EAU Guidelines on Management of Non-Neurogenic Female Lower Urinary Tract Symptoms

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1. INTRODUCTION

Lower urinary tract symptoms (LUTS) encompass storage, voiding and post-micturition symptoms [1]. Storage symptoms include frequency, urgency, nocturia and urinary incontinence (UI) (stress UI [SUI], urgency UI [UUI] and mixed UI [MUI]). Voiding symptoms include hesitancy, intermittency, slow stream, straining, splitting or spraying of the urinary stream and terminal dribble. Post-micturition symptoms include post-micturition leakage and feeling of incomplete bladder emptying. Lower urinary tract symptoms are often broadly classified into clinical syndromes/entities such as overactive bladder (OAB), underactive bladder (UAB), UI, nocturia, dysfunctional voiding, or genitourinary fistulae.

Lower urinary tract symptoms are common in women [2-5] and cause a great deal of distress and embarrassment [6], as well as significant costs to both individuals and society [7]. Estimates of prevalence vary according to the definition and population studied. However, there is universal agreement about the importance of the problem in terms of human suffering and economic cost [7]. The panel regards the sustainability and environmental impact of interventions (such as materials for pads or catheters) for LUTS as an important consideration when deciding on treatments [8].

1.1 Aim and objectives

These guidelines from the European Association of Urology (EAU) Working Panel on Non-neurogenic Female LUTS are written by a multidisciplinary group, primarily for urologists, but are likely to be referred to by other professional groups. The guidelines aim to provide sensible and practical evidence-based guidance on the clinical problems associated with female LUTS rather than an exhaustive narrative review. Such reviews for UI and other LUT syndromes are already available from the International Consultation on Incontinence (ICI) [9] and other sources. These EAU Guidelines do not describe the causation, basic science, epidemiology and pathophysiology of LUTS/UI in detail. The focus of these guidelines is on assessment and treatment, reflecting clinical practice, and they do not consider women with LUTS caused by neurological disease, or LUTS occurring in children, as these are covered by complementary EAU Guidelines [10, 11].

The current guidelines provide:

- A clear description of the assessment and treatment of common clinical problems. This can provide the basis for both individual patient management and 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 in those areas of practice for which there is little or no high-quality evidence utilising both expert clinician and patient representative opinion.

In recent years the guideline has seen a significant expansion of scope from UI to non-neurogenic female LUTS. The primary consideration here is to include the significant population of women with functional urological conditions not necessarily associated with UI that were hitherto not accounted for in previous guidelines. Secondary considerations are to align more cohesively with the existing Non-neurogenic Male LUTS Guidelines. As a consequence of the anatomical and physiological differences between the male and female LUT, the prevalence, pathophysiology, diagnostic approach and management of male and female LUTS may differ widely.

1.2 Panel composition

The EAU Non-neurogenic Female LUTS Panel consists of a multidisciplinary group of experts, including urologists, a uro-gynaecologist, a urodynamic scientist, a physiotherapist, a functional urology nurse practitioner, and patient advocates. All experts involved in the production of this document have submitted potential conflict of interest statements that can be viewed on the EAU website:
https://uroweb.org/guidelines/non-neurogenic-female-luts/panel.

1.3 Available publications

A quick reference document, the Pocket Guidelines, is available in print. This is an abridged version which may require consultation together with the full text version. Several scientific publications are available. All documents are accessible through the EAU website Uroweb:
https://uroweb.org/guideline/non-neurogenic-female-luts/.

An EAU Guidelines App for iOS and Android devices is also available containing the Pocket Guidelines, interactive algorithms and calculators, clinical decision support tools, guidelines cheat sheets and links to the extended guidelines.

1.4 Publication history

The first EAU Urinary Incontinence Guidelines were published in 2001. The guidelines have been modified since 2021 to broaden its scope, specifically to include other female LUTS. All sections of the previous (2023) Female LUTS Guidelines have been fully updated following a full literature search.

2. METHODS

2.1 Introduction

For the 2025 Non-neurogenic Female Lower Urinary Tract Symptoms guidelines, databases searched included Medline, Embase, and the Cochrane Libraries, covering a time frame between 20 February 2022, and 1st of May 2024, with a focus on high-level evidence only (systematic reviews [SR] and meta-analyses). A total of 1,423 unique records were identified, retrieved, and screened for relevance. Detailed search strategies are available: https://uroweb.org/guideline/non-neurogenic-female-luts/?type=appendices-publications.

Recommendations within the Guidelines are developed by the panel to prioritise clinically important care decisions. The strength of each recommendation is determined by the balance between desirable and undesirable consequences of alternative management strategies, the quality of the evidence (including certainty of estimates), and the nature and variability of patient values and preferences. This decision process, which can be reviewed in the strength rating forms which accompany each guideline statement, addresses a number of key elements:

1. the overall quality of the evidence which exists for the recommendation [12];
2. the magnitude of the effect (individual or combined effects);
3. the certainty of the results (precision, consistency, heterogeneity and other statistical or study related factors);
4. the balance between desirable and undesirable outcomes;
5. the impact and certainty of patient values and preferences on the intervention.

Strong recommendations typically indicate a high degree of evidence quality and/or a favourable balance of benefit to harm and patient preference. Weak recommendations typically indicate availability of lower quality evidence, and/or equivocal balance between benefit and harm, and uncertainty or variability of patient preference [13].

Additional methodology information and a list of associations endorsing the EAU Guidelines can be found in the online: https://uroweb.org/eau-guidelines/methodology-policies.

2.2 Review

The 2025 guidelines were extensively peer reviewed prior to publication.

2.3 Future goals

- A SR of Patients' Values, Preferences, and Expectations for the Diagnosis and Treatment of FLUTS.

3. DIAGNOSIS

3.1 History and physical examination

Taking a thorough clinical history and carrying out a focused physical examination are fundamental to the process of clinical evaluation. Despite the lack of supportive high-level evidence, there is universal agreement that they should be the first step in the assessment of anyone with LUTS.

The history should include a full evaluation of LUTS, as well as sexual, gastrointestinal, and neurological symptoms. The history should categorise LUTS as storage, voiding and post-micturition symptoms, and broadly classify UI as SUI, UUI or MUI whilst acknowledging that there may be other causes of UI such as uro-genital fistulae, overflow incontinence or anatomical abnormalities [14].

The history should also identify patients who need onward referral to an appropriate clinic/specialist. These may include patients with associated pain, haematuria, history of recurrent urinary tract infection (UTI), pelvic surgery or radiotherapy, continuous incontinence suggesting a fistula (see Section 4.8), new-onset enuresis or suspected neurological disease. A neurological, obstetric, and gynaecological history may help to understand the underlying cause and identify factors that may affect treatment decisions. Guidance on history-taking and diagnosis in relation to UTIs, neuro-urological conditions and chronic pelvic pain (CPP) can be found in the relevant EAU Guidelines [11, 15, 16]. Patients should also be asked about other comorbidities as well as smoking status, previous surgical procedures, and current medications, as these may affect LUTS.

Examination should include abdominal examination, to detect an enlarged urinary bladder or other abdominal masses, and digital examination of the vagina and rectum. Pelvic examination in women includes assessment of oestrogen status, pelvic floor muscle (PFM) function and careful assessment of any associated pelvic organ prolapse (POP). A cough stress test is necessary to look for SUI. A focused neuro-urological examination should also be routinely undertaken.

3.1.1 Summary of evidence and recommendation for history taking and physical examination

Summary of evidence	LE
History-taking including symptoms and comorbidity, and focused physical examination are essential parts of the evaluation of women with LUTS.	4

Recommendation	Strength rating
Take a complete medical history including symptoms and comorbidity and perform a focused physical examination for evaluation of women with LUTS.	Strong

3.2 Patient questionnaires

This includes symptom scores, symptom questionnaires/scales/indices, patient-reported outcome measures (PROMs) and health-related quality of life (HRQoL) measures. Questionnaires should have been validated for the language in which they are being used, and, if used for outcome evaluation, should have been shown to be sensitive to change. The US Food and Drug Administration (FDA) published guidance for industry on PROM instruments (questionnaires) in 2009 [17].

Although many studies have investigated the validity and reliability of urinary symptom questionnaires and PROMs, most of these studies included mixed populations (men and women). This limits the extent to which results and conclusions from these studies can be applied to particular LUT syndromes in women. A SR included 22 studies that assessed eleven case-finding tools for OAB. All tools were found to have good sensitivity and specificity for OAB or incontinence symptoms [18]. Some questionnaires are responsive to change and may be used to measure outcomes, although evidence for this is inconsistent [19, 20].

Another SR including 73 studies assessed 27 specific and six generic instruments that measure quality of life (QoL) in women with UI. In this review, the incontinence QoL (IQoL) questionnaire was found to be the most psychometrically robust disease-specific tool for use in English-speaking women with UI. Evidence on the performance of generic QoL tools for this population is limited [21]. There is no evidence to indicate whether use of QoL or condition-specific questionnaires has an impact on outcome of treatment.

Detailed description of the different urinary symptoms questionnaires and PROMs is beyond the scope of these guidelines. For more information, we recommend the 7th ICI review on PROM assessment [22]. Clinicians must evaluate the tools that exist, for use alone or in combination, for assessment and monitoring of treatment outcome [23]. The questionnaires can be found on the following websites:
www.iciq.net, https://eprovide.mapi-trust.org, www.ncbi.nlm.nih.gov.

3.2.1 Summary of evidence and recommendation for patient questionnaires

Summary of evidence	LE
Validated condition-specific symptom scores assist in the screening for and categorisation of LUTS.	3
Validated symptom scores measure the severity of UI and LUTS.	3
Both condition-specific and general health status questionnaires measure current health status and appear sensitive to change following treatment.	3
Patient questionnaires cannot replace a detailed patient consultation and should only be used as part of a complete medical history.	4

Recommendation	Strength rating
Use a validated symptom score questionnaire including bother and quality of life assessment during the initial assessment of female LUTS and for re-evaluation during and/or after treatment.	Strong

3.3 Bladder diaries

Measurement of the frequency and severity of LUTS is an important step in the evaluation and management of LUT dysfunction. Bladder diaries are a semi-objective method of quantifying symptoms, such as frequency of UI events, number of nocturia episodes, etc. They also quantify urodynamic variables, such as voided volume, 24-hour urine volume or nocturnal total urine volume.

Fluid intake and voided volume measurement can be used to support diagnoses and management planning and for identifying polyuria. Diaries can also be used to monitor treatment response but in patients with severe UI, a bladder diary is unlikely to accurately report 24-hour urine output.

Consensus terminology is now well-defined and widely accepted [1, 24]. However, the terms micturition diary, frequency/volume chart, bladder diary and voiding diary, have been used interchangeably for many years, but only bladder diaries include information on fluid intake, times of voiding, voided volumes, UI episodes, pad usage, degree of urgency and severity of UI recorded for at least 24 hours. When reviewing the evidence, all synonymous search terms have been included.

Two studies have demonstrated the reproducibility of diaries in both men and women [25, 26]. Another two studies have shown the feasibility, reliability, and validity of the bladder diary [27, 28]. Further studies have demonstrated variability of diary data within a 24-hour period and compared voided volumes recorded in diaries with those recorded by uroflowmetry [29, 30]. Another study found that keeping a bladder diary had a therapeutic benefit [31].

A number of observational studies have demonstrated a close correlation between data obtained from bladder diaries and standard symptom evaluation [32-35]. The optimum number of days required for bladder diaries appears to be based on a balance between accuracy and compliance [36, 37].

3.3.1 Summary of evidence and recommendations for bladder diaries

Summary of evidence	LE
Bladder diaries of three to seven days duration are reliable tools for objective measurement of mean voided volume, day- and night-time frequency, urgency episodes, UI episode frequency fluid intake and pad usage.	2b
Bladder diaries are sensitive to change and are a reliable outcome measure.	2b

Recommendations	Strength rating
Ask patients with LUTS to complete a bladder diary as part of the standardised initial assessment and follow-up of female LUTS.	Strong
Use a bladder diary with a duration of ≥ 3 days.	Strong

3.4 Urinalysis and urinary tract infection

Reagent strip (dipstick) urinalysis may indicate proteinuria, haematuria or glycosuria, or suggest UTI requiring further assessment. Please refer to the Urological Infections Guidelines for diagnosis and treatment of UTI [15].

Urine dipstick testing is a useful adjunct to clinical evaluation in patients in whom urinary symptoms are suspected to be due to UTI. Urinalysis negative for nitrite and leukocyte esterase may exclude bacteriuria in women with LUTS [38], and should be included, with urine culture when necessary, in the evaluation of all patients with LUTS. Urinary incontinence or worsening of LUTS may occur during UTI [39] and existing UI may worsen [40]. The rate and severity of UI were unchanged after eradication of asymptomatic bacteriuria in nursing home residents [41].

3.4.1 Summary of evidence and recommendations for urinalysis

Summary of evidence	LE
Urinalysis negative for nitrite and leukocyte esterase may exclude bacteriuria in women with LUTS.	3
The presence of UTI worsens existing symptoms of UI.	3
Elderly nursing home patients with UI do not benefit from treatment of asymptomatic bacteriuria.	2

Recommendations	Strength rating
Perform urinalysis as a part of the initial assessment of patients with LUTS.	Strong
If a urinary tract infection is present with LUTS, reassess the patient after treatment.	Strong
Do not routinely treat asymptomatic bacteriuria in elderly patients with the aim of improving urinary incontinence.	Strong

3.5 Post-void residual volume

Post-void residual (PVR) volume is the amount of urine that remains in the bladder after voiding. It is a measure of voiding efficiency, and results from a number of contributing factors. The detection of significant PVR volume is important because it may worsen symptoms and, more rarely, may be associated with UTI, upper urinary tract (UUT) dilatation and renal insufficiency. Both bladder outlet obstruction (BOO) and/or detrusor underactivity (DU) can potentially contribute to the development of significant PVR volume. Post-void residual volume can be measured by catheterisation or ultrasound (US).

Most studies investigating PVR volume have assessed mixed populations including those with neurogenic UI, so results should be applied with caution to women with non-neurogenic LUTS. Studies investigating the best method of measuring PVR volume [41-46] conclude that US measurement of PVR volume is preferable to catheterisation due to its favourable risk-benefit profile.

There is no consensus on what constitutes a significant PVR volume in women [47-52], therefore the Panel prefers the use of bladder voiding efficiency (BVE) - the proportion of the total bladder volume that is voided by the patient. Bladder voiding efficiency can be calculated as a percentage: BVE = voided volume (VV)/(VV+PVR) × 100. This may be a more reliable parameter to evaluate poor voiding [53].

3.5.1 Summary of evidence and recommendations for post-void residual volume

Summary of evidence	LE
Patients with lower urinary tract symptoms have a higher PVR volume compared to asymptomatic population groups.	2

Recommendations	Strength rating
Measure post-void residual (PVR) volume in patients with LUTS during initial assessment.	Strong
Use ultrasound to measure PVR volume.	Strong
Monitor PVR volume in patients receiving treatments that may cause or worsen voiding dysfunction.	Strong
Provide bladder voiding efficiency as an additional parameter when measuring PVR volume.	Weak

3.6 Urodynamics

Urodynamic testing is widely used as an adjunct to clinical diagnosis, in the belief that it may help to provide or confirm a diagnosis, predict treatment outcome, or facilitate discussion during counselling. The simplest form of urodynamic evaluation is uroflowmetry. The maximum flow rate (Q_{max}), the volume voided and the shape of the curve in addition to the PVR volume (see above) are the most important aspects to be assessed [54]. The bladder should be sufficiently full because of the volume dependency of Q_{max} [55, 56]. A minimum voided volume of 150 mL is advised in men, but there is little evidence to suggest a volume threshold in women. It is relevant to ask the patient whether or not the voiding is representative.

Invasive urodynamic tests include multichannel cystometry and pressure-flow studies, ambulatory monitoring and video-urodynamics, and different tests of urethral function, such as urethral pressure profilometry. The International Continence Society (ICS) and the United Kingdom Continence Society (UKCS) provide standards to optimise urodynamic test performance and reporting [57, 58]. A characteristic of a good urodynamic study is that the patient's symptoms are replicated, recordings are checked for quality control, and results interpreted in the context of the clinical problem, remembering that there may be physiological variability within the same individual [57]. Non-invasive alternatives for measurement of detrusor pressure and BOO include transabdominal wall near-infrared spectroscopy and US detrusor wall thickness analysis, but as yet, these techniques have not been adopted into routine clinical practice [54].

Further condition-specific information regarding the role of urodynamic testing in OAB, SUI, BOO and UAB can be found in respective sections of these guidelines.

3.6.1 Variability

In common with most physiological tests there is variability in urodynamic results. This has consequences for the reproducibility, diagnostic accuracy, and predictive value of urodynamic testing. The ICS Good Urodynamic Practice Guidelines state [57] that, at least in the case of cystometry and pressure-flow studies, one set of measurements suffices, but only if the patient's symptoms have been replicated; however, some studies contradict this [59, 60]. There is also conflicting evidence about the reproducibility of maximum urethral closure pressure (MUCP) measurement [59, 60]. Valsalva leak point pressure (VLPP) measurement is not standardised and there is also minimal evidence about its reproducibility.

3.6.2 Diagnostic accuracy

Clinical diagnosis and cystometric findings sometimes do not correlate [61, 62] and asymptomatic women may have abnormalities on urodynamic testing. The diagnostic accuracy of urethral pressure profilometry [63] and urethral retro-resistance pressure measurement in SUI is poor [54]. Valsalva leak point pressure did not reliably assess UI severity in a cohort of women selected for surgical management of SUI [64]. Urethral pressure reflectometry may have greater diagnostic accuracy but its clinical role remains unclear [65]. Ambulatory urodynamics may detect unexpected physiological variance from normal more often than conventional cystometry does, but the clinical relevance of this is also uncertain [66, 67].

A pressure-flow study, that is, the simultaneous measurement of flow rate and detrusor pressure during voiding, can reveal whether a poor flow rate and PVR volume are due to BOO, DU, or a combination of both. Also, it may provide information on the degree of pelvic floor relaxation and thus diagnose dysfunctional voiding. Several proposals to define BOO in women have been made. These definitions are based on detrusor pressure, either $P_{det}Q_{max}$ or the maximum value $P_{det \cdot max}$, and in combination with the Q_{max} value. These measures are sometimes combined with the findings during fluoroscopic imaging as part of a video urodynamic study (see Section 4.5.4.8) [68, 69]. Unlike the situation in men, there is no universally accepted threshold for BOO diagnosis in women. Bladder contraction strength parameters are derived from detrusor pressure and flow rate during a pressure-flow study or from stop tests [69], but again, validation is poor. Although these parameters estimate the strength of the contraction, they ignore its speed and duration (see Section 4.4.3.2) [70]. A video-urodynamic study can be useful to detect the site of obstructed voiding, which may be anatomical or functional [71]. Also, video-urodynamics may detect urethral diverticula, bladder diverticula or gross reflux as a pressure-absorbing reservoir.

3.6.3 ***Predictive value***

Performing urodynamic evaluation is only useful if it leads to more effective clinical care and better outcomes. A Cochrane review of eight randomised controlled trials (RCTs) showed that use of urodynamic tests in women with UI increased the likelihood of prescribing drugs but reduced the likelihood of undergoing surgery. However, there was no evidence that this altered the clinical outcome [72]. A recent SR and meta-analysis of eight trials (six with exclusively female SUI patients) concluded that urodynamic studies did not improve outcomes from the treatment of SUI [73]. A meta-analysis including four RCTs comparing surgical outcomes in women with self-reported SUI (or stress-predominant MUI) who were investigated via urodynamics with women who had symptom review and physical examination only, found that there was no difference in cure and complication rates [74]. Furthermore, a large retrospective multicentre study found that only 36% of patients were defined as uncomplicated according to the definitions used in large RCTs [75]. The urodynamic observations were not consistent with the pre-urodynamic diagnosis in 1,276 out of 2,053 patients (62.2%). Voiding dysfunctions were urodynamically diagnosed in 394 patients (19.2%) and planned surgery was cancelled or modified due to the urodynamic findings in 304 of 1,582 patients (19.2%) in whom data were available [76]. A large UK multi-centre RCT is underway designed to evaluate the effectiveness and cost-effectiveness of invasive urodynamic investigations in management of women with refractory OAB symptoms [77].

The predictive value of urethral function tests remains unclear. In observational studies, there was no consistent correlation between the results of these tests and subsequent success or failure of SUI surgery [33-35, 78]. The same was true in a secondary analysis of an RCT [79].

The presence of pre-operative detrusor overactivity (DO) in women with stress-predominant MUI has been associated with post-operative UUI but did not predict overall treatment failure following mid-urethral sling (MUS) surgery or colposuspension [79]. The urodynamic diagnosis of DO has no predictive value for treatment response in studies on antimuscarinics, onabotulinumtoxinA (onabotA) and sacral nerve stimulation (SNS) in patients with OAB symptoms [80, 81]. Augmentation cystoplasty aims to abolish DO, improve bladder compliance, and increase functional bladder capacity but there is no evidence to guide whether or not pre-operative urodynamics are predictive of outcome. Most clinicians would, however, consider pre-operative urodynamics as essential prior to contemplating augmentation cystoplasty.

A pressure-flow study is capable of discriminating BOO from DU as a cause of voiding dysfunction. A low pre-operative flow rate and a low detrusor voiding pressure have been shown to correlate with voiding dysfunction after both tension-free vaginal tape (TVT) and autologous fascial sling procedures [82-84]. Bladder contraction strength parameters combining flow rate and detrusor pressure only poorly predicted voiding dysfunction after autologous fascial sling [85]. *Post-hoc* analysis of two high-quality surgical trials of TVT, Burch colposuspension and autologous fascial sling showed that no pre-operative urodynamic parameter predicted post-operative voiding dysfunction in a selected population of women with low pre-operative PVR volume [86, 87].

The Panel recognises that it is often valuable to use urodynamic test results to select the optimum management strategy; however, there is inconsistent evidence regarding the predictive value of such tests. When urodynamics and clinical assessment (i.e., by history and examination) are in disagreement, there needs to be a careful re-evaluation of the clinical symptoms and investigation results to ensure that the diagnosis is correct before invasive treatments are contemplated.

3.6.4 ***Summary of evidence and recommendations for urodynamics***

Summary of evidence	**LE**
Urodynamics provide comprehensive analysis of LUT function underlying different clinical conditions.	4
Most urodynamic parameters show variability within the same session and over time.	3
Different techniques of measuring urethral function may have good test-retest reliability, but do not consistently correlate to other urodynamic tests or to the severity of UI.	3
There may be inconsistency between history and urodynamic results.	3
Urodynamic diagnosis of DO does not influence treatment outcomes in patients with OAB.	1a
Pre-operative urodynamics in women with uncomplicated, clinically demonstrable SUI does not improve the outcome of surgery for SUI.	1b
There is no consistent correlation between the results of urethral function tests and subsequent success or failure of SUI surgery.	3

There is no consistent evidence that pre-operative DO is associated with surgical failure of MUS in women.	3
The presence of pre-operative DO may be associated with persistence of urgency post-operatively in women undergoing surgery for SUI.	3

Recommendations	Strength rating
Adhere to good urodynamic practice standards as described by the International Continence Society when performing urodynamics in patients with LUTS.	Strong
Do not routinely carry out urodynamics when offering treatment for uncomplicated stress urinary incontinence.	Strong
Do not routinely carry out urodynamics when offering first-line treatment to patients with uncomplicated overactive bladder symptoms.	Strong
Perform urodynamics if the findings may change the choice of invasive treatment, and/or if there is diagnostic uncertainty.	Weak
Do not use urethral pressure profilometry or leak point pressure to grade severity of urinary incontinence.	Strong

3.7 Pad testing

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

The clinical utility of pad tests in woman with UI has been assessed in three SR's [88-90]. One SR included eighteen studies and concluded that one hour pad test was more accurate but less reproducible when compared to the longer duration pad tests. A recent crossover trial showed that twenty minute pad testing was acceptable to patients and comparable to a 60 minute pad test for assessing the severity of SUI [91]. A one hour pad test using a standardised exercise protocol, and a diagnostic threshold of 1.4 g shows good specificity but low sensitivity for symptoms of SUI and MUI. A 24-hour pad test using a threshold of 4.4 g is more sensitive but is difficult to standardise, with variation according to activity level [92].

The usefulness of pad tests in quantifying severity and predicting outcome of treatment is uncertain [88, 93, 94]. Pad tests are responsive to change following successful treatment [95]. Pad testing using a standardised bladder volume (50% of cystometric capacity) was suggested to allow for a more reliable assessment of UI in a small study of 25 women [96]. There is no evidence that one type of pad test is superior to another.

3.7.1 Summary of evidence and recommendations for pad testing

Summary of evidence	LE
A pad test can diagnose UI accurately.	2
Standardisation of bladder volume and degree of provocation improves reproducibility.	2
Longer duration (> 1 hour) pad tests may increase sensitivity but are more difficult to standardise.	3
Twenty-minute pad test may provide equivalent objective assessments of UI compared to 60-minute protocols.	1b
Change in leaked urine volume on pad tests can be used to measure treatment outcome.	2
Pad tests can be a useful tool in the research setting and are an optional investigation in clinical practice.	4

Recommendations	Strength rating
When a pad test is performed, use a standardised duration and activity protocol.	Strong
Use a pad test when quantification of urinary incontinence is required, especially to assess response to treatment.	Weak

3.8 Imaging

In clinical practice, imaging is used to understand the relationship between anatomy and function. This can be assessed simultaneously using video urodynamic studies. For further details please see the condition specific sections. Ultrasound and magnetic resonance imaging (MRI) have largely replaced X-ray imaging in the evaluation of the pelvic floor. Ultrasound is sometimes preferred to MRI because of its ability to produce three-dimensional (3D) and 4D (dynamic) images at lower cost and wider availability.

There is no need for UUT imaging unless a high-pressure bladder, severe POP or chronic urinary retention is suspected or diagnosed, or abnormal renal function tests are observed. In cases of suspected UI caused by an UUT anomaly or uretero-vaginal fistula, UUT imaging (urography, computed tomography [CT]) may be indicated [97].

3.8.1 Ultrasound

Ultrasonography of the LUT plays a role in the evaluation of women with LUTS.

Ultrasonography using different imaging approaches, such as abdominal, transvaginal, transrectal, perineal and transurethral are described. The bladder neck and urethra are easily visible, and measurements can be done at rest and during straining, coughing and pelvic floor contraction. The parameters assessed may include bladder neck mobility or descent, urethro-vesical angle, and urethral rotation and can be useful particularly in the evaluation of SUI [98, 99]. Ultrasonography can be used to assess PFMs and their function. Contraction of PFM results in displacement of pelvic structures that can easily be imaged on US. Integrity of the levator ani muscle can be determined by 3D transperineal US. Ultrasound may also provide information on the anatomical changes of the LUT, and pelvic floor associated with persistence of symptoms post-treatment [100].

Ultrasound is also used to measure detrusor wall thickness which has been studied for its diagnostic utility in OAB and BOO. The details are presented in the relevant sections of this guideline. In summary no consensus exists as to the relationship between OAB/BOO and/or increased bladder wall thickness (BWT)/detrusor wall thickness (DWT) [101], and there is no evidence that BWT/DWT imaging improves management of OAB. There is no widely accepted standardised bladder volume for BWT measurement.

A retrospective study including 227 women with voiding symptoms (hesitancy, intermittency, and poor stream) revealed that DWT was not associated with any urodynamic parameters that may indicate BOO [102].

3.8.2 Magnetic resonance imaging

There is a general consensus that MRI provides good global pelvic floor assessment, including POP, defecatory function and integrity of the pelvic floor support [103]. However, there is a large variation in MRI interpretation between observers [104] and little evidence to support its clinical usefulness in the management of LUTS/UI. There is no conclusive evidence that MRI evaluation of POP is more clinically useful than vaginal examination. Studies have assessed the use of imaging to assess the mechanism of MUS insertion for SUI. One study suggested that MUS placement decreased mobility of the mid-urethra but not of the bladder neck [105]. Following MUS, a wider gap between pubic symphysis and sling (assessed by imaging) has been shown to correlate with a lower chance of cure of SUI [106].

3.8.2.1 Summary of evidence and recommendation for imaging

Summary of evidence	LE
There is no consistent evidence that routine urinary tract imaging is useful in the evaluation or management of LUTS.	3
There is no consistent evidence that BWT/DWT measurement is useful in the management of OAB or female BOO.	3

Recommendation	Strength rating
Do not routinely carry out imaging of the upper or lower urinary tract (apart from post-void residual estimation) as part of the initial assessment of female LUTS.	Strong

3.9 Urinary Biomarkers and Microbiota

Interest in the role of urinary biomarkers for the diagnosis of LUT dysfunction has increased in recent years. Nerve growth factor (NGF), brain derived neurotrophic factor (BDNF), prostaglandin E2, adenosin triphosphate (ATP) and purinergic receptors (P2X) in bladder tissue have been studied as biomarkers for OAB. Serum beta natriuretic peptide (BNP), urinary 6-sulfaoxymelatonin and C-reactive protein (CRP), melatonin, vasopressin levels have been studied in relation to nocturia. Regarding BOO, currently, there are no validated biomarkers for female BOO available but one SR has suggested that NGF levels are elevated in women with BOO when compared with normal controls [107].

For SUI, urinary IL 12-70, urinary (uNGF) and N-telopeptide of type I collagen (NTx) have been studied. Currently, studies investigating urinary biomarkers are methodologically limited often due to failing to control for confounding variables and consequently results are conflicting [108].

Another area of discovery is the role of urinary microbiota in identifying and differentiating various types of UI and other LUT disease in women. A SR described studies showing differences in the types and relative proportions of bacteria such as *Lactobacillus, Gardnerella, and Atopobium vaginae,* among women with different types of UI compared with healthy controls. Urinary microbiota has also been shown to differ depending on women's response to anticholinergic treatment response [109]. Further research is needed before the place of urine microbiota assessment in the clinical pathway for women with LUTS is fully defined.

Further information on the diagnostic efficacy of biomarkers in OAB can be found in Section 4.1.3.4.

3.9.1 Summary of evidence and recommendation for urinary biomarkers

Summary of evidence	LE
There is insufficient evidence on the diagnostic accuracy and validity of urinary biomarkers for LUT disease in women.	3
Differences in the urinary microbiota have been found to be associated with different types of LUT dysfunction in women, including UI, and with different responses to treatment.	3

Recommendation	Strength rating
Do not routinely use urinary biomarkers or estimation of the urinary microbiota in the diagnosis and management of LUT disease in women.	Strong

4. DISEASE MANAGEMENT

4.1 Overactive bladder

4.1.1 Epidemiology, aetiology, pathophysiology

Overactive bladder syndrome is defined by the ICS as *"urinary urgency, usually accompanied by frequency and nocturia, with or without UUI, in the absence of UTI or other obvious pathology"* [110]. Overactive bladder is a chronic condition that can have debilitating effects on QoL. The hallmark urodynamic feature is DO but the diagnosis of OAB is exclusively based on symptoms.

The EPidemiology of InContinence (EPIC) study [111] was a cross-sectional telephone survey of adults conducted in five countries and demonstrated an overall prevalence of OAB symptoms of 11.8% (10.8% in men and 12.8% in women).

Various theories have been proposed to explain the pathophysiology of OAB, mainly relating to imbalances in inhibitory and excitatory neural pathways to the bladder and the urethra or sensitivity of bladder muscle receptors.

4.1.2 Classification

Overactive bladder is generally classified into wet and dry, based on the presence or absence of associated UUI.

4.1.3 Diagnostic evaluation

Evaluation of symptoms of OAB follows the general pathway of evaluation of women with LUTS.

4.1.3.1 Bladder diaries

Diaries are particularly helpful in establishing and quantifying symptoms of frequency, urgency and UI, and may be valuable in assessing change over time or response to treatment. Several observational studies have demonstrated a close correlation between data obtained from bladder diaries and standard symptom evaluation [32-35]. The optimum number of days required for bladder diaries appears to be based on a balance between accuracy and compliance, with three to seven days routinely used in the literature. For further information, please review Section 3.3.

4.1.3.2 Urodynamics

Urodynamics is essential in establishing the presence of DO, but its absence does not preclude diagnosis of OAB, which is based on symptoms alone.

A Cochrane review of seven RCTs showed that use of urodynamic tests increased the likelihood of prescribing drugs or avoiding surgery, without altering the clinical outcome of treatment [72]. A sub-analysis of an RCT comparing fesoterodine to placebo [81] showed that the urodynamic diagnosis of DO was not predictive of treatment response.

4.1.3.3 Summary of evidence and recommendations regarding OAB diagnosis

Summary of evidence	**LE**
Bladder diaries of three to seven days' duration may be helpful in quantifying symptoms of OAB and assessing response to treatment.	3
Urodynamic diagnosis of DO does not influence treatment outcomes in patients with OAB.	1a

Recommendations	**Strength rating**
Request that patients complete at least a three-day bladder diary at initial evaluation for overactive bladder (OAB).	Strong
Do not routinely carry out urodynamics when offering first-line treatment to patients with uncomplicated OAB symptoms.	Strong

4.1.3.4 Urinary biomarkers

A SR and meta-analysis indicated that uNGF, BDNF to creatinine ratio and uNGF to creatinine ratio were all increased in female OAB patients compared to healthy controls, whereas no difference was found for the PGE2/Cr and ATP/Cr ratios [112]. The current data is inadequate to assess any other potential biomarkers in the diagnosis or management of OAB in female patients.

4.1.4 ***Disease management***

4.1.4.1 Conservative management

In clinical practice, it has long been the convention that non-surgical therapies are recommended first because they usually carry the lowest risk of harm. While this remains true for non-pharmacological conservative managements (e.g., pelvic floor muscle training [PFMT]), increasing concerns regarding the adverse events of some pharmacological treatments used to treat OAB (e.g., anticholinergic drugs), particularly regarding cognitive function, have emerged and patients should be fully counselled regarding this potential risk. The utilisation of a shared decision-making approach has been recommended by recent international guidelines and the panel would fully support this [113].

4.1.4.1.1 Addressing associated medical co-morbidities

Lower urinary tract symptoms, especially in elderly patients, are associated with multiple comorbid conditions including:

- cardiac failure;
- chronic renal failure;
- diabetes;
- chronic obstructive pulmonary disease;
- neurological disease;
- general cognitive impairment;
- sleep disturbances, e.g., sleep apnoea;
- depression;
- metabolic syndrome.

If a change in comorbidity or a new treatment for any associated comorbidity has been linked to an improvement or deterioration in LUTS, then this should be reviewed.

One study involving middle-aged women with type one diabetes mellitus showed that 10% had UUI. The study showed no correlation between early intensive insulin treatment vs. conventional insulin treatment and the occurrence of UUI. The same study found no difference in the prevalence of UI in these patients later in their lives [114].

One RCT of 60 patients with OAB symptoms and obstructive sleep apnoea (OSA) reported better improvement in OAB symptoms in those who used tolterodine in combination with continuous positive airway pressure (CPAP) vs. CPAP alone [115]. However, there was significant improvement in the OAB V8 score in the CPAP alone arm compared to baseline.

4.1.4.1.2 Adjustment of other medication

Although LUTS are listed as adverse effects of many drugs, this mainly derives from uncontrolled individual patient reports and post-marketing surveillance. Few controlled studies used the occurrence of LUTS as a primary outcome or were powered to assess the occurrence of statistically significant LUTS, or worsening rates against placebo. In most cases, it is therefore not possible to be sure that any drug directly causes OAB/LUTS.

A structured scoping review failed to identify any studies addressing whether adjustment of specific medications could alter existing symptoms of OAB.

4.1.4.1.2.1 Summary of evidence and recommendations for conservative management of OAB

Summary of evidence	**LE**
There is low level evidence that improvement in associated medical conditions such as obstructive sleep apnoea and obesity may improve OAB symptoms.	3

Recommendations	**Strength rating**
Identify and address comorbidities associated with overactive bladder (OAB) such as obstructive sleep apnoea and obesity.	Weak
Take a history of current medication use from all patients with OAB.	Strong
Review any new medication associated with the development or worsening of OAB symptoms.	Strong
Use a shared decision-making process involving both clinicians and patients when selecting the appropriate conservative management for OAB.	Strong

4.1.4.1.3 Urinary containment

Urinary containment is important for people with OAB wet when active treatment does not cure the problem, is delayed, not available or possible. Some individuals may prefer urinary containment rather than active treatment with its associated risks. Containment includes the use of absorbent pads, urinary catheters, external collection devices and intravaginal devices. Detailed literature summaries can be found in the current International Consultation on Urological Diseases (ICUD) monograph [9] and in a European Association of Urology Nurses guidance document [116]. The sustainability of reusable vs. disposable pads and catheters is an important consideration.

Moderate to high certainty evidence related to urinary containment:

- Superabsorbent pads are more effective than standard pads, from an SR of five RCTs [117].
- Disposable insert pads (within washable pouch pants) were most effective for women with light UI and disposable pull-up pants were more effective for moderate/heavy UI, from a series of three crossover RCTs [118].
- One type of catheter material is not superior to any other in terms of controlling leakage, from a Cochrane review of three RCTs [119].
- There are no differences in UTI outcome or UUT changes between use of suprapubic or urethral catheter drainage; however, patients with suprapubic catheters are less likely to have urethral complications according to an SR of non-randomised studies [120].

- Antibiotic prophylaxis in patients performing IC reduces rate of symptomatic UTIs but at the cost of increased antimicrobial resistance, from a Cochrane review summarising eight trials [121] and a UK multicentre RCT [122].

Low or very low certainty evidence related to urinary containment:
- Disposable pads are better than washable pads in preventing skin problems (inconsistent evidence from an SR of five RCTs) [117].
- Anticholinergics can reduce catheter-related bladder discomfort (inconsistent and indirect evidence from clinical trials in the post-operative setting) [123-126].
- Intravesical botulinum toxin injection can help prevent bladder pain and discomfort, catheter bypass/leakage, improve QoL and reduce leakage by up to 83% (evidence from one retrospective study; therefore, the risk of bias is high, and consistency cannot be assessed).

4.1.4.1.3.1 Summary of evidence and recommendations for urinary containment

Summary of evidence	**LE**
Pads are effective in terms of containing urine.	1b
Catheters are effective in terms of containing urine and there is no evidence that one type of catheter material is superior to any other.	1a
Antibiotic prophylaxis may help reduce incidence of UTI in patients who have an indwelling catheter or use IC but may lead to increasing antimicrobial resistance.	1a

Recommendations	**Strength rating**
Ensure that women with overactive bladder (OAB) and/or their carers are informed regarding available treatment options before deciding on urinary containment alone.	Strong
Offer incontinence pads and/or containment devices for management of OAB wet, either for temporary symptom control or when other treatments are not planned or possible.	Strong
Offer prophylactic antibiotics to patients with recurrent urinary tract infection only after discussion regarding the risk of increasing antimicrobial resistance.	Strong

4.1.4.1.4 Lifestyle interventions

Examples of lifestyle factors that may be associated with UI include obesity, smoking, level of physical activity, regulation of bowel habit, and fluid intake. Modification of these factors may improve symptoms of OAB.

4.1.4.1.4.1 Caffeine intake

A scoping review of fourteen interventional and twelve observational studies reported that reduction in caffeine intake may reduce symptoms of urgency, but the certainty of evidence was low, with significant heterogeneity in study populations [127].

