results of imaging influence the choice, help predict outcome or help evaluate outcome of treatments for UI?

2.8.2 ***Evidence***

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

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

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

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

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

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

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

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3. CONSERVATIVE TREATMENT

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

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

3.1 Simple clinical interventions

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

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

- cardiac failure (1)
- chronic renal failure
- diabetes (1,2)
- chronic obstructive pulmonary disease (3)

- neurological disorders
- stroke
- dementia
- multiple sclerosis
- general cognitive impairment
- sleep disturbances, e.g. sleep apnoea.

It is possible that correction of the underlying disease may reduce the severity of urinary symptoms. However, this is often difficult to assess as patients often suffer from more than one condition. In addition, interventions may be combined and individualised, making it impossible to decide which 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 narrative review found there was only weak evidence for a causative effect for most medications associated with the adverse effect of new, or worsening, UI (2). A case-control study found that women with hypertension 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).

Systemic oestrogen therapy for post-menopausal women was shown by a meta-analysis (5) to be associated with the development and worsening of UI. Systemic oestrogen, compared to placebo, worsened symptoms of UI, both in women who had undergone a hysterectomy, and in those who had not (5). In addition, data from a single large RCT (6) showed that previously continent women treated with systemic oestrogen were more likely to develop symptoms of UI compared to women given a placebo. These more recent analyses have superseded conflicting results from earlier and smaller studies of the effect of oestrogen replacement therapy on UI. However, the number of women who gain relief from UI through stopping systemic oestrogen replacement is likely to be small since there has been a decline in the use of oestrogen replacement therapy by post-menopausal women, due to concerns about the development of cancer and the association of oestrogen replacement therapy with UI.

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

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

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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***

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

3.1.4.1 Question

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

3.1.4.2 Evidence

There was a lack of consistency in the evidence reviewed. There have been two consensus statements in the 4th International Consultation on Incontinence (1) and one RCT comparing conservative treatment with urinary pads (2). There have been Cochrane reviews of devices (3) and pads (4), and three small trials of devices with differing outcomes (5-7). Few studies have been carried out in urinary catheterisation; these included an RCT comparing condom catheters with indwelling urinary catheters (8). A small open crossover RCT (9) evaluated different penile clamps and showed that none completely controlled urine leakage, but penile blood flow was reduced. Another crossover RCT compared penile sheaths to absorbent pads in incontinent (10) men. Penile sheaths are only useful if they can be applied easily and independently.

Two RCTs have shown that the use of a vaginal pessary is equivalent to bladder training (BT) for the treatment of SUI (6,11).

Evidence summary	**LE**
Pads are not effective as a treatment for UI.	1b
Different pads have different advantages and disadvantages.	1b
Intermittent catheterisation carries a lower risk of UTI and bacteriuria than indwelling catheterisation.	1b
Containment devices are better than no treatment.	4
Penile sheaths offer better containment, and higher QoL, than absorbent products in men with UI.	1b
Penile sheaths are safer than indwelling catheters if no residual urine is present.	1b

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

3.1.4.3 Research priority

How does a simple intravaginal device compare to conventional conservative treatment in the cure or sustained improvement of UI?

3.1.4.4 References

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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. The pharmacological actions of caffeine include CNS stimulation, diuresis and smooth muscle relaxation. Anecdotal evidence of urinary symptoms being aggravated by excessive caffeine intake has 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). A lack of knowledge about the caffeine content of different drinks has made the role of caffeine reduction in alleviating UI more complex.

3.2.1.1 Question

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

3.2.1.2 Evidence

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

3.2.2.3 References

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

3.2.3.1 Question

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

3.2.3.2 Evidence

The few RCTs provide inconsistent evidence. In most studies, the instructions for fluid intake 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***

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

3.2.4.1 Question

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

3.2.4.2 Evidence

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

Two systematic reviews concluded that weight loss was beneficial in improving symptoms of UI (4,5). Five further RCTs reported a similar benefit beneficial effect on incontinence following surgical weight reduction programmes (6-9) (10).

Two large studies in diabetic women, for whom weight loss was the main lifestyle intervention showed UI did not get better but there was a lower subsequent incidence of UI among those who lost weight (6,11). There have been other cohort studies and case-control studies suggesting similar effects, including surgery for the morbidly obese (12-19). 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 therapy/scheduled voiding

Behavioural therapies include all those interventions initiated by the sufferer themselves but which require some form of training or supervision at their outset. These include bladder training (BT), scheduled voiding (prompted voiding and timed voiding). Almost always in clinical practice, these will be introduced as part of a package of care including lifestyle changes and possibly physical therapies as well. The detail 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.

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

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

*3.3.1 **Prompted voiding***

Prompted voiding is the giving of positive reinforcement for requesting toileting assistance, either spontaneously or following verbal prompts from a caregiver. A high-quality systematic review from Flanagan et al. (1) examined the effectiveness of prompted voiding as an intervention for elderly people with UI, who are living in an assisted care setting, such as a nursing home. The review included nine RCTs, which all showed a positive effect on continence outcomes of prompted voiding in comparison to standard care using intervals of 1, 2, or 3 hours (1).

Both the Flanagan et al. review (1) and a further Cochrane review (2) 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 (1) also included another two RCTs that showed no added clinical benefit for incontinence from oxybutinin or oestrogen combined with prompted voiding.

There was only one RCT of timed voiding which showed inconsistent improvement in continence compared with standard care in cognitively impaired adults (timed voiding is defined as fixed, pre-determined, time intervals between toileting, applicable for those with or without cognitive impairment. An assisted toileting programme is included for those unable to undertake independent toileting). Overall, the findings were consistent with previous systematic reviews (3,4).

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
Timed voiding reduces leakage episodes in cognitively impaired men and women.	1b

For recommendations, see section 3.4.5.

*3.3.2 **Bladder training***

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.

3.3.3 *Questions*

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

3.3.4 *Evidence*

There have been four systematic reviews covering the effect of BT compared to standard care (5-8). Two key RCTs, which compared BT with no intervention, found that UI was improved, but not cured, by timed bladder voiding at intervals of between 2.5 and 4 hours (9,10). 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 (11).

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 (12-17).

Studies have shown that the addition of BT to antimuscarinic therapy provides no added benefit for an improvement in UI compared with antimuscarinic treatment alone (12, 13, 17). However, BT combined with antimuscarinic therapy does provide a greater benefit in reducing urinary frequency and nocturia (17, 18). Bladder training does not improve an individual's capacity to discontinue drug therapy and maintain improvement of UUI (12). However, the addition of BT to antimuscarinic drugs may increase patient satisfaction with pharmacological treatment (19), including in patients previously dissatisfied with the antimuscarinic treatment (20).

Bladder training combined with PFMT is better than standard care for controlling UI in elderly women living in institutions (21). However, BT alone is inferior to a high-intensity programme of PFMT to improve SUI in elderly women (22). 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.

Evidence summary	**LE**
There is limited evidence that behavioural interventions are better than no treatment in women with UI	1b
The effectiveness of bladder training diminishes after the treatment has ceased.	2
There is inconsistent evidence to show whether bladder training is better than drug therapy.	2
The combination of bladder training with antimuscarinic drugs does not result in greater in improvement of UI but may have other benefits.	1b
Bladder training is better than pessary alone.	1b

For recommendations see section 3.4.5.

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3.4 Physical therapies

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

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

Traditionally, following vaginal examination and pelvic floor assessment by a trained professional, patients are taught to contract their pelvic floor muscles, as hard as they can and for as long as they can, and to repeat these exercises a number of times every day. This training can be delivered in many ways, including women teaching themselves (e.g. using an information leaflet), group training in classes, or intensive one-to-one supervision from a highly trained physical therapist. 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, electrical stimulation or vaginal cones. Additional techniques, such as kinseitherapy (1), proprioception training (2) and trunk stabilisation (3) have been proposed, but the benefits are unclear.

3.4.1.1 Methods used to augment PFMT

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

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

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

3.4.1.2 Question

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

3.4.1.3 Evidence

Although there have been many randomised trials of PFMT, the trials vary widely in terms of quality, mode of delivery, intensity and duration of treatment, and the details of contractions and repetitions. In a recent UK Health Technology Appraisal (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 (4). This extensive meta-analysis reviewed data from 37 interventions and 68 direct comparisons, while the mixed treatment comparisons examined combinations of 14 different types of intervention from 55 separate trials. The mixed treatment comparison used both indirect and direct comparisons and has probably provided

more accurate estimates of effect. Where relevant, the Technology Appraisal has influenced the evidence and recommendations in these Guidelines. The Agency for Healthcare Research and Quality (AHRQ) review of non-surgical treatment of UI in adult women also included indirect comparison methods as well as conventional meta-analysis (5).

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

This question has been addressed by several systematic reviews (4-6), all report inconsistency between studies because of poor reporting of technique and different outcome measures. Meta-analysis showed that PFMT achieved cure or improvement of incontinence more often compared to no treatment and the magnitude of effect is large. The most recent Cochrane review compares different approaches to delivery of PFMT. From 21 RCTs, they were able to conclude only that increasing contact with the health professional delivering the therapy improves response and that there is no consistent difference between group therapy and individualised treatment sessions (7). 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. Half of patients had progressed to surgery, though the functional outcomes in those who had undergone surgery were less satisfactory than those who did not have surgery (8).

Augmentation of PFMT and comparison with other techniques

The AHRQ review concluded from two RCTs that the addition of BT to PFMT provided no additional benefit compared to BT alone in terms of curing UI (5).

The addition of biofeedback to PFMT was reviewed by Herderschee on the basis of 24 studies (9) and concluded that biofeedback may provide additional benefit. However, the AHRQ review (5) arrived at an opposite conclusion. Thus, although the addition of biofeedback may appear to add to the effectiveness of PFMT, it is not clear whether this effect is caused by feedback (e.g. from exposure to a health professional) or the 'bio' component. When the UK HTA reviewed the addition of electrical stimulation to PFMT (4), they found no difference in continence outcomes.

Comparison of PFMT to other treatments was extensively reviewed by both AHRQ and the 2010 UK HTA (4,5), 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.

3.4.1.5 Efficacy of PFMT in childbearing women

The Cochrane review in 2008 (10) reviewed 16 RCTs in pregnant or postpartum women, which included PFMT in one arm of the trial. Five trials were in postpartum women who had developed UI. Eight trials reported mixed treatment and prevention groups. Treatment of UI with PFMT in the postpartum period increased the chances of continence at 12 months' postpartum.

3.4.1.6 PFMT in the elderly

An RCT assessing PFMT versus BT in women aged more than 65 years showed that PFMT was significantly better at improving and curing SUI. However, the use of pad tests to quantify leakage limited the clinical usefulness of the comparison (11).

In a study of Japanese women aged ≥ 70 years with UI, PFMT with general fitness training was effective for cure and improvement of UI after a 3-month period of supervised exercise (12).

A programme of supervised education and skill building around PFMT and BT for women aged ≥ 65 years was effective in decreasing the impact of UI, but there was no change in overall QoL compared with no intervention (13).

3.4.1.7 Efficacy of PFMT in men with SUI following radical prostatectomy

A Cochrane review of conservative management for post-prostatectomy urinary incontinence (PPI) (up to Nov 2009) concluded that the benefits of conservative treatment of PPI were uncertain (14). There have been further RCTs which create uncertainty about whether or not PFMT leads to earlier recovery of continence (15-17). Two additional RCTs have shown that written instructions alone offer similar levels of improvement to supervised PFMT (18, 19). 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 (20).

3.4.1.8 Preventive value of PFMT in childbearing women and post-radical prostatectomy men

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

Ten RCTs of variable quality compared the preventative effect of PFMT prior to radical prostatectomy versus various different types of control treatments. These were generally small studies, which were difficult to compare with each other because of different times of delivery and different outcomes (21-29). However, one study was well designed and provided level 2 evidence confirming that pre-operative PFMT speeds up the recovery of continence post-operatively (30).

PFMT as monotherapy	**LE**
PFMT is better than no treatment for reducing episodes of UI and improving QoL in women with SUI and MUI. There is no evidence that PFMT is better than no treatment in providing a cure.	1
Higher-intensity regimes, or the addition of biofeedback, confer greater benefit, but differences are not sustained long term.	1
A taught/supervised programme of PFMT is more effective than self-taught PFMT.	1
Group-based PFMT is as effective as treatment delivered individually.	1
Short-term benefits of intensive PFMT are not maintained at 15 years' follow-up.	2
PFMT appears effective for improvement of UI in elderly women	1b
PFMT does not result in measurable improvement in quality of life.	2
PFMT compared with other conservative treatments	**LE**
PFMT results in better reduction in leakage episodes than training using vaginal cones, but no difference in self-reported cure or improvement.	1
PFMT results in fewer incontinence episodes than electrical stimulation.	1
PFMT is better than bladder training for improvement of leakage and quality of life, in women with SUI.	2
Intensive PFMT is more effective than bladder training in older women with SUI	1
PFMT is as effective as duloxetine in women with SUI and has fewer side effects.	2
PFMT is better tolerated than oxybutynin for UUI.	2
PFMT for UI in childbearing women	**LE**
PFMT commencing in early pregnancy reduces the risk of incontinence in late pregnancy, and up to 6 months postpartum.	1
PFMT commencing in the early postpartum period improves UI in women for up to 12 months.	1
PFMT for post-prostatectomy UI	**LE**
Supervised PFMT does not cure UI in men post prostatectomy.	1b
There is conflicting evidence whether men undergoing some form of PFMT, before or after radical prostatectomy, achieve continence more quickly than untreated men.	2
Men with post-prostatectomy UI, who have had no behavioural intervention, may still benefit from starting behavioural therapy, even years after surgery.	2
There is conflicting evidence on whether the addition of electrical stimulation or biofeedback or supervised training increases the effectiveness of PFMT alone.	2
There is no evidence that pre-operative PFMT prevents UI following radical prostatectomy. As with post-operative PFMT, it appears to lead to earlier recovery of continence.	2

For recommendations see section 3.4.5.

3.4.1.9 Research priorities

- What is the comparative effectiveness of different regimens for PFMT?
- What is the long-term durability of PFMT?
- What is the effectiveness of augmenting PFMT by the addition of electrical stimulation or vaginal cones?

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

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

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

3.4.2.1 Question

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

3.4.2.2 Evidence

Most evidence on electrical stimulation refers to women. Five recent systematic reviews of electrical stimulation were found (1-5), although there was no specific Cochrane review. The five reviews included analysis of

15 RCTs, of which eight were comparisons to no treatment or sham treatment. Seven of the studies were comparisons to other physical or behavioural therapies and a further eight studies were comparisons of electrical stimulation combined with other therapies, usually PFMT. There were no new studies identified in 2011/12.

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

The role of electrical stimulation is uncertain due to a lack of knowledge of how it might work in UI.

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

Evidence summary	**LE**
The evidence is inconsistent for whether electrical stimulation alone can improve UI.	2
Electrical stimulation is no more effective than antimuscarinic therapy for improvement of patients with UUI.	1

For recommendations see section 3.4.5.

3.4.2.3 References

1. Berghmans LC, Hendriks HJ, Bo K, et al. Conservative treatment of stress urinary incontinence in women: a systematic review of randomized clinical trials. Br J Urol 1998 Aug;82(2):181-91. http://www.ncbi.nlm.nih.gov/pubmed/9722751
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*3.4.3 **Magnetic stimulation***

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

3.4.3.1 Question

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

3.4.3.2 Evidence

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

Three RCTs induced magnetic stimulation in women with UI, using a coil placed over the sacral foramina. Two

were poor-quality RCTs, with a short follow-up and an inconclusive effect in SUI and UUI or OAB (1,2). The third better-quality RCT observed no improvement in UUI or OAB after a longer 12-week follow-up and did not recommend treatment with magnetic stimulation (3).

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

In adult women with SUI, an RCT using the NeoControl chair found no improvement (6). A cohort study for 6 weeks, but with a follow-up of 2 years, showed a moderate improvement in UI measured by pad test (7), while another cohort study found no improvement (8). A further poor-quality RCT using the NeoControl chair also found no benefit in women with UUI or OAB (9). No clinical benefits were reported when magnetic stimulation using the NeoControl chair was also compared to functional electrical stimulation with surface electrodes (10) or to conventional PFMT (11).

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 3.4.5.

3.4.3.3 References

1. Fujishiro T, Enomoto H, Ugawa Y, et al. Magnetic stimulation of the sacral roots for the treatment of stress incontinence: an investigational study and placebo controlled trial. J Urol 2000 Oct;164(4): 1277-9. http://www.ncbi.nlm.nih.gov/pubmed/10992380
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11. Apolikhina I et al. Clinical efficacy of extracorporeal magnetic innervation versus pelvic floor muscle training with biofeedback for the treatment of stress urinary incontinence in women. Int Urogynecol J Pelv Floor Dysfunct 2011;22:S960-S96.

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

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

3.4.4.1 Question

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

3.4.4.2 Evidence

The reviewed studies included two RCTs of PTNS against sham treatment (1,2) and one comparing PTNS to tolterodine in patients with UUI (3). A further RCT compared transcutaneous PTNS to standard treatment with PFMT in older women (4).

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) (5).

Evidence summary	**LE**
PTNS is effective for improvement of UUI, in women who have had no benefit from antimuscarinic medication.	1b
PTNS is no more effective than tolterodine for improvement of UUI in women.	2b
No serious adverse events have been reported for PTNS in UUI.	3

*3.4.5 **Recommendations for behavioural and physical therapies***

Recommendations	**GR**
Offer supervised 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 supervised PFMT to continent women in their first pregnancy to help prevent incontinence in the postnatal period.	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 urge 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 urinary incontinence.	A
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 urge urinary incontinence.	A
Offer, if available, PTNS as an option for improvement of urge 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; PTNS = posterior tibial nerve stimulation.

3.4.6 ***Research priorities***

- Which aspect of behavioural modification is effective for the cure or sustained improvement of UI?
- Which method of delivering PFMT is most effective for the cure or sustained improvement of UI?
- Is PTNS effective in treatment of UI in men?

3.4.7 ***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. They act by blocking muscarinic receptors in the bladder wall. This reduces detrusor contractility and also alters sensation. Antimuscarinic agents differ in their pharmacological profiles, e.g. muscarinic receptor affinity and other modes of action, in their pharmacokinetic properties, e.g. lipid solubility and half-life, and in their formulation, e.g. immediate release (IR), 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, these reviews noted that the 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 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, how do antimuscarinic drugs, compare to 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

Drug	No. of Studies	Patients	Relative risk (95% CI)	Number needed to treat (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 formulations of antimuscarinic agents are effective for improvement and cure of UUI.	1b
ER formulations of antimuscarinic agents result in higher rates of dry mouth compared to placebo.	1b

4.1.1.3 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 that address this question (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 AHQR 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 both 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 resulted in 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.