4.1.4.1.4.2 Fluid intake

Modification of liquid intake, particularly restriction, is a strategy commonly used by people with OAB. Any advice on liquid intake given by health care practitioners (HCPs) should be based on 24-hour intake and urine output measurements as retrieved from the bladder diary. From a general health point of view, it should be advised that liquid intake should be sufficient to avoid thirst and that an abnormally low or high 24-hour urine output should be investigated. The few published RCTs involving women provide inconsistent evidence [128-130]. In most studies, the instructions for liquid intake were individualised and it was difficult to assess participant adherence. An RCT showed that a reduction in liquid intake by 25% improved symptoms in patients with OAB but did not improve UUI [130]. Personalised fluid advice compared to generic advice made no difference to continence outcomes in people receiving anticholinergics for OAB, according to an RCT comparing drug therapy alone to drug therapy with behavioural advice [131]. Patients should be warned of the potential consequences of liquid restriction such as worsening of constipation or development of UTI.

4.1.4.1.4.3 Weight loss

Being overweight or obese has been identified as a risk factor for LUTS in epidemiological studies [132, 133]. There is evidence that the prevalence of both UUI and SUI increases proportionately with body mass index (BMI) [134]. However, the evidence base largely relates to obesity and SUI rather than UUI and OAB. Therefore, no definite inference can be drawn between obesity and the prevalence of OAB.

4.1.4.1.4.4 Smoking cessation

Smoking cessation is a general public health measure and has been shown to be weakly associated with improving urgency, frequency, and UI [135, 136]. The effect of smoking cessation on LUTS was described as uncertain in a health technology assessment review [137].

4.1.4.1.4.5 Summary of evidence and recommendations for lifestyle interventions

Summary of evidence	**LE**
Reduction of caffeine intake may reduce symptoms of frequency and urgency.	2
Reduction in liquid intake by 25% may help improve symptoms of OAB but not UUI.	1b
Personalised liquid intake advice when added to pharmacotherapy provides no additional benefit in patients with OAB receiving medical therapy.	2
Obesity is a risk factor for UI in women, but the relationship to other OAB symptoms remains unclear.	1b
There is weak evidence that smoking cessation improves symptoms of OAB.	3

Recommendations	**Strength rating**
Advise adults with overactive bladder (OAB) that reducing caffeine intake may improve symptoms of urgency and frequency, but not incontinence.	Strong
Review type and amount of liquid intake in patients with OAB.	Weak
Encourage overweight and obese adults with OAB/urinary incontinence to lose weight and maintain weight loss.	Strong
Provide smoking cessation strategies to patients with OAB who smoke.	Strong

4.1.4.1.5 Behavioural and physical therapies

Behavioural and physical therapies are often introduced as part of a package of care including lifestyle changes and patient education.

4.1.4.1.5.1 Prompted voiding and timed voiding

The term 'prompted voiding' implies that carers, rather than the patient, initiate the patient going to void with the aim of preventing or reducing UI. This applies largely to an assisted care setting. A SR (nine RCTs including mostly women with UI), comparing prompted voiding to standard care, suggested evidence of short-term benefit for management of UI [138].

Timed voiding is defined as fixed, predetermined, time intervals between voids and is applicable for those with or without cognitive impairment. A Cochrane review of timed voiding included four RCTs and found inconsistent improvement in continence compared with standard care in cognitively impaired adults [139].

4.1.4.1.5.2 Bladder training

Bladder training (BT) is a programme of patient education along with a scheduled voiding regimen with gradually increasing intervals. Specific goals are to correct faulty patterns of frequent urination, improve control over bladder urgency, prolong voiding intervals, increase bladder capacity, reduce incontinent episodes and restore patient confidence in controlling bladder function. The ideal form or intensity of a BT programme for OAB/UI is unclear.

Cognitive behavioural therapy (CBT) involves the analysis of or change to a thought process related to the sensation of urgency or employment of a specified thought process during an episode of urgency. This includes mental distraction (the most common), relaxation and mindfulness practices.

The evidence for these strategies is of low or very low certainty:

- More patients reported improvement with anticholinergics compared to BT alone, and combination therapy resulted in more subjective improvement but no difference in objective improvement [140].
- Behavioural therapy that includes a cognitive component shows promise for OAB treatment, but its relative importance has not been well evaluated nor rigorously studied [141]. Overall, the cognitive components of behavioural therapies for OAB are neither well described nor rationalised.
- Cognitive behavioural therapy may improve symptom severity, QoL, psychological symptoms and patient satisfaction when compared with placebo. However, results were inconsistent with some studies showing no difference in objective parameters such as bladder capacity [142].

4.1.4.1.5.3 Pelvic floor muscle training

Pelvic floor muscle contraction can lead to simultaneous inhibition of urgency, detrusor contraction and incontinence [143]. Intensive and regular strength training of the PFMs over time increases both PFM contraction strength and endurance, and changes the morphology of the pelvic floor, which may yield more effective inhibition of the detrusor and help to stabilise the proximal urethra and improve urethral function. There is a lack of basic and mechanistic studies to confirm that change in pelvic floor morphology improves OAB symptoms.

A SR of eleven RCTs [144], including women with OAB, compared the efficacy of PFMT to inactive control, usual care, other lifestyle modification or other intervention. Pelvic floor muscle training significantly reduced OAB symptoms (frequency and UUI) in five RCTs, while the remaining six reported no significant difference. Significant heterogeneity in protocols and outcomes was noted.

4.1.4.1.5.4 Electrical stimulation

The methods of delivery of electrical stimulation (ES) vary considerably. Electrical stimulation of the PFM can also be combined with other forms of conservative therapy, e.g., PFMT with and without biofeedback. Electrical stimulation is often used to assist women who cannot initiate contractions to identify their PFMs and in patients with OAB and UUI with the aim of inhibiting detrusor contraction. There is, however, a lack of basic and mechanistic studies to confirm this theory.

Moderate certainty evidence for ES:

- Electrical stimulation is more likely to improve OAB symptoms compared to sham control, no treatment, PFMT, and drug treatment, from a Cochrane review [145].
- There is no difference between intravaginal stimulation and transcutaneous posterior tibial nerve stimulation (T-PTNS) in terms of urinary frequency, nocturia and QoL scores according to a SR of nine RCTs [146].
- Percutaneous posterior tibial nerve stimulation (P-PTNS) compared with T-PTNS showed no difference in urinary urgency, frequency and QoL scores [146].
- Percutaneous or transcutaneous posterior tibial nerve stimulation are most likely to result in improvement of UUI episodes or pad use compared to other methods of ES [147].

Low or very low certainty evidence for ES:

- Electrical stimulation is more effective than placebo/sham for UUI [145].
- Tibial nerve stimulation (NS) may be more effective than sacral NS for improvement in urgency incontinence episodes but with no difference in frequency/urgency/nocturia episodes or QoL, according to an SR of nine RCT's [146].
- There is not enough evidence to determine the difference in adverse event rates between ES and placebo/sham and the other active treatments.

4.1.4.1.5.4.1 Posterior tibial nerve stimulation

Electrical stimulation of the posterior tibial nerve delivers electrical stimuli to the sacral micturition centre via the S2-S4 nerve roots. Stimulation is percutaneous with a fine needle, inserted just above the medial malleolus of the ankle (P-PTNS). Transcutaneous stimulation (T-PTNS) is also available that delivers stimulation via surface electrodes which do not penetrate the skin. The optimal treatment schedule has not been determined, with daily and weekly regimens described [148]. These two tibial nerve stimulation methods had similar clinical efficacy but with slight differences: T-PTNS had shorter preparation time, less discomfort level and higher patient satisfaction than P-PTNS [149].

High certainty evidence for PTNS:

- The results of studies of PTNS in women with OAB consistently showed significant and sustained improvement in symptoms from baseline, with similar improvement compared to treatment with tolterodine [150-155].

Moderate certainty evidence for PTNS:

- Posterior tibial nerve stimulation techniques were significantly more effective than antimuscarinics in the reduction of UUI episodes with no significant difference in the reduction of overall symptoms score, frequency episodes or urgency episodes, according to an SR conducted by the panel [156].
- This SR also showed combination therapy (PTNS + antimuscarinics) added no statistically significant difference to PTNS monotherapy in the reduction of mean symptoms score, frequency episodes, nocturia episodes, or UUI episodes [156].
- Percutaneous or transcutaneous posterior tibial nerve stimulation is most likely to result in improvement of UUI episodes or reduced pad use compared to other methods of ES [147].

Low level evidence for PTNS:

- Transcutaneous posterior tibial nerve stimulation resulted in mean reduction in total international consultation on incontinence modular questionnaire (ICIQ) Urinary Incontinence Short Form (ICIQ-UI-SF) of −3.79 points in a narrative review of ten studies [157].
- Addition of T-PTNS to standard treatment (PFMT and BT) is more likely to achieve improvement [158].
- Percutaneous posterior tibial nerve stimulation and T-PTNS were more effective than BT alone in one small RCT [149].

4.1.4.1.5.5 Acupuncture

A Cochrane SR with meta-analysis [159] of fifteen RCTs reported that acupuncture might result in higher rates of cure or improvement of OAB symptoms compared to medication, with lower incidence of adverse events (low certainty evidence). The evidence is very uncertain when comparing acupuncture to no treatment or sham treatment in the same review.

A SR of 30 RCT's reported somewhat different results, with acupuncture resulting in reduction of OAB symptom scores and frequency episodes compared to sham treatment, as well as equivalent outcomes to drug therapy. Certainty of evidence from this SR remains very low, with risk of bias across almost all studies being unclear or high.

4.1.4.1.5.6 Summary of evidence and recommendations for behavioural and physical therapies

Summary of evidence	**LE**
Prompted voiding, either alone or as part of a behavioural modification programme, improves continence in elderly, care-dependent, people in the short-term.	1b
Bladder training is effective for improvement of UUI in women, but efficacy appears to be lower than that of pharmacotherapy.	1b
Pelvic floor muscle training may improve symptoms of frequency of OAB in women.	1b
Electrical stimulation may improve symptoms of OAB in some women, but the type and mode of delivery of ES remains variable and poorly standardised.	1a
Posterior tibial nerve stimulation is more effective than antimuscarinics in reducing UUI episodes but with no difference in improving other OAB symptoms.	1a
A maintenance programme of P-PTNS has been shown to be effective for up to three years.	2a
Transcutaneous-PTNS appears to be effective in reducing OAB symptoms compared to sham treatment.	1a
Transcutaneous-PTNS is not inferior to P-PTNS with regard to improvement in urinary urgency, frequency, and QoL scores.	1a
Acupuncture may result in improvement of OAB symptoms, but results compared with sham treatment, placebo and drug therapy are mixed.	1a

Recommendations	Strength rating
Offer prompted voiding to adults with overactive bladder (OAB) who are cognitively impaired.	Strong
Offer bladder training as a first-line therapy to adults with OAB/urgency urinary incontinence (UUI).	Strong
Ensure that pelvic floor muscle training programmes are as intensive as possible.	Strong
Offer posterior tibial nerve stimulation as an option for symptomatic improvement of OAB/UUI.	Strong
Consider acupuncture as an option for the management of OAB symptoms.	Weak

4.1.4.2 Pharmacological management

4.1.4.2.1 Anticholinergic drugs

Anticholinergic (antimuscarinic) drugs are currently the mainstay of treatment for OAB. Different agents vary in their pharmacological profiles, such as muscarinic receptor affinity and other modes of action and in their pharmacokinetic properties, such as lipid solubility and half-life. The panel would encourage a shared decision making prior to the use of anticholinergic drugs with particular emphasis on their effect on comorbidities such as glaucoma, cognitive impairment, chronic constipation etc., and certain aspects of lower urinary tract function such as bladder emptying efficiency.

High certainty evidence for anticholinergics:

- Antimuscarinics were significantly more effective than placebo in improving mean symptom score on OAB questionnaire (OAB-Q), reducing daily frequency episodes, reducing daily urgency episodes and UUI episodes, and increasing bladder functional capacity in the panel SR [156] and a Cochrane review [160].
- Differences across the drugs in terms of alteration in symptoms were small [161].
- Antimuscarinics caused significantly higher adverse events than placebo including dry mouth, cognitive impairment, UTI and constipation [156].
- Immediate-release (IR) anticholinergic preparations provide maximum dosage flexibility, including an off-label on-demand use, at the cost of higher risk of adverse events [162].

Cure of UUI is deemed to be the most important outcome measure. Table 1 shows a summary of the findings from a SR of RCTs including only women [163]. All agents showed superiority compared to placebo, but the absolute size of the effect was small.

Table 1: Summary of cure and discontinuation rates of anticholinergic drugs from RCTs [163]

Drug	No. of studies	No. of patients	RR (95% CI) (of curing UI)	NNT (95% CI) (to achieve one cure of UI)
Cure of incontinence				
Oxybutynin (includes IR)	4	992	1.7 (1.3-2.1)	9 (6-16)
Trospium (includes IR)	4	2,677	1.7 (1.5-2.0)	9 (7-12)
Solifenacin	5	304	1.5 (1.4-1.6)	9 (6-17)
Propiverine (includes IR)	2	691	1.4 (1.2-1.7)	6 (4-12)
Fesoterodine	2	2,465	1.3 (1.1-1.5)	8 (5-17)
Tolterodine (includes IR)	4	3,404	1.2 (1.1-1.4)	12 (8-25)
Discontinuation due to adverse events				
			RR (95% CI) (of discontinuation)	**NNT (95% CI) (for one discontinuation)**
Tolterodine (includes IR)	10	4,466	1.0 (0.6-1.7)	
Darifenacin	7	3,138	1.2 (0.8-1.8)	
Solifenacin	7	9,080	1.3 (1.1-1.7)	78 (39-823)
Trospium (includes IR)	6	3,936	1.5 (1.1-1.9)	56 (30-228)
Oxybutynin (includes IR)	5	1,483	1.7 (1.1-2.5)	16 (8-86)
Fesoterodine	4	4,433	2.0 (1.3-3.1)	33 (18-102)
Propiverine (includes IR)	2	1,401	2.6 (1.4-5)	29 (16-77)

CI = confidence interval; IR = immediate release; NNT = number to treat; RR = relative risk; UI = urinary incontinence.

The cure rates for darifenacin were not included in the US Agency for Healthcare Research and Quality (AHRQ) review. Continence rates were 29-33% for darifenacin compared to 17-18% for placebo [163]. Transdermal oxybutynin showed a significant improvement compared with placebo and other oral formulations in the number of incontinence episodes and micturitions per day but cure of UI was not reported as an outcome [160]. Oxybutynin topical gel was superior to placebo for improvement of UUI, with a higher proportion of participants being cured [163, 164].

4.1.4.2.1.1 Comparison of different anticholinergic agents

Head-to-head comparison trials of the efficacy and adverse effects of different anticholinergic agents are of interest for decision-making.

High certainty evidence for comparisons between anticholinergic agents:

- A network meta-analysis of 54 trials reported that oxybutynin 15 mg/d was most effective in reducing incontinence episodes, imidafenacin 0.5 mg/d and solifenacin 10 and 5 mg/d in reducing micturition episodes, fesoterodine 4 and 8 mg/d and solifenacin 10mg/d in reducing urgency episodes, imidafenacin 0.5 mg/d and solifenacin 10 mg/d in reducing UUI episodes, and solifenacin 10 mg/d, vibegron 50 mg/d, and fesoterodine 8 mg/d in improving the voided volume [165].
- Solifenacin 5 mg/day was significantly more effective than tolterodine 4 mg/day for reducing UUI episodes, but significantly less effective than solifenacin 10 mg/day for reducing micturition episodes. Solifenacin 5 mg/day showed significantly lower risk of dry mouth compared with other anticholinergics but no significant differences for the risk of blurred vision or constipation [166].
- Extended-release formulations are associated with lower rates of dry mouth than IR preparations [167, 168].
- Oxybutynin IR shows higher rates of dry mouth than tolterodine IR and trospium IR but lower rates of dry mouth than darifenacin 15 mg daily [167, 168].
- Oxybutynin ER causes higher rates of dry mouth than tolterodine ER does, although the incidence of moderate or severe dry mouth is similar [167].
- Solifenacin 10 mg daily has higher rates of dry mouth than tolterodine ER [167].
- Fesoterodine 8 mg daily has a higher rate of dry mouth than tolterodine 4 mg daily [169-171].

It is notable that nearly all the primary studies in this category were industry sponsored. In general, these studies have been designed to achieve regulatory approval. Upward dose titration is often included in the protocol for the experimental arm but not for the comparator arm. They have short treatment durations (twelve weeks) and a primary outcome of a change in OAB symptoms rather than a cure of, or an improvement in, UUI, which were generally analysed as secondary outcomes. The clinical utility of these trials in real-life practice is therefore debatable. Most trials were of low or moderate quality [167].

4.1.4.2.1.2 Anticholinergic drugs combined with conservative management

More than 100 RCTs and high-quality reviews are available detailing relative efficacy of anticholinergic drugs and conservative management strategies [140, 167, 172-175]. Most of these were independent studies. The main focus of the reviews was to compare the different drugs used to treat UUI. A U.S. health technology assessment [173] found that the vast majority of trials were of a low or moderate quality.

Low certainty evidence for anticholinergic drugs combined with other therapies:

- The combination of BT and solifenacin in female patients with OAB confers no additional benefit in terms of continence compared with solifenacin monotherapy [176].
- There is insufficient evidence of any benefit in terms of improving continence by adding PFMT to drug treatment [177].
- Antimuscarinics alone were less effective than a combination of antimuscarinics plus another treatment modality (topical oestrogen, pregabalin, Stroller neurostimulation [SANS], PFMT, and behavioural therapy) in reducing urgency episodes, frequency and nocturia episodes and in improving the mean symptoms score but no significant differences were found in rates of dry mouth, constipation or voiding dysfunction [156].

4.1.4.2.1.3 Anticholinergic drugs: adherence and persistence

Most studies on anticholinergic medication are short term (twelve weeks). Adherence in clinical trials is considered to be higher than in clinical practice [178]. Discontinuation rates were high for tolterodine at twelve months, and particularly high (68-95%) for oxybutynin. Two open-label extensions of RCTs of fesoterodine 8 mg showed adherence rates at two years of 49-84% [179, 180].

A longitudinal disease analyser database study has indicated an increasing discontinuation rate, following treatment with anticholinergics, from 74.8% at one year to 87% at three years [181].

Several of the RCTs tried to identify the factors associated with low/lower adherence or persistence of anticholinergics. These were identified as:

- low level of efficacy (41.3%);
- adverse events (22.4%);
- cost (18.7%), although higher adherence rates were observed when drugs were provided at no cost to patients [182].

Other reasons for poor adherence included:

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

4.1.4.2.1.4 Summary of evidence and recommendations for anticholinergic drugs

Summary of evidence	**LE**
Anticholinergic drugs are effective in improving OAB symptoms, decreasing UUI episodes, decreasing daily urgency and frequency episodes and increasing mean voided volumes, compared with placebo.	1a
Anticholinergic drugs caused higher adverse events than placebo including dry mouth, cognitive impairment, and constipation.	1a
Once daily extended-release formulations are associated with lower rates of adverse events compared to IR preparations.	1b
Transdermal oxybutynin is associated with lower rates of dry mouth than oral anticholinergic drugs but has a higher rate of withdrawal due to skin reactions.	1b
Higher doses of anticholinergic drugs are more effective to improve OAB symptoms but exhibit a higher risk of adverse effects.	1a
No anticholinergic drug is clearly superior to another for cure or improvement of OAB/UUI.	1a
The combination of antimuscarinics plus another treatment modality was more effective than antimuscarinics alone in improving OAB.	1a
Adherence to anticholinergic treatment is low and decreases over time because of lack of efficacy, adverse events and/or cost.	2a
Most patients will stop anticholinergic agents within the first three months.	2a

Recommendations	**Strength rating**
Use a shared decision-making process involving both clinicians and patients when selecting the appropriate pharmacotherapy for overactive bladder (OAB).	Strong
Offer anticholinergic drugs to woman with OAB who fail conservative management.	Strong
Consider extended-release formulations of anticholinergic drugs whenever possible.	Strong
If an anticholinergic treatment proves ineffective, consider dose escalation, offering an alternative anticholinergic formulation, or the use of a beta-3 agonist (alone or in combination with an anticholinergic).	Strong
Encourage early review (of efficacy and adverse effects) of patients on anticholinergic medication for OAB.	Strong

4.1.4.2.2 Beta-3 Agonists

Beta-3 adrenoceptors are the predominant beta receptors expressed on detrusor smooth muscle cells and their stimulation is thought to induce detrusor relaxation. Mirabegron was the first clinically available beta-3 agonist. Vibegron is another beta-3 agonist commercially available in some countries.

High certainty evidence for beta-3 agonists at three months:

- Mirabegron at doses of 25, 50 and 100 mg results in significantly greater reduction in UI episodes, urgency episodes and micturition frequency than placebo, with no difference in the rate of common adverse events in an SR [183]. The dry rates in most of these trials are 35-40% for placebo and 43-50% for mirabegron. In all trials the significant differences were consistent only for improvement but not for cure of UI.
- The most common adverse events in the mirabegron groups were hypertension (7.3%), nasopharyngitis (3.4%) and UTI (3%), with the overall rate similar to that with placebo [184-186].
- Vibegron (75 mg or 100 mg) resulted in significant improvement of urgency episodes and UUI episodes and mean voided volume compared to placebo [185] and also compared to imidafenacin and tolterodine [187].
- There was no statistical difference between mirabegron and anticholinergics in decreasing OAB symptoms on bladder diaries and symptom questionnaires on short-term follow-up (up to twelve weeks). However, at one year follow-up, there was statistically significant decrease in OAB symptoms in favour of mirabegron [188].
- Beta-3 agonists were significantly more effective than antimuscarinics in reducing nocturia episodes [156].

Moderate certainty evidence for beta-3 agonists at three months:

- No risk of QTc prolongation [189] and no raised intraocular pressure [190] were observed up to the 100 mg dose of mirabegron; however, patients with uncontrolled hypertension or cardiac arrhythmia were excluded from these trials. There is no significant difference in the rate of adverse effects at different doses of mirabegron [186].
- Combination treatment with mirabegron 50 mg and solifenacin 5 mg had a higher chance of achieving clinically meaningful improvement in UI as compared to dose escalation of solifenacin [191].
- Both vibegron and mirabegron were more efficacious than placebo at reducing the frequency of micturition, incontinence, urgency, urgency incontinence, and nocturia in an SR of eleven studies. Only mirabegron had a higher risk of nasopharyngitis and cardiovascular adverse events compared to placebo [192].

Low certainty evidence for beta-3 agonists versus anticholinergics:

- There is no significant differences between antimuscarinics and beta-3 agonists in reduction of mean symptoms score, urgency episodes, frequency episodes UUI episodes, or voided volumes at three months [156], but mirabegron may be more effective at one year [188].
- An SR of five studies reported that Vibegron 75 mg results in greater reduction in total UI episodes compared to mirabegron 50 mg and tolterodine 4 mg [193].
- Data from a large Canadian Private Drug Plan database suggest a higher adherence rate for mirabegron compared to anticholinergics [194].

4.1.4.2.2.1 Summary of evidence and recommendation for Beta-3 agonists

Summary of evidence	**LE**
Mirabegron and vibegron are better than placebo for improvement of OAB/UUI symptoms.	1a
Adverse event rates with mirabegron and vibegron are similar to those of placebo.	1a
Beta-3 agonists are as effective as antimuscarinics in the management of OAB but with lower dry mouth rates.	1a
Patients inadequately treated with solifenacin 5 mg may benefit more from the addition of mirabegron rather than dose escalation of solifenacin.	1b

Recommendations	**Strength rating**
Offer beta-3 agonists to women with OAB who fail conservative management.	Strong
Offer mirabegron as an additional therapy in patients who are inadequately treated with solifenacin 5 mg.	Weak

4.1.4.2.3 Anticholinergics and beta-3 agonists: elderly patients and cognition

Systematic reviews have included sections on the efficacy and safety of anticholinergics in elderly patients [163, 167] but an older SR found inconclusive evidence of the impact of anticholinergics on cognition [195].

Two more longitudinal cohort studies in patients using anticholinergic drugs showed deterioration in cognitive function, alteration in central nervous system metabolism and an association with brain atrophy [196, 197]. As most of the study periods are short (four to twelve weeks), the long-term impact of anticholinergic agents specifically approved for OAB treatment on specific patient cohorts are poorly understood [198-201].

- *Oxybutynin:* There is evidence that oxybutynin IR may cause/worsen cognitive dysfunction in adults [198, 200, 202, 203]. Whilst short-term trials showed no effect on recent memory or other cognitive functions [203], prospective studies showed cumulative cognitive deterioration associated with prolonged use (mean follow-up, 7.3 years) of anticholinergic medication including oxybutynin [196]. Another prospective cohort study including 376 nursing home residents aged 65 and older taking oxybutynin and tolterodine showed a decline in activities of daily living after a median follow-up of 141 days, in spite of concomitant treatment with cholinesterase inhibitors [204].

- *Solifenacin:* One pooled analysis [205] showed that solifenacin did not increase cognitive impairment in elderly patients. No age-related differences in the pharmacokinetics of solifenacin in different age groups were found, although more frequent adverse events in patients aged > 80 years were observed. No cognitive effect on healthy elderly volunteers was shown [206]. In a sub-analysis of a large trial, solifenacin 5-10 mg improved symptoms and QoL in people aged ≥ 75 years who had not responded to tolterodine [207]. In patients with mild cognitive impairment, aged ≥ 65 years, solifenacin showed no difference in efficacy between age groups and a lower incidence of most adverse effects compared to oxybutynin IR [203, 208].

- *Tolterodine:* No change in efficacy or adverse effects related to age has been reported, although a higher discontinuation rate was found for both tolterodine and placebo in elderly patients [198]. Two RCTs in elderly patients found similar efficacy and adverse effect profile to those in younger patients [209-212]. *Post hoc* analysis has shown little effect on cognition. One non-randomised comparison showed lower rates of depression in elderly participants treated with tolterodine extended release compared to oxybutynin IR [213]. Duration of the RCTs was short (twelve weeks).

- *Darifenacin:* Two RCTs in the elderly population (one in patients with UUI and the other in volunteers) concluded that, compared with placebo, darifenacin was effective with no risk of cognitive change, measured as memory scanning tests [214, 215]. Another study on darifenacin and oxybutynin ER in elderly people concluded that the two agents had similar efficacy, but that cognitive function was more often affected in the oxybutynin ER arm [200].

- *Trospium chloride:* Trospium does not appear to cross the blood-brain barrier in healthy individuals due to its molecular characteristics (quaternary amine structure and hydrophilic properties). Two studies in healthy volunteers using electroencephalography showed no effect from trospium, while tolterodine caused occasional changes and oxybutynin caused consistent changes [216, 217]. No evidence as to the comparative efficacy and adverse effect profiles of trospium in different age groups are available. However, there is some evidence that trospium does not impair cognitive function in Alzheimer's disease patients if combined with cholinesterase inhibitors over a six month period [201], or in non-cognitively impaired patients over shorter periods (twelve weeks) [218] and that it is effective compared to placebo in the elderly [219].

- *Fesoterodine:* Pooled analyses of the RCTs of fesoterodine confirmed the efficacy of 8 mg but not 4 mg dose in patients aged > 75 years [179]. Adherence was lower in patients aged > 75 years but effects on mental status were not reported [171, 179, 220]. Another RCT showed efficacy of fesoterodine in vulnerable elderly people with no differences in cognitive function at twelve weeks [221].

- *Mirabegron:* Analysis of pooled data from three RCTs showed efficacy and safety of mirabegron in elderly patients *[222]*.

4.1.4.2.3.1 Applicability of evidence to the general elderly population

It is not clear how much the data from pooled and subgroup analyses from large RCTs can be extrapolated to a general ageing population. Community-based studies of the prevalence of anticholinergic adverse effects may be the most helpful [223]. When starting anticholinergics in elderly patients, mental function should be assessed and monitored [224]. No consensus exists as to the best mental function test to detect changes in cognition [204, 225].

4.1.4.2.3.2 Anticholinergic burden

Several drugs have anticholinergic effects and, if another anticholinergic drug is prescribed, possible cumulative effects on cognition should be considered. Lists of drugs with anticholinergic properties are available from several sources [226].

Two SRs of largely retrospective cohort studies showed a consistent association between long-term anticholinergic use and cognitive dysfunction [227, 228]. Longitudinal studies in older people over two to four years have found increased rates of cognitive decline in patients on anticholinergics or drugs with anticholinergic effects [196, 197, 229, 230]. It is unclear whether there is a direct correlation between cognitive dysfunction caused by medication and the long-term risk of development of dementia.

4.1.4.2.3.3 Summary of evidence and additional recommendations for use of anticholinergic and beta-3 agonists in elderly patients

Summary of evidence	**LE**
Anticholinergic drugs are effective in elderly women suffering from OAB/UUI.	1b
Mirabegron has been shown to be efficacious and safe in elderly women suffering from OAB.	1b
In older women the cognitive impact of drugs with anticholinergic effects is cumulative and increases with length of exposure.	2
Oxybutynin may worsen cognitive function in elderly women.	2
Darifenacin, fesoterodine, solifenacin and trospium have not been shown to cause cognitive dysfunction in elderly women in short-term studies.	1b

Recommendations	**Strength rating**
Long-term anticholinergic treatment should be used with caution in elderly women, especially those who are at risk of, or have pre-existing cognitive dysfunction.	Strong
Assess anticholinergic burden and associated comorbidity in women being considered for anticholinergic therapy for overactive bladder syndrome.	Strong

4.1.4.2.4 Oestrogens

Oestrogen treatment for UI has been tested using oral, transdermal, and vaginal routes of administration. Vaginal (local) treatment is primarily used to treat symptoms of vaginal atrophy in post-menopausal women. Available evidence is related mainly to SUI, and although some reviews include participants with UUI, it is difficult to generalise the results to women with predominantly OAB/UUI.

The association of LUTS with genitourinary syndrome of menopause (GSM) should be considered [231]. Genitourinary syndrome of menopause is a new term that describes various menopausal symptoms and signs associated with physical changes of the vulva, vagina and LUT. These include mucosal pallor/erythema, loss of vaginal rugae, tissue fragility/fissures, vaginal petechiae, urethral mucosal prolapse, introital retraction and vaginal dryness. There is evidence from a SR to suggest benefit from vaginal oestrogen therapy in GSM [232]. All vaginal oestrogens demonstrated superiority in objective and subjective end points of GSM compared with placebo. Only some trials demonstrated superiority vs. placebo in urogenital symptoms (UI, recurrent UTI, urgency, and frequency). No significant difference was observed between various doses and dosage forms of vaginal oestrogen products. Vaginal oestrogen showed superiority over vaginal lubricants and moisturisers for the improvement of objective clinical end points of vulvovaginal atrophy but not for subjective end points [232].

Available evidence suggests that vaginal treatment with oestradiol and oestriol is not associated with increased risk of thromboembolism, endometrial hypertrophy, and breast cancer that is seen with systemic administration [233-235].

4.1.4.2.4.1 Summary of evidence and recommendation for oestrogen therapy

Summary of evidence	**LE**
Vaginal oestrogen therapy may improve symptoms associated with GSM, of which OAB may be a component.	1a

Recommendation	Strength rating
Offer vaginal oestrogen therapy to women with LUTS and associated symptoms of genitourinary syndrome of menopause.	Weak

4.1.4.2.5 Placebo and nocebo

Placebo has a clear effect on the improvement of OAB signs and symptoms, and the overall placebo responses in various outcomes studied are statistically significant and, for some of the outcomes, possibly clinically significant. A SR including 57 studies with 12,901 patients showed a standardised mean difference of -0.45 for daily micturition episodes, -0.33 for daily nocturia episodes, -0.46 for UUI episodes, -0.50 for daily urgency episodes, -0.51 for daily incontinence episodes, and 0.25 for volume voided per micturition [236]. The same group published a SR with meta-analysis of data retrieved from 57 RCTs on the nocebo effect of pharmacotherapy in patients with OAB (up to 80% females). They reported dry mouth as the most common reported adverse event with mean rate of 4.9%, followed by constipation 2.6%. The authors concluded that HCPs should appreciate the possible positive and negative patient expectation regarding pharmacotherapy for OAB in order to optimise the individual outcomes [236]. The placebo response seems to be non-negligible in OAB, supporting the requirement for placebo control in RCTs.

4.1.4.2.6 Saw palmetto extract

Saw palmetto has been investigated for its anticholinergic properties. An RCT of 76 patients reported an improvement in frequency and nocturia symptoms with 320mg of saw palmetto extract vs. placebo [237]. Further large, high-quality trials are needed to corroborate these findings before it can be more widely recommended.

4.1.4.3 Surgical management

4.1.4.3.1 Bladder wall injection of botulinum toxin A

OnabotulinumtoxinA (onabotA; BOTOX®) 100 U is licenced in Europe to treat OAB with persistent or refractory UUI in adults of both sexes [238, 239]. Surgeons should be aware that other doses of onabotA and other formulations of botulinumtoxin A, abobotulinumtoxin A and incobotulinumtoxin A, are not licensed for use in OAB/UUI. Doses for onabotA are not transposable to the other brands of onabotulinumtoxinA. The continued efficacy of repeat injections is usual, but discontinuation rates may be high [240, 241]. The most important adverse events related to onabotA 100 U injection detected in the regulatory trials were UTI and an increase in PVR volume that may require IC [242].

A SR included ten studies on 2,055 patients comparing intravesical onabotA injection with placebo. OnabotulinumtoxinA was more effective than placebo in improvement of mean symptoms score, reduction of mean urgency episodes, mean UUI episodes, mean frequency episodes, mean nocturia episodes [156]. No statistically significant difference was found between onabotA and placebo in change of mean voided volumes or maximum cystometric capacity.

OnabotulinumtoxinA was associated with significantly higher rates of voiding dysfunction compared to placebo at both 100-unit dose and 200-unit dose, and significantly higher rates of UTI both at 100-unit dose and 200-unit dose.

A Cochrane review reported no significant difference in PVR volume between the onabotA and placebo groups [243].

Quality of life was substantially improved in the onabotA arm, as shown by the > 2.5 times improvement in Incontinence Quality of Life Questionnaire (I-QOL) scores compared to baseline. Cohort studies have shown the effectiveness of bladder wall injections of onabotA in elderly and frail elderly people [244], although the success rate might be lower and the PVR volume (> 150 mL) higher in this group.

The median time to request retreatment in the pooled analysis of the two RCTs was 24 weeks [239, 242]. Follow-up over 3.5 years showed consistent or increasing duration of effect for each subsequent treatment, with a median of 7.5 months. Considerable differences were noted in patients' outcomes on secondary analysis [245].

Two RCTs on 545 patients compared onabotA injections with antimuscarinics. OnabotulinumtoxinA was significantly more effective in curing UUI, but no significant difference was noted in the reduction of mean UUI episodes. However, it was associated with significantly higher rates of voiding dysfunction than antimuscarinics, and UTIs [156].

A meta-analysis of six studies reported no significant difference between sub-urothelial and intradetrusor injection techniques in any efficacy parameters and with no difference in rate of adverse events [246].

Identification of DO in urodynamics does not appear to influence the outcome of onabotA injections in patients with UUI [247].

4.1.4.3.1.1 Summary of evidence and recommendations for bladder wall injection of onabotulinumtoxinA

Summary of evidence	**LE**
A single treatment session of onabotA (100 U) injected in the bladder wall is more effective than placebo at curing and improving UUI/OAB symptoms and improving QoL.	1a
There is no evidence that repeated injections of onabotA have reduced efficacy, but discontinuation rates are high.	2a
There is a risk of voiding dysfunction, increased PVR volume and UTI with onabotA injections.	1a
The risk of bacteriuria after onabotA (100 U) injection is high but the clinical significance of this remains uncertain.	1b
OnabotulinumtoxinA is more effective in curing UUI but similarly effective in reducing mean UUI episodes compared with antimuscarinics.	1a
OnabotulinumtoxinA is associated with higher rates of voiding dysfunction than antimuscarinics.	1a
There is no difference in outcomes between sub-urothelial and intradetrusor onabotA injection techniques.	1a

Recommendations	**Strength rating**
Offer bladder wall injections of onabotulinumtoxinA (100 U) to patients with overactive bladder/urgency urinary incontinence refractory to conservative therapy or drug treatment.	Strong
Warn patients of the limited duration of response, risk of urinary tract infection and possible prolonged need for intermittent catheterisation prior to offering treatment with onabotulinumtoxinA.	Strong

4.1.4.3.2 Sacral nerve stimulation

Sacral nerve stimulation involves placing electrodes adjacent to the sacral nerve roots and delivering an electric current to the area via an attached battery implanted in the buttock. This delivers low-amplitude stimulation resulting in modulation of neural activity and stabilisation of bladder electrical activity through a mechanism that is, as yet, not fully understood. In most centres, test stimulation with a temporary or permanent electrode is performed to assess response, before undertaking permanent stimulator implantation. Currently, the only reliable predictor for treatment success in SNS is test stimulation. A SR did not find predictive factors of success due to low level of evidence of included studies (small, retrospective, and heterogeneous populations) [248].

All randomised studies suffer from the limitation that patients cannot be blinded to the treatment allocation since all recruited patients have to respond to a test phase before randomisation.

The ROSETTA trial randomised 386 women with refractory UUI to SNS (n = 194 women) or intradetrusor injection of onabotA (n = 192 women) [249]. At two years, the authors found no statistically significant difference between SNS and onabotA in improvement of mean symptoms scores on OABq-SF or in reducing the mean UUI daily episodes. Patients reported significantly higher satisfaction with onabotA, but also significantly higher rates of recurrent UTIs than SNS (24% vs. 10%, respectively). On the other hand, SNS was associated with 9% removal rate and 3% revision rate at two-years follow-up.

The INSITE trial randomised 70 (94% women) patients to SNS implantation and 77 patients (92% women) to receive antimuscarinics [250]. At six months follow-up, results showed statistically significant higher success rate for SNS compared to antimuscarinics - success was defined as > 50% improvement in daily UUI or frequency episodes. Adverse events occurred in 30% and 27% of SNS and antimuscarinics trial arms, respectively, none were serious. SNS was associated with higher rates of UTIs and was associated with implant site infection and lead migration in 3.4% of cases each.

A Cochrane review [251] identified three RCTs that investigated SNS in patients with refractory UUI. The majority of studies compared a strategy of immediate implantation with delayed implantation. One study compared implantation to controls who stayed on medical treatment and received delayed implantation at six months. Fifty percent of the immediately implanted group had > 90% improvement in UUI at six months compared with 1.6% of the control group [252]. The effect on QoL measured by the SF-36, was unclear as it differed between the groups in only one of the eight dimensions. The other RCT achieved similar results, although these patients had already been included in the first report [253].

The three-year results from the French SOUNDS study [254] a multicentre registry-based study reported 72% response rate (defined as > 50% improvement in UUI symptoms) with a 33% revision rate and 13% removal rate. At five years these results were 68% response rate, 39% revision rate and 15% removal [255]; 44% of participants remained cured (continent) at five years.

Another SR of studies including SNS with ≥ 6 months follow-up reported dry rates of 43-56% [256]. Adverse events occurred in 50% of implanted cases, with surgical revision necessary in 33-41% [257, 258]. In a sub-analysis of the RCT similar success rates were found in patients with or without urodynamic DO [259].