In conclusion, there is no consistent evidence for the superiority of one antimuscarinic agent over another the size of effect. There is good evidence that ER, once daily, and transdermal preparations, are associated with lower rates of dry mouth than ER preparations, although discontinuation rates are similar.

Evidence summary	LE
There is no consistent evidence that one antimuscarinic drug is superior to an alternative antimuscarinic drug for cure or improvement of UUI.	1a
The ER formulation of oxybutynin is superior to the ER and IR formulations of tolterodine for improvement of UUI.	1b
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

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 less economically developed countries, conservative treatment remains a cheap, effective alternative treatment to drug therapy, with a low risk of side effects.

4.3.1 ***Question***

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

4.3.2 ***Evidence***

There is a large body of evidence comparing non-drug and drug treatment, including more than 100 RCTs and 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 bladder training, multicomponent behavioural approaches and electrical stimulation. Only one of these studies showed superiority for behavioural therapy. In one study, multicomponent behavioural modification produced significantly greater reductions in incontinence episodes compared to oxybutynin and higher patient satisfaction for behavioural versus drug treatment.

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

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

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

*4.3.3 **References***

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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 8m show 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 provides 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.

Muscarinic receptors exist throughout the body and are involved in many physiological processes. Most anticholinergics used to treat OAB are directed against the M2 and M3 receptors. The M1 receptor is involved in memory processes. The specificity of a drug for one or another receptor and the degree of penetration into the CNS through the blood-brain barrier may 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). Meta-analyses have been limited by study heterogeneity, dosing inconsistency and reporting bias. There is a need for more detailed, standardised measurement of age-stratified CNS outcomes in clinical trials to provide better information to patients and clinicians about the CNS risks associated with antimuscarinic agents.

Studies on antimuscarinic effects have been done in elderly persons (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 substantial evidence that oxybutynin IR may cause or worsen cognitive dysfunction in adults (7,9,11).

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 (12) but secondary analysis revealed no change in incontinence (13). 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 (14).

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 (15). 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 (16) has shown that solifenacin has good efficacy and does not increase cognitive impairment in the elderly. Another RCT found no age-related differences in the pharmacokinetics of solifenacin between elderly, middle-aged or younger patients. One post-marketing surveillance study reported more frequent adverse events in subjects over 80 years old. Another study on healthy elderly volunteers showed no cognitive effect (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 (17).

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. Post-hoc analysis from other RCTs has shown little effect on cognition. One trial showed lower rates of depression amongst elderly participants treated with tolterodine ER compared to oxybutynin IR (18).

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 (19,20). 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 (21, 22).

No published evidence was found regarding the comparative efficacy and side effect profiles of trospium in the elderly compared with younger patients. However, there is some evidence that trospium does not impair cognitive function (10, 23, 24) and that it is effective compared to placebo in this group (25).

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 in the elderly confirmed the efficacy of the 8 mg but not the 4 mg dose in over-75 year olds. Adherence was lower in the over-75 year-old group but the effect on mental status was not reported (26, 27).

4.5.2.7 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 (28).

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

Recommendations for antimuscarinic drugs	GR
Offer IR or ER formulations of antimuscarinic drugs as initial drug therapy for adults with urge urinary incontinence.	A
If IR formulations of antimuscarinic drugs are unsuccessful for adults with urge 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 urge urinary incontinence (< 30 days).	A
When prescribing antimuscarinic drugs to elderly patients, be aware of the risk of cognitive side effects, especially in those receiving cholinesterase inhibitors.	C
Avoid using oxybutynin IR in patients who are at risk of cognitive dysfunction.	A
Consider use of trospium chloride in patients known to have cognitive dysfunction.	B
Use antimuscarinic drugs with caution in patients with cognitive dysfunction.	B
Do an objective assessment of mental function before treating patients whose cognitive function may be at risk.	C
Check mental function in patients on antimuscarinic medication if they are at risk of cognitive dysfunction.	C

IR = immediate release; ER = extended release.

*4.5.3 **Research priority***

- All drug trials should report 'dry' 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.

A review of relevant literature and web-based resources (2) identified conference abstracts of two RCTs on the use of mirabegron ER, a beta-adrenoceptor agonist, for the treatment of patients with overactive bladder and UUI (3,4). The use of mirabegron ER (50 and 100 mg) resulted in modest reduction (improvement) in episodes of UUI compared to placebo. Adverse effects were similar to placebo, although mirabegron ER use was associated with an average rise in pulse rate of 2 beats per minute and 4% of participants withdrew due to adrenergic side effects. The European-Australian study (3) included tolterodine 4 mg ER as a comparative arm, but the results were not reported in the abstract. The North American trial (4) has now been published in full (5). Mirabegron ER has been approved for use in people with OAB and UUI at a dose of 25 mg and 50 mg in both the USA and Japan and is under consideration by the European Medicines Agency (EMA) and NICE in the UK.

Evidence summary	**LE**
Mirabegron ER is more effective than placebo for improvement of UUI.	1b
Adrenergic-mediated side effects of mirabegron appear mild and not clinically significant.	2

Recommendation	**GR**
Offer mirabegron extended release to people with urge urinary incontinence depending on local licensing arrangements.	B

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 reduce 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 (6,7) including 10 RCTs (8-17) and one subsequent RCT (10). The typical dose of duloxetine was 80 mg daily, with dose escalation up to 120 mg daily allowed in one study (9), 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 (12).

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 (8). An improvement in I-QoL was not found in the study using I-QoL as a primary endpoint (12). A further study compared duloxetine, 80 mg daily, with PFMT alone, PFMT + duloxetine, and placebo (18). 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 (19,20). 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 (21). Episodes of UUI were also significantly reduced by duloxetine.

One study (22) 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, can improve 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 80mg - 120mg 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.	A
Duloxetine should be initiated using dose titration because of high adverse effect rates.	A

4.7.3 ***References***

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4.8 Intravaginal oestrogen

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

4.8.1 *Question*

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

4.8.2 *Evidence*

A recent Cochrane systematic review including 33 trials looked at the use of oestrogen therapy in post-menopausal women (1) given local oestrogen therapy. There is also a more recent narrative review of oestrogen therapy in urogenital diseases (2). However, since the Cochrane review, no new RCTs have been published up to September 2012.

Local oestrogen therapy can be given as conjugated equine, oestriol or oestradiol in vaginal pessaries, vaginal rings or creams. Besides improving vaginal atrophy (3), local oestrogen therapy reduces UI and frequency and urgency in OAB. Local oestrogens were more effective than placebo at improving or curing UI and reducing frequency (1). The current data do not allow differentiation among the various types of oestrogens or delivery methods. Moreover, the ideal duration of this type of therapy and the long-term effects have been poorly studied. One RCT compared oestradiol ring pessary with treatment with oxybutynin ER showing no difference in outcomes (4).

Evidence summary	LE
Local oestrogen therapy in post-menopausal women may improve or cure UI.	1a
There is no evidence available on the neoadjuvant or adjuvant use of local oestrogens at the time of surgery for UI.	1a

Recommendations	GR
Offer post-menopausal women with urinary incontinence local oestrogen therapy, although the ideal duration of therapy and best delivery method are unknown.	A

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

4.9.3 ***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. Surgeons performing operations for UI should be properly trained and perform an adequate number of procedures to maintain expertise. Most importantly, they should be able to demonstrate their competence by being aware of the outcomes of individual operations in their own hands, and should share this information with their patients.

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

The section considers surgical options for the following situations:

- Women with uncomplicated SUI. This means no history of previous surgery, no neurological LUTD, no bothersome genitourinary prolapse, and not considering further pregnancy.
- Women with complicated SUI. Neurogenic LUTD is reviewed in the EAU Guidelines on Neurogenic Lower Urinary Tract Dysfunction (1).
- Associated genitourinary prolapse has not been included in these Guidelines, but will be reviewed for 2013.

- Men with SUI, 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.

5.1 Women with uncomplicated SUI

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

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

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

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

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

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

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

5.1.1.1 Question

In women with SUI, what is 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 (1-4), but no RCTs comparing any operation to a sham procedure.

Open colposuspension

The Cochrane review (5) 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 (6). One trial compared open colposuspension with antimuscarinic treatment, while another compared it with periurethral injection of bulking agents. Colposuspension resulted in superior outcomes, but had significantly higher rates of adverse events.

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

Anterior colporrhaphy
Anterior colporrhaphy is now mainly considered to be an obsolete operation for UI. In a Cochrane review (3), 10 trials compared anterior colporrhaphy (385 women) with colposuspension (627 women). The failure rate for 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 (3,7) described 26 RCTs, including 2284 women undergoing autologous sling procedure in comparison to other operations. The trials did not identify those women undergoing repeat surgery for recurrent UI. No further studies have been reported.

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

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

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

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

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

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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.

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 (2-15). The overall patient-reported cure rate was 75%. There was weak evidence of higher clinician-reported cure rates at 12 months after mid-urethral sling (83%) compared to colposuspension (78%) (2,7,9-15). However, longer-term follow-up for up to 5 years reported no difference in effectiveness, though the numbers of participants lost to follow-up was high (2,6,16). 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) (4,5,7,17,18).

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

Insertion using a skin-to-vagina direction versus a vagina-to-skin direction
A Cochrane systematic review and meta-analysis found that the skin-to-vagina direction (outside in) for retropubic insertion of mid-urethral slings was less effective than the vagina-to-skin (inside out) direction and was associated with higher rates of voiding dysfunction, bladder perforation and vaginal erosion (21). 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 (22). 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 (21).