4.1.4.3.2.1 Summary of evidence and recommendation for sacral nerve stimulation

Summary of evidence	**LE**
Sacral nerve stimulation is more effective than continuation of failed conservative management for OAB/UUI, but no sham controls have been used.	1b
Sacral nerve stimulation is as effective as onabotA 200 U injection at 24 months.	1b
In patients who have been implanted, at least 50% improvement of UUI is maintained in ≥ 50% of patients and up to 40% may remain cured at five years. Surgical revision rates of 30-40% at three to four years is common.	3

Recommendation	**Strength rating**
Offer sacral nerve stimulation to patients who have overactive bladder/urgency urinary incontinence refractory to anticholinergic therapy.	Strong

4.1.4.3.3 Laser treatment

A SR evaluated the use of vaginal lasers in the treatment of OAB in short term studies detailing minimal improvement [260]. No RCTs were included, the quality of reported studies were weak and long-term safety data were also lacking.

4.1.4.3.3.1 Summary of evidence and recommendation for laser treatment

Summary of evidence	**LE**
Vaginal laser therapy shows minimal OAB symptom improvement in the short term in uncontrolled trials, with minimal complications; however, long-term efficacy and safety data is lacking.	3

Recommendation	**Strength rating**
Do not offer vaginal laser therapy to treat overactive bladder symptoms outside of a well-regulated clinical research study.	Strong

4.1.4.3.4 Cystoplasty/urinary diversion

4.1.4.3.4.1 Augmentation cystoplasty

In augmentation cystoplasty (also known as clam cystoplasty), a detubularised segment of bowel is inserted into the bivalved bladder wall. Most of the evidence pertaining to cystoplasty comes from patients with neuropathic bladder dysfunction. One study did not find any difference between bivalving the bladder in the sagittal or coronal plane [261, 262]. The procedure can be done, with equal success by open or robotic techniques, although the latter takes more time [263].

There are no RCTs comparing bladder augmentation to other treatments for patients with OAB/UUI.

A large case series of bladder augmentation in a mixed population of idiopathic and neurogenic UUI included 51 women [264]. 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. The results for idiopathic DO (58%) were less satisfactory than for neurogenic UUI (90%). Malignant transformation was not reported in this series; however, it has been documented in other series and a SR [265-267]. Fewer than 60 cases have been reported worldwide, and almost all are exclusively beyond ten years after the original cystoplasty [268].

Adverse effects are common and have been summarised in a review with five to seventeen years follow-up of > 267 cases; 61 of which had non-neurogenic UUI [269]. Short-term complications include bowel obstruction (2%), infection (1.5%), thromboembolism (1%), bleeding (0.75%) and fistula (0.4%). In the long term, patients may require IC to obtain adequate bladder emptying (38%). Other long-term effects include asymptomatic bacteriuria (70%), changes in bowel symptoms (25%), UTI (20%), metabolic disturbances (16%), urinary tract stones (13%), deterioration in renal function (2%), and bladder perforation (0.75%).

It is unclear if mucolytic agents reduce mucus accumulation. The only RCT comparing various mucolytic agents did not find significant benefits with the use of N-acetylcysteine, aspirin, or ranitidine. In one small study (n = 40), subcutaneous octreotide immediately before, and for fifteen days after surgery yielded significant reductions in mucus production, the need for bladder irrigation to clear blockages, and mean duration of hospital stay [270]. Before cystoplasty, all potential complications should be outlined, and before and after surgery patients should be well supported by stoma/continence nurses.

Depending on the relative costs of onabotA and augmentation cystoplasty, the latter can be cost-effective within five years if the complication rate is low and duration of effect of onabotA is < 5 months [271].

4.1.4.3.4.2 Detrusor myectomy (bladder auto-augmentation)
Detrusor myectomy aims to increase bladder capacity and reduce storage pressure by incising or excising a portion of the detrusor muscle, to create a bladder mucosal bulge or pseudo-diverticulum. It was initially described as an alternative to bladder augmentation in children [272].

Two case series in adult patients with idiopathic and neurogenic bladder dysfunction demonstrated poor long-term results caused by fibrosis of the pseudo-diverticulum [273, 274]. This technique is rarely, if ever, used nowadays.

4.1.4.3.4.3 Urinary Diversion
Urinary diversion remains a reconstructive option for patients with intractable UI after multiple pelvic procedures, radiotherapy or pelvic pathology leading to irreversible sphincteric incompetence or fistula formation. Options include ileal conduit urinary diversion, orthotopic neobladder and heterotopic neobladder with continent catheterisable conduit. There is insufficient evidence to comment on which procedure leads to the most improved QoL.

A small study comparing ileal with colonic conduits concluded that there are no differences in the relative risks (RR) of UUT infection and uretero-intestinal stenosis. However, no studies have specifically examined these techniques for treatment of intractable OAB/UUI [261]. Therefore, careful consideration of which operation is undertaken depends on thorough pre-operative counselling, access to stoma/continence nurses, as well as patient factors to allow for fully informed patient choice.

4.1.4.3.4.4 Summary of evidence and recommendations for cystoplasty/urinary diversion

Summary of evidence	**LE**
There is limited evidence of the effectiveness of augmentation cystoplasty and urinary diversion specifically for treatment of idiopathic OAB or UUI.	3
Augmentation cystoplasty and urinary diversion are associated with high risks of short- and long-term severe complications.	3
The need to perform IC following augmentation cystoplasty is common.	3
There is no evidence comparing the efficacy or adverse effects of augmentation cystoplasty to urinary diversion.	3
Detrusor myomectomy is associated with poor long-term results.	3

Recommendations	Strength rating
Ensure patient counselling and life-long support both prior to and after major surgery as a treatment for overactive bladder (OAB) is provided by a specialist nurse or equivalent health care provider.	Strong
Offer augmentation cystoplasty to patients with OAB/urgency urinary incontinence (UUI) who have failed all other treatment options and have been informed about all possible complications.	Weak
Inform patients undergoing augmentation cystoplasty of the high risk of intermittent catheterisation (ensure they are willing and able to do so) and that they will need life-long surveillance.	Strong
Do not offer detrusor myectomy as a treatment for UUI.	Weak
Only offer urinary diversion to patients who have failed less-invasive therapies for the treatment of OAB/UUI, who will accept a stoma and have been warned about the possible small risk of malignancy.	Weak

4.1.5 ***Follow-up***

Follow-up for women with OAB is guided by the type of treatment instituted and local service capacity. Standardisation of follow-up pathways can therefore be difficult. Here, we provide recommendations based on best practice and standards from clinical trials.

4.1.5.1 Recommendations for follow-up of patients with overactive bladder

Recommendations	Strength rating
Offer early follow-up to women who have been commenced on anticholinergic or beta-3 agonist therapy.	Strong
Offer repeat injections of onabotulinumtoxinA, as required, to women in whom it has been effective (refer to the manufacturer's guidance regarding the minimum timeframe for repeat injections).	Strong
Offer life-long surveillance to women who have a sacral nerve stimulation implant to monitor for lead displacement, malfunction, and battery wear.	Strong
Offer cystoscopic surveillance to women who are ten years or more post-augmentation cystoplasty due to the small risk of malignancy.	Weak

4.2 Stress urinary incontinence

4.2.1 ***Epidemiology, aetiology, pathophysiology***

Stress urinary incontinence, defined as the involuntary loss of urine on effort or physical exertion, is a significant health problem worldwide with social and economic impact on women and society. It is estimated that the number of women in the USA with UI will have increased from 18.3 million in 2010 to 28.4 million in 2050 [275]. The prevalence of SUI appears to peak between 45 and 59 years of age [276].

Data regarding the association of UI with ethnicity are conflicting. In several studies, SUI is more common in white women than in women of African American or Asian American origin [277, 278]. Other factors positively associated with SUI include parity, obesity [279], previous hysterectomy or pelvic surgery, diabetes mellitus [280] and pulmonary disease [281]. Mild-to-moderate physical activity decreases the risk of UI, but female athletes are about three times more likely to have SUI compared to controls [282]. A meta-analysis including six studies with a total sample size of 3,678 cases showed that the risk for SUI in women with metabolic syndrome was three times those without [283].

Two common, often overlapping, mechanisms for SUI have been described: (1) urethral hypermobility resulting from loss of support of the bladder neck and urethra; and (2) weakness of the urinary sphincter itself (intrinsic sphincter deficiency), which can result from trauma, radiotherapy, previous pelvic or uro-gynaecological surgery, neurological disease, or ageing.

The mechanism behind urethral hypermobility as a cause of SUI is based on the "vaginal hammock" hypothesis [284]. The endopelvic fascia, which is attached to the upper (abdominal) side of the PFMs, links the muscles to the vagina and represents the "hammock", which can compress the urethra during rest and activity. This compression, combined with intrinsic urethral sphincter pressure, supports, and maintains the urethra in the

correct and closed position, preventing involuntary loss of urine, despite any increases in intravesical pressure. Damage to the supporting tissues (particularly the arcus tendinous fasciae pelvis, the central part of the fascia) can result in urethral hypermobility. Consequently, rather than being compressed at times of increased intra-abdominal pressure, the urethra moves caudally, funnelling the bladder neck, and is no longer compressed, resulting in SUI [284, 285]. In general, almost all treatments are used for both subtypes of SUI, but in general most treatments are more successful in patients with some degree of urethral hypermobility than for isolated intrinsic weakness of the urinary sphincter [286].

*4.2.2 **Classification***

Patients with SUI can be classified as uncomplicated and complicated [287]. The Panel has reached a consensus on the definition to be used throughout this guideline document:

- Women with uncomplicated SUI: no prior surgery for SUI, extensive pelvic surgery, or pelvic radiotherapy; no neurogenic LUT dysfunction; no bothersome genitourinary prolapse; absence of OAB or voiding symptoms; and no medical conditions that affect the LUT. In cases where additional significant storage symptoms, especially OAB, are present, consider a possible diagnosis of MUI (see Section 4.3).
- Women with complicated SUI: previous surgery for incontinence or extensive pelvic surgery; history of pelvic irradiation; presence of anterior or apical POP; presence of voiding symptoms or neurogenic LUT dysfunction; concomitant OAB/UUI; congenital abnormalities such as bladder exstrophy. Neurogenic LUT dysfunction is reviewed in the EAU Guidelines on Neuro-Urology and will not be considered further in these guidelines [11]. The treatment of LUTS associated with genitourinary prolapse has been included in these guidelines (see Section 4.7).

*4.2.3 **Diagnostic evaluation***

4.2.3.1 History and physical examination

There is universal agreement that taking a history and carrying out physical examination, should be the first steps in the assessment of anyone with UI despite the lack of evidence to show that it affects patient outcomes. When the history categorises UI as probable SUI, the presence of complicated or uncomplicated SUI can also be determined. Those patients who require rapid referral to an appropriate specialist can also often be identified from the clinical history.

Initial assessment should include abdominal examination, vaginal examination and careful assessment of any associated POP, examination of the perineum and evaluation of PFM strength, as well as a focussed neurological examination. An attempt to reproduce the SUI should be made. A standing cough test has greater sensitivity for diagnosis of SUI compared with a supine cough test [288]. Despite this, the ICS has proposed a standardisation of the female cough stress test that includes a supine/lithotomy position with 200-400 mL fluid in the bladder and one to four coughs [289].

4.2.3.1.1 Summary of evidence and recommendation for history and physical examination

Summary of evidence	LE
A standing cough stress test is more sensitive than a supine test.	1b

Recommendation	Strength rating
Take a full clinical history and perform a thorough physical examination including standardised cough stress test in all women presenting with stress urinary incontinence.	Strong

4.2.3.2 Patient questionnaires

To date, there is not one questionnaire that fulfils all requirements for the assessment of women with SUI. Some questionnaires are used for prevalence studies; others are responsive to change and may be used to measure outcomes, although evidence on their sensitivity is inconsistent [19, 20].

According to a SR the top five reported validated PROMs are Patient Global Impression of Improvement (PGI-I), Urogenital Distress Inventory-Short Form (UDI 6), International Consultation on Incontinence Questionnaire-Urinary Incontinence-Short Form (ICIQ-UI SF), Incontinence Impact Questionnaire-Short Form (IIQ-7) and King's Health Questionnaire (KHQ). There is no evidence to indicate whether use of QoL or condition-specific questionnaires has an impact on treatment outcome [290].

4.2.3.2.1 Summary of evidence and recommendation for patient questionnaires

Summary of evidence	LE
Validated condition-specific symptom scores assist in the screening for and categorisation of UI.	3
Validated symptom scores measure the severity and associated bother of SUI.	3
Both condition-specific and general health status questionnaires measure current health status and are responsive to change following treatment.	3

Recommendation	Strength rating
Use a validated condition-specific questionnaire as part of the standardised assessment of patients with stress urinary incontinence.	Strong

4.2.3.3 Post-void residual volume

It is important to evaluate PVR volume in patients with SUI; particularly in those who also have voiding symptoms or POP. The prevalence of a significant PVR volume in patients with SUI is uncertain, partly because of the lack of a standard definition of an abnormal PVR volume. Most studies investigating PVR volume have not included patients with SUI. In general, the data on PVR volume can only be applied with caution to adults with non-neurogenic SUI. In a cohort study of > 900 women with SUI, there was good correlation between PVR volume estimated by US and measured by catheterisation and the documented PVR was on average less than 50 ml [52].

4.2.3.3.1 Summary of evidence and recommendations for post-void residual volume

Summary of evidence	LE
The majority of women with SUI do not have a significant PVR volume.	3
There is good correlation between PVR volume estimated using US and measured via catheterisation in women with SUI.	3

Recommendations	Strength rating
Measure post-void residual (PVR) volume in patients presenting with stress urinary incontinence (SUI), particularly when assessing those with voiding symptoms or complicated SUI.	Strong
When measuring PVR volume, use ultrasound in preference to catheterisation.	Strong
Monitor PVR volume in patients scheduled for treatment that may cause or worsen voiding dysfunction, including surgery for SUI.	Strong

4.2.3.4 Urodynamics

The role of urodynamics in SUI evaluation remains poorly defined and is still under debate.

Clinical diagnosis of incontinence and cystometric findings often do not correlate [61, 62]. The diagnostic accuracy of urethral pressure profilometry [63] and VLPP measurement in SUI is generally poor [54]. Measurement of MUCP correlates, albeit weakly, with incontinence severity [63], and there is conflicting evidence about its reproducibility [59, 60]. Methods of recording MUCP cannot be compared meaningfully [291]. Valsalva leak point pressures are not standardised and there is minimal evidence about reproducibility. Valsalva leak point pressures did not reliably assess incontinence severity in a cohort of women selected for surgical management of SUI [64]. The predictive value of the tests regarding treatment outcome remains unclear.

A Cochrane review including seven RCTs showed that urodynamic tests increased the likelihood of avoiding surgery for SUI. However, there is no evidence that this influence on decision-making alters the clinical outcome of treatment within trial populations [72].

A high-quality RCT (n = 630) compared office evaluation without urodynamics, to office evaluation including urodynamics in women with clinically demonstrable SUI about to undergo surgery. While urodynamics changed the clinical diagnosis in 56% of women [292], there was no difference in severity of SUI or any secondary

outcome at twelve months' follow-up after SUI surgery [75]. Another study also found that omission of urodynamics in the pre-operative work-up of SUI did not lead to inferior results [293]. Patients in whom urodynamics were discordant with clinical assessment (*n* = 109) were randomly allocated to receive either immediate surgery or individually tailored therapy based on the urodynamic findings. In this trial, performing immediate surgery, irrespective of the result of urodynamics, did not result in inferior outcomes [294]. An RCT, in which 145 women were randomised to retropubic or trans-obturator MUS, concluded that when patients were stratified according to pre-operative VLPP (≤ or > 60 cm H_2O), it was not linked to outcome after both synthetic MUS procedures [295]. Another study reported conflicting evidence with Valsalva leak point pressures or MUCP in the lowest quartile was predictive of synthetic MUS failure at twelve months [79].

The Panel recognises that it is often valuable to use urodynamic test results to help select the optimum surgical procedure, but the evidence outlined above suggests that performing urodynamics in patients with uncomplicated SUI, which can be diagnosed based on detailed clinical history and demonstrated at examination, is not necessary. The role of urodynamics in complicated SUI is still under debate [296]. However, the Panel consensus is that urodynamics should definitely be considered in cases of SUI with associated storage symptoms; cases in which the type of incontinence is unclear; cases in which voiding dysfunction is suspected; and cases with associated POP or prior surgery for SUI. This is in line with other guideline documents in this area [61, 73].

4.2.3.4.1 Summary of evidence and recommendations for urodynamics

Summary of evidence	**LE**
Pre-operative urodynamic testing in women with uncomplicated, clinically demonstrable, SUI does not improve surgical outcome for SUI.	1b
There is no consistent correlation between urethral function tests and subsequent success or failure of SUI surgery.	3
There is no consistent evidence that pre-operative DO is associated with surgical failure of MUS in women.	3

Recommendations	**Strength rating**
Perform pre-operative urodynamic tests in cases of stress urinary incontinence (SUI) with co-existing additional storage symptoms; cases in which the type of incontinence is unclear; cases in which voiding dysfunction is suspected; and cases with associated pelvic organ prolapse or prior surgery for SUI.	Weak
Perform urodynamic tests if the findings may change the choice of invasive treatment.	Weak
Do not use urethral pressure profilometry or leak point pressure to grade severity of incontinence.	Strong

4.2.3.5 Pad testing

Please refer to section 3.7 for the diagnostic accuracy and predictive value of using pad testing to quantify the presence and severity of SUI. The summary of evidence and recommendations can be found in section 3.7.1.

4.2.3.6 Imaging

The role of imaging in SUI patients is limited. Studies using US and MRI have found that SUI cannot be identified by specific urethro-vesical movement patterns [297]. Increased urethral mobility after childbirth does not appear to be associated with *de novo* SUI [298]. Pelvic floor muscle training can change PFM and external urethral sphincter anatomy, specifically higher bladder neck position and narrower levator hiatus dimensions, thicker external urethral sphincter, increased cross-sectional area of PFM, and improvement in PFM damage and blood flow. Research on MUS (mid-urethral sling) mechanisms indicates MUS placement reduces mid-urethra mobility but not bladder neck mobility [105]. A wider gap between the symphysis and sling post-MUS surgery correlates with lower SUI cure rates [106]. Trans-labial US has been studied to assess tape functionality, with findings suggesting tape position relative to the urethra affects treatment outcomes [299]. The general role of US in evaluating and following up on SUI in women remains unclear, needing further research to define its clinical relevance [300].

Various imaging studies have examined the relationship between sphincter volume and function [301], and sphincter volume and surgical outcomes in women [302]. However, no imaging test has predicted SUI treatment outcomes. Pelvic floor imaging can identify levator ani detachment and hiatus size, but evidence linking these findings to clinical benefits post-SUI treatment is limited.

4.2.3.6.1 Summary of evidence and recommendation for imaging

Summary of evidence	**LE**
Imaging can reliably be used to measure bladder neck and urethral mobility, although there is no evidence of clinical benefit for patients with UI.	2b

Recommendation	**Strength rating**
Do not carry out imaging of the upper or lower urinary tract as part of the routine assessment of stress urinary incontinence.	Strong

4.2.4 ***Disease management***

4.2.4.1 Conservative management

4.2.4.1.1 Obesity and weight loss

Being overweight or obese are significant risk factors for LUTS and SUI, as shown in many epidemiological studies [133, 134]. Both UUI and SUI prevalence increase proportionately with BMI [303]. The proportion of overweight or obese patients undergoing incontinence surgery is higher than in the general population [134]. Conversely, young elite athletes and women who work out for fitness also exhibit a high prevalence of UI/SUI [282, 304].

Three SRs concluded that weight loss improves UI overall [132, 133, 305]. Five RCTs also reported beneficial effects on incontinence in general following surgical weight reduction programs [306-310]. The improvement in which subtype of incontinence specifically improved was not included in these papers.

A prospective study of 160 women who underwent bariatric surgery showed that weight loss significantly improved pelvic floor disorders, including UI [311]. Similar results from prospective single-centre studies indicated that bariatric surgery significantly reduced UI at eleven months and three years' post-surgery [312, 313].

4.2.4.1.1.1 Summary of evidence and recommendation for obesity and weight loss

Summary of evidence	**LE**
Obesity is one of the risk factors for LUTS and UI in women.	3
Non-surgical weight loss improves UI in overweight and obese women.	1a
Surgical weight loss improves UI in obese women.	1b

Recommendation	**Strength rating**
Encourage overweight and obese women with LUTS/stress urinary incontinence to lose weight and maintain weight loss.	Strong

4.2.4.1.2 Urinary containment

The evidence for urinary containment derives from the same literature as for containment in OAB-wet. The readers are therefore referred to Section 4.1.4.1.3. The summary of evidence and recommendations for urinary containment can be found in Section 4.1.4.1.3.1.

4.2.4.1.3 Pelvic floor muscle training

Pelvic floor muscle training is used to improve functional and morphological parameters of the pelvic floor, thus improving urethral stability [300]. An immediate effect of a single PFM contraction is narrowing of the levator hiatus area, increase of urethral closure pressure, and lifting of the bladder and rectum thus preventing occurrence of SUI [314-316]. In an RCT comparing intensive PFMT over a six-month period with no treatment, there were increased muscle strength and endurance, narrowing of the levator hiatus, reduced PFM length,

increased muscle volume, and lifting of the bladder neck and rectal ampulla [317]. Pelvic floor muscle training may be used to prevent SUI, e.g., in childbearing women before birth, or as part of a planned recovery programme after childbirth. Most often, PFMT is used to treat existing SUI; sometimes in combination with observation and/or palpation of the muscle contraction by the therapist, or biofeedback (using an apparatus measuring the contraction either by electromyography, manometry, dynamometry, US or MRI). Electrical stimulation and vaginal cones are also used in treatment of SUI based on an assumption of the same mechanism of action. A recent SR including five RCTs demonstrated that PFMT using telerehabilitation is a feasible and effective approach and highlighted its efficacy in patients with UI [318].

4.2.4.1.3.1 Efficacy of pelvic floor muscle training

A Cochrane review compared PFMT with no treatment or inactive control treatment and found that women with SUI in the PFMT groups were eight times more likely to report cure [319]. The review also documented significant improvement in SUI and improvement in UI QoL. Pelvic floor muscle training reduced leakage by an average of one episode per day in women with SUI. Women with SUI in the PFMT groups lost significantly less urine in short (up to one-hour) pad tests. The comparison of short pad tests showed considerable heterogeneity, but the findings still favoured PFMT when using a random-effects model. Women in the PFMT group were also more satisfied with treatment and their sexual outcomes were better. Adverse events were rare and minor.

Comparison training programs on the effect of using biofeedback together with PFMT and PFMT alone must include the same amount of attention and training dosage. In a RCT (61.3% had MUI) comparing the exact same training dosage and attention between groups, use of biofeedback did not yield any additional effect [320]. Group training is cost-effective in treatment of SUI/UI compared to individual treatment [321]. Another Cochrane review concluded that combination of individual assessment/education and group training was equally effective compared to individual treatment, but again the dosage and attention differed between comparison groups [322]. In another RCT with the exact same training dosage and attention in individual and group training, group training was not inferior to individual treatment [321]. It is worth noting that all of the PFMT interventions in these reviews follow individual assessment and teaching before starting PFMT, and most interventions use some sort of measurement tool (biofeedback) in the assessment.

Both the Cochrane review and the ICI concluded that the use of vaginal cones to train the PFMs is more effective than no treatment, but it is inconclusive whether it is more or less effective than structured PFMT [319, 323, 324]. Some women are unable to maintain the cone inside, and some report discomfort and motivation problems and adherence may be low [323].

The Cochrane review [319], the ICI [324] and the National Institute for Health and Care Excellence (NICE) guidelines (2019) [61] all conclude that there is the highest level evidence (1a) to support PFMT in the treatment of SUI/MUI. All SRs conclude that PFMT is less effective if women with MUI and UUI are included in the studies and more effective with more intensive and supervised training. According to the NICE guidelines literature review, PFMT is as effective as surgery for around half of women with SUI, and due to the risks following surgery and absence of adverse effects of PFMT, they recommend three months of supervised PFMT as first-line treatment for SUI and MUI [61].

Pelvic floor muscle training supervised by certified pelvic floor physiotherapists was compared to synthetic MUS surgery in an RCT involving 460 women with moderate to severe SUI [325]. Crossover between treatment arms was allowed and 49% of women in the physiotherapy group and 11.2% of women in the surgery group crossed over to the alternative treatment. Subjective improvement was reported by 90.8% of women in the surgery group and 64.4% of women in the physiotherapy group at twelve months [325].

4.2.4.1.3.2 Long-term efficacy of pelvic floor muscle training

In a SR including nineteen studies, 1,141 women were followed-up for one to fifteen years after PFMT for SUI [326]. Meta-analysis was not performed due to high heterogeneity of outcome measures and training dosage (frequency, intensity, duration and adherence). Only two studies provided interventions during follow-up. Losses to follow-up ranged between 0% and 39%. Long-term adherence to PFMT varied between 10% and 70%. Five studies reported that the initial success rate on SUI and MUI was maintained in the long term. Long-term success based on responders in the original trial varied between 41% and 85%. Surgery rates in the long term varied between 4.9% and 58%. It was concluded that short-term outcome of PFMT can be maintained at long-term follow-up without incentives for continued training, but there is a high heterogeneity in both interventional and methodological quality in short and long-term PFMT studies [326].

4.2.4.1.3.3 Efficacy of pelvic floor muscle training in the peri-natal period

Pelvic floor muscle training to prevent SUI has been studied during pregnancy and in the postpartum period and the results are not reported separately for SUI and other subgroups of UI. A Cochrane review concluded that PFMT in women with and without UI (combined primary and secondary prevention) during pregnancy, produced a 26% reduced risk of UI during pregnancy and the mid-postnatal period [327]. Furthermore, pregnant continent women (primary prevention) who exercised the PFM during pregnancy were 62% less likely to experience UI in late pregnancy and had 29% lower risk of UI three to six months after giving birth. There is insufficient evidence for a long-term effect of antenatal PFMT beyond six to twelve months postpartum. Compared with usual care, there is no evidence that antenatal PFMT in incontinent women decreases incontinence in late pregnancy (very low-quality evidence), or in the mid- (low-quality evidence) or late postnatal periods (very low-quality evidence). The latter is based on only two RCTs with contradictory results.

There have been fewer RCTs in the postpartum period than during pregnancy [327]. No primary prevention studies were found in women after birth. For PFMT started after delivery, in a mixed group of continent and incontinent women, there was uncertainty about the effect on UI risk in the late postnatal period (three trials, 826 women; moderate-quality evidence). In postnatal women with persistent UI, PFMT has shown to be effective [22], but there is no evidence that PFMT results in a difference in UI at more than six to twelve months postpartum (three trials; 696 women; low-quality evidence). However, another RCT found that UI was less frequent in the intervention group, with 57% of patients still symptomatic, compared to 82% of controls, as was bladder-related problems with a prevalence of 27% in the intervention vs. 60% in the control group [328]. Randomised controlled trials of high interventional and methodological quality are needed in the postpartum period.

4.2.4.1.3.4 Pelvic floor muscle training in elderly women

There have been only a few RCTs on conservative management of SUI in elderly women (> 65 years) and many of the studies combined different modalities, such as BT, lifestyle modifications and PFMT [329]. Some of the studies on PFMT and SUI in the general population have included women > 65 years and PFMT seems to be equally effective in elderly women. A SR on conservative management included 23 trials, with nine of moderate-to-high methodological quality and concluded that PFMT in combination with physical training was effective in reducing SUI and improving QoL [330]. Prompted voiding and toileting assistance with functional exercise reduced UI. Other behavioural interventions such as night-time prompted voiding and waking routine had no effect on UI reduction. The most recent ICI consensus publication stated that although there are limited studies of PFMT on UI in frail elderly populations, age and frailty alone should not preclude the use of PFMT in appropriate patients with sufficient cognition to participate [22]. More high-quality RCTs, both in frail and healthy older women (> 80 years of age) are needed.

4.2.4.1.3.5 Continence Pessaries

A Cochrane review examined the evidence for continence pessaries in comparison to and in addition to other conservative management modalities [177]. The authors reported moderate to high certainty evidence that PFMT was superior to continence pessary in terms of reduction in the Urinary Distress Inventory score and continence pessary plus PFMT was superior to continence pessary alone in terms of global improvement (PGI-I).

4.2.4.1.3.6 Composite treatments for PFMT

A Cochrane review found insufficient evidence to state whether there were additional effects by adding PFMT to other active treatments (including vaginal cones, electromagnetic stimulation [EMS], biofeedback, continence pessary, drugs) when compared with the same active treatment alone for female SUI or mixed UI. However, these results should be interpreted with caution as most of the comparisons were investigated in small, single trials. Also, none of the included trials reported data on adverse events associated with the PFMT regimen, thereby making it very difficult to evaluate the safety of PFMT [177].

In an RCT, 132 women assessed by vaginal palpation to have 0-1 on the modified Oxford grading scale (unable to contract the PFM) were randomly assigned to an eight-week intervention of learning to contract via palpation, palpation with pelvic tilt, intravaginal ES, or verbal instruction [331]. The results showed palpation was significantly more effective than ES, but one third of the ES group had learned a correct PFM contraction [331]. The effect on UI measured by ICIQ-UI-SF was significantly better in the palpation group. An RCT [332] compared ES with untreated control in 64 women with 0-1 on the modified Oxford grading scale. After the intervention, the ability to contract the PFM was acquired by 36% of the experimental group and 12% of the control group. The experimental group also improved by a mean of two points more than the control group on the ICIQ-UI-SF score.

A single-blind RCT evaluated whether peri-operative supervised PFMT was superior to standard care (handout) in terms of improvements in SUI symptoms, cure rate, and/or post-operative filling or voiding symptoms among women undergoing synthetic MUS insertion for SUI. The results showed that supervised PFMT improves SUI cure rates associated with synthetic MUS insertion with OR > 3 when considering symptoms of SUI, but does not improve post-operative continence function as measured by a pad test, nor does it lead to fewer post-operative voiding or filling symptoms [333].

4.2.4.1.3.7 Summary of evidence and recommendations for pelvic floor muscle training

Summary of evidence	**LE**
Pelvic floor muscle training is better than no treatment for improving SUI and QoL in women with SUI and MUI across a range of outcomes, including cure rate, improvement rate, QoL, number and volume of urine leaks and treatment satisfaction.	1a
Pelvic floor muscle training exhibits very few adverse events and no serious adverse events.	1a
Higher-intensity, supervised treatment regimens confer greater benefit in women receiving PFMT.	1a
There is no extra benefit of combining PFMT with biofeedback.	1b
Short-term benefits of intensive PFMT can be maintained in the long term.	2a
Pelvic floor muscle training in the antenatal period is associated with a reduced risk of UI in late pregnancy and in the short term postnatally.	1a
Postpartum PFMT is effective in women with persistent UI.	1b
Mid-urethral sling surgery is superior to PFMT in women with moderate-to-severe SUI.	1b
Pelvic floor muscle training commencing in the early postpartum period improves UI in women for up to six months.	1b
There is conflicting evidence on whether the addition of ES increases the effectiveness of PFMT alone.	2a
There is low to moderate certainty evidence suggesting benefit of ES in patients with SUI, but it may be useful for learning a correct PFM contraction.	1b
There is moderate to high certainty evidence that PFMT is superior to continence pessaries in terms of urinary symptom reduction.	1a
There is moderate to high certainty evidence that the addition of PFMT to continence pessary treatment improves patients' global impression of outcome.	1a

Recommendations	**Strength rating**
Offer supervised intensive pelvic floor muscle training (PFMT), lasting at least three months, as first-line therapy to all women with stress urinary incontinence (SUI) or mixed urinary incontinence (including elderly women and pre- and postnatal women).	Strong
Ensure that PFMT programmes are as intensive as possible.	Strong
Balance the efficacy and lack of adverse events from PFMT against the expected effect and possible complications from invasive surgery for SUI.	Strong
Consider electrical stimulation for treatment of SUI, or as an adjunct for teaching PFM contraction.	Weak

4.2.4.1.4 Electromagnetic stimulation

Electromagnetic stimulation has been evaluated for its role in SUI therapy. In a double-blind RCT of EMS including 70 women with SUI, no effect of EMS over sham in any outcome was recorded [334].

4.2.4.1.5 Electrical stimulation

There is lack of consensus regarding the use of ES to treat SUI. For subjective cure of SUI, a Cochrane review found moderate-quality evidence that ES is probably better than no active treatment [335]. Similar results were found for cure or improvement of SUI, but the quality of evidence was low. There is uncertainty as to whether there is a difference between ES and sham treatment in terms of subjective cure alone because of the very low quality of evidence. For subjective cure or improvement, ES may be better than sham treatment. Any comparison between ES and PFMT and other treatments is hampered by low-quality evidence. One assessor blinded RCT found that PFMT was significantly better than either the use of vaginal cones or ES. Only PFMT showed improvement in PFM strength and SUI compared to control [336]. Adverse effects such as pain and discomfort have been reported, and ES is not tolerated by all women [335].

4.2.4.1.6 Electroacupuncture

A SR including fifteen RCTs and women with SUI treated by electroacupuncture (EA) demonstrated that EA for SUI was effective. The ICIQ-SF scores improved, and one-hour urine leakage decreased in patients undergoing EA compared with those receiving sham EA, physical exercise or medication [337].

4.2.4.1.7 Summary of evidence and recommendations for electromagnetic stimulation and Electroacupuncture.

Summary of evidence	**LE**
The outcomes of EMS for SUI do not differ from sham procedure.	1b
Electroacupuncture improved SUI outcomes.	1a

Recommendations	**Strength rating**
Do not offer EMS for SUI unless it is a part of a well-regulated and closely monitored research study.	Strong
Offer electroacupuncture in women with SUI.	Strong

4.2.4.2 Pharmacological management

4.2.4.2.1 Oestrogen

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

Oestrogen treatments for SUI have been tested via oral, transdermal, and vaginal routes. Evidence indicates that vaginal oestrogen (oestradiol and oestriol) does not carry the same risks of thromboembolism, endometrial hypertrophy, and breast cancer as systemic administration [233-235] and is mainly used for vaginal atrophy symptoms in post-menopausal women.

A Cochrane review found that vaginal oestrogen improved SUI symptoms short-term. Small, low-quality trials compared vaginal oestrogen with phenylpropanolamine, PFMT and ES, and its use as a surgery adjunct. Local oestrogen was less effective than PFMT but showed no differences compared to other treatments. The use of local oestrogen prior to mid-urethral synthetic sling surgery did not improve outcomes [233]. One trial found no significant adverse effects from vaginal oestradiol over two years [338].

In an ancillary analysis of a randomised, double-blind trial, in post-menopausal women with ≥ stage two apical and/or anterior prolapse, scheduled for transvaginal native tissue apical repair, conjugated oestrogen intravaginal cream was compared to placebo administered before and for one year post-operatively. Although the improvement in tissue quality, limited results on incontinence, sexual function, and atrophy symptoms were demonstrated [339].

Vaginal oestrogen can be administered as conjugated equine oestrogen, oestriol, or oestradiol in pessaries, rings, or creams, but optimal duration and long-term effects remain uncertain. A SR found that vaginal rings, favoured over pessaries, improved UI compared to placebo [340].

One RCT showed that adding intravaginal oestriol to vaginal ES and PFMT benefitted female SUI [341].

Local vaginal oestrogen treatment given to post-menopausal patients after MUS procedures can reduce the symptoms of daytime frequency and urinary urgency [342]. Studies of systemic HRT found that conjugated equine oestrogens increased UI risk, with no SUI improvement [335-340], while raloxifene showed no UI effect [343]. Two small RCTs using oral oestriol or oestradiol as HRT for vulvovaginal atrophy suggested that UI symptoms were improved although the evidence was unclear [61, 344].

4.2.4.2.1.1 Summary of evidence and recommendations for oestrogens

Summary of evidence	LE
Vaginal oestrogen therapy improves SUI for post-menopausal women in the short term.	1a
Neoadjuvant or adjuvant use of local oestrogens is ineffective as an adjunct to synthetic mid-urethral sling surgery for SUI.	2b
Systemic HRT using conjugated equine oestrogens does not improve SUI and may worsen pre-existing UI.	1a

Recommendations	Strength rating
Offer vaginal oestrogen therapy to post-menopausal women with stress urinary incontinence (SUI) and symptoms of vulvovaginal atrophy.	Strong
In women taking oral conjugated equine oestrogen as hormone replacement therapy (HRT) who develop or experience worsening SUI, discuss alternative HRT.	Strong

4.2.4.2.2 Duloxetine

Duloxetine inhibits the presynaptic reuptake of serotonin (5-HT) and noradrenaline (NE). In the sacral spinal cord, increased 5-HT and NE levels enhance stimulation of pudendal motor neuron receptors, boosting the resting tone and contraction strength of the urethral sphincter.

Three SRs assessed duloxetine for female SUI or MUI, showing improvement compared to placebo with no clear differences between SUI and MUI [172, 345, 346]. One study reported a 10% cure rate for UI, though no improvement in UI QoL scores was found. Another study compared duloxetine (80 mg daily) with PFMT alone, PFMT + duloxetine, and placebo, finding reduced leakage and better global improvement and QoL for combined therapy over no treatment [347].

Two open-label studies with follow-up of ≥ 1 year found high withdrawal rates due to lack of efficacy and adverse events (e.g., nausea, vomiting, dry mouth, constipation, dizziness, insomnia, somnolence, and fatigue) [348, 349].

An SR highlighted duloxetine's efficacy over placebo in women with SUI but noted increased adverse events, including mental health issues and suicidal ideation [346]. A meta-analysis of four RCTs with 1,910 women reported no suicidality, violence, or akathisia events, though discontinuation due to adverse events was about one in seven, suggesting potential harm may outweigh benefits [350]. Another meta-analysis of twelve placebo-controlled trials involving nearly 3,000 patients with major depressive disorders found no significant differences in suicide-related events between duloxetine and placebo [351].

4.2.4.2.2.1 Summary of evidence and recommendations for duloxetine

Summary of evidence	LE
Duloxetine improves SUI in women, but the chances of cure are low.	1a
Duloxetine may cause significant gastrointestinal and central nervous system adverse effects, leading to a high rate of treatment discontinuation, although these symptoms may be limited to the first weeks of treatment.	1a

Recommendations	Strength rating
Offer duloxetine (where licensed) to selected patients with stress urinary incontinence unresponsive to other conservative managements and who want to avoid invasive treatment, counselling carefully about the risk of adverse events.	Weak
Duloxetine should be initiated and withdrawn using dose titration because of the high risk of adverse events.	Strong

4.2.4.2.3 Adrenergic agonists

A Cochrane SR including 22 RCTs involving 673 women and seven different adrenergic drugs (phenylpropanolamine in eleven trials, midodrine in two, norepinephrine in three, clenbuterol in another three, terbutaline in one, eskornade in one and Ro 115-1240 in one) found weak evidence that adrenergic agonists may improve SUI. Moreover, side effects did occur but were usually minor. More evidence is needed to compare adrenergic drugs with other drugs for SUI and, also with PFMT [352].

4.2.4.3 Surgical management

4.2.4.3.1 General considerations

4.2.4.3.1 General considerations

The use of polypropylene mesh as synthetic MUS for the treatment of SUI has recently come under scrutiny following concerns about long-term complications. In some European countries such as the UK, the use of synthetic MUS has been paused and pelvic mesh was the subject of a parliamentary review published in July 2020 [353]. This review concluded that *"For many women mesh surgery is trouble free and leads to improvements in their condition. However, this is not the case for all. There is no reliable information on the true number of women who have suffered complications. While they may be in the minority, that does not diminish the catastrophic nature of their suffering or the importance of providing support to them and learning from what has happened to them"*.

The range of complications highlighted during the process of this parliamentary review included [353]:

- pain;
- recurrent infections;
- mobility issues;
- recurring or new incontinence/urinary frequency;
- recurring or new prolapse;
- haemorrhage;
- bowel issues;
- erosion of mesh; this can be into the vagina and/or other organs;
- sexual difficulties; including pain on intercourse and a loss of sex life;
- autoimmune issues;
- psychological impacts.

When considering the choice of surgical managements for SUI the Panel advises individual clinicians to abide by any national or local rules that may be in place regarding mesh surgery and to ensure they discuss initial non-surgical management such as PFMT. It is essential for clinicians to point out the deficiencies in the long-term evidence regarding mesh use in SUI with specific reference to the complications highlighted above.

In line with the recommendations from NICE [61] and the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) paper [354], the Panel agrees that surgeons and centres performing surgery should:

- be trained in the field of incontinence and for each surgical procedure they perform/offer;
- perform sufficient numbers of a procedure to maintain expertise of him/herself and the surgical team;
- be able to offer alternative surgical managements;
- be able to deal with the complications of surgery;
- provide suitable arrangements for long-term follow-up.

The establishment of accurate and complete databases registering the interventions, patient profiles and surgical complications or all surgical managements for SUI is recommended to allow the generation of robust long-term data.

Many surgical procedures are available for uncomplicated SUI patients and the Panel analysed the results of the different procedures in terms of clinical effectiveness, safety and cost-effectiveness based on the ESTER SR and economic evaluation [355] and previous SRs including those from the Cochrane Collaboration [356-360].

The outcome parameters used to evaluate surgery for SUI have been limited to:

- continence rate;
- patient-reported outcome measures;
- general and procedure-specific complications;
- generic, specific (UI) and associated (sexual and bowel) QoL.

In this context, it has to be taken into account that a number of products may no longer be available and therefore the recommendations may not be transferable to current devices. The Panel makes a strong recommendation that new devices are only used as part of a structured research programme and their outcomes monitored in a registry, until there is adequate evidence of safety and efficacy.

4.2.4.3.1.1 Shared decision making

The Panel recognises that a shared decision-making approach is paramount when any treatments are proposed but felt particular emphasis should be made for the topic area of surgical management for SUI. There are a number of different options available for patients which vary in both efficacy and safety profile. Consequently, the amount of information given to patients considering surgery for SUI is substantial. The Panel would unequivocally advise adherence to the fundamental principles of the shared decision-making process which include:

- full participation from the patient;
- delivery of factual information regarding benefits and risks of a full range of potential treatments, if possible adapted to the specific situation of the patient;
- delivery of information about the experience and expertise of the HCP/institution delivering the treatment, especially for highly specialised procedures such as complex SUI and mesh removal surgery;
- confirmation that the patient understands the information given;
- clinician understanding and documenting individual patient preferences;
- facilitation of deliberation and initial decision-making;
- patient opportunity to consider and confirm any decisions made;
- clinician assistance with implementation of the final decision.

4.2.4.3.1.2 Recommendations for surgical treatment

Recommendations	Strength rating
Employ a shared decision-making approach when deciding on appropriate treatment for stress urinary incontinence (SUI).	Strong
Offer patients who have explored/failed conservative management options, which should include pelvic floor muscle training, a choice of different surgical procedures, where appropriate, and discuss the advantages and disadvantages of each approach.	Strong
Use new devices for the treatment of SUI only as part of a structured research programme. Their outcomes must be monitored in a registry or as part of a well-regulated research study.	Strong

4.2.4.3.2 Surgery for women with uncomplicated stress urinary incontinence

The principal procedures evaluated are:

- open and laparoscopic colposuspension;
- autologous “traditional” slings;
- bulking agents;
- synthetic MUS.

4.2.4.3.2.1 Open- and laparoscopic colposuspension surgery

Open Burch colposuspension was once the standard for SUI surgery and often served as a comparator in trials of newer techniques.

Open colposuspension

A number of SRs and a Cochrane review, including 55 trials with 5,417 women, have documented high initial continence rates (85-90%) within the first year [355, 357-360]. Failure rates were 17% up to five years and 21% beyond five years, with a reoperation rate of 6% within five years and 10.8% within nine years. The specific reoperation rate for UI was only 2%. However, open colposuspension had higher rates of enterocoele/vault/cervical prolapse (42%) and rectocele (49%) compared to TVT (23% and 32%, respectively), with similar cystocoele rates (37% vs. 41%). The Cochrane review concluded that about 70% of women remain dry five years post-surgery [360].

Laparoscopic colposuspension

A Cochrane review of twelve trials comparing laparoscopic and open Burch colposuspension found similar subjective cure rates but suggested poorer objective outcomes for laparoscopic procedures [358]. The ESTER SR [355], based on network meta-analysis, indicated that open colposuspension was more effective than

laparoscopic colposuspension at twelve months, but this was based on low-quality evidence. The surface under the cumulative ranking curve (SUCRA) scores were 76.7% for open colposuspension and 48.9% for laparoscopic. Laparoscopic colposuspension was associated with shorter hospital stays and might be slightly more cost-effective after 24 months.

Single-port laparoscopic Burch is a potential alternative, but data on its efficacy are limited [361].

Complications
Voiding difficulties were more common after laparoscopic colposuspension compared to retropubic MUS (7.5% vs. 5.1%) [355]. There was no significant difference between open colposuspension and retropubic MUS (7.8% vs. 7.5%) [355]. Rates of new urgency or UUI symptoms did not favour either open colposuspension or retropubic MUS (11% vs. 8%). Bladder or urethral perforation rates were higher in laparoscopic colposuspension compared to open colposuspension (3.7% vs. 0.7%) [355].

4.2.4.3.2.1.1 Summary of evidence and recommendation for open and laparoscopic colposuspension surgery

Summary of evidence	**LE**
High subjective cure rates are associated with both open and laparoscopic colposuspension for treatment of SUI.	1a
Objective cure rates are higher for open compared to laparoscopic colposuspension.	1a
Colposuspension is associated with a higher long-term risk of POP than MUS.	1a
Laparoscopic colposuspension has a shorter hospital stay and may be more cost-effective than open colposuspension.	1a
Laparoscopic colposuspension is associated with higher rates of intraoperative bladder perforation and post-operative voiding dysfunction compared to open colposuspension.	1a
The rates of *de novo* urinary urgency following colposuspension are similar to other surgical managements for SUI.	1a

Recommendation	**Strength rating**
Offer colposuspension (open or laparoscopic) to women seeking surgical management for stress urinary incontinence following a thorough discussion of the risks and benefits relative to other surgical modalities.	Strong

4.2.4.3.2.2 Autologous sling
Historically, autologous, cadaveric, xenograft, and synthetic materials have been used for bladder neck pubovaginal slings. Today, autologous tissues, such as rectus sheath or Fascia lata, are the most studied and supported by evidence [362].

Effectiveness
The ESTER SR reviewed trials comparing autologous slings with open colposuspension, retropubic MUS, and transobturator MUS. Although evidence quality was very low, pooled estimates suggested higher cure rates for autologous slings at one year compared to open colposuspension (OR: 1.24), retropubic MUS (OR: 1.06), and transobturator MUS (OR: 1.44), though these were not significant. The SUCRA score for autologous fascial sling cure rates was 89.4%. A Cochrane sub-analysis indicated better effectiveness for autologous slings compared to colposuspension at one to five years' follow-up. In an RCT comparing Burch colposuspension and autologous slings, continence rates at five years were 24.1% for colposuspension and 30.8% for slings, with higher satisfaction in the sling group (83% vs. 73%) [363].

Complications
Adverse event rates were similar for Burch (10%) and sling (9%) groups, though post-operative obstruction occurred only in the sling group [361]. Voiding difficulties were more common with autologous slings (15.4% vs. 10.2%; OR: 1.46) compared to retropubic MUS. Bladder or urethral perforation rates were lower for traditional slings (0.6%) than for open colposuspension (3.0%; OR: 0.20) [355].

4.2.4.3.2.2.1 Summary of evidence and recommendation for autologous sling

Summary of evidence	LE
High cure rates are associated with autologous sling placement for treatment of SUI.	1a
Autologous sling is more effective in terms of cure rate than colposuspension.	1a
Autologous sling has a similar rate of adverse events compared to open colposuspension, with higher rates of voiding dysfunction and post-operative UTI, but lower rates of POP and bladder or urethral perforation.	1a

Recommendation	Strength rating
Offer autologous sling placement to women seeking surgical management for stress urinary incontinence following a thorough discussion of the risks and benefits relative to other surgical modalities.	Strong

4.2.4.3.2.3 Urethral bulking agents

Urethral bulking agents are used to enhance continence by creating artificial cushions around or under the urethra. Various substances, such as Ethylene vinyl alcohol copolymer (Uryx™), glutaraldehyde cross-linked collagen (Contigent©), and others like porcine dermal implant (Permacol©) and solid silicone elastomer (Macroplastique©), have been studied. However, a Cochrane SR concluded that evidence remains insufficient to definitively guide clinical practice [364].

A SR of 56 studies highlight Bulkamid© and Macroplastique© as promising options, with short-term efficacy ranging from 30% to 90% and 40% to 85%, respectively. Long-term effectiveness varies from 42% to 70% for Bulkamid© and 21% to 80% for Macroplastique©, with Bulkamid© demonstrating a more favourable safety profile due to minimal product erosion or migration reported [365].

A SR of 23 studies on Macroplastique© show significant improvements in continence rates, with 75% improvement reported, including a 43% dry rate at less than six months and a 64% improvement with a 36% cure rate at more than eighteen months post-injection [366]. Other trials involving elderly women with SUI showed a reduction in pad weight in 73% of cases at one-year follow-up, regardless of the injected material [367]. Most of the studies showed a tendency for short-term improvement in UI, with the exception of one RCT, which did not find a difference between saline and fat injection [368]. The heterogeneity of the populations, the variety of materials used and the lack of long-term follow-up limit guidance for practice.

Safety-wise, urethral bulking agent injections are generally safe, with UTI being the most common adverse event. However, caution is advised against using autologous fat or hyaluronic acid due to risks like fatal embolism or local abscess formation, respectively [368, 369].

Comparison with other surgical procedures

Comparative studies with conventional surgeries for SUI indicate that while open surgeries may offer greater efficacy, they also come with higher complication rates [370, 371]. In a trial comparing midurethral TVT slings to Bulkamid®, TVT slings showed better satisfaction and higher cure rates based on objective measures like negative cough stress tests [372].

Overall, SRs indicate that urethral bulking agents are generally less effective compared to traditional surgical procedures for SUI, particularly in terms of subjective improvement. However, these conclusions are limited by study heterogeneity and the absence of standardised outcome measures across trials.

In conclusion, while urethral bulking agents like Bulkamid® and Macroplastique® offer viable options for managing SUI, clinicians should consider individual patient factors, long-term efficacy data, and comparative effectiveness with traditional surgeries when making treatment decisions.

4.2.4.3.2.3.1 Summary of evidence and recommendations for urethral bulking agents

Summary of evidence	LE
Urethral bulking agents may provide short-term improvement and cure in women with SUI.	1b
Bulking agents are less effective than MUS, Burch colposuspension or autologous sling for cure of SUI and repeat injections may be required in order to achieve sustained benefits.	1b
Autologous fat and hyaluronic acid as bulking agents have a higher risk of adverse events.	1a
Adverse event rates for urethral bulking agents are lower compared to open surgery.	2a
There is no evidence that one type of bulking agent is better than another.	1b
The periurethral route of injection of bulking agents may be associated with a higher risk of urinary retention compared to the transurethral route.	2b

Recommendations	Strength rating
Offer urethral bulking agents to women seeking surgical management for stress urinary incontinence (SUI) following a thorough discussion of the risks and benefits relative to other surgical modalities.	Strong
Offer urethral bulking agents to women with SUI who request a low-risk procedure with the understanding that efficacy is lower than other surgical procedures, repeat injections are likely, and long-term durability and safety are not established.	Strong
Do not offer autologous fat and hyaluronic acid as urethral bulking agents due to the higher risk of adverse events.	Strong

4.2.4.3.2.4 Laser treatment

Laser therapy to the vagina and surrounding tissues aims to improve continence by inducing collagen contraction, new collagen formation, vascularisation, growth factor infiltration, restoration of elasticity, and thickening of the vaginal epithelium. Several SR have evaluated laser treatment for SUI. One SR of sixteen studies (including only one RCT) reported on 899 patients and found significant improvements in the ICIQ-SF score at one, two, and six months (-5.49, -4.97, and -5.48, respectively) and improvements in the one hour pad weight test results at one, three-, and twelve-months post-treatment (-5.59, -4.96, and -5.82, respectively). The PISQ-12 score increased by 5.39 following treatment. Adverse effects were mild or moderate, affecting a small number of patients, and generally resolved without medical intervention. This SR concluded that vaginal laser therapy appears to be a safe, effective, and minimally invasive treatment for SUI, well tolerated by patients [373].

Another SR of 31 studies (including only one RCT) with 1,530 women confirmed beneficial effects of laser therapy on prolapse and UI. However, the evidence level remains low, with no clear recommendation on the type of laser to use. Moreover, no long-term cost-effectiveness studies are available, making it difficult to compare laser treatment longevity with surgical results [374].

A third SR of 27 studies on Er:YAG and Fractional CO_2 lasers reported that the overall quality of studies was poor, with most being case series. The Er:YAG laser showed modest reductions in mild SUI cases, with benefits lasting up to sixteen months. The Fractional CO_2 laser showed improvement in mild SUI in a few studies, but no long-term data are available. Adverse events were generally insignificant but not systematically reported [260].

A randomised double-blind sham-controlled study on women with SUI showed a significant reduction in the ICIQ-UI SF score after Er:YAG laser therapy compared to sham treatment [375]. However, only 21% of the women were subjectively dry compared to 4% in the sham group.

The literature on vaginal lasers has limitations, including lack of high quality RCTs, variation in laser settings and protocols, short-term follow-up, lack of urodynamic evaluation, and poor reporting of objective measures and adverse events. Consequently, lasers cannot currently be recommended as a treatment option for SUI based on available evidence.

4.2.4.3.2.4.1 Summary of evidence and recommendations for laser treatment

Summary of evidence	LE
Several limitations have been noted in the current literature regarding vaginal laser treatment for SUI. These include variation in laser settings and protocols, short term follow-up, lack of urodynamic evaluation, poor reporting of appropriate objective measures and adverse events and lack of high-level evidence.	1b

Recommendations	Strength rating
Do not offer vaginal laser therapy to treat stress urinary incontinence symptoms unless it is part of a well-regulated and closely monitored research study.	Strong

4.2.4.3.2.5 Mid-urethral slings

Mid-urethral slings are widely used in Europe for treating SUI in women, utilizing synthetic, monofilament, nonabsorbable materials like polypropylene [376].

Transobturator route versus retropubic route

A Cochrane meta-analysis found comparable short-term subjective cure rates for retropubic and transobturator slings [377]. However, the ESTER SR based on network meta-analysis [355] including 36 trials of overall moderate quality, showed that at twelve months retropubic MUS was more effective than transobturator MUS (OR: 0.74). The SUCRA scores for women cured after retropubic MUS were 89.1% vs. 64.1% after transobturator MUS. Long-term studies showed retropubic MUS also had higher objective cure rates than transobturator slings after five years, though patient satisfaction remained high for both [378, 379].

Data on long-term complications are limited. One study reported *de novo* OAB in 14% of patients ten years post-transobturator tape (TVT-O) surgery [380]. Retropubic TVT showed high objective and subjective cure rates at ten years, with 82.6% patient satisfaction [381]. Long-term prospective studies on transobturator slings also reported sustained cure rates over time [382, 383]. The ESTER network meta-analysis indicated that retropubic and transobturator MUS, along with traditional slings, were the most effective for SUI [355].

Complications of synthetic mid-urethral slings

The ESTER network meta-analysis noted that comparative assessment of adverse events between different procedures was not always possible due to the lack of available data [355]. Regarding adverse events, retropubic MUS was associated with higher bladder perforation rates compared to transobturator MUS. Groin pain was more frequent with transobturator MUS, while suprapubic pain was more common with retropubic MUS. Vaginal erosion rates were low and similar between both types of MUS. A Scottish population-based study reported similar complication rates between mesh and non-mesh surgeries [384]. However, a UK study found a significant 9.8% complication rate with MUS, suggesting the need for comprehensive informed consent [385].

A SR described the association between surgeon operative volume and the risk of reoperation after MUS. The likelihood of a repeat incontinence procedure was almost 30% higher if the surgery was carried out by a low-volume surgeon, although these results need to be interpreted with caution as the definition of low-volume vs. high-volume surgeon varied between studies [386].

In general, the available published evidence would suggest that MUS does not seem to be associated with significantly higher rates of morbidity and complications compared to other surgeries for SUI, but in general the quality of the literature, particularly long-term follow up studies is low. Pelvic organ prolapse is more common after colposuspension while voiding dysfunction occurs more often after MUS [360]. The ESTER review has commented that the level of detail regarding short-to-medium adverse event data is poor for all SUI surgeries [355] and the Panel is aware of the findings from the Independent Medicines and Medical Devices Safety Review in the UK that has raised the possibility that the level of complications from synthetic MUS may be higher than the medical literature would suggest [353]. The NICE guideline on UI and pelvic organ prolapse does not recommend the use of transobturator synthetic mid-urethral slings for the treatment of SUI and specifically notes the potential difficulty in achieving full removal should complications occur [61].

Health economic analyses of MUS procedures yielded conflicting results. Some studies indicated that transobturator MUS might be cost-effective compared to retropubic MUS [387] while others favoured retropubic MUS over a lifetime [355].

Surgical technique for Synthetic MUS
The Cochrane review on MUS for female SUI found no significant difference in short- and medium-term subjective cure rates between the vagina-to-skin (inside-out) and skin-to-vagina (outside-in) approaches [388]. Voiding dysfunction was more common with the inside-out transobturator tape (TOT) method, which, however, had a lower frequency of vaginal perforations. The lower rate of vaginal perforations might contribute to fewer instances of vaginal tape erosions, though the evidence quality is low. A meta-analysis of RCTs confirmed no significant efficacy difference between the two approaches, but again noted fewer vaginal perforations with the inside-out method [389]. Five-year data from a prospective, non-randomised trial showed high objective success rates for both techniques (82.6% vs. 82.5%), with no notable difference in outcomes [390]. Additionally, a secondary analysis of the E-TOT study, which examined transobturator MUS in women with urodynamic MUI, reported no significant difference in patient-reported success rates between the inside-out and outside-in groups (63.2% vs. 65.5%) at nine years follow-up [391].

Overall, while MUS does not appear to have higher morbidity rates than other SUI surgeries based on existing literature, the ESTER review and other findings suggest the need for better reporting and longer follow-up to fully understand the complication profiles, particularly in the longer term.

Single-incision mid-urethral slings
Despite numerous studies on single-incision MUS, significant differences in technical design between devices complicate generalisations about their efficacy and safety. Some devices, like TVT Secur®, Minitape, and MiniArc®, have been withdrawn from the market, yet their data still influence current meta-analyses. Single-incision slings are quicker to perform and cause less post-operative thigh pain, but there's no difference in chronic pain rates compared to other methods. Insufficient evidence exists for direct comparisons among single-incision slings, preventing definitive conclusions about their relative efficacy.

The ESTER SR, based on low-quality evidence, indicated that at twelve months, retropubic and transobturator MUS were more effective than single-incision slings (TVT, OR: 0.50; TOT, OR: 0.68). However, the SUCRA score for single-incision slings was 39.8%, and not all devices have been evaluated in comparative RCTs, making it unsafe to assume uniformity in efficacy or technical similarity [355].

Following the publication of ESTER, a multicentre noninferiority RCT comparing single-incision slings (Ajust® and Altis®) with conventional MUS found that 72.0% of single-incision sling patients reported success at 36 months, compared to 66.8% of MUS patients, suggesting noninferiority of single-incision slings in terms of patient-reported success [392].

Complications of single-incision slings
Complication rates between single-incision slings and transobturator MUS were similar, with mesh erosion or extrusion rates at 4.8% and 3.7%, respectively. Post-operative pain was higher after retropubic MUS (19.2% vs. 6.8%). At 36 months, groin or thigh pain was comparable between single-incision slings (14.1%) and MUS (14.9%). Tape or mesh exposure occurred in 3.3% of single-incision sling cases and 1.9% of MUS cases, with reoperation rates for SUI at 2.5% and 1.1%, respectively [392].

Immediate post-operative pain was lower for single-incision slings, though *de novo* dyspareunia was higher. No significant differences in objective cure rates were reported at twelve months (90% vs. 88%) [393]. Single-incision slings had higher rates of unspecified pain at twelve and twenty-four months and more repeat surgeries compared to transobturator MUS (5.1% vs. 2.9%). At over three years post-procedure, repeat surgery rates were 10.3% for single-incision slings versus 7.6% for transobturator MUS [355].

Sexual function after synthetic mid-urethral sling surgery
A SR examining the effect of synthetic MUS on female sexual function suggested different and contradictory results between studies. More studies have shown an improvement, or no change, in sexual function because of a reduction in coital incontinence, anxiety and avoidance of sex. Dyspareunia was the most common cause of worsening of sexual function and the precise incidence is difficult to estimate as many studies did not report it [394]. A meta-analysis of outcome measures in trials of sling procedures suggests that single-incision slings are associated with a significantly higher improvement in sexual function; however, conflicting evidence was seen, compared to standard MUS procedures [395]. An RCT comparing single-incision slings with MUS showed similar

outcomes with respect to QoL and sexual function in the two groups, with the exception of dyspareunia. Among the 290 women responding to a validated questionnaire, dyspareunia was reported by 11.7% in the single-incision group and 4.8% in the MUS group [392].

4.2.4.3.2.5.1 Summary of evidence and recommendations for mid-urethral slings

Summary of evidence	LE
The retropubic MUS appears to provide better patient-reported subjective and objective cure of SUI, compared with colposuspension.	1a
Synthetic MUSs inserted by the transobturator or retropubic route provide equivalent patient-reported outcomes at one year.	1a
Synthetic MUSs inserted by the retropubic route have higher patient-reported cure rates in the longer term.	1b
Long-term analyses of MUS cohorts showed a sustained response beyond ten years.	2b
The retropubic route of insertion, compared with the transobturator route, is associated with a higher intraoperative risk of bladder perforation and a higher rate of voiding dysfunction.	1a
The transobturator route of insertion is associated with a higher risk of groin pain than the retropubic route.	1a
Long-term analysis of MUS showed no difference in terms of efficacy for the skin-to-vagina (outside-in) compared to vagina-to-skin (inside-out) directions up to nine years.	2a
The top-to-bottom (inside-out) direction in the retropubic approach is associated with a higher risk of post-operative voiding dysfunction.	1b
The comparative efficacy of Ajust® and Altis® single-incision slings against conventional MUS at fifteen and 36 months is non-inferior.	1b
Operating times for insertion of single-incision MUSs are shorter than for standard retropubic slings.	1b
Blood loss and immediate post-operative pain are lower for insertion of single-incision slings compared with conventional MUS.	1b
The rate of mesh exposure, repeat SUI surgery and dyspareunia at three years is higher for single incision slings (Ajust ® and Alits®) compared to conventional MUS.	1b
There is no evidence that other adverse outcomes from surgery are more or less likely with single-incision slings than with conventional MUS.	1b
In women undergoing MUS surgery for SUI, coital incontinence is likely to improve.	3
Overall, there is conflicting evidence regarding sexual function following MUS surgery for SUI.	1a

NB: Most evidence on single-incision slings is from studies using the TVT secur® device, and although this device is no longer available, it is, however, still included in many SRs and meta-analyses.

Recommendations	Strength rating
Offer a mid-urethral sling (MUS) to women seeking surgical management for stress urinary incontinence following a thorough discussion of the risks and benefits relative to other surgical modalities.	Strong
Perform cystoscopy to check for intraoperative bladder perforation when inserting a synthetic MUS.	Strong
Inform women that long-term outcomes from MUS inserted by the retropubic route are superior to those inserted via the transobturator route.	Strong
Inform women of the complications associated with MUS procedures and discuss all alternative treatments in the light of recent publicity surrounding surgical mesh.	Strong
Inform women who are being offered single-incision slings (Ajust® and Altis®), that short term efficacy appears equivalent compared to conventional MUS.	Strong
Inform women who are being offered a single-incision sling that long-term efficacy remains uncertain.	Strong

4.2.4.3.2.6 Other treatments for uncomplicated stress urinary incontinence

Intravesical balloon treatment, exemplified by the Vesair® gas-filled intravesical balloon, has been investigated for women with SUI. Unlike other treatments, this method aims to mitigate intravesical pressure fluctuations caused by abdominal pressure increases, rather than increasing outlet resistance or reducing urethral hypermobility [396, 397]. Two sham-controlled RCTs demonstrated significant reductions in incontinence symptoms and pad weight with the Vesair® balloon, though QoL improvements were not significantly different between treatment and control groups [396, 398]. Both trials reported high rates of adverse events, including dysuria, urgency, gross haematuria, and UTIs, leading to substantial numbers of withdrawals and device removals.

Mechanical devices have long been used to manage SUI, functioning by either supporting the bladder neck or urethra to counteract urethral hypermobility or occluding the urethral lumen. However, the evidence for their efficacy is limited. A Cochrane review of eight RCTs, including three small trials comparing mechanical devices to no treatment, found inconclusive evidence of benefit [399]. Another SR similarly concluded that there is insufficient evidence to support the use of mechanical devices for women with SUI [400]. The efficacy of these devices remains uncertain, necessitating large, well-conducted trials for better evaluation. There is also no substantial evidence favouring one specific device over others, and few studies compare mechanical devices to other treatment forms [399].

Compression devices, such as adjustable compression therapy and artificial urinary sphincter (AUS) devices, have been supported by SRs [401, 402]. Although typically reserved for patients with recurrent or complicated SUI, some recent literature suggests their use for uncomplicated SUI. These reviews indicate a potential role for compression devices in the broader management of SUI, though their application remains primarily for more complex cases.

4.2.4.3.2.6.1 Summary of evidence and recommendations for other treatments for uncomplicated stress urinary incontinence

Summary of evidence	**LE**
Implantation of an AUS can improve or cure incontinence in women with uncomplicated SUI.	3
Implantation of the adjustable compression therapy (ACT®) device may improve uncomplicated SUI.	3
Complications, mechanical failure and device explantation often occur with both the artificial sphincter and the ACT®.	3

Recommendations	**Strength rating**
Do not offer mechanical devices to women with mild-to-moderate stress urinary incontinence unless it is part of a well-regulated and closely monitored research study.	Strong
Inform women receiving artificial urinary sphincter or adjustable compression device (ACT®) that, although cure is possible, even in expert centres there is a high risk of complications, mechanical failure, or a need for explantation.	Strong

4.2.4.3.3 Surgery for women with complicated stress urinary incontinence

This section addresses surgical management for women with complicated SUI as defined in Section 4.2.2.

Women with associated genitourinary prolapse are included in Section 4.7.

The principal procedures included are:

- Colposuspension or MUS (synthetic or autologous) following failed primary SUI surgery;
- External compression devices: adjustable compression therapy (ACT®) and AUS;
- Adjustable slings.

4.2.4.3.3.1 Colposuspension or mid-urethral sling (synthetic or autologous) following failed primary stress urinary incontinence surgery

Urinary incontinence following SUI surgery may indicate persistent or recurrent SUI, or the development of *de novo* UUI, or both. Careful evaluation, including urodynamics, is essential for these patients.

Most data on surgery for SUI refer to primary operations. Even when secondary procedures are included, outcomes in this subgroup are rarely reported separately. When reported, patient numbers are usually too small for meaningful comparisons, making it difficult to recommend the best modality for treating recurrent SUI. Previous SRs have highlighted the lack of evidence, suggesting clinicians rely on expert opinion or personal experience for treatment advice [403].

The ESTER network meta-analysis indicated that women with transobturator MUS were more likely to undergo repeat surgery than those with retropubic MUS. Retropubic MUS was associated with fewer repeat operations compared to other interventions. An update of two Urinary Incontinence Treatment Network trials [404] compared retreatment-free survival rates by initial surgical procedure. Five-year retreatment-free survival rates were 87%, 96%, 97%, and 99% for Burch colposuspension, autologous fascial sling, transobturator, and retropubic MUS, respectively. Types of surgical retreatment included autologous fascial sling (19), bulking agent (18), and synthetic sling (1), suggesting MUS may not be preferred for recurrent SUI [404].

In these cohorts, 6% of women underwent surgical retreatment within five years, mostly with injection therapy or autologous fascial sling. Not all women with recurrent SUI opted for surgical retreatment.

A Cochrane review attempted to summarise data on different types of MUS procedures for recurrent SUI after failed primary surgery [405]. The literature search identified 58 records, but all were excluded from quantitative analysis for not meeting eligibility criteria. Consequently, no data were available to recommend or refute any management strategies for recurrent or persistent SUI after failed MUS surgery. Another SR on MUS effectiveness in recurrent SUI included twelve studies, reporting an overall subjective cure rate of 78.5% at an average of 29 months follow-up [406]. The subjective cure rate following MUS after previous failed MUS was 73.3% at sixteen months follow-up. This review noted a lower cure rate with transobturator compared to retropubic tape for recurrent SUI. Conflicting evidence from another SR assessed various surgical procedures for recurrent SUI, analysing data from 350 women in ten RCTs with an 18.1-month mean follow-up [407]. The SR found no difference in patient-reported and objective cure/improvement rates between retropubic and transobturator MUS for recurrent SUI. No significant difference was observed between Burch colposuspension and retropubic MUS regarding patient-reported improvement or objective cure/improvement.

A SR of older trials of open surgery for SUI suggested that long-term outcomes of repeat open Burch colposuspension may be poor compared to autologous fascial slings [408]. Similarly, one large non-randomised comparative series reported cure rates after more than two previous operations were 0% for open Burch colposuspension and 38% for autologous fascial sling [409].

4.2.4.3.3.1.1 Summary of evidence for surgery in those with recurrent stress urinary incontinence following failed primary surgery

Summary of evidence	**LE**
Failure rates of single-incision slings appear higher than with other types of MUS.	1a
The incidence of repeat surgery is higher in those women who underwent primary transobturator compared to retropubic MUS.	1a
The five-year failure rate of Burch colposuspension appears higher than for synthetic or traditional sling procedures.	2b
Some studies suggest that retropubic synthetic MUS procedures appear to be more effective than transobturator MUS for the treatment of recurrent SUI, but this is not a consistent finding in the literature.	1a
Most procedures are less effective when used as second-line procedures.	2a
Burch colposuspension has similar short-term patient-reported or objective cure rates when compared to TVT for treatment of recurrent SUI.	1b
Autologous sling appears superior to Burch colposuspension for treatment of recurrent SUI.	2b

4.2.4.3.3.2 Adjustable slings

Although adjustable slings are most commonly used for treatment of complicated SUI, they may also be considered for uncomplicated SUI. There are no RCTs investigating outcome of adjustable sling insertion for women with SUI. There are limited data from cohort studies on adjustable tension slings with variable selection criteria and outcome definitions. Few studies have included sufficient numbers of patients or have long enough follow-up to provide useful evidence.

One adjustable sling is the Remeex system (Neomedic International®, Terrassa, Spain), which was investigated in a prospective study of 230 women with SUI [410]. After a mean follow-up of 89 months, 165 patients were cured of SUI (71.7% in the intention-to-treat [ITT] analysis, 80.5% in per protocol [PP] analysis). Forty patients remained incontinent (17.4% in ITT, 19.5% in PP) and 88 patients required readjustment of the sling during follow-up.

The tension was increased in 82 cases due to recurrence of SUI and reduced in six due to outlet obstruction. The currently available adjustable sling devices have differing designs, making it difficult to draw general conclusions about them as a class of procedure.

4.2.4.3.3.2.1 Summary of evidence for adjustable slings

Summary of evidence	**LE**
There is only low-level evidence to suggest that adjustable MUS devices may be effective for cure or improvement of SUI in women.	3
There is no evidence that adjustable slings are superior to standard MUS.	4

4.2.4.3.3.3 External compression devices

External compression devices are usually used for treatment of recurrent SUI after failure of previous surgery but can be considered for primary treatment. Studies have largely included patients with profound intrinsic failure of the sphincter mechanism, characterised by low VLPP or urethral closure pressure [401, 402]. The two intracorporeal external urethral compression devices available are the adjustable compression therapy (ACT®) device and AUS.

ACT®: Using US or fluoroscopic guidance, the ACT® device is inserted by placement of two inflatable spherical balloons; one on either side of the bladder neck. The volume of each balloon can be adjusted through a subcutaneous port placed within the labia majora. A SR including eight studies published between 2007 and 2013 with follow-up of one to six years revealed 15-44% of patients considered that their SUI had been cured and 66-78.4% were satisfied [401]. The explantation rate was 19-31%. In these studies, a significant reduction in the number of pads used daily was consistently observed after ACT® balloon placement and QoL was significantly improved. The authors concluded that ACT® balloons constitute a reasonable, minimally-invasive alternative for treatment of female SUI due to intrinsic sphincter deficiency, especially in patients who have already experienced failure of standard surgical management.

AUS: The major advantage of AUS over other anti-incontinence procedures is the perceived ability to be able to void normally [399]. There have been a few case series of AUS in women, with populations of 45-215 patients and follow-up of one month to 25 years [411-414]. 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 cure in 59-88%. Common adverse effects included mechanical failure requiring revision (≤ 42% at ten years) and explantation (5.9-15%). In a retrospective series of 215 women followed-up for a mean six years, the risk factors for failure were older age, previous Burch colposuspension and pelvic radiotherapy [414].

Early reports of laparoscopically implanted AUS do not have sufficient patient populations or sufficient follow-up to be able to draw any conclusions [415, 416].

A systematic review that included seventeen studies, all of which were retrospective or prospective non-comparative case series [402] reported that most patients had undergone at least one anti-incontinence surgical procedure prior to AUS implantation (69.1-100%). Outcomes revealed that complete continence rates were 61-100%. The rates of explantation were 0-45%, erosion rates were 0-22% and mechanical failure rates were 0-44%. The authors concluded that AUS could provide excellent functional outcomes in women with SUI resulting from intrinsic urethral sphincter deficiency but at the cost of high morbidity.

4.2.4.3.3.3.1 Summary of evidence for external compression devices

Summary of evidence	**LE**
Implantation of an artificial sphincter improves or cures incontinence in women with SUI caused by sphincter insufficiency.	3
Implantation of the AUS device may improve complicated SUI.	3

Implantation of the ACT® device may improve complicated SUI.	3
Complications, mechanical failure, and device explantation often occur with both the artificial sphincter and ACT®.	3
Explantation of AUS is more frequent in older women and among those who have had previous Burch colposuspension or pelvic radiotherapy.	3

4.2.4.3.3.4 Recommendations for complicated stress urinary incontinence

Recommendations	**Strength rating**
Management of complicated stress urinary incontinence (SUI) should only be offered in centres with appropriate experience (see Section: 4.2.4.3.1).	Strong
Base the choice of surgery for recurrent SUI on careful evaluation, including individual patient factors and considering further investigations such as cystoscopy and multichannel urodynamics, as appropriate.	Strong
Inform women with recurrent SUI that the outcome of a surgical procedure, when used as second-line treatment, is generally inferior to its use as first-line treatment, both in terms of reduced efficacy and increased risk of complications.	Weak
Do not use adjustable mid-urethral sling for primary surgical management for SUI unless it is part of a well-regulated and closely monitored research study.	Strong
Consider secondary synthetic sling, bulking agents, Burch colposuspension, autologous sling or artificial urinary sphincter (AUS) as options for women with complicated SUI.	Weak
Inform women receiving AUS or ACT® device that, although cure is possible, even in expert centres, there is a high risk of complications, mechanical failure, or a need for explantation.	Strong

4.2.4.3.4 Surgery for stress urinary incontinence in special patient groups

4.2.4.3.4.1 Stress urinary incontinence surgery in obese women

The outcomes of incontinence surgery in obese women are debated. An RCT comparing retropubic and transobturator tapes showed that obese women (BMI ≥ 30) had inferior outcomes compared to non-obese women (BMI < 30). At one-year, objective dry rates were 67.8% for obese women versus 85.6% for non-obese women, and at five years, 65.9% versus 87.4%. Subjective cure rates were also lower for obese women at both time points [417, 418].

However, short-term outcomes for single-incision MiniArc® and Altis® slings showed similar objective cure rates between obese and non-obese women at two years (MiniArc®: 81% vs. 86%; Altis®: 87% vs. 88%) with comparable improvements in urinary distress and impact scores [419, 420].

Further research is needed to evaluate long-term outcomes and efficacy among different surgical options for SUI in obese women.

4.2.4.3.4.2 Stress urinary incontinence surgery in elderly women

Age significantly affects outcomes of SUI surgery, though evidence is mixed. An RCT with 537 women comparing retropubic to transobturator tape found age over 50 to be an independent risk factor for surgical failure [421]. Another RCT with 162 women comparing TVT to TVT-O also identified age as a risk factor for SUI recurrence at one year [422]. A sub-analysis of a cohort of 655 women over two years indicated that elderly women were more likely to have a positive stress test at follow-up, report less improvement in stress and UUI, and need retreatment for SUI, with no difference in the time to post-operative normal voiding [423]. Another RCT comparing immediate TVT to no surgery (or delayed TVT) in older women confirmed surgery's efficacy for quality of life and satisfaction but noted more complications [424]. A SR found mid-urethral sling surgery successful in older patients (≥ 65 years), with 5.2-17.6% reporting persistent SUI, and no significant difference in *de novo* UUI, persistent UUI, or persistent SUI [357].

4.2.4.3.4.3 Summary of evidence and recommendations for stress urinary incontinence surgery in special patient groups

Summary of evidence	LE
Incontinence surgery may be safely performed in obese women; however, outcomes may be inferior.	1
The risk of failure from surgical repair of SUI, and the risk of adverse events, appears to increase with age.	2b
There is no evidence that any surgical procedure has greater efficacy or safety in older women than another procedure.	4

Recommendations	Strength rating
Inform obese women with stress urinary incontinence (SUI) about the increased risks associated with surgery, together with the lower probability of benefit.	Weak
Inform older women with SUI about the increased risks associated with surgery, together with the likelihood of lower probability of benefit.	Weak

4.2.5 ***Follow-up***

The follow-up of patients with SUI is dependent on the treatment given. For conservative and physical therapies, sufficient time should be allowed for the demonstration of a therapeutic effect. For pharmacological treatment, early follow-up is recommended. For most surgical interventions, short-term follow-up should be arranged to assess efficacy and identify any early post-operative complications.

The Panel is supportive of long-term outcome assessment via registries and recognises the paucity of high-quality long-term data, specifically regarding complications from surgery.

4.3 Mixed urinary incontinence

The term MUI is broad because it may refer to equal stress and urgency symptoms, stress-predominant symptoms, urgency-predominant symptoms, urodynamic stress urinary incontinence (USUI or USI) with DO or USUI with clinical urgency symptoms, but no DO [425]. The challenge of this broad definition is that it leads to inconsistencies when evaluating treatment options and outcomes.