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

The results of the EAU Panel meta-analysis (20) were consistent with those of the Cochrane systematic review (21), 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 (23) 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 (24). In addition, our results and recommendations are consistent with those of the Society of Obstetricians and Gynaecologists of Canada (25) and those of NICE in the UK (26).

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 (27). One recent RCT (28) and another cohort study (29) 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 post-operative sexual function nor between any of the techniques used (30).

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 (31). 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 (32). 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 urge UI, and are more likely to undergo retreatment for SUI (OR 3.9, 95% CI 1.3-11.48). There was no difference in time to post-operative normal voiding (33).

Another RCT comparing immediate TVT versus delayed TVT in older women confirmed significant efficacy in women undergoing surgery, but the cohort as a whole suffered higher complication rates, particularly bladder perforation (22%) and urinary retention (13%) (34).

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 (35).

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 (top-down) direction of both retropubic and transobturator insertion is associated with a higher risk of post-operative 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 post-operative sexual dysfunction differs between midurethral sling procedures.	3

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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. These procedures are usually performed as day cases under local anaesthesia.

5.1.3.1 Questions

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

5.1.3.2 Evidence

Although there have been many studies published on single-incision devices, it should be noted that there are significant differences in design between devices and it may be misleading to make general statements about them as a class of operations. It should also be noted that the TVTS device has now been withdrawn from the market, however, much of the evidence on single incisions slings applies to this device.

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

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

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

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

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

Another recent RCT compared in 80 women a transobturator tape against the single incision sling Tissue Fixation System (TFS). Cure rates were significantly higher with the TFS tape (84% vs. 90%, respectively) (10).

There are a number of case series with a minimum of 12 months' follow-up, including five series using the Miniarc device (11-16), two series using the TVTS device (14, 17) and one series using the Minitape® device (18). The 12-month outcomes range from 52% objective cure to 92% subjective cure. Results from one study reporting outcome at 2 years found that only 10% of included participants remained cured (18). One study reported a 24% rate of de novo urgency, but generally there were few reported adverse effects (14).

The Ajust® device is a self-fixing single incision sling that allows adjustment of tension during insertion. A short-term RCT compared Ajust to obturator tape in 137 women with similar efficacy but lower pain levels and earlier return to normal activity (19). A single cohort study reported an 80% success rate (patient's global impression of improvement) in 90 women after 12 months of follow-up (19).

There are no RCTs relating to the Solyx® device. There is one retrospective review of 63 women with short-term follow-up (20), and one report of 12 months' follow-up of the Ophira® device 176 women (21). These studies did not report outcomes of interest for these Guidelines.

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

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

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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 is limited data from cohort studies on adjustable tension slings with variable selection criteria and outcome definition. Few studies include sufficient numbers of patients or have a long enough follow-up to provide useful evidence. The available devices have differing designs, making it difficult to use existing data to make general conclusions about adjustable slings as a class of procedure. Three adjustable sling devices were reviewed: Remeex®, Safyre®, Ajust®. The latter is an adjustable single-incision sling.

Remeex®

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

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

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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 review (1,2) and one independent SR (3) (Ghoneim et al.), 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 2006 (6) 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 (BulkamidTM)
No RCT data are available. There is a single multicentre case series of 135 women, which reported 66% success rate with 35% participants requiring re-injection (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 to women with uncomplicated stress urinary incontinence as the preferred surgical intervention whenever available.	A
Offer colposuspension (open or laparoscopic) or autologous fascial sling to women with stress urinary incontinence if mid-urethral sling cannot be considered.	A
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.	C
Warn women who are being offered a retropubic insertion synthetic sling about the relatively higher risk of peri-operative complications compared to transobturator insertion.	A
Warn women who are being offered transobturator insertion of mid-urethral sling about the higher risk of pain and dyspareunia in the longer term.	A
Warn women undergoing autologous facial sling that there is a high risk of voiding difficulty and the need to perform clean intermittent self-catheterisation; ensure they are willing and able to do so.	A
Do a cystoscopy as part of retropubic insertion of a mid-urethral sling, or if difficulty is encountered during transobturator sling insertion, or if there is a significant cystocoele.	C
Women being offered a single-incision sling device should be warned that long-term efficacy remains uncertain.	C
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.	C
Do not offer bulking agents to women who are seeking a permanent cure for stress urinary incontinence.	A

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 gold standard operations in treatment of women with SUI?
- What is the effect of varying tension of a midurethral 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 2013 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 urodynamic evaluation 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 EAU 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 refers 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 latest 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 confirmed higher failure rates for both SUI and other complications of surgery, for all women undergoing second-line surgery, whichever intervention they had undergone (7-10). However a history of prior surgery for UI is not an independent predictor of failure at 2 years in women undergoing open colposuspension or autologous fascial sling (8).

One large non-randomised comparative series suggested that cure rates after more than two previous operations were 0% for open colposuspension and 38% for abdominal perineal 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 midurethral 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
The risk of treatment failure from surgery for SUI is higher when women have had prior surgery for incontinence or prolapse.	1
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 for intrinsic sphincter deficiency***

Some of the earliest techniques for treating SUI simply applied intra-corporeal compression external to the urethra. External compression devices are still widely used in the treatment of recurrent SUI after the failure of previous surgery. They are also commonly used in women with neurological LUTD, in whom there is thought to be profound intrinsic failure of the sphincter mechanism, characterised by very low leak point pressures or low urethral closure pressures. 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
Do not undertake open colposuspension in women who have had more than two previous operations for incontinence.	C
Implantation of AUS or ACT for women with complicated stress urinary incontinence should only be offered in high-volume centres.	C
Warn women receiving AUS or ACT that, even in high-volume centres, there is a high risk of complications, mechanical failure or a need for explantation.	C

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

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 and asymptomatic), and to assess the value of prophylactic anti-incontinence surgery in women with no evidence of UI.

5.3.1 ***Questions***

- In women with both SUI and POP, does combined surgery for POP and SUI provide better cure or improvement of UI compared to surgery for POP or SUI alone?
- In continent women with POP alone does combined surgery for POP and SUI reduce the incidence of post-operative UI compared to POP surgery alone?
- In women with POP and occult SUI (i.e. seen only on urodynamics), does combined surgery for POP and SUI reduce the incidence of post-operative UI compared to POP surgery alone?

5.3.1.1 Evidence

Women with POP and associated UI

A Cochrane review in 2011 included six trials of moderate quality (1).

Incontinence post-operative rates were 15% for combined surgery (where a mid-urethral sling was used as the incontinence operation) versus 44% with POP surgery alone, and this significant difference persisted beyond 12 months. There is significant heterogeneity among trials and the results are mainly driven by one study which compared a mid-urethral sling + anterior repair versus anterior repair alone. No other studies in this group used a mid-urethral sling as a comparator in the combined surgery arm. There was a significantly higher rate of adverse events reported in the combined surgery group.

A recent RCT has shown no difference in the 5-year outcomes when colposuspension was used as the incontinence procedure (persistent UI in 56.5% with combined surgery vs. 40.9% with POP surgery alone)

(2), although the longer-term outcomes suggested higher UI rates in women undergoing colposuspension (3). The addition of this study to the Cochrane meta-analysis makes no difference to the conclusions. Another two small RCTs showed no difference in outcomes (4,5).

Continent women with POP
The 2011 Cochrane review included three trials of moderate quality showing that post-operative incontinence rates at < 12 months were 21.7% in the combined surgery group versus 31.7% in POP surgery alone, mainly driven by one study (6).

One trial reported better QoL outcomes following combined surgery. There was no difference in rate of adverse events reported.

Two other trials have shown significantly higher rates of post-operative UI for women undergoing prolapse surgery alone, but the incidence of adverse events such as bladder perforation, UTI, bleeding, and voiding dysfunction was higher in the combined surgery patients. The number needed to treat to prevent incontinence in one woman was 6.3 at 12 months (2,7).

Women with POP and occult UI
In this group of women, the presence of occult UI was dependent on a urodynamics diagnosis which, in turn, is dependent on the performance of the prolapse reduction stress test. The 2011 Cochrane review included five trials of moderate quality addressing this point. Overall, 83% of women are free of objective evidence of SUI at 12 months with combined surgery versus 52% with prolapse surgery alone. There was no reported difference in the incidence of adverse events. The 2011 OPUS trial (n = 337) showed that women had an eight-fold higher risk of UI if the POP surgery was not accompanied by an operation for SUI (7). The prolapse reduction stress test was positive in 29.6% women in the combined treatment arm (using TVT) and 71.9% women in the POP repair + sham incision treatment arm.

It is difficult to generalise the results of trials using very different procedures to treat UI. 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. The evidence suggests that most women may be dry after prolapse surgery alone but the risks of repeat surgery, should it become necessary, may outweigh the potential benefits.

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 post-operatively	1a
• The addition of a prophylactic anti-incontinence procedure reduces the risk of post-operative UI	1b
• The addition of a prophylactic anti-incontinence procedure increases the risk of adverse events to the same extent	1b
Women with prolapse and occult SUI	
• Surgery for POP + 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	1b

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

POP = pelvic organ prolapse.

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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, this difference was significant, but in patients with moderate and mild incontinence, the difference was less.

Evidence summary	LE
There is no evidence that bulking agents cure post-prostatectomy incontinence.	2a
There is weak evidence that bulking agents can offer temporary, 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 post-prostatectomy incontinence. Fixed slings are positioned under the urethra and fixed by a retropubic or transobturator approach. The tension is adjusted during the surgery and cannot be re-adjusted post-operatively.

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

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

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 have poor outcomes 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 post-operatively. 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 post-operative 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 ***Compressive devices in males***

External compression devices can be divided into two types: circumferential and non-circumferential compression of the urethral lumen (1). The artificial urinary sphincter (AUS) has been used for more than 30 years and is the standard treatment for moderate-to-severe male SUI. Most data available on the efficacy and adverse effects of AUS implantation is from older retrospective cohort studies with RCTs not performed due to

the lack of a comparator. Several modifications of the standard single-cuff transperineal technique have been described, including transcorporeal implantation, double-cuff implants and trans-scrotal approaches (2). Men considering insertion of an AUS should understand that they must be able to operate a scrotal pump, requiring adequate dexterity and cognitive function. If the ability of an individual to operate the pump is uncertain, it may not be appropriate to implant an AUS. There are several recognised complications of AUS implantation, e.g. mechanical dysfunction, urethral constriction by fibrous tissue, erosion and infection.

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

5.4.4.1 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).

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

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 high volume centres.	C
Warn men receiving AUS or ACT that, even in high volume 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?

5.4.4.4 References

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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. The effects of repeat injection have not been well studied in patients with UUI. The most important adverse event is an increase in PVR that may require clean intermittent catheterisation (CIC), which is itself associated with an increased risk of UTIs (1,2).

5.5.1.1 Question

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

5.5.1.2 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. It included data from a new dose-finding study (4) and supplementary data obtained from the authors (5), including dry rates at 6 and 12 weeks (results summarized in Table 6). The rate of de novo CIC was 9.1% for 100 U and 18.2% for 200 U. Higher cure rates but also higher PVR requiring CIC were found with higher doses.

Table 6: (summarising the likelihood of achieving continence for varying doses of botulinum toxin)

BTX (onabotulinumtoxinA), dosage (U)	Odds ratio for becoming dry (95% CI)
50	2.28 (0.95-5.49; p = 0.07)
100	4.39 (1.91-10.12; p = 0.0005)
150	4.96 (2.14-11.53; p = 0.0002)
200	4.34 (2.49-7.59, p < 0.00001)
300	7.05 (2.68-18.51, p < 0.0001)

Although 300 U was shown to be the most efficacious dose, it is not a recommended dose because of the high rates of PVR requiring CIC. A dose of 100-200 U seems to have comparable efficacy in the meta-analysis. As part of this meta-analysis, two small RCTs comparing BTX doses between 100 and 200 units (6,7) showed no difference in efficacy for different doses. A further large RCT has been presented in abstract form at both American Urological Association and International Continence Society meetings, confirming the efficacy of onabotulinumtoxinA 100 U against placebo (8).

The QoL after onabotulinumtoxin administration has been shown to be sustained for 36 weeks (5) and in another study the gains in QoL achieved by increasing the dose, were marginal (9).

Successful UUI treatment with onabotulinumtoxinA does not appear to be related to the existence of DO. In a

subanalysis of the Dmochowsky dose-finding study, no differences were found regardless of the occurrence of DO at baseline (5). Likewise, onabotulinumtoxinA improved UUI in a cohort of 5 male and 27 female patients with OAB and without DO (10).

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 (11), whilst another study showed superior symptomatic improvement if the trigone was included in the injection protocol (2), though UUI was no specifically evaluated in the latter study.

Cohort studies have shown the effectiveness of botulinum toxin injections in the elderly and frail elderly (12), 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 (11).

A recent RCT compared onabotulinumtoxinA injection to solifenacin (with dose escalation or switch to trospium possible in the solifenacin group) and showed a similar reduction in urge urinary incontinence episodes over the course of 6 months (13). Patients receiving onabotulinumtoxinA were more likely to have complete resolution 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.

Dowson et al. (14) reported in a cohort of 100 patients a rapid decline of the patients willing to receive repeated onabotulinumtoxinA 200 U injections. In fact, 25 patients abandoned the treatment after the first injection and more 12 after the second injection. Fear of de novo CIC, poor response and treatment invasiveness were given as the major reasons for discontinuation.

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 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 botulinumtoxinA have reduced efficacy.	3
There is a high risk of increased PVR when injecting elderly frail patients.	3
There is a high risk of UTI in those who require CIC.	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 in curing severe forms of UUI.	1a
Repeated injections of onabotulinumtoxinA may be associated with a high discontinuation rate.	2

Recommendations	**GR**
Offer botulinum toxin A intravesical injections to patients with urge urinary incontinence refractory to antimuscarinic therapy.	A
Always check the botulinum toxin brand before injection, as units among the available brands are not interchangeable.	A
Offer onabotulinumtoxinA 100 U as initial dose to minimise the risk of urinary retention and urinary tract infection.	A
Warn patients of the limited duration of response, the possible prolonged need to self-catheterise (ensure that they are willing and able to do so) and the associated risk of urinary tract infection.	A
Patients should also be informed of the licensing status of botulinumtoxinA, and that long-term adverse effects, although improbable, remain uncertain.	A

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?

5.5.1.4 References

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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

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

5.5.2.3 Research priority

A RCT comparing a strategy of botulinum toxin injection, repeated as required, against a strategy of test and permanent sacral nerve neuromodulation, with 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

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 post-operative 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 longterm 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

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APPENDIX A: MIXED URINARY INCONTINENCE

A.1 Introduction

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

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

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

A.2 Question

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

A.3 Evidence

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

However, a Cochrane report on pelvic floor muscle training (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.3.1 ***RCTs in MUI population, which compare one treatment to another***

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

A.3.1.1 Duloxetine

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

A.3.1.2 Transvaginal obturator tape

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

A.3.1.3 Tolterodine

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

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

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

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

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 (7).

A.3.2.1 Drugs

Duloxetine was found to have equal efficacy for SUI and MUI in an RCT (n = 553) following secondary analysis of subpopulations (8). In another study, secondary analysis showed that tolterodine compared to placebo (n = 1380) was equally effective in reducing urgency and UUI symptoms, regardless of whether there was associated SUI (9). Similar findings apply to solifenacin (10,11).

A.3.2.2 Surgery

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

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

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

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

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 (15).

A.3.3.1 Surgery for SUI

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

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

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

One cohort of 450 women, undergoing midurethral sling surgery, had significantly worse outcomes for increased amounts of urgency. In urgency-predominant MUI, the success rate fell to 52% compared to 80% in stress-predominant MUI (22). In a second study in 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 (23).

A.4 Evidence statements

Evidence summary	**LE**
Pelvic floor muscle training is less effective for mixed UI than for SUI alone.	2
Electrical stimulation is equally effective for mixed UI and SUI.	1b
Antimuscarinic drugs are equally effective in improving symptoms of urgency and UUI in patients with MUI as in patients with UUI alone.	1a
Duloxetine is equally effective in improving SUI in patients with MUI as in patients with SUI alone.	1a
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

A.5 Recommendations

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

A.6 Research priority

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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APPENDIX B: OLDER PEOPLE WITH URINARY INCONTINENCE

B.1 Introduction

For the purposes of the Guidelines, older people can be defined by age thresholds, which are typically greater than 65 years or greater than 75 years, or in terms of level of physical or cognitive impairment, i.e. 'frailty'. However, it should be noted that such impairment requiring people to live in supervised environments, such as care homes, can also be experienced by younger people. 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, coordination or balance or impaired cognition and may require specific interventions, such as timed, prompted or assisted toileting.

Comorbidities also increase the risk of adverse drug effects, such as cognitive impairment with antimuscarinic medication. Ageing of the pelvic tissues may compromise success of surgery for SUI. At an individual level, expectations of assessment and treatment may need to be modified to tailor offered management to specific circumstances, needs, and preferences, while taking into account any loss of capacity for consent on the part of the patient.

B.2 Conservative treatment of elderly people with UI

B.2.1 ***Correcting underlying disease***

In patients with existing UI, particularly the elderly, it may be difficult or impossible to distinguish between the effects on UI of medication, comorbidity or ageing. Urinary incontinence, especially in the elderly, can be worsened or caused by underlying diseases, especially conditions that cause polyuria, nocturia, increased abdominal pressure or CNS disturbances. These conditions include:

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

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

Only one study was found that addressed the question of whether correcting underlying disease could improve symptoms of UI. The study found no correlation between earlier intensive treatment of type 1 diabetes mellitus and the prevalence of UI in later life versus conventional treatment (4). This was despite the known benefit of close control of blood glucose levels on other known consequences of type 1 diabetes mellitus, including renal and visual impairment. A higher prevalence of UI was associated with an increase in age and body mass index in this study.

B.2.2 ***Adjustment of medication***

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

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

Several case series have suggested a link between drugs with a CNS site of action and UI (4). A secondary analysis of a large observational database of elderly Italians found a higher risk of UI among those taking benzodiazepines.

B.2.3 ***Constipation***

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

B.2.4 ***Caffeine***

A further interventional study in the elderly showed borderline significance for the benefit of reducing caffeine intake on UI (5).

B.2.5 ***Physical activity***

Three RCTs in the elderly confirmed that exercise, as a component of a multidimensional regime, including pelvic floor muscle training (PFMT) and weight loss, was effective in improving UI in women. It is not clear which component of such a regimen is most important (6-8).

B.2.6 ***Behavioural therapy***

Bladder training (BT) combined with PFMT is better than standard care for controlling UI in elderly women living in institutions (9). However, BT alone is inferior to a high-intensity programme of PFMT to improve stress urinary incontinence (SUI) in elderly women (10). Bladder training is better than intravaginal pessaries to control SUI, although the improvement may only be short term.