4.3.1 ***Epidemiology, aetiology and pathophysiology***

Prevalence rates of MUI vary widely due to inconsistent consideration and reporting of UI subtypes in epidemiological studies. The literature is unclear about the population prevalence and risk factors for different UI subtypes, with significant heterogeneity in urinary symptom questionnaires, population parameters, response rates, definitions of MUI, and outcome measures [426]. Despite this variability, MUI is the second most common form of UI after SUI, with most studies reporting a 7.5-25% prevalence [426]. Approximately one-third of women with UI are estimated to have MUI [427]. In a secondary analysis of a large clinical trial involving 655 women, 50-90% reported MUI based on subjective questionnaires, but only 8% were categorised as having MUI based on objective urodynamic findings [428].

Mixed urinary incontinence is typically caused by a combination of factors responsible for SUI and UUI. Potential causes include oestrogen deficiency, histomorphological abnormalities, and microstructural changes [429]. One hypothesis suggests that an incompetent sphincter and bladder neck cause urine to enter the proximal urethra during stress, triggering a urethro-detrusor reflex and involuntary detrusor contraction, leading to urgency and UUI [430]. Another theory indicates that urine flow across the urethral mucosa increases the excitability of the micturition reflex [431]. It is likely that multiple factors and disturbances contribute to the development of MUI and its symptoms, rather than a single cause [429].

4.3.2 ***Diagnostic evaluation***

Assessment of patients with MUI begins with a thorough history of the patient's urinary symptoms and follows the recommendations set out in the general evaluation and diagnosis of LUTS section 3. It is conventional to try and categorise MUI as either stress or urgency predominant.

Mixed urinary incontinence is difficult to diagnose, as the condition comprises many phenotypes. Some women exhibit detrusor contractions provoked by physical stressors, some have unprovoked detrusor contractions, and many have no abnormal detrusor contractions, but still report urine leakage with the sensation of urgency. Some

women with urgency symptoms do not manifest UUI because their urethral sphincter is strong and often able to prevent urine leakage [432].

The role of urodynamics in MUI is unclear but establishing objective degrees of SUI and DO incontinence may help in counselling patients about the most appropriate initial treatment option and are almost universally utilised in women with MUI.

4.3.2.1 Summary of evidence and recommendations for the diagnosis of mixed urinary incontinence

Summary of evidence	**LE**
Urodynamics can help to evaluate the most predominant cause(s) in patients with MUI.	4
There is no evidence that urodynamics affects outcomes of treatment for MUI.	3

Recommendations	**Strength rating**
Complete a thorough history and examination as part of the assessment of mixed urinary incontinence (MUI).	Strong
Characterise MUI as either stress-predominant or urgency-predominant where possible.	Weak
Use bladder diaries and urodynamics as part of the multimodal assessment of MUI to help inform the most appropriate management strategy.	Strong

4.3.3 ***Disease management***

4.3.3.1 Conservative management

Managing MUI presents unique challenges due to its typically more severe symptoms and variable treatment responses compared to SUI or UUI [433]. Conservative management strategies are recommended initially, with surgery considered as a last resort option [432].

4.3.3.1.1 Pelvic floor muscle training

Pelvic Floor Muscle Training plays a central role in conservative management for MUI. Research findings indicate that PFMT, often supplemented with audiotapes or other forms of guidance, effectively reduces the frequency of incontinence episodes and improves quality of life for women with MUI [434]. Studies, including RCTs, have consistently shown that PFMT can significantly enhance PFM strength and decrease UI episodes compared to no treatment.

A Cochrane review comparing PFMT with no or sham treatment included 31 RCTs from fourteen countries, but there was only one study including women with MUI and one with UUI and none of them reported data on cure, improvement, or number of episodes of these subgroups [319].

The effect of combining biofeedback with PFMT has already been fully addressed in Section 4.2.4.1.3, and there was no evidence of any additional benefit in a population with predominantly MUI.

4.3.3.1.2 Bladder training

Details on BT programmes are given in Section 4.2.4. The ICI 2017 [324] concluded that PFMT and BT are effective first-line therapies for MUI and UUI. An RCT assigning 108 women with SUI, UUI, or MUI to six weeks of BT combined with PFMT versus BT alone demonstrated superior outcomes in the combined treatment arm in terms of symptom improvement and cure rates, particularly in the MUI subgroup [435].

4.3.3.1.3 Electrical stimulation

Electrical Stimulation has been explored as a treatment option for SUI and stress-predominant MUI. A Cochrane review highlighted that while ES showed promise in subjective cure or improvement of SUI, the evidence quality varied. Some trials were criticised for biases such as baseline differences between groups and industry funding. Electrical stimulation for OAB and SUI is covered in Sections 4.1.4.1.5.4 and 4.2.4.1.5.

Clinicians are advised to exercise caution when interpreting study results and implementing treatment plans, as the efficacy of interventions like PFMT and BT can vary depending on patient characteristics and adherence to therapy protocols. Further research is needed to refine treatment guidelines and better understand the long-term effectiveness of conservative therapies for managing MUI.

In conclusion, while surgery remains an option for refractory cases, conservative management strategies such as PFMT, BT, and potentially ES offer effective initial approaches to alleviate symptoms and improve quality of life for women with MUI.

4.3.3.2 Summary of evidence and recommendations for conservative management in mixed urinary incontinence

Summary of evidence	**LE**
Pelvic floor muscle training appears less effective for MUI than for SUI alone.	2
Pelvic floor muscle training is better than no treatment for improving UI and QoL in women with MUI.	1a
Bladder training combined with PFMT may be beneficial in the treatment of MUI.	1b

Recommendations	**Strength rating**
Treat the most bothersome symptom first in patients with mixed urinary incontinence (MUI).	Weak
Offer bladder training as a first-line therapy to adults with MUI.	Strong
Offer supervised intensive pelvic floor muscle training, lasting at least three months, as a first-line therapy to all women with MUI (including elderly and postnatal women).	Strong

4.3.3.3 Pharmacological management

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

4.3.3.3.1 Anticholinergics

In an RCT of 854 women with MUI, tolterodine ER was effective for improvement of UUI but not SUI, suggesting that the efficacy of tolterodine for UUI was not altered by the presence of SUI [436]. In another study (n = 1,380), tolterodine was equally effective in reducing urgency and UUI symptoms, regardless of whether there was associated SUI [437]. Similar results were found for solifenacin [438, 439].

4.3.3.3.2 Mirabegron

In a *post-hoc* analysis of phase IIb and phase III trials mirabegron reduced voiding frequency, and the effect size increased over time. Improvements in most other OAB symptoms apart from the cardinal symptom of urinary urgency. Mirabegron showed larger improvements versus placebo in all quality-of-life domains [440].

4.3.3.3.3 Duloxetine

In one RCT of duloxetine vs. placebo, 588 women were stratified into either stress-predominant, urgency-predominant or balanced MUI groups. Duloxetine was effective for improvement of incontinence and QoL in all subgroups, although results in the stress-predominant groups were better [441]. Treatment-emergent adverse event rate in the duloxetine group was 61.3% with discontinuation rates of 15.7%. Adverse event rates were higher in those participants taking other concomitant antidepressant agents.

Duloxetine was found to have equal efficacy for SUI and MUI in an RCT (n = 553) following secondary analysis of respective subpopulations, but no adverse events data were reported [442].

4.3.3.3.4 Summary of evidence and recommendations for pharmacological management of mixed urinary incontinence

Summary of evidence	**LE**
Limited evidence suggests that anticholinergic drugs are effective for improvement of the UUI component in patients with MUI.	2
Mirabegron may improve OAB symptoms in patients with MUI but appears to have minimal effect on urgency.	3
Duloxetine is effective for improvement of both SUI and MUI symptoms, but adverse event rates are high.	1b

Recommendations	Strength rating
Treat the most bothersome symptom first in patients with mixed urinary incontinence (MUI).	Weak
Offer anticholinergic drugs or beta-3 agonists to patients with urgency-predominant MUI.	Strong
Offer duloxetine (where licensed) to selected patients with stress-predominant MUI unresponsive to other conservative managements and who want to avoid invasive treatment, counselling carefully about the risk of adverse events.	Weak

4.3.3.4 Surgical management

Surgical management options for MUI encompass procedures commonly used for SUI, detailed in Section 4.2.4.3 of the guidelines. Despite many RCTs including MUI patients alongside those with pure SUI or UUI, few studies report separate outcomes for MUI subgroups.

Post hoc analyses indicate that outcomes for procedures like autologous fascial sling and Burch colposuspension may be less favourable in women with pre-operative urgency symptoms [423]. Studies comparing transobturator and retropubic MUS suggest that greater pre-operative urgency severity correlates with increased likelihood of treatment failure [94], although earlier studies suggest comparable outcomes regardless of urgency presence, particularly in cases with urodynamic DO.

Combining surgical approaches with botulinum toxin A injections has shown significant improvements in continence and QoL compared to single treatments [443]. Long-term follow-up studies on transobturator TVTs in urodynamic MUI patients indicate similar success rates between different sling insertion techniques over extended periods [391].

Challenges include the applicability of evidence from meta-analyses on single-incision slings primarily to SUI cases, rather than MUI or severe POP. Future research should focus on well-defined MUI subtypes to better guide surgical decisions and optimise treatment outcomes.

4.3.3.4.1 Summary of evidence and recommendations for surgery in patients with mixed urinary incontinence

Summary of evidence	LE
Women with MUI are less likely to be cured of their UI by SUI surgery than women with SUI alone.	2
The response of pre-existing urgency symptoms to SUI surgery is unpredictable but those with pre-operative urinary urgency are more likely to experience unfavourable surgical outcomes or treatment failure.	1b

Recommendations	Strength rating
Treat the most bothersome symptom first in patients with mixed urinary incontinence (MUI).	Weak
Warn women that surgery for MUI is less likely to be successful than surgery for stress urinary incontinence alone.	Strong
Inform women with MUI that one single treatment may not cure urinary incontinence; it may be necessary to treat other components of the incontinence problem as well as the most bothersome symptom.	Weak

4.4 Underactive bladder

Underactive bladder is a common clinical entity, defined by the ICS as: *"a symptom complex characterised by a slow urinary stream, hesitancy, and straining to void, with or without a feeling of incomplete bladder emptying sometimes with storage symptoms"* [444]. Diagnosis of UAB is based on clinical symptoms and the presentation and aetiology can be variable.

This differs from DU, which is a diagnosis based on urodynamic studies. Detrusor underactivity is defined by the ICS as: *"a detrusor contraction of reduced strength and/or duration, resulting in prolonged bladder emptying and/or failure to achieve complete bladder emptying within a normal time span"* [1]. Acontractile detrusor is specified when there is no measurable detrusor contraction.

Female voiding dysfunction is defined by the ICS as: *"a diagnosis based on symptoms and urodynamic investigations characterised by abnormally slow and/or incomplete micturition, based on abnormally slow urine flow rates and/or abnormally high PVR volume"* [110]; ideally on repeated measurement to confirm abnormality. Pressure-flow studies may be required to determine the precise cause of the voiding dysfunction [24].

4.4.1 ***Epidemiology, aetiology, pathophysiology***

4.4.1.1 Epidemiology

Underactive bladder as an entity remains difficult to characterise, partly because its corresponding urodynamic correlate, DU, remains loosely defined, leading to significant variability in diagnostic criteria across research studies and significant overlap of symptoms with other conditions. As a consequence of the variable definition, reported prevalence also varies and ranges from 12-45% in women, with increased prevalence seen with age [70] and in institutionalised elderly women [445].

Several studies have demonstrated similar prevalence rates for DU in the ambulatory setting of around 12-19% [446-448]. As would be expected, voiding symptoms consistent with UAB are higher. In a large cross-sectional, population-based internet survey conducted in the USA, UK and Sweden including 15,861 women aged ≥ 40 years, 20.1% had weak flow, 27.4% had incomplete bladder emptying and 38.3% had terminal dribbling [5].

Both DO during filling and DU in the voiding phase of urodynamic studies can co-exist (formerly known as detrusor hyperactivity with impaired contractility; [DHIC]) and one study showed the prevalence of this finding was over 30% in elderly women [445].

4.4.1.2 Aetiology

The presence of DU in diverse clinical groups suggests multifactorial aetiology [449]. Idiopathic DU is probably partly an age-dependent decrease in detrusor contractility with no other identifiable causes, but young women can also have DU. There are many secondary causes of DU, including neurogenic (e.g., multiple sclerosis, multiple systemic atrophy, spinal cord injury, spina bifida, Parkinson's disease, hydrocephalus, transverse myelitis, stroke, Guillain-Barré syndrome, diabetes mellitus, and pelvic nerve injury), myogenic (prolonged bladder overdistension, diabetes mellitus, and BOO) and iatrogenic (pelvic surgery) causes [450].

4.4.1.3 Pathophysiology

Many pathways are involved in normal detrusor contraction, and there are different possible sites of dysfunction [75] with a variety of mechanisms involved in UAB (see Figure 1):

- Central circuits and centres (prefrontal cortex, periaqueductal gray, pontine micturition centre and hypothalamus): failure of integration or processing.
- Efferent pathways (sacral cord, sacral nerves, pelvic nerves, and postganglionic neurons): impaired detrusor activation.
- Afferent pathways (peripheral afferent nerves, anterolateral white column, and posterior column): early termination of voiding reflex.
- Muscle (detrusor myocytes and extracellular matrix): loss of intrinsic contractility.

Different aetiologies can share common pathophysiological mechanisms: for example, diabetes mellitus affects mainly afferent pathways and the detrusor muscle; and neurogenic diseases affect central circuits and efferent/afferent pathways.

Figure 1: Management and treatment of women presenting with urinary incontinence, site of dysfunction, major aetiological factors, mechanisms

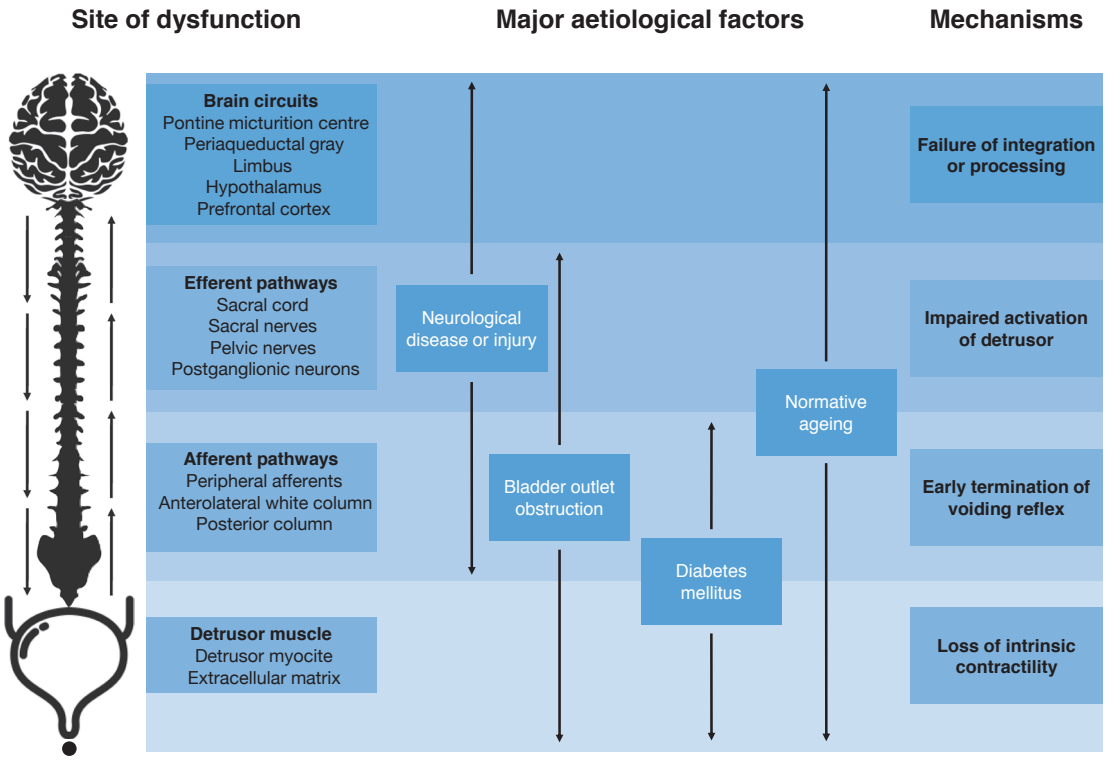

**Figure reproduced with permission from the publisher, from Osman N. et al. [451].*

4.4.2 Classification

There is no current classification system of UAB. Patients can be classified according to presumed aetiology or pathogenic mechanism, but without sufficient longitudinal data or high-level evidence to establish prognostic factors, the classification of UAB patients in terms of relevant clinical characteristics or risk of complications is not possible.

4.4.3 Diagnostic evaluation

4.4.3.1 Symptoms associated with detrusor underactivity

A retrospective study correlated LUTS with urodynamic findings in 1,788 patients (1,281 women). Women with DU, defined as detrusor pressure at maximum flow rate ($P_{det}Q_{max}$) < 20 cmH_2O, maximum flow rate (Q_{max}) < 15 mL/s, BVE < 90% and no sign of obstruction on video-urodynamic studies, had a significantly higher occurrence of reduced and/or interrupted stream, hesitancy, feeling of incomplete bladder emptying, palpable bladder, and absent and/or decreased sensation compared with women with normal pressure and flow [452]. A qualitative study on a small sample of male and female patients diagnosed with DU reported a variety of LUTS and associated impact on QoL. Storage symptoms of nocturia, increased daytime frequency, and urgency, and the voiding symptoms of slow stream, hesitancy, and straining were reported by over half of the patients. A sensation of incomplete emptying and post-micturition dribble were also frequently described. The impact of their symptoms on QoL was variable, but in general, storage symptoms were more bothersome [453].

Based on current data, it is not possible to find a pivotal symptom or collection of symptoms to identify DU patients. The ICI Questionnaire-Underactive Bladder (ICIQ-UAB) has been developed as a research PROM tool [454].

4.4.3.2 Urodynamic studies

Non-invasive studies like uroflowmetry, PVR volume measurement and BVE determination are potentially useful to identify women who might have DU. There is considerable symptomatic overlap with BOO, and uroflowmetry and PVR volume findings may also be similar. Only invasive urodynamics with pressure-flow studies can reliably distinguish DU from BOO and these urodynamic diagnoses can coexist. Diagnosis in women is particularly difficult as they can void by relaxing the pelvic floor, that is, without detectable detrusor contraction during pressure-flow study and without increased abdominal pressure [455]. The simplest methods to define and diagnose DU are based on the use of cut-off values of Q_{max} and $P_{det}Q_{max}$, possibly combined with cut-off values of PVR volume and BVE. However, there is no consensus on which cut-off values should be used [456] and the prevalence of

DU therefore depends on the criteria used. For example, in a retrospective study of 1,015 women, DU was found in 14.9% when using Q_{max} < 12 mL/s or PVR volume > 150 mL; in 9.6% when using $P_{det}Q_{max}$ < 30 cm H_2O and Q_{max} < 10 mL/s; and in 6.4% when using $P_{det}Q_{max}$ < 20 cm H_2O, Q_{max} < 15 mL/s and BVE < 90% [457].

More elaborate methods combine urodynamic data into an index or a physical quantity that reflects bladder contraction strength. A value below a certain threshold would thus diagnose DU. Again, there is no consensus regarding what is normal/abnormal. Table 4 provides an overview of the best-known parameters, their background, and typical values.

Another method of quantifying bladder contraction strength involves stop tests. One study compared three types of direct measurement of isovolumetric pressure: (1) the voluntary stop test, in which the patient voluntarily interrupted flow; (2) the mechanical stop test, in which flow was interrupted by a balloon catheter; and (3) the continuous occlusion test, in which the subject tried to void against a blocked outlet. The latter had the best reliability and best detected drug-induced changes, though the results of the mechanical stop tests were similar [458].

All parameters discussed above give some information about the strength of detrusor contraction in a given void. They do not necessarily reflect what the detrusor might potentially achieve under optimum conditions [459]. Also, they give no information on voiding duration. No parameters for this are available. Finally, abnormally low bladder contraction strength does not necessarily imply insufficient bladder contraction strength to achieve optimal voiding.

Table 4: Most used parameters to measure detrusor contraction in female patients

Parameter	Basis	Population	Values
Watt's factor [460]	Hill equation of muscle contraction in a spherical organ, with fixed constants obtained from experimental and clinical studies	Eight asymptomatic female volunteers aged 28-45 years (median 34 years)	Ideal voiding (bell-shaped flow curves): WF_{max} 11-24 W/m^2 Non-ideal voiding: WF_{max} 5–10 W/m^2 Normally: WF_{max} > 7 W/m^2 (expert opinion, unspecified population) [461]
Projected isovolumetric pressure (cm H_2O) and BCI, using PIP as an index [53, 462]	Bladder output relation, simplified to a straight line with fixed slope of 5 cm H_2O/mL/s (formula: $P_{det}Q_{max} + 5xQ_{max}$)	Unspecified population, mainly men with BPO	Classification based on expert opinion: > 150: strong contraction 100–150: normal contraction 50–100: weak contraction < 50: very weak contraction
Projected isovolumetric pressure 1 (cm H_2O) [463]	Comparison of Q_{max} and $P_{det}Q_{max}$ values with stop test results (Formula: $p_{det}Q_{max} + Q_{max}$)	100 women with UUI aged 53–89 (mean 70) years	5th-95th percentile: 29–78 cm H_2O Mean: 49 cm H_2O Median: 48 cm H_2O Proposed typical values: 30-75 cm H_2O
Continuous occlusion test [458]	Direct measurement of isovolumetric voiding contraction	70 women with UUI aged 53–89 (mean: 70) years	Mean ± SD: 48.7 ± 24.4 cm H_2O

BCI = Bladder contractility index; PIP = Projected isovolumetric pressure; UUI = urgency urinary incontinence; WF = Watt's factor.

4.4.4 ***Disease management***

As there are different possible causes and pathogenic mechanisms involved in female UAB, preventive and therapeutic strategies are difficult to define. Among preventive strategies, early recognition after major surgery or labour might prevent long-term problems associated with prolonged bladder over-distension. Nerve-sparing techniques for radical pelvic surgery are more favourable in terms of early recovery of bladder function [464, 465].

Treatment of female DU includes strategies to ensure bladder drainage, increase bladder contraction, decrease urethral resistance, or a combination of the two [461]. The management goals for UAB are to improve symptoms and QoL, to reduce the risk of complications, and to identify situations where interventions may not be appropriate.

4.4.4.1 Conservative management

4.4.4.1.1 Behavioural interventions

Regular or timed voiding in women with impaired bladder sensations have been done to avoid bladder over-distention. Assisted voiding by abdominal straining with adequate relaxation of the PFM, double or triple voiding are potential strategies to improve bladder emptying. However, none of these manoeuvres has proven efficacy in an RCT. Furthermore, there is a possible association between voiding by excessive abdominal straining and the risk of POP [466]. A small retrospective study in women with neurogenic acontractile detrusor secondary to spina bifida showed that Valsalva voiding may increase the risk of rectal prolapse compared with IC [467].

4.4.4.1.2 Pelvic floor muscle relaxation training with biofeedback

Theoretically PFM relaxation may reduce outlet resistance and therefore potentially improve voiding parameters. There are no RCTs on PFM relaxation training in adult women with UAB. Contrary to common beliefs, one study found significant relaxation of the PFMs after contraction [468] and another study found that PFM relaxation training over time increased the speed of relaxation after a single contraction [469]. There is some evidence from the paediatric literature, including one RCT that compared efficacy of PFM relaxation with biofeedback plus combined therapy (including hydration, scheduled voiding, toilet training and diet) vs. combined therapy alone in children with non-neuropathic UAB and voiding dysfunction. Mean number of voiding episodes was significantly increased in the relaxation training group compared with the group with only combined treatment. Post-void residual volume and voiding time decreased considerably, whereas maximum urine flow increased significantly in the relaxation group compared with the combined treatment group [470, 471].

4.4.4.1.3 Intermittent catheterisation

Intermittent catheterisation (IC) is the most commonly used therapy to manage high PVR volume and urinary retention [116]. It reduces the risk of complications such as UTI, UUT deterioration, bladder stones and overflow UI, etc. It has not yet been established whether the incidence of UTI, other complications and user satisfaction, are affected by either sterile or clean intermittent catheterisation (CIC), coated or uncoated catheters or by any other strategy [472]. The use of hydrophilic catheters may be associated with a lower rate of UTI, but further evidence is needed, as current data comes from neurogenic patients [473]. The average frequency of catheterisation is four to six times per day [474] and the catheter sizes most often used are 12-16 Fr. In aseptic IC, an optimum frequency of five times showed a reduction of UTI [474]. Frequency of catheterisation needs to be based on individual need and capability, to prevent chronic and repeated over-filling of the bladder [475]. Thorough counselling regarding techniques, frequency, equipment, and adverse effects of IC should be given to all potential patients in line with good medical practice.

For people using IC, a Cochrane review found no evidence that one type of catheter or regimen of catheterisation was better than another [472]. However, a narrative review suggests that, in certain populations, single-use catheters may reduce urethral trauma and UTI [476].

4.4.4.1.4 Indwelling catheter

Indwelling urinary catheter may be an option for some women who have failed all other treatments and are unable to perform IC. Complications include UTI, stone formation, and urethral damage. Suprapubic catheterisation may be preferable over urethral catheterisation to minimise the risk of urethral trauma and pain [477].

4.4.4.1.5 Intravesical electrical stimulation

Intravesical electrical stimulation (IVES) can be used to improve bladder dysfunction by stimulating A-delta mechanoreceptor afferents but requires intact afferent circuits and healthy detrusor muscle. One retrospective study in sixteen patients (eleven females) found that two-thirds of patients with a weak detrusor after prolonged bladder over-distension regained balanced voiding after IVES due to detrusor reinforcement [478].

4.4.4.2 Pharmacological management

4.4.4.2.1 Parasympathomimetics

Theoretical approaches to UAB pharmacological treatment include direct stimulation of detrusor cell muscarinic receptors using parasympathomimetic agents such as carbachol or bethanechol or acetylcholinesterase inhibitors such as distigmine, pyridostigmine or neostigmine.

A SR on the use of parasympathomimetics in patients with UAB included ten RCTs (controls typically received placebo or no treatment). Three studies reported significant improvements relative to the control group, but six did not and one even reported significant worsening of symptoms. There was no evidence for differences between individual drugs, specific uses of such drugs, or in outcome measures [479]. The review concluded that the available studies do not support the use of parasympathomimetic for treating UAB, especially when frequent and/or serious adverse effects (gastrointestinal upset, blurred vision, bronchospasm, and bradycardia) are taken into account.

4.4.4.2.2 Alpha-adrenergic blockers

In order to improve bladder emptying, decreasing outlet resistance through sympathetic blockade at the bladder neck/urethra has been investigated. One prospective study with tamsulosin showed similar improvement in terms of uroflowmetry parameters (specifically in the percentage of patients who had a good therapeutic response) in women with BOO (39.4%) or DU (32.7%) [480]. Another longitudinal study including fourteen women with DU showed clinical and urodynamic improvements after tamsulosin [481]. A prospective single-blind RCT in female patients with DU compared the efficacy of alpha-blocker, cholinergic drugs, or combination therapy, with the latter exhibiting the best results [482].

4.4.4.2.3 Prostaglandins

Prostaglandins are prokinetic agents that promote smooth muscle contraction. Prostaglandins E2 and F2 have been used intravesically to treat urinary retention after surgery. A Cochrane review showed a significant association between intravesical prostaglandin and successful voiding among post-operative patients with urinary retention. However, the success rate was low (32%) with wide 95% CI, compared to placebo. The RCTs included in the pooled analysis were underpowered with methodological limitations and the event rate was very low, indicating a very low certainty of the evidence [483]. Intravesical prostaglandin treatment is rarely used, and further research is necessary before it can be taken up more widely.

4.4.4.3 Surgical management

4.4.4.3.1 Sacral nerve stimulation

Sacral nerve stimulation is often used for therapy of non-obstructive urinary retention. The mechanism of action has not been fully elucidated, but activation of afferent sensory pathways, modulation-activation of the central nervous system, and inhibition of inappropriate activation of the guarding reflex are some of the mechanisms proposed.

An RCT included 37 patients in the implantation arm and 31 in the standard medical therapy arm, showing a mean decrease in PVR volume and a mean increase in voided PVR volume compared to standard treatment [484]. A meta-analysis of seven studies also showed a mean difference in PVR volume reduction of 236 mL and a mean voided volume increase of 299 mL [485]. The response rate during the trial phase ranged from 33-90% (mean 54.2%) and the success rate of permanent implantation ranged from 55-100% (mean 73.9%), highlighting that patient selection is crucial [486].

The importance of careful patient selection has been emphasised with one study suggesting women with evidence of anatomical BOO, suspected loss of intrinsic detrusor contractility or neurogenic bladder dysfunction show lower response rates [487].

4.4.4.3.2 Onabotulinumtoxin A

OnabotulinumtoxinA injections in external striated urethral sphincter may improve voiding in patients with DU by reducing outlet resistance and reducing the guarding reflex. Some retrospective case studies have shown improvement in voiding symptoms, recovery of spontaneous voiding, and improvement in urodynamic parameters (reduction of voiding pressure and/or urethral closure pressures, reduced PVR volume) [488, 489]. The duration of symptomatic relief is short; typically, three months but the reported incidence of *de novo* SUI is low.

4.4.4.3.3 Transurethral incision of the bladder neck

Transurethral incision of the bladder neck has been described in a small series of women with refractory DU. In a retrospective case study, 40/82 (48.8%) women achieved satisfactory outcomes (spontaneous voiding with voiding efficiency ≥ 50%), but five (6.1%) patients developed SUI and two (2.4%) developed a vesico-vaginal fistula [490].

4.4.4.3.4 Myoplasty

One retrospective multicentre study reported the long-term results of latissimus dorsi detrusor myoplasty in patients with bladder acontractility, with 71% recovering complete spontaneous voiding, with a mean PVR volume of 25 mL [491]. No other groups have published their experience to reproduce these findings.

4.4.4.3.5 Intravesical electrical stimulation

One RCT from China has reported improvement in mean PVR compared to placebo with this technique [492] but further evaluation in larger multicentre studies is required.

4.4.4.4 Summary of therapeutic evidence on detrusor underactivity

The level of evidence for most therapeutic interventions for DU is low. Only IC remains as a gold standard to reduce the adverse consequences of a high PVR volume and incomplete voiding, in spite of the low level of evidence that supports this statement.

4.4.4.4.1 Summary of evidence and recommendations for underactive bladder

Summary of evidence	**LE**
Abdominal straining with relaxation of the PFM may improve bladder emptying but increases the risk of POP.	3
Pelvic floor muscle relaxation training may increase voiding episodes, decrease post-void residual volume and voiding time.	3
Intermittent catheterisation has proven efficacy in terms of effecting bladder emptying in patients who are unable to do so.	3
Indwelling transurethral catheterisation and suprapubic cystostomy are associated with a range of complications as well as a risk of recurrent UTI.	3
Intravesical electrical stimulation may be useful in some patients after prolonged bladder over-distension, but long-term efficacy remains unproven.	1b
Oral parasympathomimetics do not improve clinical or urodynamic parameters of UAB and frequent and/or serious adverse effects may arise.	1b
Alpha-adrenergic blockers in women with UAB may be effective in improving voided volume and reducing PVR volume.	2b
Intravesical prostaglandins may promote successful voiding in patients with urinary retention after surgery, but further research is necessary.	1a
Sacral nerve stimulation improves voided volume and decreases PVR volume in women with DU.	1b
There is limited evidence for the effectiveness of onabotA external urethral sphincter injections to improve voiding in women with UAB.	3
Transurethral bladder neck incision may improve voiding in women with DU, but complications (SUI, vesico-vaginal fistulae) may occur.	3
There is very limited evidence for the effectiveness of detrusor myoplasty for bladder acontractility.	3

Recommendations	**Strength rating**
Encourage double voiding in those women who are unable to completely empty their bladder.	Weak
Warn women with underactive bladder (UAB) who use abdominal straining to improve emptying about pelvic organ prolapse risk.	Strong
Use intermittent catheterisation (IC) as a standard treatment in patients who are unable to empty their bladder.	Strong
Thoroughly instruct patients in the technique and risks of IC.	Strong
Offer indwelling transurethral catheterisation and suprapubic cystostomy only when other modalities for urinary drainage have failed or are unsuitable.	Weak
Do not routinely recommend intravesical electrical stimulation in women with UAB.	Weak
Do not routinely recommend parasympathomimetics for treatment of women with UAB.	Strong
Offer alpha-adrenergic blockers before more-invasive techniques.	Weak
Do not use intravesical prostaglandins in women with urinary retention unless it is part of a well-regulated and closely monitored research study.	Weak

Offer onabotulinumtoxinA external sphincter injections before more-invasive techniques as long as patients are informed that the evidence to support this treatment is of low quality.	Weak
Offer sacral nerve stimulation to women with UAB refractory to conservative management.	Strong
Do not routinely offer detrusor myoplasty as a treatment for detrusor underactivity.	Weak

4.4.5 Follow-up

Natural history and clinical evolution at long-term follow-up of women with DU is not well known. No longitudinal cohort studies are described in the literature. The interval between follow-up visits depends on patient characteristics, treatments given and the frequency of urinary complications.

4.5 Bladder outlet obstruction

4.5.1 Introduction

Bladder outlet obstruction is defined by the ICS as: *"obstruction during voiding, characterised by increased detrusor pressure and reduced urine flow rate"* [1]. Its precise diagnosis requires urodynamic evaluation including an assessment of pressure and flow.

Voiding dysfunction has previously been defined in Section 4.4. In women, voiding dysfunction can be caused by BOO or DU [1]. There are also non-obstructive causes and therefore voiding dysfunction, and BOO should not be used interchangeably. Another term that must be differentiated from BOO and voiding dysfunction is dysfunctional voiding, which is a specific and discrete form of voiding dysfunction characterised by an intermittent and/or fluctuating flow rate due to involuntary intermittent contractions of the pelvic floor or periurethral striated muscles during voiding in neurologically normal individuals [110].

4.5.2 Epidemiology, aetiology, pathophysiology

4.5.2.1 Epidemiology

Estimates of prevalence of BOO among women vary from 2.7-29% [493]. One large series of women undergoing urodynamic evaluation for LUTS found that ~20% are diagnosed with BOO. The wide variance is due to several factors, including differences in definitions and diagnostic criteria for female BOO, differences in study populations, and variation in study methods. The estimated prevalence rates of LUTS due to BOO in women are lower than those reported in men (18.7-18.9% vs. 24.3-24.7%) [494].

Prevalence of voiding LUTS is associated with age [47, 495, 496], parity [47, 497], prolapse [47, 497] and prior continence surgery [47, 497]. Bladder outlet obstruction has long been postulated to cause mainly voiding symptoms [498] but recent data from a series of 1,142 women referred for evaluation of LUTS suggest that storage symptoms may be predominant in women diagnosed with BOO, and excess daytime urinary frequency was the most common symptom reported by 69% [493].

4.5.2.2 Pathophysiology and aetiology

Bladder outlet obstruction can be either anatomical (mechanical) or functional. In anatomical BOO, there is a physical or mechanical obstruction to the outflow of urine, whereas in functional BOO there is a non-anatomical, non-neurogenic obstruction of the outlet usually resulting from non-relaxation of the bladder neck, sphincter or PFM. Other causes of functional BOO would include increased urethral sphincter tone or PFM contraction during voiding, as observed in patients with dysfunctional voiding [498]. The exact causes of this lack of relaxation, or contraction, are often elusive but might be due to sympathetic hyperactivity or hypertrophy of the bladder neck smooth muscle for primary bladder neck obstruction [499] or maybe behavioural for dysfunctional voiding [500].

Mechanisms for anatomical (mechanical) obstruction include external compression, fibrosis, stricture or injury to the urethra and kinking of the urethra due to POP. Progressive fibroblastic reaction around the urethra induced by mesh tapes or slings used in incontinence surgery may also cause anatomical (mechanical) obstruction [450]. In a retrospective review of 192 women diagnosed with BOO, 64% had mechanical obstruction [493].

In primary bladder neck obstruction, the bladder neck fails to open adequately during voiding, in the absence of an anatomical obstruction [501]. It is estimated that 4.6-16% of women presenting with voiding symptoms have primary bladder neck obstruction [499].

Dysfunctional voiding is due to involuntary intermittent contractions of the periurethral striated or PFM during voiding in neurologically normal women and is thought to be caused by faulty learned toileting behaviour [450]. There is also some evidence of a link between dysfunctional voiding and a history of sexual abuse [502].

Fowler's syndrome, is a primary disorder of the urethral striated sphincter with hypertrophy of the muscle fibres, which exhibits complex repetitive discharges and deceleration bursts on electromyography. Fowler's Syndrome is characterized by urinary retention associated with decreased detrusor contractility via enhancement of the guarding reflex (high tone non-relaxing sphincter). It is seen most often, but not exclusively, in young women and is characterised by increased urinary sphincter volume and activity/tone, commonly associated with polycystic ovarian syndrome (PCOS) and endometriosis [503, 504].

Alpha-adrenergic agonists, such as pseudoephedrine commonly contained in decongestants, can lead to some form of functional obstruction due to their stimulatory effects, which may contract the bladder neck and lead to urinary retention [505].

Neurological conditions can also bring about functional BOO in women. These conditions are not considered in these guidelines and are covered elsewhere [11].

Table 5: Main causes of female bladder outlet obstruction [11]

Functional BOO	Anatomical BOO
• Primary bladder neck obstruction • Dysfunctional voiding • Idiopathic urinary retention (Fowler's) syndrome • Increased tone of PFM or sphincter	• Urethral stricture • Anti-incontinence surgery • Pelvic organ prolapse • Urethral diverticulum • Urethral caruncle • Urethral malignancies • Paraurethral masses

4.5.2.3 Recommendation for classification of bladder outlet obstruction

Recommendation	Strength rating
Use standardised classification of bladder outlet obstruction in women (anatomical or functional), and research populations should be fully characterised using such classification.	Strong

4.5.3 ***Diagnostic evaluation***

Diagnosis of BOO in women, although dependent on formal pressure-flow studies, may be suggested by several clinical and other non-invasive assessments.

4.5.3.1 Clinical history

In terms of clinical history, a range of LUTS may be elicited and these may not be confined to voiding LUTS. Women may not present until they have the possible complications of BOO, such as recurrent UTI, chronic urinary retention or acute/chronic kidney disease [493]. The evidence regarding clinical utility of symptoms for the diagnosis of BOO is inconclusive and limited to small retrospective studies [506, 507]. Perhaps some of the difficulty in evaluating the diagnostic accuracy of urinary symptoms comes from the observation that a significant proportion of women presenting with obstruction also have concomitant storage symptoms, making urodynamic evaluation essential. In a large study of > 5,000 women with urinary symptoms including 163 with BOO, additional urodynamic diagnoses were noted in 54% [508].

4.5.3.2 Clinical examination

There are no studies evaluating the clinical utility of physical examination in women with suspected BOO; nevertheless, it is widely considered as a key part of the medical assessment. It allows for visual inspection of the urethra and vagina for possible causes of mechanical obstruction. EMG assessment, dynamometry and manometry of the pelvic floor may be utilised to look for possible causes of functional obstruction.