A high-quality systematic review by Flanagan et al. examined the effectiveness of prompted voiding (the giving of positive reinforcement for requesting toileting assistance either spontaneously or following verbal prompts from a caregiver), as an intervention for elderly people with UI living in assisted care setting such as nursing homes (11). The review included nine RCTs, which all showed a positive effect on continence outcomes of prompted voiding in comparison to standard care using intervals of 1, 2 or 3 hours. This review (11) and a further Cochrane review (12) also identified five RCTs that consistently showed that a 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. (11) included two RCTs that showed no added clinical benefit of oxybutinin or oestrogen when combined with prompted voiding. This review found one RCT of timed voiding (defined as fixed, pre-determined time intervals between toileting, applicable for those with or without cognitive impairment; an assisted toileting programme was used for those unable to undertake independent toileting) that showed inconsistent improvement in continence over standard care among cognitively impaired adults. Overall, the findings were consistent with previous systematic reviews (13).

B.2.7 ***PFMT in the elderly***

An RCT assessing PFMT versus bladder training in 83 women > 65 yrs old showed that PFMT was significantly better (PFMT median leakage on stress test 0.0 g, 95% CI 0.2-0.9; BT median 0.3 g, 95% CI 0.2-1.7). Although this difference was significant, the practical value of this difference is debatable, as is the method of using stress tests to quantify leakage (10).

In a study of Japanese women aged ≥ 70 years with UI, PFMT with general fitness training was effective for cure and improvement of UI after a 3-month period of supervised exercise (6).

A programme of supervised education and skill building around PFMT and BT for women aged ≥ 65 years was effective in decreasing the impact of UI, but there was no change in overall quality of life compared with no intervention (14). Electrical stimulation of the pelvic floor using an intravaginal device was no more effective in a group of women aged ≥ 65 years with UI compared to patient-led home-based PFMT with verbal instruction (15).

One RCT found that a multimodal intervention in elderly patients, involving assisted toileting, fluid intake, etc, reduced the occurrence of UI and constipation, while behavioural therapy appeared to improve both constipation and UI (8). Another study found bowel function improved after successful treatment of voiding problems with sacral nerve stimulation (16). A different study recommended the simultaneous treatment of constipation and urinary disorders in children and adolescents with LUTS.

B.2.8 ***Evidence summary for conservative treatment of elderly people with UI***

Evidence summary	LE
Elderly nursing home patients with established UI do not benefit from treatment of asymptomatic bacteriuria.	2
Improved diabetic control neither resolves nor improves UI.	3
Diuretics in elderly patients does not cause or worsen UI.	3
Multimodal behavioural therapy improves both constipation and UI in the elderly.	1b
Moderate exercise is associated with lower rates of UI in middle-aged or older women.	2b
Prompted voiding, either alone or as part of a behavioural modification programme, improves continence in elderly, care-dependent people.	1a
The inclusion of prompted voiding in behavioural modification programmes improves continence in elderly, care-dependent people.	1b
Timed voiding may reduce leakage episodes in elderly cognitively impaired people.	2
Pelvic floor muscle training appears effective for improvement of UI in elderly women.	1b

B.2.9 Recommendations

Recommendations for conservative treatment of elderly people with incontinence	GR
Do not treat asymptomatic bacteriuria in elderly patients to improve urinary incontinence.	B
Support other healthcare professionals in use of rehabilitation programmes, including prompted voiding for the care of elderly care-dependent people with urinary incontinence.	A
For adults with urinary incontinence, treat co-existing constipation.	C
Offer pelvic floor muscle training to elderly women with urinary incontinence.	B

B.3 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.

There have been two systematic reviews of antimuscarinic agents in elderly patients (13, 17). One review was confined to evidence on nursing home residents with UUI (13). A community-based cohort study on the burden of antimuscarinic drugs in an elderly population (n = 372) found a high incidence of cognitive dysfunction (18). The Oregon systematic review of treatments for OAB reported specifically on outcomes in elderly patients (19). A further systematic review with a search cut-off date of December 2011 focused in part on the efficacy and safety of antimuscarinic drugs in the elderly (20). One recent review included nine studies in which the cognitive impact of antimuscarinics was tested but evidence was found to be inconclusive (21).

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 (22, 23). Meta-analyses have been limited by study heterogeneity, dosing inconsistency and reporting bias. There is a need for more detailed, standardised measurement of age-stratified CNS outcomes in clinical trials to provide better information to patients and clinicians about the CNS risks associated with antimuscarinic agents.

Studies on antimuscarinic effects have been performed in elderly persons (24) and in people with dementia with UUI (25). 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. However post-hoc analysis of healthy elderly sub-groups from RCTs of antimuscarinic agents provide some lower-level evidence of relative harms.

B.3.1 ***Oxybutynin***

Two studies in the elderly demonstrated additional benefit for UI from oxybutynin IR combined with scheduled

voiding versus scheduled voiding alone. Another study found no differences in efficacy or harms between oxybutynin ER and IR in elderly patients (26). Subanalysis of an elderly subgroup from a RCT population assessing oxybutinin 5 mg ER showed no significant improvement compared to placebo in UUI over a 4-week period (27).

There is some evidence that oxybutynin IR may cause or worsen cognitive dysfunction in adults (24, 28, 29). A crossover RCT in elderly volunteers given oxybutynin IR reported increased cognitive dysfunction with oxybutynin, but a short-term RCT of oxybutynin ER in elderly women with cognitive dysfunction observed no increase in delirium (30).

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 (31).

B.3.2 ***Solifenacin***

One pooled analysis from several RCTs (32) suggested that solifenacin was effective and did 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 (29). In a subanalysis of a large trial, solifenacin 5-10 mg appeared effective for symptom and quality of life improvement among people aged older than 75 years who had not responded to tolterodine (33).

B.3.3 ***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 (28). Two RCTs of tolterodine specifically designed in the elderly found that tolterodine showed a similar efficacy and side effect profile, as in younger patients. Post-hoc analysis from other RCTs has shown little effect on cognition. One trial showed lower rates of depression amongst elderly participants treated with tolterodine ER compared to oxybutynin IR (34).

B.3.4 ***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 (35, 36). 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 (24).

B.3.5 ***Trospium chloride and fesoterodine***

No published evidence was found regarding the comparative efficacy and side effect profiles of trospium or fesoterodine in the elderly compared with younger patients. However, there is some evidence that trospium does not impair cognitive function (25, 37, 38) and that it is effective compared to placebo in this group (39).

Two separate pooled analyses of the same two RCTs of fesoterodine in the elderly confirmed the efficacy of the 8 mg but not the 4 mg dose in the over-75s. Adherence to treatment was lower in the over-75-year-old group, but the effect on mental status was not reported (40, 41).

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 (42).

B.3.6 ***Evidence summary***

Evidence summary	**LE**
Oxybutynin IR may worsen cognitive function.	1b
Oxybutynin IR is less effective in people with impaired orientation, cerebral cortical underperfusion and reduced bladder sensation.	2
The effectiveness and risk of adverse events of solifenacin, tolterodine and darifenacin do not differ with patient age.	3

B.3.7 ***Recommendations***

Recommendations for antimuscarinic drugs	GR
Offer IR or ER formulations of antimuscarinic drugs as initial drug therapy for adults with urge urinary incontinence.	A
If IR formulations of antimuscarinic drugs are unsuccessful for adults with urge 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 urge urinary incontinence (< 30 days).	A
When prescribing antimuscarinic drugs to elderly patients, be aware of the risk of cognitive side effects, especially in those receiving cholinesterase inhibitors.	C
Avoid using oxybutynin IR in patients who are at risk of cognitive dysfunction.	A
Consider use of trospium chloride in patients known to have cognitive dysfunction.	B
Use solifenacin, tolterodine and darifenacin with caution in patients with cognitive dysfunction.	B
Do an objective assessment of mental function before treating patients whose cognitive function may be at risk.	C
Check mental function in patients on antimuscarinic medication if they are at risk of cognitive dysfunction.	C

IR = immediate release; ER = extended release.

B.4 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 (43). 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 (44). 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 urge UI, and are more likely to undergo retreatment for SUI (OR 3.9, 95% CI 1.3-11.48). There was no difference in time to normal post-operative voiding (45).

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%) (46).

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 (47).

A case series of 157 elderly (> 70 years) women with OAB given botox for the first time divided them into frail elderly (52), elderly without impaired activities of daily living (47) and those aged 58-70 years old (58). 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 (48).

Cohort studies have shown the effectiveness of botulinum toxin injections in the elderly and frail elderly (49), 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.