4.5.3.3 Uroflowmetry and post-void residual volume

Reduced Q_{max} and incomplete bladder emptying can result from weakness in the contractile strength of the detrusor muscle, or increased outlet resistance due to functional or anatomical/mechanical BOO. The use of uroflowmetry to differentiate between anatomical and functional BOO was explored in a retrospective study of 157 women [500], which concluded that Q_{max} was significantly lower in patients with anatomical obstruction, but a large degree of overlap was noted. The largest evaluation of the diagnostic utility of urine flow studies and PVR volume estimation was a retrospective analysis of > 1,900 patients with symptoms of voiding dysfunction,

of whom > 800 were diagnosed with BOO based on urodynamic assessment [509]. Functional BOO was > 6 times more common than anatomical/mechanical obstruction, which inconsistent with most of the other epidemiological literature for female BOO. The authors found that although urine flow rate alone was not accurate enough to diagnose BOO, PVR of ≥ 200 mL could differentiate bladder neck dysfunction from the other causes of BOO, with a receiver-operator characteristics (ROC) area under the curve (AUC) of 0.69. Conversely, in a retrospective study involving 101 women primarily presenting with SUI, a good correlation between abnormal uroflowmetry and urodynamic obstruction (phi = 0.718) was found [510]. In a retrospective study a novel predictive model of fBOO based on clinical features and non-invasive test parameters in female patients with LUTS was validated; 728 women were investigated for BOO ($P_{det.}Q_{max} - 2.2 \times Q_{max} > 5$ [BOOIf > 5]) by urodynamic test; 249 (34.2%) and they were randomly assigned to a model development group and a model validation group. Older age, lower Q_{max}, longer flow time, and lower voiding efficiency were identified as factors predicting BOO. This nomogram could be easily used in clinical practice as it includes non-invasive clinical and diagnostic factors obtained by simple uroflowmetry [511].

4.5.3.4 Ultrasound

The major utility of US scanning in women with BOO is to detect possible complications such as increased BWT/DWT or upper tract dilatation/hydronephrosis. However, the diagnostic capabilities of US have been investigated in a SR of sixteen non-randomised studies and reported a moderate pooled sensitivity and high specificity for DWT, while six studies evaluating US-estimated bladder weight (UEBW) reported a high sensitivity and specificity [512]. A prospective case-control study of 27 patients with cystoscopically confirmed bladder neck obstruction [513] reported the diagnostic value of shear wave elastography (SWE) and acoustic radiation force impulse imaging (ARFI) for female BOO was compared and the authors concluded that ARFI was more accurate than SWE, but a combination of the techniques was superior to either one alone.

4.5.3.5 Magnetic resonance imaging

Magnetic resonance imaging in patients with pathological urethral stricture can determine the degree of periurethral fibrosis, although the prognostic and clinical significance of such a finding has not been established [514].

4.5.3.6 Electromyography

Electromyography (EMG) is considered the most accurate means of assessing PFM tone and intraurethral straited muscle sphincter activity [515, 516]. It has been most extensively studied in the subgroup of women with BOO due to idiopathic urinary retention caused by a high-tone non-relaxing sphincter (Fowler's syndrome). Abnormal urethral EMG activity may be associated with non-relaxation of the striated sphincter, abnormally high urethral pressure, and, through an exaggerated guarding reflex, poor bladder sensation and reduced detrusor contractile strength [502, 517]. Complex repetitive discharges and decelerating bursts are specific urethral EMG abnormalities that have been described in patients with high-tone non-relaxing sphincter, although these abnormalities have also been noted in asymptomatic volunteers [518, 519]. A SR of voiding dysfunction in women included 65 studies with only a small number addressing the diagnostic utility of PFM EMG [450]. The authors commented that increased EMG activity of the PFM can be seen during voiding or non-relaxation, and when this is coupled with pressure-flow information from urodynamics, it may be useful to differentiate between functional and anatomical obstruction. Further evidence for this comes from a retrospective study of 157 women with roughly equal numbers of women with functional and anatomical obstruction, which concluded that a low level of PFM EMG activity is characteristic of anatomical obstruction [500]. Additional neurophysiological tests, such as anal sphincter EMG, bulbocavernosus reflex, and pudendal sensory evoked potentials can assess the integrity of the somatic S2-4 nerve roots; however, their clinical utility in the context of non-neurogenic female BOO needs to be better defined [502].

4.5.3.7 Cystourethroscopy

Cystourethroscopy can be useful to visualise any anatomical/mechanical obstruction and provide information regarding its nature, location and calibre. Given that pelvic malignancy may cause anatomical BOO, cystourethroscopy is considered an essential part of the diagnostic pathway. Formal urethral calibration may be useful for women with BOO secondary to pathological urethral stricture and various different urethral calibre thresholds have been used, from 14-20 Fr [520].

4.5.3.8 Urodynamics and video-urodynamics

Pressure-flow studies are the mainstay of BOO diagnosis and the characteristic abnormalities are a combination of low flow and concomitant high detrusor pressure [501]. However, while the general definition of BOO is well established, with some data supporting its clinical validity in male patients [521], the urodynamic definition of female BOO remains controversial [68, 498]. Several urodynamic criteria have been introduced but none has been established as a standard due to lack of clinical validation [498, 522]. The Blaivas and Groutz nomogram, which plots free Q_{max} and maximum detrusor pressure ($P_{det \cdot max}$) measured during urodynamic studies, is one of the most popular [523] but has been suggested to overestimate obstruction [524]. The addition of fluoroscopic imaging suggested by Nitti and colleagues introduces a video-urodynamic criterion for obstruction [71]. However, both methods lack data supporting their clinical validity, especially regarding their predictive value for therapeutic intervention outcomes [69].

In a large retrospective study of 1,914 patients, 810 of whom were diagnosed with BOO, several urodynamic cut-off values were determined by receiver-operating characteristic (ROC) curve analysis to optimise the diagnostic accuracy of video-urodynamic studies [509]:

- $P_{det}Q_{max} \geq 30$ cm H_2O for differentiating BOO from bladder dysfunction and normal studies (ROC AUC = 0.78);
- the Abrams-Griffiths number > 30 for differentiating anatomical from functional BOO (ROC AUC = 0.66);
- $P_{det}Q_{max} \geq 30$ cm H_2O for differentiating dysfunctional voiding from poor relaxation of the external sphincter (ROC AUC = 0.93).

More recently, Solomon and Greenwell devised a female BOO nomogram that parallels the ICS nomogram used for male BOO [525]. It allows the calculation of an alternative BOO female index (BOOIf), using a formula closely aligned to its male counterpart: $BOOIf = P_{det}Q_{max} - 2.2Q_{max}$.

It is interpreted with a different algorithm however:

- BOOIf < 0: < 10% probability of obstruction;
- 5 < BOOIf < 18: equivocal, ≥ 50% likelihood of obstruction;
- BOOIf > 18: 90% likelihood of obstruction.

The Solomon-Greenwell nomogram was the first to be tested for clinical validity. In a series of 21 unselected consecutive women treated for BOO, the authors observed significant improvement of all urodynamic parameters (Q_{max}, $P_{det}Q_{max}$ and BOOIf) in female patients who became asymptomatic post-operatively [526].

An alternative urodynamic parameter of area under the detrusor pressure curve during voiding (corrected for voided volume) has been proposed following a prospective study of 103 women [527]. The authors concluded that this variable appears to be the most discriminating urodynamic parameter for the diagnosis of female BOO. This suggested diagnostic method has not been independently validated.

Voiding cystourethrography (VCUG) alone or in conjunction with concomitant pressure-flow studies may be useful in delineating the site of obstruction. Characteristic features include:

- radiographic evidence of obstruction between the bladder neck and distal urethra in the presence of
- sustained detrusor contraction [71];
- lack of funnelling appearance of the bladder neck/tight bladder neck in primary bladder neck obstruction;
- proximal dilatation of the urethra with distal narrowing in women with urethral stricture disease or pelvic-floor hypertonicity.

It is not uncommon for women with voiding dysfunction, specifically functional BOO, to be unable to provide a flow during (video)urodynamic testing. Failure to relax the PFM can enhance the guarding reflex, limiting detrusor contractility.

The complexity of the diagnosis of BOO was highlighted in a recent SR from the panel that concluded that the evaluation should be multidisciplinary and may include a detailed history, neurological and uro-gynaecological examination, EMG, video urodynamics, urethral pressure profilometry, ultrasound and cystourethroscopy [68].

4.5.3.9 Summary of evidence and recommendations for diagnosis of bladder outlet obstruction

Summary of evidence	LE
Evaluation of LUTS by history and examination alone is insufficient to accurately diagnose female BOO.	3
Urine flow studies cannot accurately diagnose BOO in women.	3
Ultrasound is unable to accurately diagnose BOO in women.	2b
Electromyography alone is unable to accurately diagnose BOO in women, although it may be of use in combination with pressure-flow studies and in differentiation of anatomical vs. functional BOO.	3
Cystourethroscopy can be useful to visualise any anatomical/mechanical obstruction and provide information regarding its nature, location, and calibre.	4
Video urodynamics is the standard test for evaluating female BOO.	3

Recommendations	Strength rating
Take a full clinical history and perform a thorough clinical examination in women with suspected bladder outlet obstruction (BOO).	Strong
Do not rely on measurements from urine flow studies alone to diagnose female BOO.	Strong
Perform cysto-urethroscopy in women with suspected anatomical BOO.	Strong
Perform urodynamic evaluation (preferably with video fluoroscopy) in women with suspected anatomical BOO.	Strong
Use electromyography when evaluation of PFM or sphincter tone is required.	Strong

4.5.4 ***Disease management***

Therapeutic interventions for BOO aim to decrease outlet resistance in order to increase urinary flow, improve bladder emptying and thus reduce voiding and storage LUTS [69, 498, 522]. Treatment choice is commonly dictated by the underlying cause of the obstruction, whether it is an anatomical (mechanical), or a functional obstruction.

4.5.4.1 Management of Anatomical Bladder Outlet Obstruction

4.5.4.1.1 Conservative Management

4.5.4.1.1.1 Use of vaginal pessary

Intravaginal devices such as pessaries aim to relieve voiding symptoms and improve bladder emptying by physical correction of the obstruction caused by a POP. In a prospective study of eighteen women with grade three or four cystocoeles and diagnosed with BOO by urodynamics (defined as $P_{det}Q_{max}$ > 25 cm H_2O, Q_{max} < 15 mL/s), normal voiding was noted in seventeen (94%) immediately after placement of a vaginal pessary. No other outcomes were available in this series [528]. No long-term data are available on the use of vaginal pessary for BOO.

4.5.4.1.1.2 Urinary containment

The use of containment devices in BOO is to achieve social continence in patients with urinary retention and associated overflow UI (due to elevated bladder pressures or urethral sphincter weakness or both) and is often only a temporary measure. There are no published studies on the outcomes or adverse events associated with the use of urinary containment devices for the management of female BOO, though there are many involving women with UI who may have BOO as an underlying cause.

4.5.4.1.1.3 Urinary catheterisation

Significant urinary retention from BOO may be addressed by actively bypassing the obstruction and draining the residual urine. Catheterisation may be used as a treatment itself or as an adjunct to an initial treatment of urethral dilatation or urethrotomy or bladder neck incision. There are two ways of using a catheter: IC or indwelling catheterisation [116].

After UI surgery, BOO may be managed by short-term catheterisation in most patients who have transient post-operative voiding difficulty. For a few women who develop chronic urinary retention, IC or indwelling catheterisation may be offered [450].

In a series of twenty patients with voiding dysfunction after TVT who were put on an IC programme, overall cure rate was 59%, with cure defined as consistent residual volume < 100 mL. Half of these patients were voiding normally within twelve weeks [529].

See Section 4.4.4.1.3 for further evidence related to IC.

4.5.4.1.1.4 Intraurethral inserts

An intraurethral insert is a short silicone catheter containing an internal valve and pump mechanism positioned in the female urethra. The valve-pump mechanism is operated by an external control unit, which activates to open the valve and the pump to draw urine from the bladder and allow voiding. At the end of urination, the pump ceases, and the valve closes to regain continence. The insert is routinely replaced once a month.

One study reported the use of this device in 92 women with voiding dysfunction of various aetiologies including multiple sclerosis, prior pelvic surgery, pelvic radiation, diabetes mellitus, spinal stenosis and injury. The device was removed within seven days of insertion in 60% of the cases due to discomfort, peri-catheter leakage or technical difficulty. An additional 20% of patients had late discontinuation. All those who continued to use the device were satisfied, with PVR volumes remaining < 100 mL. Adverse events included migration into the bladder in six cases and symptomatic UTI in four cases [530, 531]. Extended, long-term data on the use of urethral inserts are not available.

4.5.4.1.1.5 Summary of evidence and recommendations for conservative management of anatomical bladder outlet obstruction

Summary of evidence	**LE**
In women with large (grade three or four) cystocoeles causing BOO, placement of a vaginal pessary may improve voiding efficiency.	3
Regular IC after urethrotomy is better than no catheterisation to prevent recurrence of urethral strictures.	1b
An IC programme in women with voiding dysfunction after TVT has a cure rate of 59%.	3
Women who use an intraurethral device have lower PVR volume, but most require its removal due to complications.	3

Recommendations	**Strength rating**
Offer the use of a vaginal pessary to women with grade three or four cystocoeles and bladder outlet obstruction (BOO) who are not eligible/inclined towards other treatment options.	Weak
Offer urinary containment devices to women with BOO to address urinary leakage as a result of BOO, but not as a treatment to correct the condition.	Weak
Offer clean intermittent self-dilatation to women with urethral strictures or post-urinary incontinence surgery for BOO.	Weak
Do not offer an intraurethral device to women with BOO.	Strong

4.5.4.1.2 Surgical Management

4.5.4.1.2.1 Pelvic organ prolapse surgery

Pelvic organ prolapse surgery may relieve BOO by correcting the urethral kinking caused by the prolapse or by relieving the urethral compression brought about by the prolapsing organ [69, 498, 522].

Bladder outlet obstruction due to POP may be addressed by corrective surgery. Based on reviews, the majority of patients who had BOO caused by POP who had repair of their cystocoele demonstrated improvement of their voiding difficulties [450, 532].

A multicentre prospective study involving 277 women with at least grade two symptomatic POP who underwent surgery demonstrated a significant reduction in voiding symptoms and PVR volume one year post-operatively [533].

A retrospective study of 50 women who underwent laparoscopic sacrocolpopexy for POP showed a significant increase in mean post-operative Q_{max} and decrease in $P_{det}Q_{max}$ and PVR in those aged ≥ 65 years. The OAB symptom score improved but there was no significant difference in the ICIQ-SF score post-operatively [534].

4.5.4.1.2.2 Urethral dilatation

Urethral dilation involves the passage of sequentially greater diameter dilators into the urethra, causing the obstructing fibrotic tissue to break open, thereby widening the lumen. It is considered the primary procedure of choice for women suspected of urethral stricture disease [520]. Dilation of up to 30-40 Fr has been done. There is no standard dilatation technique; dilatation of up to 43 Fr has been described, although other authors suggest dilating to 30 or 35 Fr.

A SR of female urethral stricture management included three trials involving urethral dilatation. Pooled analysis of data from 93 women showed a mean success rate of 49% after urethral dilation to 41 Fr with a mean follow-up of 46 months. Mean time to failure was twelve months. In treatment-naïve patients, success rate (as defined by trialists) was 58%, compared with 27.2% in patients who had undergone previous dilatation [535].

An RCT of 50 women with OAB syndrome and associated urodynamically confirmed BOO (defined as a Q_{max} < 15 mL/s with a voided volume of ≥ 100 mL and/or PVR volume > 200 mL, not due to urethral stricture) compared the effect of cystoscopy and bladder distension with urethral dilatation (n = 22) and cystoscopy only (n = 28) after six weeks' follow-up. Significantly more patients who had cystoscopy only had persistent urgency at six weeks and six months post-operatively. Urodynamic parameters did not significantly change pre- and post-operatively in both groups. The greater improvement in QoL scores based on the King's Health Questionnaire domain scores seen in the non-urethral dilatation group in this trial should be interpreted cautiously because of the higher baseline scores. There were no significant changes in Q_{max}, PVR volume, voided volume or $P_{det}Q_{max}$ in any of the two groups at six weeks, questioning the role of either of these two options for therapeutic management of BOO. Also, six patients (12%) developed post-operative SUI [536].

A prospective trial of 86 women with primary urethral stricture compared on-demand vs. intermittent urethral dilatation to 24 Fr every two months. It showed an overall increase in Q_{max} and decrease in PVR volume post-dilatation. Significantly greater improvements were seen in the intermittent urethral dilatation group [537].

Worsening or new-onset SUI is a concern with urethral dilatation, but it is less of a concern than after urethrotomy or surgical reconstruction. Patients have also reported frequency and urgency post-dilatation [538].

4.5.4.1.2.3 Urethrotomy

Urethrotomy involves incision of the urethra endoscopically or using a urethrotome. It addresses the urethral narrowing by cutting open the scar tissue which is causing the obstruction [69, 498, 522, 538].

A prospective study of ten women with urethral strictures investigated the effect of Otis urethrotomy to 40 Fr followed by six weekly dilatations. There was significant improvement in IPSS, QoL, voided volume, Q_{max} and PVR volume at six months. Only the improvements in PVR volume and QoL were maintained on long-term follow-up (mean 82 months) [539].

A small RCT investigated the effectiveness of self-dilatation to prevent recurrence after internal optical urethrotomy for urethral stricture disease. In the treatment group, self-dilatation was done twice a day for one week, and once a day for four weeks, then once weekly for seven weeks post-urethrotomy. Freedom from stricture recurrence, determined by urethrography and uroflowmetry performed twelve weeks post-operatively, was higher in the self-dilatation group compared to the group with no self-dilatation (78.5% vs. 55.4%) [540]. This finding mirrors the Cochrane review on self-dilatation for urethral stricture among men that showed less recurrence with the performance of self-dilatation [541].

4.5.4.1.2.4 Bladder neck incision/resection

Transurethral bladder neck incision decreases resistance at the bladder neck by cutting open the hypertrophic bladder neck smooth muscle in patients with primary bladder neck obstruction. Transurethral incision of the bladder neck may be performed with a unilateral incision at the twelve o'clock position or with bilateral incisions at the five and seven o'clock, two and ten o'clock or three and nine o'clock positions, or four incisions at the three, six, nine and twelve o'clock positions. This may be done using a resectoscope with a Collin's knife, cold knife, or using laser energy. Some authors report additional resection of the bladder neck between the five and seven o'clock positions.

A review of non-comparative studies on bladder neck incision for the treatment of bladder neck obstruction in women reports success rates of 76-100% [501].

Bladder neck incision was compared with V-Y-reconstruction using Nesbit's technique in a retrospective study of seventeen women with BOO, diagnosed by various uroradiological, endoscopic and urodynamic investigations. The results showed similar symptomatic improvement rates and post-operative PVR volume between the two groups. V-Y plasty had a longer operating and catheter time, lower uroradiological improvement rate, higher transfusion rate, and higher adverse event rate [542].

Several prospective case series consistently reported significant improvements in IPSS, QoL, Q_{max}, $P_{det}Q_{max}$ and PVR volume after treatment compared to baseline, regardless of the site of the incision, type of energy used or the length of follow-up [543-546].

The largest case series with 84 patients diagnosed with primary bladder neck obstruction (based on lack of funnel shape of the bladder neck during voiding-on-voiding cysto-urethrography, P_{det} > 20 cm H_2O and Q_{max} < 12 mL/s) showed success in 84.5% of patients with improvement in IPSS, QoL, Q_{max} and $P_{det}Q_{max}$ after mean follow-up of 27.4 months (6-78 months). Complications included vesico-vaginal fistula (VVF) (3.6%), SUI (4.7%) and urethral stricture (3.6%) [543].

No comparisons have been made between the different incision techniques (location, length, and depth of incision, implement used - cold knife vs. hot knife vs. laser, with or without resection). However, in a case series of 84 patients, complications of VVF and SUI were noted in the cohort of patients who had their incisions at five and seven o'clock positions, and not in those who had their incisions at two and ten o'clock [543].

Adverse events include SUI, requirement for reoperation, and recurrence. Post-operative SUI was reported in 3- 33% [501].

4.5.4.1.2.5 Urethroplasty/urethral reconstruction
Surgical reconstruction of the female urethra has been used in the management of extensive urethral stricture. Several urethroplasty techniques include the use of vaginal or labial flaps, as well as vaginal and buccal grafts after cutting open the fibrotic tissue causing the urethral obstruction [547]. The use of bladder flaps has also been reported [548], and laboratory-engineered tissue grafts have also been used [548].

The surgical approaches have been described based on the position relative to the urethra; dorsal, ventral, or circumferential. The dorsal approach is believed to provide better mechanical support and a more vascularised bed for a graft or flap. However, there is greater risk of damage to the sphincter and clitoral bodies with this approach. The ventral approach is more familiar to most surgeons and requires less urethral mobilisation. However, it is reported as being more prone to urethrovaginal fistulae, although it is not clear to what extent [520].

Reviews of studies reporting outcomes of urethroplasty state success rates of 57-100% [549]. Pooled analysis from six studies using vaginal or labial flaps showed a mean success rate of 91% with a mean follow-up of 32 months. Vaginal or labial graft urethroplasty was reported to have an 80% success rate with a mean follow-up of 22 months.

Oral mucosal grafts, reported in seven studies, had a mean success of 94% after a mean follow-up of fifteen months [520]. A later review of studies on dorsal buccal mucosal graft reported success rates of 62-100%, with a pooled success rate of 86% [550]. A long-term study with a mean follow-up of 32 months showed a stricture recurrence rate of 23.1% [549].

A SR performed by the panel indicated that urethroplasty results in better QoL and Q_{max} compared to both urethral dilatation and urethrotomy [148].

The EAU Guidelines on Urethral Strictures presents an algorithm on the management of urethral strictures in women presenting with refractory frequency, urgency, poor flow and incomplete emptying [551].

4.5.4.1.2.6 Urethrolysis
Bladder outlet obstruction in women occurring as a complication of surgery for SUI may be managed surgically by urethrolysis, to regain urethral mobility. Urethrolysis may involve removal of periurethral anti-incontinence sutures, scar tissue and fibrosis.

Case series showed success rates measured as improved voiding and lower residual volumes, improvement, or resolution of symptoms and QoL, and improvement of urodynamic parameters after treatment [552-554]. *De novo* SUI was reported in 39% in one study [554]. Another study reported an association of persistent post-operative bladder symptoms with greater delay to performing urethrolysis [555].

4.5.4.1.2.7 Removal/excision/section/loosening of mid-urethral sling

In women who develop BOO after placement of a mid-urethral sling, surgical management may include tape loosening, incision or division, and excision and/or removal of the tape [450].

Several small retrospective reviews of cases using different techniques of sling revision (incision, partial excision, or excision) showed good success rates in terms of symptom reduction, resumption of voiding with significant reduction in PVR volume and improvement of urodynamic parameters. Stress urinary incontinence recurs in a small proportion of patients and often to a lesser degree than prior to the sling procedure. Studies have shown long-term efficacy, including preservation of continence.

In a series of 63 women who presented with voiding dysfunction and persistent PVR volume > 100 mL after tape surgery for UI, different techniques were compared. Comparisons involved sling revision: sling division (n = 46) vs. partial sling excision (n = 13) vs. sling revision (division or excision) with an additional anti-SUI procedure (n = 4). The authors reported an overall success rate of 87% (PVR volume < 150 mL). No significant difference in success rates was demonstrated among the different revision techniques. There was a greater need for surgery for recurrent SUI in the partial sling excision group without an anti-SUI procedure (23% vs. 2.2 and 0) [556].

One study showed that patients who underwent surgical release > 180 days after initial anti-UI surgery had significantly less recurrent SUI compared with patients who underwent the release sooner (15% vs. 46%) [557]. Sling revision in women who presented with urinary retention or voiding problems and significant PVRs after sling surgery for UI resulted in improvements in symptoms and urodynamic parameters, resumption of voiding and reductions in PVRs [558].

Beyond the lack of consensual definition and diagnostic approach, well-designed prospective studies on surgical management of BOO are lacking. Evidence to support surgical management is scarce according to the SR performed by the EAU guideline on FLUTS panel [148].

4.5.4.1.2.8 Summary of evidence and recommendations for surgical management of anatomical bladder outlet obstruction

Summary of evidence	**LE**
Repair of POP improved PVR and voiding symptoms.	3
Urethral dilatation in women with BOO results in significant improvement in OAB symptoms, but improvements in urodynamic parameters of voiding are inconsistent.	1b
Programmed intermittent surgical urethral dilatation results in better outcomes compared with on-demand dilatation.	3
Effects of urethral dilatation are poorly sustained, requiring repeat intervention in the long term.	3
Internal urethrotomy followed by regular dilatations resulted in significant improvement in symptoms and urodynamic parameters in women with BOO.	3
Regular self-dilatation after urethrotomy is better than no self-dilatation in terms of preventing recurrent urethral strictures.	1b
Bladder neck incision in females with BOO results in improvements in symptoms and urodynamic parameters.	3
Complications of bladder neck incision are not common, but include VVF, SUI, and urethral stricture.	3
Urethroplasty using grafts or flaps in women with BOO due to urethral stricture have good success rates with significant improvements of symptoms, QoL scores and urodynamic parameters compared to baseline.	3
Urethroplasty results in better QoL and Q_{max} compared to both urethral dilatation and urethrotomy.	2
Long-term results showed significant stricture recurrence rate after urethroplasty.	3
Urethrolysis performed on women with voiding problems after anti-UI surgery resulted in improvements in symptoms, QoL and urodynamic parameters post-operatively.	3

Delayed urethrolysis was associated with persistent post-operative bladder symptoms.	3
Sling revision in women who presented with urinary retention or voiding problems and significant PVRs after sling surgery for UI resulted in improvements in symptoms and urodynamic parameters, resumption of voiding and reductions in PVRs.	3
Sling revision is associated with the risk of recurrent SUI.	3

Recommendations	Strength rating
Inform women with voiding symptoms associated with pelvic organ prolapse that symptoms may improve after surgical repair.	Weak
Offer urethral dilatation to women with urethral stricture causing bladder outlet obstruction (BOO) but advise on the likely need for repeated intervention.	Weak
Offer internal urethrotomy with post-operative urethral self-dilatation to women with BOO due to urethral stricture disease but advise on its limited long-term improvement and the risk of post-operative urinary incontinence (UI).	Weak
Do not offer urethral dilatation or urethrotomy as a treatment for BOO to women who have previously undergone mid-urethral synthetic tape insertion due to the theoretical risk of causing urethral mesh extrusion.	Weak
Inform women of limited long-term improvement (only in terms of post void residual volume and quality of life) after internal urethrotomy.	Weak
Offer bladder neck incision to women with BOO secondary to primary bladder neck obstruction.	Weak
Inform women who undergo bladder neck incision on the small risk of developing post operative stress urinary incontinence (SUI), vesico-vaginal fistula or urethral stricture.	Strong
Offer urethroplasty to women with BOO due to recurrent urethral stricture after failed primary treatment.	Weak
Inform women on the possible recurrence of strictures on long-term follow-up after urethroplasty.	Strong
Offer urethrolysis to women who have voiding difficulties after anti-UI surgery.	Weak
Offer sling revision (release, incision, partial excision, or excision) to women who develop urinary retention or significant voiding difficulty after tape surgery for UI.	Strong
Inform women about the risk for recurrent SUI and the need for a repeat/concurrent anti-UI surgery after sling revision.	Strong

4.5.4.2 Management of Functional Bladder Outlet Obstruction

4.5.4.2.1 Conservative Management

4.5.4.2.1.1 Behavioural modification

Behavioural modification interventions are often tailored to individual patients' needs, symptoms and circumstances and can include elements such as education regarding normal voiding function, self-monitoring of symptoms, changes in lifestyle factors that may affect symptoms, avoidance of constipation, and alteration of voiding technique. Ultimately, techniques aim to improve the coordination between the detrusor and sphincter, resulting in their synergistic action [69, 498, 522].

These individual components of self-management have not been evaluated separately and most recommendations are derived from consensus methodology. They may help reduce symptoms resulting from BOO, but no quantification of their effect is possible.

4.5.4.2.1.2 Pelvic floor muscle training +/- biofeedback

In the context of BOO, physiotherapy aims to teach patients to relax their PFMs and striated urethral sphincter during voiding. Pelvic floor muscle contraction, particularly in women with pelvic floor dysfunction, has been shown to significantly reduce vaginal resting pressure and surface EMG activity [468].

In a narrative review examining the effect of PFM relaxation training on muscle tone and female BOO symptoms, three RCTs compared different types of exercise, and no trial compared relaxation training with no or sham treatment. None of the trials reported the effect between groups on the reduction of PFM tone but all three trials showed improvement of BOO symptoms [471]. The authors concluded that there was an urgent need for studies to define normal values of PFM tone and also to explore the association between PFM tone and symptoms [471].

4.5.4.2.1.3 Electrical stimulation
Application of electrodes that help the woman to perform controlled contraction and relaxation of the PFMs may theoretically facilitate the relaxation of the external sphincter and pelvic floor, but no critical evaluation of this intervention in women with BOO has been published.

4.5.4.2.1.4 Extracorporeal magnetic stimulation
Extracorporeal magnetic stimulation involves the patient sitting on a device that induces consistent PFM contraction and relaxation at a set frequency and interval by repeated magnetic stimulation of motor nerve fibres. It is postulated that patients therefore learn to spontaneously contract or relax the PFM, which may enhance their ability to relax their pelvic floor while voiding [559].

In a small (n = 60) prospective non-randomised trial, alfuzosin was compared to EMS and to the combination of alfuzosin + EMS in women with functional BOO. They observed significant increase of Q_{max} and significant decrease of International Prostate Symptom Score (IPSS) in all groups and significantly greater improvement in the QoL question of the IPSS in the combination therapy group [559].

4.5.4.2.1.5 Summary of evidence and recommendations for conservative management of functional bladder outlet obstruction

Summary of evidence	**LE**
Pelvic floor muscle relaxation training with biofeedback may improve symptoms associated with BOO.	1b
There is no available evidence in the published literature on the clinical effect of ES for management of female BOO.	NA
Extracorporeal magnetic stimulation combined with alfuzosin may be more effective than either of these therapies alone in women with functional BOO.	2a

Recommendations	**Strength rating**
Offer pelvic floor muscle training (PFMT) aimed at pelvic floor muscle relaxation to women with functional bladder outlet obstruction (BOO).	Strong
Prioritise research that investigates and advances understanding of the mechanisms and impact of PFMT on the coordinated relaxation of the pelvic floor during voiding.	Strong
Offer urinary containment devices to women with BOO to address urinary leakage as a result of BOO, but not as a treatment to correct the condition.	Weak

4.5.4.2.2 Pharmacological management
4.5.4.2.2.1 Alpha-adrenergic blockers
Alpha-adrenergic blockers are postulated to relieve LUTS caused by BOO in women via smooth muscle relaxation in the bladder neck, thus decreasing bladder outlet resistance [560].

Systematic reviews on the use of alpha-blockers in women generally involve studies with a population that includes women complaining of LUTS and voiding dysfunction. Confirmation of BOO is often not required in the trials included [561, 562]. These reviews showed significant improvements in symptoms and urodynamic parameters associated with their use [561-563]. A meta-analysis of fourteen RCTs comparing alpha-blockers and placebo in women with LUTS showed significant symptom relief after alpha-blocker treatment relative to placebo, but no significant difference in Q_{max}, PVR volume and adverse event rates [561]. This is in contrast to prospective non-comparative trials that consistently showed improvements in voiding and storage symptoms, bother scores, and urodynamic parameters (Q_{max}, PVR, $P_{det}Q_{max}$, MUCP after alpha-blocker use compared to baseline) [480, 481, 564-566].

A SR performed by the Panel of studies on alpha-blockers used specifically for women with BOO included one placebo-controlled RCT, one RCT comparing two types of alpha-blockers, and six prospective non-comparative studies [148]. In the only placebo-controlled RCT reporting subgroup analyses in women with urodynamically proven BOO (based on the Blaivas-Groutz nomogram) no significant difference was observed in the changes of IPSS, IPSS sub scores, Q_{max}, PVR volume and bladder diary after eight weeks of alfuzosin (n = 58) vs. placebo (n = 59). Of note, no EMG and/or voiding cysto-urethrography was used to distinguish between dysfunctional voiding and primary bladder neck obstruction [567].

Information on the comparative effectiveness of the different types of alpha-blockers was limited to one RCT. A small trial of 37 women with IPSS > 8, Q_{max} < 12 mL/s and PVR volume > 50 mL, compared tamsulosin and prazosin over a three-month treatment period. More patients treated with tamsulosin were completely satisfied with their treatment (16/20 vs. 9/20). Both treatment groups showed significant improvement in symptom scores from baseline but no further statistical comparison between the groups was done. However, a larger decrease in AUA symptom score was seen in the tamsulosin group compared with the prazosin group. More adverse events were reported with prazosin (thirteen vs. one case) [568].

4.5.4.2.2.2 Striated muscle relaxants

Baclofen is a gamma-aminobutyric acid (GABA) agonist that exerts its effect on the GABAergic interneurons in the sacral inter-mediolateral cell column responsible for the relaxation of the striated urethral sphincter during voiding.

A randomised placebo-controlled crossover trial investigated the efficacy and safety of a four-week course of oral baclofen 10 mg three times/day in 60 women diagnosed with BOO, based on increased EMG activity with sustained detrusor contraction during voiding. It showed a lower number of voids, significant improvements in Q_{max} and $P_{det}Q_{max}$ with baclofen compared with placebo. Post-void residual volume, maximum cystometric capacity and MUCP were not significantly different between the groups. Adverse event rates were also similar, with the most common being somnolence, dizziness, and nausea. An important limitation of this study was the lack of patient-reported outcomes to assess symptoms and QoL [569].

4.5.4.2.2.3 Oestrogens

The relative reduction in urethral wall compliance seen in atrophic urethritis due to oestrogen deprivation may be responsible for urethral obstruction in post-menopausal women. Oestrogen therapy is thus theoretically expected to improve the condition. There are no published studies on the use of oestrogens specifically for the management of female BOO.

4.5.4.2.2.4 Sildenafil

Sildenafil, by inhibiting phosphodiesterase five, might be expected to increase the levels of nitric oxide in the female urethral sphincter, thereby promoting urethral relaxation.

A placebo-controlled, randomised crossover trial that included twenty women with partial or complete retention or obstructive voiding, with high MUCP and elevated US-estimated sphincter volume (> 1.6 cm) showed that while there was significant improvement in symptom scores and urodynamic parameters from baseline with sildenafil treatment, this difference was not significant when compared with placebo [570].

4.5.4.2.2.5 Thyrotropin-releasing hormone

Intravenous thyrotropin-releasing hormone (TRH) has been postulated as a neurotransmitter that induces urethral relaxation [571]. The exact mechanism is unclear.

In a small RCT of sixteen women with voiding difficulty, eight (three with BOO) were randomised to receive 200 μg intravenous bolus of TRH, and eight (three with BOO) received saline. No difference in the decline in functional profile lengths and maximum urethral closure pressures were noted between treatment groups, despite a significant decline noted from baseline in the treatment group. No subgroup analysis of women with BOO was reported [571].

4.5.4.2.2.6 Summary of evidence and recommendations for pharmacological treatment of functional bladder outlet obstruction

Summary of evidence	LE
Alpha-adrenergic blockers are associated with significant improvement in symptom scores, PVR and Q_{max} from baseline, but not compared to placebo.	1a
Tamsulosin is associated with greater improvement in symptom score compared with prazosin.	1b
Non-specific alpha-blockers are associated with higher rates of adverse events.	1b
Oral baclofen is better than placebo in improving Q_{max} and $P_{det}Q_{max}$, but not other urodynamic parameters. Its effects on symptoms are not well reported.	1b
Sildenafil is not superior to placebo in improving symptoms or urodynamic parameters of female patients with BOO.	1b
Trials including women with voiding problems of mixed aetiologies showed no difference in urodynamic outcomes between intravenous TRH and placebo.	1b

Recommendations	Strength rating
Offer uroselective alpha-blockers, as an off-label option, to women with functional bladder outlet obstruction (BOO) following discussion of the potential benefits and adverse events.	Weak
Offer oral baclofen to women with BOO, particularly those with increased electromyography activity and sustained detrusor contraction during voiding.	Weak
Do not offer sildenafil to women with BOO unless it is part of a well-regulated and closely monitored research study.	Strong
Do not offer thyrotropin-releasing hormone to women with BOO.	Strong

4.5.4.2.3 Surgical management

4.5.4.2.3.1 Intra-sphincteric botulinum toxin injection

Botulinum toxin inhibits the presynaptic release of acetylcholine, which reduces urethral sphincter tone. It is also believed to decrease the release of noradrenaline in the urethra to counteract external urethral sphincter overactivity [572].

Evidence on the use of botulinum toxin for female BOO is limited to small case series. Most studies included mixed populations without subgroup analyses, or the diagnosis of voiding dysfunction could not be ascertained as solely resulting from BOO. No comparative trial exclusively involving female BOO patients using botulinum toxin has been identified in the literature.

A SR including several reports of small case series using variable doses of onabotA injected periurethrally in women with dysfunctional voiding showed improvements in symptoms, and reductions in residual volume and voiding detrusor pressure. Larger series in adults (both sexes) showed success rates of 86-100% [572].

A double-blind, placebo-controlled RCT (n = 73) resulted in significantly lower IPSS score and larger voided volume after 100 U onabotA compared with saline in 31 men and women with dysfunctional voiding. Dysfunctional voiding was defined by a spinning top appearance on real-time fluoroscopy, poorly relaxed urethral sphincter on EMG, and a normal-to-high voiding pressure with a low and/or intermittent urinary flow rate, a PVR volume > 300 mL, and a low voiding efficiency. Other urodynamic parameters were comparable between the groups [573]. A subgroup analysis on the female population of this study was not available.

A SR and meta-analyses on the efficacy of transurethral botulinum toxin A injections for the treatment of BOO which included 232 patients with 27% females demonstrated that at three months, in patients with detrusor sphincter dyssynergia, transurethral botulinum toxin A injections improved LUTS, QoL, and urodynamic parameters (increased Q_{max} and diminished PVR) and no serious adverse effects have been reported. Moreover, there was a significant improvement in symptomatology among patients with satisfactory outcomes both in neurogenic and non-neurogenic patients [574].

Three small case series in women with BOO reported the effects of intrasphincter 100 U onabotA. All showed improvement in symptom and bother scores and significant reduction in PVR volume [502, 575, 576]. One study reported increased Q_{max} and improved static urethral pressure profile (UPP) [502]. The average symptom-free

duration was 16.8 weeks in another study [575]. Adverse events included UTI and temporary need for IC. No SUI was reported. Another study reported failure in 3/10 women, then submitted to transurethral incision of the bladder neck. Patients with improvement in objective and subjective symptoms underwent another botulinum toxin infiltration after six months from the first one [576].

4.5.4.2.3.2 nerve stimulation

Sacral nerve stimulation is postulated to decrease urethral tone and to work by blockade of the inhibitory urethral afferent impulses, which cause inhibition of normal bladder contraction.

No comparative trial has been identified in the literature on the use of SNS for female BOO.

Most publications on SNS for voiding dysfunction are retrospective reviews of cases, involving a mix of patient populations who underwent the procedure for different indications. In studies that indicated a subgroup of patients with urinary retention, there was either no urodynamic confirmation of the nature of the retention or separate outcomes were not reported for participants with retention.

A review of 60 women who underwent SNS for urinary retention associated with outlet obstruction (defined as UPP > 100 cm H_2O, increased urethral sphincter volume > 1.8 mL, and abnormal EMG with repetitive discharges and decelerating bursts) showed an overall spontaneous voiding rate of 72% over a mean follow-up of four years. Of those who continued to require IC up to twice daily post-operatively, the frequency was less than prior to surgery (degree not specified). There were 99 adverse events and 63 surgical revisions. In this series, half of the patients underwent a one-stage SNS procedure and the other half a two-stage procedure. The proportion of patients who required IC-assisted voiding was higher in the two-stage group (27% vs. 17%). More serious adverse events (defined as events requiring admission or surgical revision to resolve issues such as loss of response, lead migration and surgical revisions) were associated with the one-stage procedure [577].

The magnitude of symptomatic improvement was explored in a prospective study and 32 women with Fowler's syndrome underwent SNS, all patients underwent percutaneous nerve evaluation before the permanent device was implanted. About 62.5% had 100% cure rate after the procedure. The cure rate was defined by lack of incontinence, resolution of need for IC, and/or negligible PVR [578].

In a large multicentre series of 357 patients with chronic urinary retention and/or slow urinary stream, the authors found that high maximum urethral closure pressure, younger age and the absence of an underlying neurological disease affecting the lower motor neuron were associated with a higher success rate of the sacral neuromodulation test phase [579].

4.5.4.2.3.3 Summary of evidence and recommendations for surgical management of functional bladder outlet obstruction

Summary of evidence	**LE**
Intrasphincteric injection of botulinum toxin results in the improvement of symptoms and urodynamic parameters.	2
Sacral nerve stimulation results in spontaneous voiding and a reduction in IC rate in the majority of female BOO patients in idiopathic urinary retention.	3
More serious adverse events and surgical revisions were associated with the one-stage neuromodulator implantation procedure.	3
High maximum urethral closure pressure, the lack of an underlying neurologic condition, and younger age could be predictive factors of SNS success in women with chronic urinary retention.	3

Recommendations	**Strength rating**
Offer intra-sphincteric injection of botulinum toxin to women with functional bladder outlet obstruction (BOO).	Weak
Offer sacral nerve stimulation to women with functional BOO.	Weak

4.5.5 Follow-up

Women with BOO should be followed up and monitored regularly due to the risk of further deterioration of voiding or renal function in case of persistence and progression of the obstruction. For those who received treatment, monitoring must be done for recurrence of BOO. In particular, women who undergo urethral dilation, urethrotomy or urethroplasty for urethral stricture need to be monitored for stricture recurrence.

4.6 Nocturia

Nocturia was defined by the ICS in 2002 as "the complaint that the individual has to wake at night one or more times to void" and quantified in an updated document in 2019 as *"the number of times an individual passes urine during their main sleep period, from the time they have fallen asleep up to the intention to rise from that period"* [580]. The EAU Guidelines Panel on Urinary Incontinence conducted a SR on nocturia in women [581]. The search covered evidence up to 2017 and this review was updated with a scoping search in 2024.

4.6.1 Epidemiology, aetiology, pathophysiology

The prevalence of nocturia varies according to age with 4-18% of women aged 20-40 years experiencing ≥ 2 episodes per night, compared to 28-62% of women aged ≥ 70 years [582]. In a study of 1,000 community-dwelling older adults, female nocturia was associated with older age, African American race, history of UI, lower limb oedema and hypertension [583]. A report on > 5,000 adults aged 30-79 years identified around 28% with nocturia and found additional correlates with increased BMI, cardiac disease, type two diabetes, and diuretic use [584]. A SR and meta-analysis with moderate certainty evidence, demonstrated that the higher incidence of nocturia among hypertensive patients was more strongly associated (1.2- to 1.3-fold) among Black and Asian women, unrelated to their age or BMI status [585]. Another SR with moderate certainty of evidence showed that nocturia was associated with a 1.2-fold increased risk of falls and possibly an approximately 1.3-fold increased risk of fractures [586]. Another SR and meta-analysis concluded that nocturia is probably associated with an ~1.3-fold increased risk of death [586]. A large, US population-representative survey showed significantly greater burden on work productivity, depression, fatigue, and daytime sleepiness is seen in women with nocturia and nocturnal polyuria, to a greater degree compared with men [587].

The aetiology of nocturia is multifactorial and can include both urological and non-urological causes. Urological conditions which may exhibit nocturia as a significant symptom include OAB syndrome, BOO, DU, and dysfunctional voiding. Non-urological causes include 24-hour polyuria, nocturnal polyuria, congestive heart failure, sleep apnoea, restless leg syndrome, peripheral vascular disease, sleep disorders, night-time food ingestion, dependent oedema, and excessive fluid intake [588]. Given the varied aetiology of this symptom, there are a range of possible pathophysiological mechanisms, including: (1) 24-hour polyuria (e.g., diabetes mellitus, primary polydipsia, and diabetes insipidus); (2) nocturnal polyuria (e.g., behavioural, peripheral oedema, OSA, glycosuria, hormonal abnormalities and cardiac dysfunction); (3) diminished bladder capacity (e.g., OAB syndrome/DO, PFM dysfunction, BOO, pharmaceuticals, LUT calculi or tumours, and neurological bladder dysfunction); and (4) primary or secondary sleep disorders [589].

In post-menopausal women the relative deficiency in endogenous oestrogen production is thought to exacerbate all major pathophysiological mechanisms that may underlie nocturia [590].

4.6.2 Classification

Classification of nocturia is dependent on bladder diary analysis and several parameters have been defined as important [591]:

- nocturnal urine volume - total volume of urine passed during the night (this includes the first morning void but does not include the last void prior to sleep);
- maximum voided volume - largest single voided volume in 24 hours;
- nocturia index - nocturnal urine volume divided by maximum voided volume;
- nocturnal polyuria index - nocturnal urine volume divided by 24-hour urine volume;
- nocturnal urine production - nocturnal urine volume divided by duration of sleep, in hours.

Analysis of these parameters allows clinical classification of nocturia based on physiological abnormalities that can cause nocturia:

- 24-hour polyuria;
- nocturnal polyuria;
- diminished bladder capacity;
- sleep disorders.

4.6.3 *Diagnostic evaluation*

Evaluation of nocturia should include a thorough medical history and physical examination with particular reference to history of sleep disorders, fluid balance, associated LUTS, cardiovascular and endocrine comorbidity, renal disease, current medications, and history of urological disease [591, 592]. There are several nocturia-specific symptom scores, such as the ICI Questionnaire-Nocturia, Nocturia Quality of Life Questionnaire (N-QoL), and Nocturia Impact Diary; some of which were developed in men. These questionnaires have shown good content and discriminant validity, reliability, and sensitivity to change as well. A further screening tool that aims to identify causes of nocturia is the Targeting the individual's Aetiology of Nocturia to Guide Outcomes (TANGO) assessment tool [593-595]. The PLANET study (PLanning Appropriate Nocturia Evaluation and Treatment) has suggested a useful tool for initial history taking called the SCREeN tool, with questions focused on evaluating areas of Sleep, Cardiovascular, Renal, Endocrine and Neurological function [596].

A bladder diary is a vital initial investigation tool in patients complaining of nocturia and further supplementary investigations are guided by any abnormalities identified. Bladder diary analysis can allow for calculation of the parameters detailed in Section 4.6.2. A low nocturnal bladder capacity or global bladder capacity will be highlighted by reduced voided volumes during nocturnal hours or both night and day. This suggests an underlying urological condition such as OAB syndrome, BOO or DU. The term 24-hour polyuria is defined as 24-hour urine production > 40 mL/kg [597] and may be present in conditions such as diabetes mellitus or diabetes insipidus. The definition of nocturnal polyuria is age dependent and the thresholds for this diagnosis range from 20% (in younger persons) to 33% (age > 65 years) of the 24-hour urine volume produced during sleep. This may also be observed in patients with loss of circadian rhythm, cardiovascular disease, sleep apnoea, or sleep disorders [591].

As an alternative to the ≥ 3-day bladder diary a nocturnal-only diary has been investigated in men [598]. The results showed acceptable sensitivity and specificity for the nocturnal bladder diary compared with the standard bladder diary for most parameters. The nocturnal-only diary was not able to diagnose 24-hour polyuria and has not yet been validated for use in women.

A 2022 SR and nominal group technique (NGT) consensus exercise recommended including blood tests for renal function, thyroid function, HbA1c calcium levels and morning urine osmolality in the initial work-up of patients presenting with nocturia in the context of an endocrine disease [599-601].

Sleep disorders are potentially highly influential in nocturia, but often overlooked. A 2022 SR and NGT expert consensus recommended the use of screening questions to reach a clinical diagnosis of sleep disorder (insomnia, restless legs syndrome/periodic limb movements of sleep and parasomnias) [600].

4.6.3.1 Summary of evidence and recommendations for diagnosis of nocturia

Summary of evidence	**LE**
A thorough medical history is an integral part of the evaluation of women presenting with nocturia, including screening for sleep disorders.	4
Nocturia-specific questionnaires are sensitive to symptom changes.	3
A bladder diary allows for calculation of important indices and can identify potential causes of nocturia.	3
Nocturnal-only bladder diaries have been evaluated in men only and show acceptable sensitivity and specificity compared with the standard bladder diary for most parameters except 24-hour polyuria.	3
Obesity and/or endocrine diseases such as, diabetes mellitus or insipidus and thyroid diseases can be associated with nocturia.	2

Recommendations	**Strength rating**
Take a complete medical history from women with nocturia, including screening for sleep disorders.	Strong
Use a validated questionnaire during assessment of women with nocturia and for re-evaluation during and/or after treatment.	Weak
Use a three-day bladder diary to assess nocturia in women.	Strong
Do not use nocturnal-only bladder diaries to evaluate nocturia in women.	Weak

Consider screening for sleep disorders and performing renal function, thyroid function, HbA1c and calcium level blood tests in the initial workup of women presenting with nocturia as predominant symptom.	Strong

*4.6.4 **Disease management***

4.6.4.1 Conservative management

The individual components of self-management have not been critically evaluated and most recommendations are traditionally derived from consensus methodology. Interventions such as those listed below may help with nocturia but, for the majority, no quantification of their effect is possible:

- reduction of fluid intake at specific times;
- avoidance/moderation of intake of caffeine or alcohol;
- distraction techniques;
- bladder retraining;
- Increase exercise;
- pelvic floor muscle training;
- reviewing medication;
- treatment of constipation.

The available data for conservative management of nocturia shows significant heterogeneity. In a SR [581], three studies [602-604] were favourable for conservative management with PFMT, with another failing to confirm a benefit [605].

The highest level of evidence comes from a secondary analysis from a RCT of patients with urgency-predominant UI. The study found that among those with nocturia, training in PFM contraction, which included four sessions of biofeedback-assisted PFMT reduced nocturia by a median 0.50 episodes per night and was significantly more effective than anticholinergic drug treatment or placebo [602]. The certainty of evidence is moderate.

A smaller RCT of 50 women with urinary complaints, randomised 1:1 to BT and PFMT compared with a control group receiving no treatment, showed a significant decrease in patients' complaints of nocturia [603]. Another RCT in only 24 women compared PFMT only to Interferential Therapy plus PFMT [604]. Although the authors did not find significant differences between the groups, the change in nocturia episodes before and after treatment was statistically significant in both groups. The certainty of the evidence from these two trials is low. A large randomised, two-arm, parallel design, superiority trial (n = 647; women), compared the effects of unsupervised behavioural PFMT programmes delivered in a two-hour class format and twenty minutes video format on UI prevention. No significant between-group differences of nocturia were observed at three months and twelve months, but at 24 months, women in the two hour class group were less likely to have fewer nocturia episodes (OR = 0.5; 95 % CI: 0.3–0.7; p = 0.005) compared with those in the twenty minutes video group, but the authors concluded that the evidence is not sufficient to support one management strategy [606].

A multicentre, open-labelled, RCT evaluated whether CBT using a self-assessment via a checklist is effective in improving nocturia in a mixed population (30/78 women). The mean rate of achievement of the CBT group was 64.4%. There was no significant difference between the two groups in night-time frequency based on the IPSS Q7 at four weeks but episodes of nocturia on the frequency volume chart (FVC) were significantly smaller in the CBT group (1.9 ± 0.9) than in the control group (2.4 ± 1.3; p = 0.039) [607].

In a secondary analysis from a RCT, 210 women with UUI were evaluated for change from baseline in the number of episodes of nocturia and nocturnal incontinence between groups allocated to medical treatment (tolterodine ER 4 mg) alone vs. medical treatment plus PFMT [605]. Both groups experienced small but significant reduction in nocturia episodes from baseline but no difference between groups was found. The certainty of the evidence from this trial is low.

An RCT has explored both individual and group PFMT with a specific secondary outcome of number of patients with two or more nocturia episodes per night [321]. The authors reported similar reductions in the proportion of patients, who had ≥ 2 episodes of nocturia at baseline no longer experiencing this level of symptoms at one year after PFMT.

One small, single-centre RCT in which functional magnetic stimulation was compared with no treatment in 39 women reported a significant decrease in nocturia (together with voiding frequency and pad use) in the treatment group compared with the control group [608].

In patients with OSA who complain of nocturia, CPAP has been shown to be effective in a SR and meta-analysis of five RCTs involving both sexes [609]. This treatment was associated with an average numerical reduction in nocturia of > 2 episodes per night. A more recent SR including eleven studies supported the efficacy of CPAP [610].

4.6.4.1.1 Summary of evidence and recommendations for conservative management of nocturia

Summary of evidence	**LE**
Individual or group PFMT appears to be equally effective for reduction in nocturia episodes.	1b
Most studies evaluating PFMT for nocturia in women with additional urinary symptoms have shown positive results compared with placebo or anticholinergic drugs.	1b
Treatment of nocturia secondary to OSA with CPAP reduces nocturia episodes.	1a

Recommendations	**Strength rating**
Offer women with LUTS lifestyle advice prior to, or concurrent with, treatment.	Strong
Offer pelvic floor muscle training for nocturia (either individually or in the group setting) to women with urinary incontinence or other storage LUTS.	Strong
Offer women with nocturia and a history suggestive of obstructive sleep apnoea a referral to a sleep clinic for assessment of suitability for continuous positive airway pressure treatment.	Strong

4.6.4.2 Pharmacological management

4.6.4.2.1 Desmopressin

Desmopressin is a synthetic analogue of the hormone vasopressin and is most often used for management of nocturia due to nocturnal polyuria. A SR identified three trials on the effect of desmopressin specifically in women [581]. The first study was a small cross-over trial of 25 women treated with 25ug desmopressin or placebo [611]. It revealed a significantly greater reduction in nocturnal urinary frequency with desmopressin. Two double-blind RCTs investigated the effects of different doses of desmopressin and placebo in women [612, 613]. Both studies showed significantly better outcomes with desmopressin compared with placebo. Significant reductions in mean nocturnal voids and nocturnal urinary volumes in a dose-response relationship were also seen with desmopressin. Women were also seen to be more sensitive to desmopressin compared to men, Adverse event rates were similar across treatment groups. Overall certainty of the evidence is high.

Desmopressin can be safely combined with anticholinergics with significant benefit in women with OAB and nocturnal polyuria [614]. A *post-hoc* analysis in the nocturnal polyuria subgroup of RCT data comparing three-month once-daily combination (desmopressin 25 µg/tolterodine 4 mg) or monotherapy (tolterodine 4 mg) revealed a significant reduction in nocturnal void volume and time to first nocturnal void in favour of combination therapy. The certainty of the evidence from this trial is low.

Pooled data from three RCTs were used to examine the adverse event profile of desmopressin, specifically hyponatraemia [615]. The authors reported that the majority tolerate desmopressin treatment without clinically significant hyponatraemia, but risk increased with age and lower baseline serum sodium concentration. They advised that desmopressin treatment in elderly patients (> 65 years) should include careful monitoring of the serum sodium concentration and should be avoided in patients with a baseline serum sodium concentration below normal range.

4.6.4.2.2 Anticholinergics for concomitant OAB

A SR [581] identified three RCTs involving anticholinergics such as oxybutynin 2.5 mg/day [602] and tolterodine 4 mg/day [605, 614]. A secondary analysis from a prospective RCT involving 131 women with nocturia followed up for eight weeks found that women receiving 2.5 mg IR oxybutynin once daily (with the possibility of self-titration and dose escalation to 5 mg three times daily) had fewer nocturia episodes than women receiving placebo [602]. Women receiving oxybutynin plus behavioural therapy also exhibited a significant decrease in

nocturia episodes compared with placebo and oxybutynin alone. A multicentre RCT with 305 women followed up for eight weeks examined the efficacy of tolterodine tartrate 4 mg alone or in combination with behavioural training [605]. Significant differences compared with baseline were observed in mean nocturia episodes and nocturnal incontinence episodes in both groups, but no difference was reported between the two treatment groups.

In an RCT including 97 women with nocturnal polyuria and OAB syndrome, comparing three months of once daily combination (desmopressin 25 µg/tolterodine 4 mg, n = 49) or monotherapy (tolterodine 4 mg/placebo, n = 57), a significant reduction in mean number of nocturnal voids compared with baseline was reported in both groups [614].

A large comparative study followed 407 women with OAB and nocturia for four weeks [616]. The patients were given tolterodine as monotherapy in one group, and tolterodine combined with estazolam (a benzodiazepine) in the other group. Significant changes from baseline in both groups for the main outcome of number of nocturia episodes were reported. Combination therapy showed a significant benefit for women with OAB and nocturia compared with monotherapy in terms of differences in number of nocturia episodes, urgency episodes in 24 hours, UUI episodes in 24 hours, and voided volume per micturition. The level of certainty of the evidence from this trial is very low.

4.6.4.2.3 Mirabegron for concomitant OAB

A small multicentre RCT compared oxybutynin patch vs. mirabegron on nocturia-related QoL in women with OAB. Both treatments showed improvements in N-QoL score at four weeks, but mirabegron showed statistical differences at eight weeks. Additionally, only mirabegron decreased nocturnal frequency and water intake, and prolonged hours of uninterrupted sleep eight weeks after administration with statistical significance, whereas oxybutynin patch did not [617]. The certainty of the evidence for this trial is low.

4.6.4.2.4 Oestrogens

One RCT compared an oestradiol-releasing vaginal ring with an oestriol vaginal pessary in 251 women followed up for six months [618]. There was no difference between the treatment groups in the number of women reporting nocturia, although they reported significant change from baseline in both treatment arms with > 50% of women responding in each arm. Most adverse events including vaginal discomfort/discharge and breast pain were reported as mild and transient. The certainty of evidence for this outcome was low.

A small study on post-menopausal women with nocturnal polyuria showed that hormonal replacement therapy resulted in significant reduction in total liquid intake but no impact on total urinary output, the mean nocturnal voided volume and number of nocturnal voids. It also observed a mild change in the circadian rhythm with a high free water clearance during daytime compared with night-time values after treatment [619].

4.6.4.2.5 Diuretic treatment

In a randomised placebo-controlled study an afternoon dose of 40 mg furosemide (taken six hours before bedtime) in an attempt to establish complete diuresis before bedtime was given to elderly men [620]. In the 43 men who completed the study, night-time frequency in the furosemide group fell by 0.5 episodes compared with placebo, and percentage night-time voided volume fell by 18%. No such study has been carried out in female patients.

4.6.4.2.6 Melatonin and melatonin-receptor antagonist

Melatonin is a sleep-enhancing hormone that regulates the sleep/wake cycles and circadian rhythm. A SR of nine trials (391 patients, 86 women) that investigated the effect of melatonin and ramelteon, a melatonin-receptor agonist on nocturia. Majority of the studies showed statistically significant reduction in the number of voids per night, improvement in symptoms scores and QoL scores. Adverse event rates were similar to that of placebo/no treatment. The certainty of the evidence for this SR is low [621].
In a high-quality placebo-controlled RCT among women, melatonin 2mg given for two weeks resulted in lower nocturia episodes by one, longer duration of first uninterrupted sleep by almost an hour, higher total and sleep/energy domain N-QoL scores with no difference in 24-hour urine volume, nocturnal polyuria index, first voided volume at night. The certainty of evidence is moderate [622].

4.6.4.2.7 Protopine and Nuciferine (Nutraceuticals)

Protopine and nuciferine are two alkaloids that affect the neurotransmitter receptors that regulate voiding. This is results in specific smooth muscle relaxation postulated to control OAB symptoms, in particular nocturia. A single arm prospective study on 30 women with OAB who received a combination of protopine and nuciferine for three months showed that more than 90% obtained marked improvement in nocturia symptoms scores.

The certainty of evidence is very low [623] and further research is needed this treatment modality can be recommended.

4.6.4.2.8 Saw Palmetto Extract

Saw palmetto extract, consumed as supplements by men with suspected BPO, is believed to attenuate urodynamic symptoms in OAB of not only males but also females. A placebo-controlled randomised trial on 72 elderly Japanese women investigated the effect of twelve weeks of 320mg saw palmetto extract on their LUTS scores. Results showed significant reduction in daytime frequency scores but not on the other symptoms. Nocturia scores were lower after saw palmetto extract intake in a subset of patients with SUI. Certainty of the evidence is low [237].

4.6.4.3 Summary of evidence and recommendations for pharmacological treatment of nocturia

Summary of evidence	**LE**
Desmopressin treatment for nocturia shows significant reductions in nocturnal urine output, nocturnal urinary frequency, and nocturnal polyuria index.	1b
Most nocturia patients tolerate desmopressin treatment without clinically significant hyponatraemia; however, the risk increases with increasing age and decreasing baseline serum sodium concentration.	1a
Treatment of nocturia in OAB patients with anticholinergic drugs shows reduction in nocturia episodes.	1b
Mirabegron improved nocturia-QoL scores, decreased nocturnal frequency and water intake, and prolonged hours of uninterrupted sleep, in women with OAB.	1b
Combination of PFMT and anticholinergics does not appear to confer additional benefit over anticholinergics alone.	1b
Combination of anticholinergic and desmopressin treatment appears to reduce nocturnal voided volume and time to first nocturnal void in women with nocturnal polyuria.	1b
Vaginal oestrogen may be beneficial in the treatment of nocturia in around 50% of women.	1b
Afternoon (timed) diuretic treatment with furosemide reduces nocturia episodes and nocturnal voided volume in men but no similar studies have been conducted in women.	1b
Assessment of clinical significance is important when evaluating trials involving treatment strategies for nocturia, as statistical significance can be achieved with small reductions in nocturia episodes.	3
Melatonin (used for up to two weeks) reduces nocturnal voids, improves LUTS symptom scores and nocturia quality of life scores with low adverse event rates.	1b
Majority of women who received protopine and nuciferine experienced improvement in nocturia symptoms.	3
Saw palmetto extract resulted in lower nocturia scores in elderly women with SUI.	1b

Recommendations	**Strength rating**
Offer desmopressin treatment for nocturia secondary to nocturnal polyuria to women, following appropriate counselling regarding the potential benefits and associated risks (including hyponatraemia).	Strong
Carefully monitor serum sodium concentration in elderly patients treated with desmopressin. Avoid prescribing desmopressin to patients with a baseline serum sodium concentration below normal range.	Strong
Offer anticholinergic treatment for nocturia to women with urgency urinary incontinence or other LUTS, following appropriate counselling regarding the potential benefits and associated risks.	Strong
Inform women with nocturia that combination of behavioural therapy and anticholinergic drugs is unlikely to provide increased efficacy compared with either modality alone.	Weak
Offer combination of anticholinergics and desmopressin to women with overactive bladder (OAB) and nocturia secondary to nocturnal polyuria, following appropriate counselling regarding the potential benefits and associated risks.	Weak
Offer mirabegron in women with OAB to improve nocturia.	Weak
Offer vaginal oestrogen treatment to women with nocturia, following appropriate counselling regarding the potential benefits and associated risks.	Weak

Offer afternoon-dosed furosemide to women with nocturia polyuria, following appropriate counselling regarding the potential benefits and associated risks.	Weak
Consider short-term use (up to two-weeks) of melatonin for symptom improvement in women with nocturia associated with sleep disturbance.	Strong

4.6.4.4 Surgical management

Considering the strong association between obesity and nocturia, a SR explored the effect of bariatric surgery and nocturia [624]. Pooled data from five cohort studies on men and women with BMI > 25 showed significant reduction of nocturia by 0.67 (95% CI: 0.24-1.10) but with high heterogeneity. Certainty of the evidence of this SR is low.

4.6.4.5 Summary of evidence and recommendations for surgical management of Nocturia

Summary of evidence	**LE**
Weight loss from bariatric surgery among obese patients may result in a reduction of nocturia episodes.	3

Recommendations	**Strength rating**
Inform overweight and/or obese women that bariatric surgery may result in a reduction in nocturia episodes.	Weak

4.6.5 ***Follow-up***

Follow-up of patients with nocturia is dependent on the underlying aetiology of this symptom and the treatment given.

4.7 Pelvic organ prolapse and lower urinary tract symptoms

4.7.1 ***Epidemiology, aetiology, pathophysiology***

Pelvic organ prolapse is a common condition in adult women. The prevalence of POP is 3-6% when bothersome symptoms are used to characterise the condition and increases to 50% when a purely anatomical definition is used [625].

The estimated lifetime risk for POP surgery is 12.6% [626]. Parity, vaginal delivery, instrumental delivery, ageing, and obesity are the most commonly recognised risk factors [627].

Although the aetiology of POP is not fully understood, birth trauma to the levator ani complex is recognised as central to its development. In normal physiology, an intact levator ani complex functionally closes the genital hiatus surrounding the vagina, limiting the pressure gradient between the intra-abdominal and intravaginal areas. During physical activities, this reduces stress on the endopelvic fascia and its condensations (e.g., ligaments), which are crucial in securing the bladder, uterus, and rectum to their surroundings. Current aetiological concepts include widening of the levator hiatus due to birth trauma, which creates a low-pressure area in the vagina and consequently increased stress on the ligaments, fascial elements, and PFMs during physical activity. When the supporting function of the muscles and connective tissues fails, POP may develop [628]. This concept also explains the time lapse between birth trauma and occurrence of POP. It has been questioned whether strenuous physical activity including heavy lifting is a risk factor for development of POP [629]. The prevalence of reported symptomatic POP in strenuous exercisers and athletes varies between 0 (small study on different sports) and 23 % (Olympic weightlifters and power lifters). Three studies evaluated the pelvic floor after a single exercise or one session of exercises and found increased vaginal descent or increased POP symptoms. One prospective cohort study reported the development of POP after six weeks of military parashot training, and one randomised trial reported increased POP symptoms after transverse abdominal training. The effect of strenuous exercise on POP development needs further prospective studies [629].

Pelvic organ prolapse and LUTS often occur simultaneously in women. In isolation, both POP and LUTS are prevalent conditions in women, although the prevalence of LUTS in women with POP exceeds that of LUTS in women without POP [625]. A multicentre prospective cohort study of treatment-seeking women with at least one urinary symptom, demonstrated a potential association between increasing prolapse in all compartments and voiding LUTS. The same study demonstrated a trend toward fewer OAB and SUI symptoms in patients presenting with LUTS and POP, especially when only considering anterior vaginal wall prolapse [630]. In contrast, other studies have demonstrated an association between POP and OAB symptoms.

In a meta-analysis and SR, consistent results demonstrated a higher prevalence of OAB symptoms and UUI in patients with POP than without POP [625, 631]. The observation that LUTS may improve or worsen after POP treatment suggests a link between these two entities [625]. Clinical examples include the occurrence of voiding symptoms in severe POP, and disappearance of SUI symptoms with progression of POP (and conversely the occurrence of SUI after treatment of POP) [632]. Pelvic organ prolapse is also associated with symptoms of bowel and/or sexual dysfunction [633].

4.7.2 ***Classification***

Since 1996, POP has been classified according to the Pelvic Organ Prolapse-Quantification (POP-Q) system [634]. For specifics on how to perform the POP-Q measurement and the nine standard points to be measured (Figures 2 and 3), we refer to the original publications [634, 635].

The vagina is divided into anterior (bladder), posterior (rectum) and apical (cervix or vaginal vault) compartments. After scoring the position of the nine POP-Q points, a prolapse of each compartment is graded numerically from stage 0 to 4, with stage 0 being no prolapse and stage 4 being complete eversion of the compartment. A crucial marker in staging POP is the hymenal remnant. Any POP with a maximum descent that is still 1 cm above the hymen (e.g., in the vagina) is considered a stage 1 POP. A maximum descent between 1 cm above and 1 cm below (outside the vagina) the hymen is a stage 2 POP. Any descent, except complete eversion, beyond 1 cm below the hymen is a stage 3 POP.

The figures below show the POP-Q staging in comparison to the Baden-Walker system (and others) used before the international consensus on the POP-Q staging was introduced as the new standard.

Figure 2: Prolapse classification system

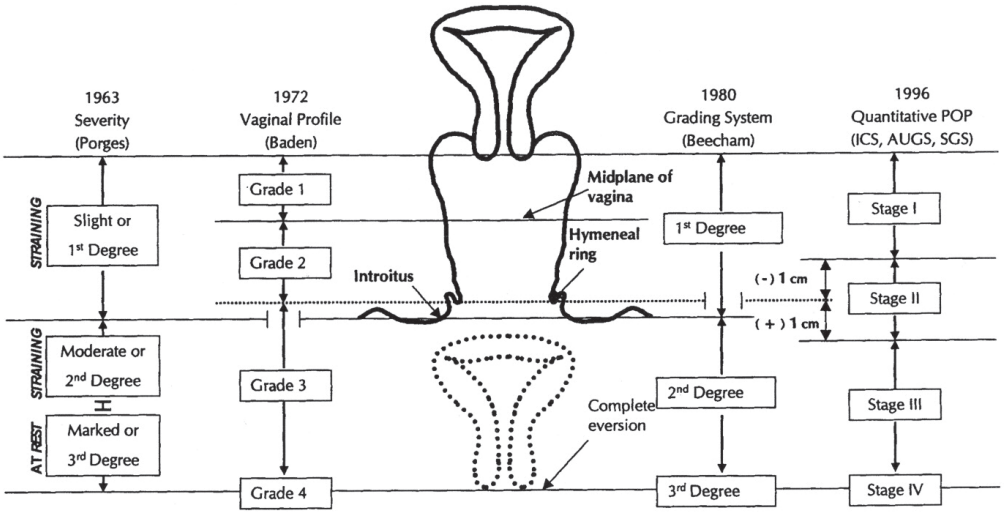

Figure reproduced with permission from the publisher, from Theofratus et al. [635].

Figure: 3: Pelvic Organ Prolapse-Quantification staging

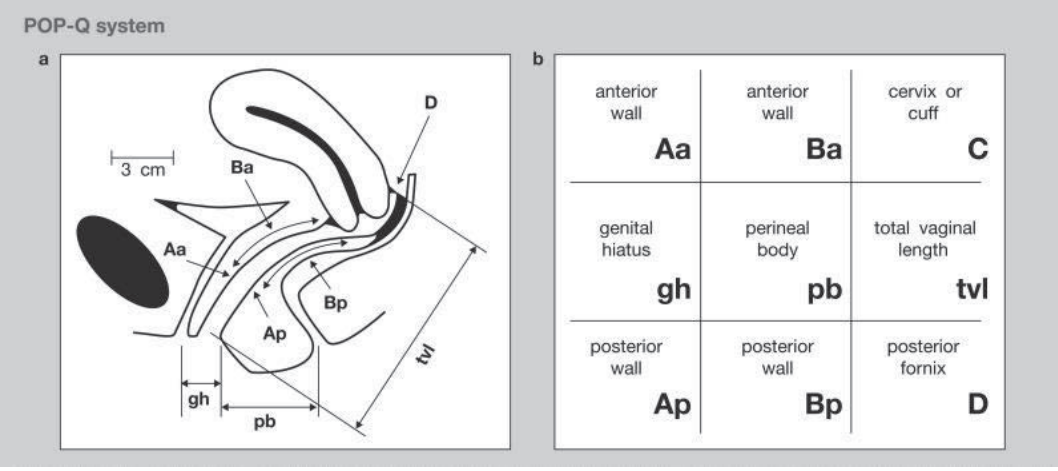

Figure reproduced with permission from the publisher, from Bump et al. [634]. The standardisation of terminology of female POP and pelvic floor dysfunction.

4.7.3 ***Diagnostic evaluation***

Pelvic organ prolapse is a clinical diagnosis and is staged according to the POP-Q system. Pelvic organ prolapse that is above the hymen should only produce mild symptoms at most [636]. In cases where there is a discrepancy between the clinical symptoms and POP-Q staging, it is advised to consider performing the POP-Q measurement in a standing rather than supine position or re-evaluating at a later time in the day. Magnetic resonance imaging assessment demonstrated a marked difference in POP staging between supine and standing position [637]. Additional diagnostic tests for POP are mainly indicated if there are accompanying symptoms like LUTS or bowel dysfunction. Imaging techniques are not advised for the routine diagnostic work-up of patients presenting with POP [61]. The role of urodynamics in the diagnostic work-up of SUI has been discussed in the SUI, Section 4.2, of this guideline.

The use of techniques to reduce POP during urodynamic evaluation to diagnose occult SUI is common practice. This information may be used to decide if additional anti-UI surgery should be offered at the time of POP surgery or to counsel patients on the possible after-effects of POP treatment.

There are several POP reduction methods that may be used during physical examination or urodynamic evaluation. In a multicentre observational study, five different cough/stress tests were compared for their ability to detect SUI in women with POP [533]. Stress urinary incontinence during at least one of the five tests occurred in 60/205 (29.2%) women without SUI symptoms. Looking at single test performance, the detection rate of occult SUI in women without symptoms increased from 4.4% in case of no reduction to 22% in case of reduction with a pessary.

A large RCT included women with POP without symptoms of SUI, who were randomised to sacro-colpopexy with or without Burch colposuspension [638]. Three hundred and twenty-two stress-continent women with stages 2-4 prolapse underwent standardised urodynamic testing, and the protocol included five prolapse reduction methods. Preoperatively, twelve of 313 (3.7%) women demonstrated urodynamic SUI without prolapse reduction. Pre-operative detection of urodynamic SUI with prolapse reduction at 300 mL was by pessary, 6% (5/88); manual, 16% (19/122); forceps, 21% (21/98); swab, 20% (32/158); and speculum, 30% (35/118). Another large trial included women with POP without SUI symptoms randomised to vaginal POP surgery with or without (sham incision) MUS [639]. Before surgery, 33.5% (111/331) of women demonstrated SUI at a prolapse-reduction cough stress test. In an observational study of 172 women with POP without SUI, 19% of women were diagnosed with occult SUI by basic office evaluation (with prolapse reduction with swab on forceps) and 29% on urodynamic evaluation [640].

In summary, SUI can be demonstrated in women with POP without symptoms of SUI after POP reduction in up to 30% of cases. There is no consensus on the best reduction technique.

Although the detection rate of occult SUI increases after reduction of POP in women without SUI symptoms, its clinical value is under debate. In one trial, pre-operative stress-continent women were evaluated during urodynamic testing with prolapse reduction to determine if they were more likely to report post-operative SUI,

regardless of concomitant colposuspension (controls 58% vs. 38% and Burch colposuspension 32% vs. 21%) [638]. In another trial, women with SUI during the cough stress test after POP reduction reported UI at three months in 29.6% in the synthetic MUS group, compared with 71.9% in the sham group [639]. Women with a positive prolapse reduction stress test before surgery appeared to receive more benefit from a synthetic MUS at three months, but not at twelve months, than did those with a negative test.

In a large observational study, women did not receive additional anti-UI surgery even if they had SUI after POP reduction preoperatively. In this scenario, 9% (16/172) of women developed post-operative *de novo* SUI and six underwent surgery for *de novo* SUI [640]. Women with demonstrable pre-operative SUI were more at risk of postoperative SUI: 28% vs. 5%. Based on urodynamic evaluation only, one more woman was predicted to have postoperative SUI, but all six women who underwent treatment for *de novo* SUI showed SUI during basic office evaluation.

In a model developed to predict the risk of *de novo* SUI in women undergoing POP surgery based on findings from two trials, twelve preoperative predictors were tested [641]. Positive SUI during a pre-operative prolapse reduction test was included in this model, but it failed to be a significant predictor of *de novo* SUI, as a single item. Pre-operative POP stage was not associated with risk of *de novo* SUI.

4.7.3.1 Urodynamics in women with pelvic organ prolapse and LUTS (without stress urinary incontinence)

The role of urodynamics is less clear in women presenting with POP and concurrent LUTS, other than SUI. Pelvic organ prolapse is a complex condition incorporating different compartments of the vagina and presenting at different stages of severity. Information about detrusor activity, as assessed with urodynamics, may provide information about the risk of developing DO after surgery, but also on the risk of urinary retention due to DU. An observational study assessed predictors for DO following POP surgery for POP-Q stage 3 or higher in 1,503 women and the authors concluded that pre-operative maximum urethral closure pressure ≥ 60 cm H_2O, Q_{max} < 15 mL/s, maximum detrusor voiding pressure (D_{max}) ≥ 20 cm H_2O and PVR volume ≥ 200 mL were independent risk factors for post-operative DO [642]. A small observational study (n = 49) evaluated patients with pre-operative DU (detrusor pressure at maximum flow was ≤ 10 cm H_2O and Q_{max} ≤ 12 mL/s) after POP surgery. Surgery objectively cured DU in 47% of women and urodynamic findings normalised after surgery [643]. The 2019 NICE Guidelines do not include a recommendation to perform urodynamics as part of the diagnostic work-up of POP, except for combination with symptomatic SUI [61].

4.7.3.2 Summary of evidence and recommendation for detection of SUI in women with POP

Summary of evidence	**LE**
Pelvic organ prolapse reduction during cough stress test, in office or during urodynamics detects SUI in ~30% of continent women.	2a
Women with SUI after POP reduction preoperatively (occult SUI) is likely to be at increased risk of developing SUI symptoms after POP surgery.	2a
Urodynamic parameters such as maximum urethral closure pressure and maximum detrusor voiding pressure may predict post-operative DO after prolapse surgery.	3

Recommendation	**Strength rating**
Perform pelvic organ prolapse (POP) reduction test in continent women to identify those with occult stress urinary incontinence and counsel them about the pros and cons of additional anti-incontinence surgery at the time of POP surgery.	Strong
Consider pre-operative urodynamic testing in women with POP and SUI undergoing surgery.	weak

4.7.4 ***Disease management***

Pelvic organ prolapse symptoms can be treated with PFMT, vaginal pessary, surgery, or a combination of these treatments. The scope of these guidelines is to focus on LUTS in women; therefore, only data on the effect of treatment of urinary symptoms are presented.

4.7.4.1 Conservative management of pelvic organ prolapse

According to the ICI 2023 [22] and IUC [644] there is level 1 evidence/grade A from eleven RCTs that PFMT is effective in reducing POP symptoms and/or improving POP stage (by one stage) in women with POP-Q stage I, II and III in the general female population. There is no evidence from none out of ten RCTs that adding PFMT pre-

and post -surgery for POP is effective. Only three RCTs compared PFMT with pessary. There are few long-term follow-up studies, and results are inconsistent. There are no serious adverse effects or complications reported related to PFMT. The scope of these guidelines is to focus on LUTS in women; therefore, only data on the effect of treatment of urinary symptoms are presented.

4.7.4.1.1 Pelvic floor muscle training versus lifestyle advice

An assessor blinded RCT (n = 109) reported that, after the six months intervention, the ICIQ-UI-SF scores improved in favour of the PFMT group (2.40 points) compared with a control group receiving lifestyle advice only (0.2 points) [317], and in another assessor blinded RCT, comparing fourteen weeks of PFMT with untreated controls, a significant improvement of PFMT in symptoms of SUI (p = 0.002) and straining to empty bladder (p = 0.031) was found [645].