B.4.1 ***Evidence summary for surgery for UI in the elderly***

Evidence statement	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

B.4.2 ***Recommendations for surgery for UI in the elderly***

Recommendation	GR
Inform older women with stress urinary incontinence about the increased risks associated with surgery, including the lower probability of success.	B

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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)
AHRQ	Agency for Healthcare Research and Quality
AUS	artificial urinary sphincter
BT	bladder training
BTX	botulinum toxin
CIC	clean intermittent catheterisation
CNS	central nervous system
DO	detrusor overactivity
EAU	European Association of Urology
ER	extended release
FS2S	first stage of two-stage (implantation of sacral neuromodulator)
GR	grade of recommendation
HRQoL	health-related quality of life
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
PNE	percutaneous nerve evaluation
PPI	post-prostatectomy urinary incontinence
PROMS	patient-reported outcome measures
PTNS	posterior tibial nerve stimulation
PVR	post-voiding residual
Q_{max}	maximum urinary flow rate
QoL	quality of life
RCT	randomised 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
US	ultrasound
UTI	urinary tract infection
UUI	urge urinary incontinence

Conflict of interest

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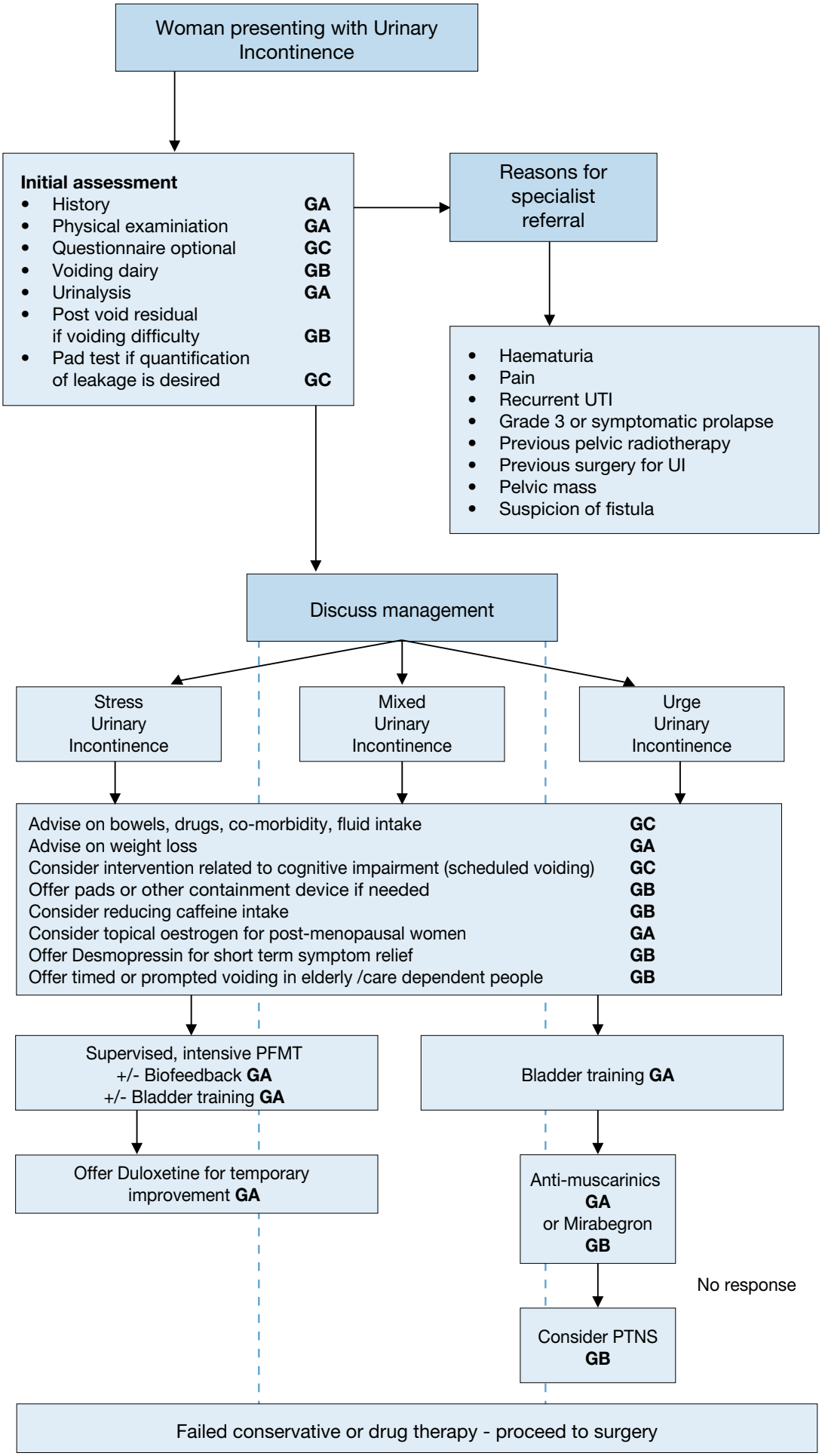
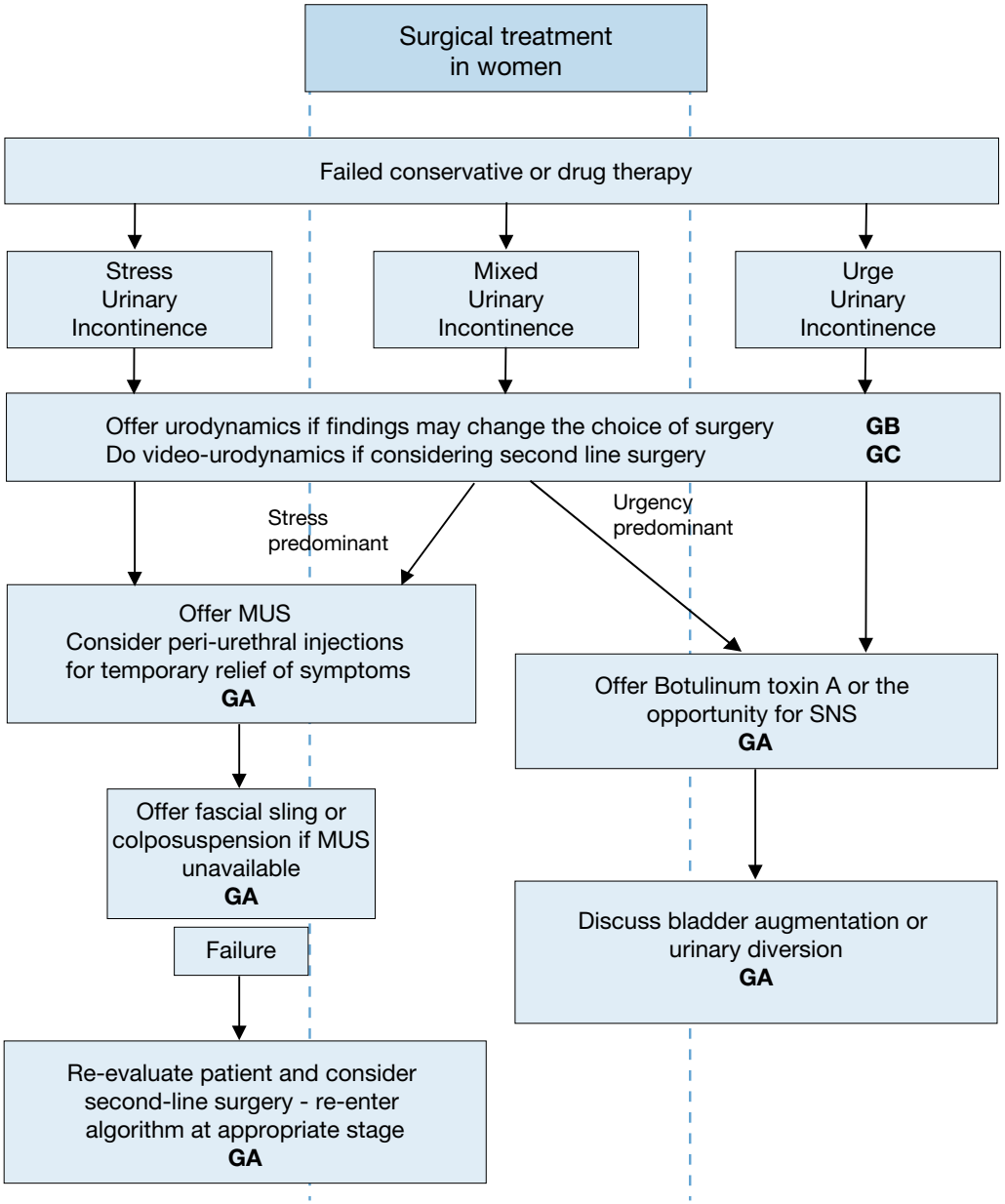
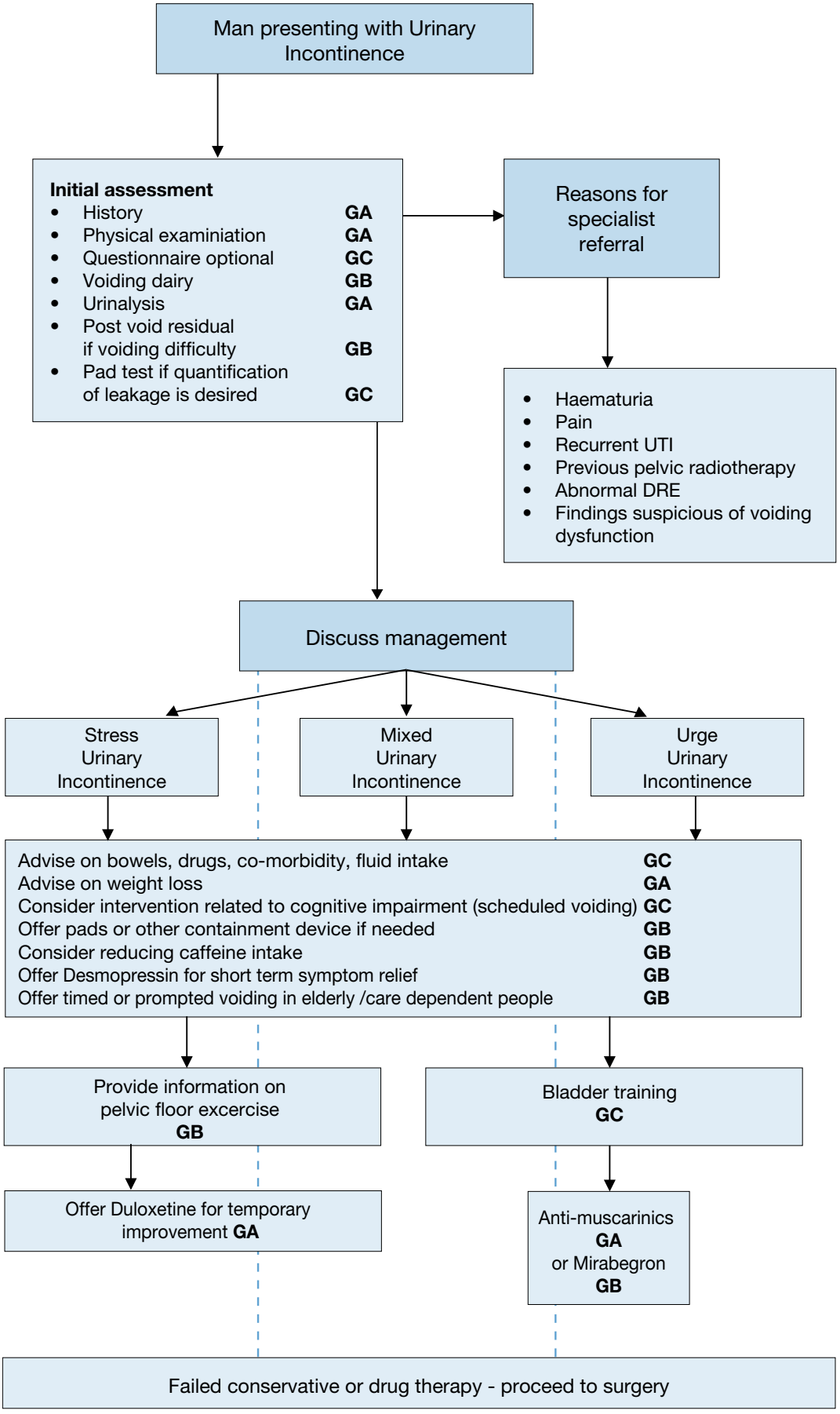
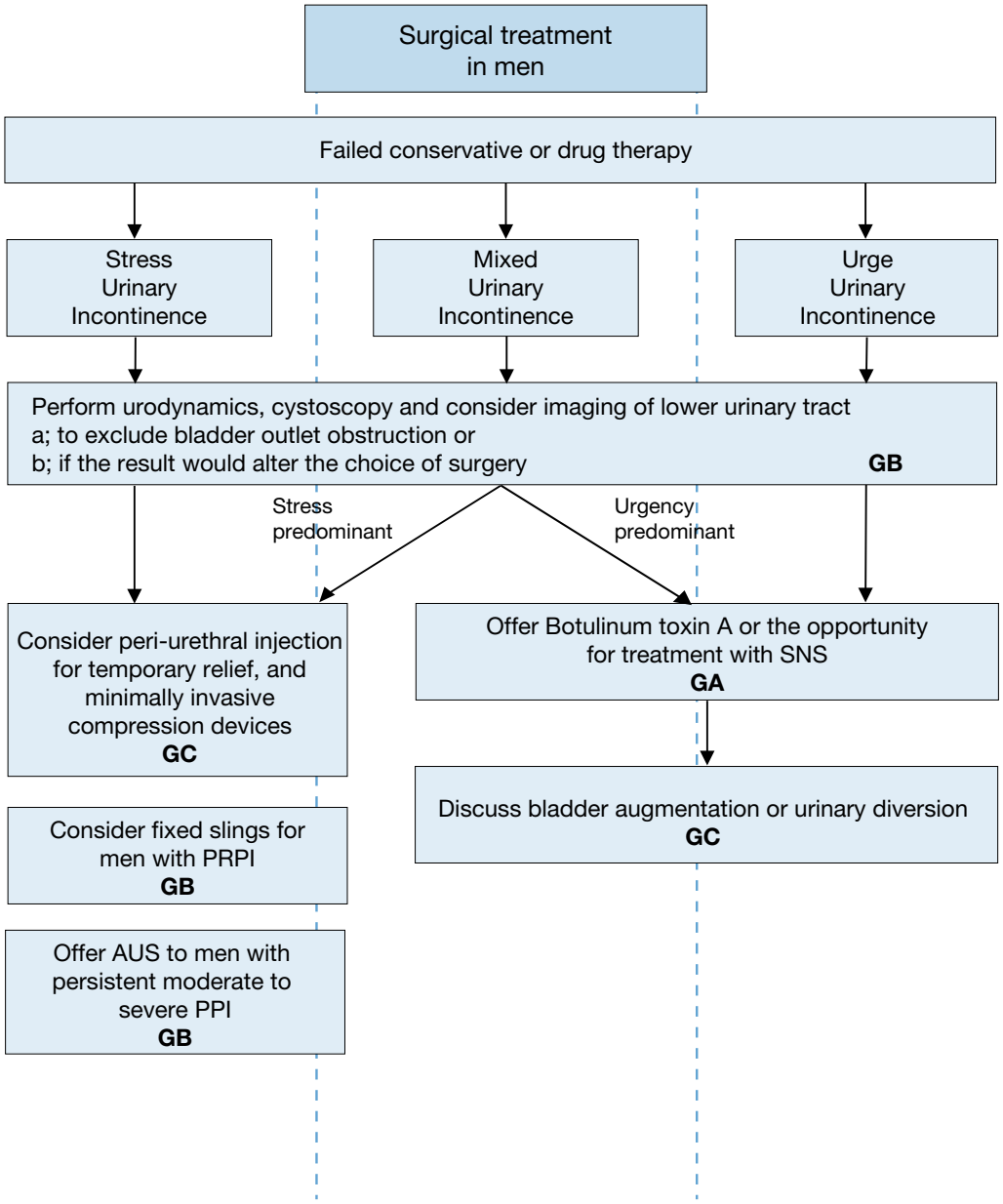

Woman presenting with Urinary Incontinence
Initial assessment
History GA
Physical examiniation GA
Questionnaire optional GC
Voiding dairy GB
Urinalysis GA
Post void residual if voiding difficulty GB
Pad test if quantification of leakage is desired GC
Reasons for specialist referral
Haematuria
Pain
Recurrent UTI
Grade 3 or symptomatic prolapse
Previous pelvic radiotherapy
Previous surgery for UI
Pelvic mass
Suspicion of fistula
Discuss management
Stress Urinary Incontinence
Mixed Urinary Incontinence
Urge Urinary Incontinence
Advise on bowels, drugs, co-morbidity, fluid intake GC
Advise on weight loss GA
Consider intervention related to cognitive impairment (scheduled voiding) GC
Offer pads or other containment device if needed GB
Consider reducing caffeine intake GB
Consider topical oestrogen for post-menopausal women GA
Offer Desmopressin for short term symptom relief GB
Offer timed or prompted voiding in elderly /care dependent people GB
Supervised, intensive PFMT +/- Biofeedback GA +/- Bladder training GA
Bladder training GA
Offer Duloxetine for temporary improvement GA
Anti-muscarinics GA or Mirabegron GB
No response
Consider PTNS GB
Failed conservative or drug therapy - proceed to surgery


Surgical treatment in women
Failed conservative or drug therapy
Stress Urinary Incontinence
Mixed Urinary Incontinence
Urge Urinary Incontinence
Offer urodynamics if findings may change the choice of surgery
Do video-urodynamics if considering second line surgery
GB
GC
Stress predominant
Urgency predominant
Offer MUS
Consider peri-urethral injections for temporary relief of symptoms
GA
Offer fascial sling or colposuspension if MUS unavailable
GA
Failure
Re-evaluate patient and consider second-line surgery - re-enter algorithm at appropriate stage
GA
Offer Botulinum toxin A or the opportunity for SNS
GA
Discuss bladder augmentation or urinary diversion
GA


Man presenting with Urinary Incontinence
Initial assessment
History GA
Physical examiniation GA
Questionnaire optional GC
Voiding dairy GB
Urinalysis GA
Post void residual if voiding difficulty GB
Pad test if quantification of leakage is desired GC
Reasons for specialist referral
Haematuria
Pain
Recurrent UTI
Previous pelvic radiotherapy
Abnormal DRE
Findings suspicious of voiding dysfunction
Discuss management
Stress Urinary Incontinence
Mixed Urinary Incontinence
Urge Urinary Incontinence
Advise on bowels, drugs, co-morbidity, fluid intake GC
Advise on weight loss GA
Consider intervention related to cognitive impairment (scheduled voiding) GC
Offer pads or other containment device if needed GB
Consider reducing caffeine intake GB
Offer Desmopressin for short term symptom relief GB
Offer timed or prompted voiding in elderly /care dependent people GB
Provide information on pelvic floor excercise GB
Bladder training GC
Offer Duloxetine for temporary improvement GA
Anti-muscarinics GA or Mirabegron GB
Failed conservative or drug therapy - proceed to surgery


Surgical treatment in men
Failed conservative or drug therapy
Stress Urinary Incontinence
Mixed Urinary Incontinence
Urge Urinary Incontinence
Perform urodynamics, cystoscopy and consider imaging of lower urinary tract
a; to exclude bladder outlet obstruction or
b; if the result would alter the choice of surgery
GB
Stress predominant
Urgency predominant
Consider peri-urethral injection for temporary relief, and minimally invasive compression devices
GC
Consider fixed slings for men with PRPI
GB
Offer AUS to men with persistent moderate to severe PPI
GB
Offer Botulinum toxin A or the opportunity for treatment with SNS
GA
Discuss bladder augmentation or urinary diversion
GC