Two publications from one RCT reported on the three-, six- and twelve-month results of lifestyle advice only vs. lifestyle advice combined with group PFMT [646, 647]. The Urogenital Distress Inventory-6 (UDI-6) and Urinary Impact Questionnaire-7 (UIQ-7) questionnaires were used to assess urinary symptoms. At three months' follow-up, both groups (53 women in the lifestyle group and 56 in the lifestyle + PFMT cohort) reported significantly improved UDI-6 scores, while the lifestyle-only group also reported significantly greater improvement in the UIQ-7 score. Between-group comparison showed no differences in UDI-6 and UIQ-7 scores at six months. At twelve months' follow-up, the majority of women had sought additional treatment (70% in the lifestyle-only group and 48% in the lifestyle/PFMT group). The number of patients remaining on the original therapy was too small to reach strong conclusions.

One RCT reported on six- and twelve-months follow-up of 225 women with POP-Q stage 1-3 randomised to individualised PFMT and 222 women randomised to lifestyle leaflet information only (control) [648]. At six months, significantly more women in the control group reported UI, the need to strain to empty their bladder, and the feeling of incomplete emptying compared to the PFMT group. The ICIQ-SF score was also significantly worse in the control group as compared to the PFMT group. However, at twelve months, there was no significant difference in these items between groups. It has to be noted that 50% in the control group received additional treatment within the twelve-month study period. Twenty-seven percent had additional PFMT, which may have had an effect on the twelve-month data.

Another RCT reported on the 24-month follow-up of 414 women with stage 1-3 POP (207 assigned to PFMT/Pilates and 207 to lifestyle advice) [649]. Urinary symptoms were assessed with the ICIQ-UI-SF and a question about UI and difficulty emptying the bladder. At 24 months, the ICIQ-UI-SF score was significantly better in the intervention group (mean difference -0.83). However, the proportion of women reporting any UI did not differ between the groups, nor did the number of pads used weekly.

4.7.4.1.2 PFMT vs. PFMT and Pessary

One RCT compared PFMT alone to PFMT and pessary for symptomatic POP [650]. Urinary tract symptom changes were assessed using UDI-6 and UIQ at six and twelve-months follow-up. At twelve months, there was no difference in the between-group comparison. With respect to the UIQ, women in the pessary/PFMT group showed a significant improvement from baseline, but the PFMT-only group did not. Women in the pessary/PFMT group reported significantly more frequent *de novo* SUI (48% vs. 22%), and more improvement of pre-existing voiding difficulty (62.5% vs. 35.5%).

4.7.4.1.3 Pelvic floor muscle training versus pessary only

One RCT reported on the 24-month follow-up of 82 women with symptomatic POP randomised to pessary therapy and 80 women randomised to PFMT [651]. Both in the ITT and per protocol analyses, the UDI-6 score did not differ significantly between groups at 24 months of follow-up.

4.7.4.1.4 Surgery alone versus surgery with pelvic floor muscle training

An assessor blinded RCT compared surgery for POP with or without additional pre-and postoperative PFMT. At twelve months after surgery, there were no significant differences between the groups on the change in scores of the UDI nor the IIQ scores [652].

Three other RCTs confirmed no additional effect of adding PFMT to surgery for secondary outcomes of LUTS in women with POP [653-655].

It is important to recognise that a benefit from PFMT is expected on typical POP symptoms, like feeling or seeing a bulge out of the vagina, but for LUTS the results differ.

4.7.4.1.5 Pessary versus surgery alone

A prospective cohort study showed that surgery in comparison with pessary treatment resulted in statistically significant more women reporting subjective improvement [656].

4.7.4.1.6 Summary of evidence and recommendation for the conservative management of pelvic organ prolapse and lower urinary tract symptoms

Summary of evidence	**LE**
Pelvic floor muscle training improves LUTS for up to six months in POP patients who do not have additional pessary or surgical management.	1b
If pessary therapy or surgical intervention is used for POP, PFMT does not show an additional benefit.	1b

Recommendations	**Strength rating**
Inform women with pelvic organ prolapse (POP), who do not need a vaginal pessary or surgical intervention, about the potential relief from LUTS from pelvic floor muscle training (PFMT).	Strong
Do not offer pre-operative PFMT to improve outcome of LUTS if pessary therapy or surgical intervention is indicated for POP.	Strong

4.7.4.2 Pelvic organ prolapse surgery and overactive bladder

Only a few studies have specifically addressed the effect of POP surgery on OAB symptoms. A SR of twelve studies, excluding women with SUI, evaluated OAB symptoms before and after surgery [631]. All but one study reported improvement of OAB symptoms. The same authors performed a prospective analysis of 505 women who had POP surgery with or without mesh [657]. Mean follow-up was 12.7 months. The incidence of bothersome urinary frequency reduced from 36.6% to 14.6%, with *de novo* symptoms occurring in 6.1%. Bothersome urgency symptoms reduced in 36.8% to 12.9% of women, with 5.0% developing *de novo* symptoms. Urgency urinary incontinence symptoms reduced from 21.2% to 6.1% of women, with 5.3% developing *de novo* symptoms.

One observational study evaluated frequency and urgency symptoms without consideration of bother in 87 women undergoing POP surgery and showed an improvement in frequency by 75%, and in urgency in 83% [658]. The effect of the POP-Q stage did not seem to influence the effect of surgery on OAB symptoms [657, 658].

Another observational study (n = 43) evaluated the effect of posterior repair on OAB/DO and showed a 70-75% improvement rate in both parameters after surgery [659].

4.7.4.3 Pelvic organ prolapse surgery and bladder outlet obstruction

The criteria for BOO are based on urodynamic assessment. POP can be categorised as anatomical BOO, which is addressed in Sections 4.5.2.2 and 4.5.4.1.

4.7.4.4 Pelvic organ prolapse surgery and stress urinary incontinence

The aim of this section is to address the options available to women who require surgery for POP and who have associated SUI (either before or after reduction of prolapse), and to assess the value of prophylactic anti-UI surgery in women with no evidence of SUI.

A SR and meta-analysis of ten trials on prolapse surgery with or without an anti-incontinence procedure was reported in 2018 [660]. In addition, a Cochrane review including nineteen trials (n = 2,717) evaluating bladder function after surgery for POP presented analyses of women with POP and SUI, women with POP and occult SUI, and women with POP who were continent [661].

4.7.4.4.1 Vaginal pelvic organ prolapse surgery in women with stress urinary incontinence

Two trials addressed postoperative SUI in patients who had been diagnosed with SUI preoperatively and had vaginal POP surgery [662, 663]. Two trials (n = 185 and 134) compared the use of MUS at initial POP surgery to POP surgery alone. The RR for postoperative SUI was 0.30 in favour of the combined POP surgery and MUS group. One of these two trials also compared the use of MUS at initial POP surgery and at three months if SUI persisted [662]. At twelve months' follow-up, there was no difference between the groups regarding postoperative UI (RR 0.41); however, 44% of the women without initial MUS never required surgery and 29% were dry.

4.7.4.4.2 Abdominal pelvic organ prolapse surgery in women with stress urinary incontinence

One RCT randomised 47 women with POP and SUI to an abdominal POP surgical procedure, e.g., sacro-colpopexy with or without Burch colposuspension. Additional SUI surgery did not improve postoperative SUI as compared to sacro-colpopexy alone (RR: 1.38) [664]. This finding remained consistent over five years' follow-up [665]. Another RCT compared the addition of a MUS or Burch colposuspension to an abdominal sacro-colpopexy in 113 women with POP and SUI [666]. At two years' follow-up, the RR for postoperative SUI was 0.54 in favour of the MUS group. Secondary analysis of a small subgroup from two RCTs concluded that the incidence of persistent or *de novo* SUI was high, but the level of bother associated with this was low [667].

4.7.4.5 Vaginal pelvic organ prolapse surgery in continent women

One RCT compared vaginal POP surgery alone with concomitant POP surgery and MUS in 220 women. Post-operative SUI occurred in 46/113 (40.7%) women who had POP surgery alone, compared to 30/107 (28.0%) who had additional MUS (RR: 0.69) [661].

Cost effectiveness of concomitant vaginal prolapse repair and mid-urethral sling placement was assessed as a planned secondary analysis of an RCT. The study demonstrated that prophylactic sling placed during vaginal prolapse surgery reduced the rate of *de novo* UI but was not cost-effective [668].

4.7.4.5.1 Abdominal pelvic organ prolapse surgery in continent women

Two RCTs compared abdominal sacro-colpopexy with (n = 180) or without (n = 187) Burch colposuspension with an outcome favouring the addition of Burch colposuspension (RR for *de novo* SUI: 0.69) [664, 669]. However, 34% of women in the prophylactic Burch colposuspension group developed *de novo* SUI (as compared to 49% in the control group). An RCT with medium-term follow-up (mean 39.5 months) showed that additional SUI surgery was needed by only 1/31 women (3%) in both groups [665, 670].

4.7.4.5.2 Vaginal pelvic organ prolapse surgery in women with prolapse and occult stress urinary incontinence

Five RCTs including a total of 194 women who had vaginal POP repair alone and 174 women who had an additional MUS at the time of primary surgery were identified [639, 671-674]. The risk of post operative SUI was lower in favour of the MUS group.

4.7.4.6 Adverse events associated with combined pelvic organ prolapse and stress urinary incontinence surgery

Data from six RCTs on vaginal POP surgery with MUS were pooled to assess adverse events [639, 662, 663, 672-674]. Urgency urinary incontinence was less frequent after combination surgery as compared to POP surgery alone, but there was a tendency towards more voiding problems. Adverse events directly related to surgery occurred more often in the combination group, as did serious adverse events such as bladder perforation, urethral injuries, and tape exposure [660].

A SR with meta-analysis conducted to determine urodynamic changes in patients undergoing surgical POP repair with or without a sling placement concluded that correction surgery for POP alone results in improved urodynamic voiding parameters, with a reduction in the prevalence of DO but with more incontinent patients after surgery [675].

In summary, it is difficult to generalise the results of trials using different procedures to treat both POP and UI. It seems that with a combined procedure, the rate of postoperative SUI is lower but voiding symptoms and complication rates are higher. Studies using MUS have shown more significant differences in UI outcomes with combined procedures than when other types of anti-UI procedure have been used. It must be considered that although more women are dry after combined surgery for POP with MUS, there are potential adverse events that should be balanced against potential benefits.

4.7.5 Summary of evidence and recommendations for surgery in women with both pelvic organ prolapse and stress urinary incontinence

Summary of evidence	**LE**
Women with POP and SUI	
Surgery for both POP and SUI show a higher rate of cure of UI in the short-term than POP surgery alone.	1a
There is conflicting evidence on the relative long-term benefit of surgery for POP and SUI vs. POP surgery alone.	1a
Combined surgery for POP + SUI carries a higher risk of adverse events than POP surgery alone.	1a

Continent women with POP	
Continent women with POP are at risk of developing SUI post-operatively.	1a
Women with POP and OAB	
There is some low-level inconsistent evidence to suggest that surgical repair of POP can improve symptoms of OAB.	2b

Recommendations for women requiring surgery for bothersome pelvic organ prolapse (POP) who have symptomatic or occult stress urinary incontinence (SUI)	**Strength rating**
Offer simultaneous surgery for POP and SUI only after a full discussion of the potential risks and benefits of combined surgery vs. POP surgery alone.	Strong
Inform women of the increased risk of adverse events with combined prolapse and anti-urinary incontinence surgery compared to prolapse surgery alone.	Strong
Recommendations for women requiring surgery for bothersome POP who do not have symptomatic or occult SUI	
Inform women that there is a risk of developing *de novo* SUI after prolapse surgery.	Strong
Do not offer concomitant anti-incontinence surgery at the time of abdominal prolapse surgery.	Strong

4.8 Urinary fistula

The evidence relating to diagnosis and treatment of urinary fistulae is generally low level and largely composed of case series and other consensus statements. In particular, the epidemiology, aetiology, diagnosis, treatment and prevention of obstetric and non-obstetric fistulae have been described in detail during the 2023 ICI conference [22]. Most non-obstetric fistulae are iatrogenic in origin, caused by pelvic surgery (e.g., hysterectomy for benign or malignant conditions, bowel resection, and urological surgery). The risks during pelvic surgery increase proportionally to the complexity of the resection, the extent of the primary disease, and with a past history of radiotherapy (especially for recurrent disease). When a fistula occurs following radiotherapy for primary treatment, this may be an indication of tumour recurrence.

*4.8.1 **Epidemiology, aetiology and pathophysiology***

4.8.1.1 Obstetric fistula

According to the WHO, fistulae affect > 2 million women, mostly from sub-Saharan African and Asian countries. The pooled prevalence of fistula from population studies is 0.29/1000 pregnancies [676]. Poor quality obstetric care, staff unaccountability, late referral, and poor nursing standards have been identified as health system causes [676]. However, obstructed labour is poorly documented. The main individual risk factors include age at first marriage, short stature, pregnancy with a male child, failure to attend antenatal care, low socio-economic status, low social class, lack of employment, and illiteracy [677-679]. Obstetric fistulae have detrimental consequences on global and individual health and are associated with malnutrition, sexual dysfunction, anxiety, depression, insomnia, social isolation, worsening poverty, and suicide [680, 681].

4.8.1.2 Iatrogenic fistula

Poor obstetric care is usually responsible for VVFs in the developing world. By contrast, in the developed world, gynaecological or pelvic surgery is the main cause of VVF. In a French epidemiological study, pelvic surgery accounted for two thirds of VVF causes [682].

4.8.1.2.1 Post-gynaecological surgery

An injury to the urinary tract during hysterectomy for benign conditions (60-75%), hysterectomy for malignant conditions (30%) and caesarean section (6%) are the main causes of postoperative VVF in the developed world [683, 684]. The risk of pelvic organ fistula following hysterectomy ranges from 0.1-4% [685].

Fistulae may also occur as a result of primary or recurrent malignancy, or as a consequence of cancer treatment by surgery, radiotherapy, and/or chemotherapy.

In a study including 536 women undergoing radical hysterectomy for invasive cervical cancer, bladder injury occurred in 1.5% with VVFs forming in 2.6% and uretero-vaginal fistulae in 2.4% of cases [686]. Overall, the rate of urogenital fistula appears to be ~9 times higher following radical hysterectomy for malignant disease as compared to that following simple hysterectomy (abdominal or vaginal for benign conditions) [687]. Bladder-sparing techniques during pelvic exenteration can increase the risk of fistula formation [688].

4.8.1.2.2 Radiation fistula

The risk of fistula seems to be higher for postoperative external beam radiation (1.9%) compared to intravaginal brachytherapy (0.8%) [689], without any predictive factor being identified [690]. This is most likely due to the heterogeneity of data regarding the tumour type and stage, the form of radiation, and the site and dose delivered.

4.8.1.2.3 Rare causes of vesico-vaginal fistula

Foreign bodies such as pessaries, sex toys, cups etc. can be a cause of delayed presentation of VVF [691-693]. Ketamine abuse has also been shown to be responsible for fistula formation [694].

4.8.1.3 Summary of evidence for epidemiology, aetiology, and pathophysiology of urinary fistula

Summary of evidence	LE
The risk of injury to the urinary tract and subsequent fistula formation is higher in women with malignant disease undergoing radical surgery than in women with benign disease undergoing simple surgical procedures.	2
The rate of fistula formation following external beam radiotherapy for gynaecological cancer appears to be of the same order as that following surgical management.	4

4.8.2 ***Classification***

Due to the plethora of VVF classification systems, a consensual classification system needs to be adopted. The Waaldijk and Goh classifications are widely used for diagnosis and follow-up [695-697] but were originally designed for obstetric fistulae and their use in iatrogenic fistulae is less relevant [698]. The WHO classification (Table 6) was originally developed for obstetric fistulae and separates fistulae into simple and complex.

Table 6: Adapted WHO Classification of fistulae [676]*

Simple fistula with good prognosis	Complex fistula with uncertain prognosis
• Single fistula < 4 cm • Vesico-vaginal fistula • Sphincters not involved • No circumferential defect • Minimal tissue loss • Ureters not involved • First attempt to repair	• Fistula > 4 cm • Multiple fistula • Recto-vaginal mixed fistula, cervical fistula • Sphincters involved • Scarring • Circumferential defect • Extensive tissue loss • Intravaginal ureters • Failed previous repair • Radiation fistula

**Although this classification was developed for obstetric fistula initially, it could be relevant for iatrogenic fistula as well.*

4.8.2.1 Recommendation for the classification of urinary fistula

Recommendation	Strength rating
Use a detailed description of anatomical and associated features to distinguish between simple and complex fistulae and standardise terminology in this subject area.	Strong

4.8.3 ***Diagnostic evaluation***

Leakage of urine is the hallmark sign of a urogenital fistula. The leakage is usually painless, may be intermittent if it is position dependent, but more usually is constant. Unfortunately, intraoperative diagnosis of a genito-urinary or gastrointestinal injury is made in only about half of the cases [699]. Diagnosis of VVF usually requires clinical assessment often in combination with appropriate imaging or laboratory studies. As for any LUTS, history taking and focused physical examination with direct visual inspection are essential parts of urinary fistula diagnostic evaluation. Cystoscopy and retrograde bladder filling with a coloured fluid with placement of a tampon into the vagina to identify staining facilitate diagnosis of VVF. A double-dye test to differentiate between UVF and VVF may be useful in some cases [684]. Testing the creatinine level in either the extravasated or collected fluid will confirm fluid leakage as urine. Contrast-enhanced CT with late excretory phase reliably

diagnoses urinary fistulae and provides information about ureteric integrity and the possible presence of associated urinoma. Magnetic resonance imaging, in particular with T2 weighting, also provides diagnostic information regarding fistulae [700].

Summary of evidence	LE
As for any LUTS, history taking and focused physical examination with direct visual inspection are essential parts of urinary fistula diagnostic evaluation.	3
Cystoscopy and retrograde bladder filling with a coloured fluid with placement of a tampon into the vagina to identify staining facilitate diagnosis of VVF.	3
Contrast-enhanced CT with late excretory phase reliably diagnoses urinary fistulae and provides information about ureteric integrity.	3
Magnetic resonance imaging, in particular with T2 weighting, also provides diagnostic information regarding fistulae.	3

Recommendations	Strength rating
Take a complete medical history and perform a focused physical examination including direct visual inspection for evaluation of women with suspicion of urinary fistula.	Strong
Use cystoscopy and retrograde bladder filling with a coloured fluid to confirm the diagnosis of urinary fistula.	Weak
Perform Contrast-enhanced CT with late excretory phase and/or magnetic resonance imaging in cases where the diagnosis of urinary fistula is challenging or when ureterovaginal fistula is suspected.	Weak

4.8.4 ***Management of fistula***

4.8.4.1 Management of vesico-vaginal fistula

4.8.4.1.1 Conservative management

4.8.4.1.1.1 Spontaneous closure

The reported spontaneous closure rate is 13 ± 23% [701], although this applies largely to small fistulae (< 1 cm) [702, 703]. Hence, immediate management is usually by urinary catheterisation or diversion; however, within the first two weeks following fistula occurrence, delayed surgical exploration and repair can be planned.

4.8.4.1.1.2 Pharmacotherapy

Several case reports describe a successful fistula closure rate following the induction of amenorrhoea by oestrogen, oestrogen/progesterone combinations or luteinising hormone releasing hormone analogues specifically for small (< 7 mm), uretero- or vesico-uterine fistulae following caesarean section [704-710]. One RCT comparing the efficacy of using fibrin glue compared to Martius flap inter-position (n = 14; < 4 cm and n = 5; > 5 cm) did not report significantly different outcomes between the two types of treatment but the closure rates were relatively low in both groups (68.4% vs. 57.9%) [711].

4.8.4.1.1.3 Palliation and skin care

During the intervening period between diagnosis and repair, UI pads with the aim of prevention of skin complications related to chronic urinary leakage can be provided and the use of a barrier cream or local oestrogen should be considered [712, 713].

4.8.4.1.2 Surgical management

Overall closure rates after surgical repair of vesico-vaginal fistulae range from 58-100% [714].

4.8.4.1.2.1 Timing of surgery

Findings from small uncontrolled case series suggest no difference in success rates for early (within four weeks) or delayed (after three months) closure of VVF [715, 716].

4.8.4.1.2.2 Surgical approaches

Vaginal procedures

There are two main types of closure techniques applied to the repair of urinary fistulae, the classical saucerisation/partial colpocleisis [701] and the more commonly used dissection and repair in layers or flap-splitting technique [717]. There are no data comparing their outcomes.

Abdominal procedures
There are no RCTs comparing abdominal and vaginal approaches. Repair by the abdominal route is indicated when high fistulae are fixed at the vaginal vault and are inaccessible via a vaginal approach. A transvesical repair has the advantage of being entirely extraperitoneal. A simple transperitoneal repair is used less often although it is favoured by some using the laparoscopic approach. A combined transperitoneal and transvesical procedure may be utilised for fistula repair following caesarean section. Results of secondary and subsequent repairs are not as successful as the initial repair [718].

Laparoscopic and robotic procedures
Small series (single figures) have reported using these techniques. In a recent analysis of the American NSQIP dataset, transvaginal and robotic/laparoscopic approaches were associated with lower morbidity compared to the open abdominal approach [719].

Trimming of fistula edge
A single RCT compared trimming of the fistula edge with no trimming. There was no difference in success rates but failed repairs in trimmed cases had larger recurrences than untrimmed cases, which were smaller [720].

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

Postoperative management
There is no high-level evidence to support any particular practice in postoperative management, but most reported series used catheter drainage for ≥ 10 days and longer periods in complex or radiation-associated fistulae (up to three weeks). The performance of post-operative cystography prior to catheter removal can theoretically miss a persistent fistula if not done with a micturition phase or if the fistula is located at the bladder neck.

4.8.4.1.3 Management of complications of vesico-vaginal fistulae
The complications of VVF repair are varied and can include:
- Persistence or recurrence of fistula;
- Persistence or recurrence of UI;
- Persistence of LUTS or occurrence of new LUTS, including *de novo* OAB and/or SUI;
- Infections: wound and UTIs/urosepsis;
- Ureteric obstruction (ligation, fibrosis or injury);
- Bladder outlet obstruction (meatal stenosis, urethral stricture or bladder neck obstruction);
- Bladder contracture;
- Vaginal stenosis;
- Sexual dysfunction (vaginismus/dyspareunia).

The literature on the treatment and management of complications of fistula repairs is scarce and is mostly experienced based. It is impossible to provide any specific evidence-based guidance.

4.8.4.2 Management of radiation fistulae
Modified surgical techniques are often required, and indeed, where the same techniques have been applied to both surgical and post-radiation fistulae, the results from the latter have been consistently poorer [721]. Due to the wide field abnormality surrounding many radiotherapy-associated fistulae, approaches include permanent urinary and/or faecal diversion [721, 722] or preliminary urinary and faecal diversion, with later undiversion in selected cases following reconstruction. In cases where life expectancy is deemed to be short, ureteric occlusion and nephrostomy insertion might be more appropriate.

4.8.4.3 Management of ureteric fistulae
Uretero-vaginal fistula occurring in the early post-operative phase predominantly after hysterectomy is the most frequent presentation of upper urinary tract fistulae in urological practice. An RCT in 3,141 women undergoing open or laparoscopic gynaecological surgery found that prophylactic insertion of ureteric stents made no difference to the low risk (1%) of ureteric injury [723].

Patients at higher risk of ureteric injury require experienced surgeons who can identify and protect the ureter and its blood supply to prevent injury and recognise injury promptly. Immediate repair of any intraoperative injury should be performed by observing the principles of debridement, adequate blood supply and tension-free anastomosis with internal drainage using stents [724]. Delayed presentation of UUT injury should be suspected in patients whose recovery after relevant abdominal or pelvic surgery is slower than expected, if there is any fluid leak, and if there is any unexpected hydronephrosis.

While there is no evidence to support the use of one surgical approach over another, there is consensus that repair should adhere to the standard principles of tissue repair and safe anastomosis and be undertaken by an experienced team. Conservative management is possible with internal or external drainage, endoluminal management using nephrostomy and stenting where available, and early (< 2 weeks) or delayed (> 3 months) surgical repair when required [725]. If endoluminal techniques fail or result in secondary stricture, the abdominal approach to repair is standard and may require end-to-end anastomosis, reimplantation into the bladder using psoas hitch or Boari flap, or replacement with bowel segments with or without reconfiguration. As a last resort, nephrectomy may be considered, particularly in the context of a poorly functioning kidney and an otherwise normal contralateral kidney [726-730]. Functional and anatomical imaging should be used to follow-up patients after repair to guard against development of ureteric stricture and deterioration in renal function.

4.8.4.3.1 Management of urethro-vaginal fistulae

4.8.4.3.1.1 Aetiology

Although urethro-vaginal fistulae are rare, most of them in adults have an iatrogenic aetiology. Causes include surgical management of SUI, surgery for urethral diverticulum and genital reconstruction. Irradiation and even conservative management of prolapse with pessaries can lead to formation of fistulae.

4.8.4.3.1.2 Diagnostic evaluation

Clinical vaginal examination, including the three-swab test, is often sufficient to diagnose urethro-vaginal fistulae. Urethroscopy and cystoscopy can be performed to assess the extent and location of the fistulae. In cases of difficult diagnosis, VCUG or US can be useful. An 3D-MRI or CT scan is becoming utilised more widely to clarify anatomy [731, 732].

4.8.4.3.1.3 Surgical management

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

One case series reported that a vaginal approach yielded a success rate of 70% at first attempt and 92% at second attempt, and that an abdominal approach only led to successful closure in 58% of cases [733]. A vaginal approach required less operating time, had less blood loss and shorter hospitalisation.

Most authors have described surgical principles that are identical to those of VVF repair, and primary closure rates of 53 - 95.4% have been described. A series of 71 women, treated for urethro-vaginal fistulae reported that 90.1% of fistulae were closed at the first vaginal intervention. Additionally, 7.4% were closed during a second vaginal intervention. Despite successful closure, SUI developed in 52% of cases. Stress urinary incontinence patients were treated with synthetic or autologous slings and nearly 60% became dry and an additional 32% improved. Urethral obstruction occurred in 5.6% and was managed by urethral dilation or urethrotomy [734].

4.8.4.3.1.4 Flaps and neo-urethra

The simplest flap is a vaginal advancement flap to cover the urethral suture line. Labial tissue can be harvested as a pedicled skin flap. This labial skin or the vaginal mucosa can be used as patches to cover the urethral defect but can also be used to create a tubular neo-urethra [735, 736]. The construction of a neo-urethra has mostly been described in traumatic aetiologies. In some cases, a transpubic approach has been used [737]. The numbers of patients reported are small and there are no data on the long-term outcome of fistula closure and continence rates.

4.8.4.3.1.5 Martius flap

In obstetrical fistula repair, the Martius labial bulbocavernosus muscle/fat flap was not found to have any benefit. However, the Martius flap is still considered by some to be an important adjunctive measure in the treatment of genitourinary fistulae for which additional bulking with well-vascularised tissue is needed [738]. The series of non-obstetrical aetiology are small and all of them are retrospective. There are no prospective data, nor randomised studies [739]. The indications for Martius flap in the repair of urethra-vaginal fistulae remain unclear.

4.8.4.3.1.6 Rectus muscle flap
Rectus abdominis muscle flaps have been described by some authors [740, 741]. However, this flap is more morbid to harvest and this flap is usually to bulky/large to fit in the vaginal cavity.

4.8.4.3.1.7 Alternative approaches
An alternative retropubic retro-urethral technique has been described by Koriatim [742]. This approach allows a urethro-vesical flap tube to be fashioned to form a continent neo-urethra.

4.8.4.4 Summary of evidence and recommendations for the management of urinary fistula

Summary of evidence	**LE**
Spontaneous closure of surgical fistulae does occur and appears more likely for small fistulae although it is not possible to establish the rate with any certainty.	3
There is no evidence that the timing of repair makes a difference to the chances of successful closure of a fistula.	3
There is no high-quality evidence of differing success rates for repair of VVFs by vaginal vs. abdominal transvesical vs. extravesical, approaches.	3
A variety of interpositional grafts can be used in either abdominal or vaginal procedures, although there is little evidence to support their benefits in any specific setting.	3
Post-radiation fistula	
Success rates are lower for irradiated fistulae than for non-radiated fistulae.	3
Ureteric fistula	
Prophylactic ureteric stent insertion does not reduce risk of ureteric injury during gynaecological surgery.	2
Antegrade endoluminal distal ureteric occlusion combined with nephrostomy tube diversion often palliates urinary leakage due to malignant fistula in the terminal phase.	4
Urethro-vaginal fistula	
Urethro-vaginal fistula repair may be complicated by SUI, urethral stricture, and urethral shortening, which may necessitate long-term follow-up.	3

Recommendations	**Strength rating**
General	
When reporting on outcomes after fistula repair, authors should make a clear distinction between fistula closure rates and post-operative urinary incontinence rates and the time at which the follow-up was organised.	Strong
Do not routinely use ureteric stents as prophylaxis against injury during routine gynaecological surgery.	Strong
Suspect ureteric injury or fistula in patients following pelvic surgery if a fluid leak or pelvicalyceal dilatation occurs post-operatively, or if drainage fluid contains high levels of creatinine.	Strong
Use three-dimensional imaging techniques to diagnose and localise urinary fistulae, particularly in cases with negative direct visual inspection or cystoscopy.	Weak
Manage upper urinary tract fistulae initially by conservative or endoluminal techniques (catheter/stent etc.) where such expertise and facilities exist.	Weak
Surgical principles	
Surgeons and other healthcare professionals involved in fistula treatment should have appropriate training, skills, and experience to select an appropriate procedure for each patient.	Weak
Attention should be given as appropriate to skin care, nutrition, rehabilitation, counselling, and support prior to, and following, fistula repair.	Weak
Tailor the timing of fistula repair to the individual patient and surgeon requirements once any oedema, inflammation, tissue necrosis, or infection, are resolved.	Weak

Ensure that the bladder is continuously drained following fistula repair until healing is confirmed (expert opinion suggests: ten to fourteen days for simple and/or post-surgical fistulae; fourteen to 21 days for complex and/or post-radiation fistulae).	Weak
Where urinary and/or faecal diversions are required, avoid using irradiated bowel segment.	Weak
Use interposition graft when repair of radiation associated fistulae is undertaken.	Weak
Repair persistent urogenital fistulas by an abdominal approach using open, laparoscopic, or robotic techniques according to availability and competence.	Weak
Urethro-vaginal fistulae should preferably be repaired by a vaginal approach.	Weak

4.9 Urethral diverticulum

A female urethral diverticulum is a sac-like protrusion composed of the entire urethral wall or only the urethral mucosa, situated between the periurethral tissues and the anterior vaginal wall.

4.9.1 Epidemiology, aetiology, pathophysiology

Urethral diverticulum is an uncommon condition with an estimated prevalence of 1-6%. A prevalence of up to 10% was reported among women with LUTS attending a tertiary referral centre [743]. However, as many patients are asymptomatic or misdiagnosed, the true incidence is unknown [744-746]. Given the rarity of the condition, most published series are small and single institutional. Urethral diverticulum is thought to arise from repeated obstruction, infection, and subsequent rupture of periurethral glands into the urethral lumen, resulting in an epithelialised cavity that communicates with the urethra [744].

Iatrogenic damage to the urethra may also play a role, as up to 20% of women with urethral diverticula are noted to have a history of urethral surgery, dilation, or traumatic delivery [744, 747]. Iatrogenic urethral diverticula formation associated with synthetic mid-urethral sling has also been reported [748-750].

4.9.2 Classification

Table 7: Classification system for female urethral diverticula based on characteristics*

Localisation	Mid-urethral Distal Proximal Full length
Configuration	Single Multi-loculated Saddle shaped
Communication	Mid-urethral No communication visualised Distal Proximal
Continence	Stress urinary incontinence Continent Post-void dribble Mixed incontinence

**Limited LNS C3 classification of urethral diverticula [747, 751, 752].*

4.9.3 Diagnostic evaluation

4.9.3.1 Anatomical evaluation

The commonly encountered symptoms for urethral diverticulum such as pain, urgency, frequency, recurrent UTIs, vaginal discharge, dyspareunia, voiding difficulties or UI [753], are common to many other LUT dysfunctions. However, in a recent prospective study, the combination of LUTS, post micturition dribble and UTI had the strongest association with the diagnosis of urethral diverticulum [754]. Many patients with urethral diverticulum are asymptomatic. However, urethral diverticulum often presents with a palpable urethral mass. It may be possible to express a purulent exudate from the urethra. Occasionally a stone may develop within the diverticulum.

No robust diagnostic accuracy studies have addressed the question of the best test to confirm the diagnosis in women with clinical suspicion of urethral diverticulum. A case series of 27 patients concluded that endoluminal (vaginal or rectal) MRI has better diagnostic accuracy than VCUG [755] and determines the size and extent of urethral diverticulum more accurately. A case series of 60 patients reported that the sensitivity, specificity, positive predictive value and negative predictive value of MRI was 100%, 83%, 92% and 100%, respectively [756]. Another case series reported 100% specificity and sensitivity of MRI in 60 patients [757]. However, a case series of 41 patients reported a 25% discrepancy between MRI and surgical findings [758]. Polyacrylamide hydrogel injection sites can mimic diverticulum on MRI and the diagnosis should be questioned in patients with an history of polyacrylamide injection [759].

Magnetic resonance imaging is the gold standard for the diagnosis and planning of surgical repair and is also useful in diagnosing diverticular inflammation or tumour [760, 761].

Urethrocystoscopy can be used to visualise the ostia of the diverticula. Knowledge of the ostias' location and number can assist with surgical planning since they need to be closed after diverticulectomy. However, given the challenges of urethroscopy in women, the ostia are only seen in 42% of cases [753].

If VCUG is performed, antero-posterior and lateral images are required to optimally characterise the configuration of the diverticulum. There is a high risk of false negatives since the ostia of the diverticula must be patent and the patients must be able to void during the study. In more complex diverticula where there is septation, the entire diverticulum may not be visualised underestimating its complexity or size [762]. The sensitivity of VCUG is 73.5% which is significantly worse than MRI [753].

Ultrasound can be performed transabdominally, trans-vaginally or trans-perineally to identify the diverticulum. In particular, the transvaginal approach allows imaging of the urethra from the meatus to the bladder neck in several planes and can identify the number, size, location, and contents of the diverticulum. This technique is challenging and requires a skilled ultrasonographer. Additionally, the probe can compress the urethra, causing distortion [762]. A meta-analysis reported that US of any kind had a sensitivity of 82.0%, which was inferior to that of MRI [762].

For patients who cannot undergo MRI and those in whom the ostia cannot be seen on cystoscopy, double balloon urethrography is an option. Sensitivity of 94.7% has been reported, which is comparable to that of MRI, but it is technically difficult, requires an experienced radiologist/radiographer and specialised equipment, can be painful for the patient and carries a risk of UTI [762].

4.9.3.2 Associated voiding dysfunction

Although the presentation of urethral diverticulum is often non-specific and variable, urethral diverticulum can be associated with voiding dysfunction and SUI or UUI.

One series reported SUI in 60% of patients with urethral diverticulum [763]. Urethral diverticulum is most often located at the level of the mid-urethra. This location often overlaps with the external sphincter. However, urethral diverticulum may also extend proximally toward the bladder neck in the vicinity of the proximal sphincter mechanism. This morphology may, in part, explain the association between urethral diverticulum and SUI, with potentially more proximal lesions at risk for post-operative SUI [764].

Urethral diverticulum may also be associated with BOO due to the mass effect of the urethral diverticulum, urinary retention, or urgency and UUI [765]. Pain and dysuria associated with urethral diverticulum may also result in acquired voiding dysfunction.

Pressure-flow studies may have a role in the pre-operative assessment of patients with urethral diverticula and coexisting voiding dysfunction or SUI [746, 766-768]. Indeed, urodynamics may evaluate coexisting detrusor dysfunction or document the presence of SUI or obstruction prior to repair [769, 770].

Urethral pressure profilometry has also been used in the assessment or diagnosis of urethral diverticulum, noting a biphasic pattern, or pressure drop at the level of the lesion [766, 768, 771]. Video-urodynamics may be helpful in differentiating SUI from paradoxical UI due to fluid accumulation in the urethral diverticulum. Additionally, resting and straining images obtained during fluoroscopic imaging may document an open bladder neck at rest. This may be a consideration in some patients with an extensive urethral diverticulum at the level of the mid-urethra, and potential implications for post-operative UI due to compromise of both sphincter mechanisms.

4.9.4 ***Disease management***

For women with minimal symptoms who would prefer to avoid invasive treatment, conservative management can be considered. Patients should be warned of the small risk of cancer (1-6%) within the diverticulum [772, 773].

4.9.4.1 Surgical treatment

No RCTs have investigated the effectiveness of surgery in women who have a bothersome urethral diverticulum. Thorough evaluation of the anatomy of the diverticulum is essential in planning reconstructive surgery.

There are three surgical approaches to treatment of diverticulum: marsupialisation, endoscopic incision, and curative treatment with diverticulectomy.

Surgical removal (diverticulectomy) is the most commonly reported treatment in contemporary case series. The principles of successful transvaginal diverticulectomy are to: dissect a well-vascularised vaginal flap; preserve the periurethral fascia for closure; remove all the diverticular wall; excise the ostium and close the urethra in a watertight fashion; close the incision in a multi-layered fashion with no overlapping suture lines; and preservation or creation of continence.

The decision to use a labial fat pad flap (commonly known as a Martius flap) varies, and the flap is used more frequently in the following situations: recurrent cases, large urethral defects or for deficient vaginal flaps for closure [747, 751] transection of the urethra required for access to a circumferential diverticulum [761] or in the case of complex configuration [765], and if there is a planned future sling procedure required for UI to facilitate the dissection at that time [747].

Marsupialisation involves incision into the mass on the vaginal side to drain the infected contents. The wall is sutured open with absorbable suture to allow drainage and prevent reaccumulating of infectious materials. This approach leaves the cystic structure in place and can theoretically cause a urethro-vaginal fistula because there is communication with the diverticular ostium, but it is a rapid procedure with little dissection required and could even be done in the office in selected patients. One recent series suggest a success rate of 100% with only 18 % rate of post-operative complications, which were all described as minor [774].

Endoscopic incision is a rarely reported treatment option [775, 776]. This procedure involves finding the narrow neck of the ostium and incising it with a resectoscope. This unroofing of the diverticulum transforms the narrow communication with the urethra that causes symptoms when it becomes obstructed into a wide-mouthed sac that drains freely.

4.9.4.2 Management of concomitant stress urinary incontinence

Many women present with concomitant SUI and urethral diverticulum and may request both conditions to be simultaneously treated. A meta-analysis reported that diverticulectomy cured SUI even without a concomitant anti-incontinence procedure. However, no data regarding symptom severity were given and it could be assumed that many of these cured patients had less-severe UI before surgery [753]. Therefore, additional surgical correction may be required [764, 776]. However, there is no consensus on appropriate timing of surgical management of these two conditions. Thus, patients with symptomatic bothersome SUI in association with urethral diverticulum may be offered simultaneous anti-UI surgery. Although historical series have shown good results with concomitant bladder neck suspension [770], more contemporary series have utilised pubovaginal fascial slings, with satisfactory outcomes [777-780]. Synthetic MUS are not recommended as a concomitant anti-UI procedure at the time of urethral diverticulectomy [781]. Synthetic material adjacent to a fresh suture line following diverticulectomy in the setting of potentially infected urine may place the patient at higher risk for subsequent urethral erosion and vaginal extrusion of the sling material, as well as urethro-vaginal fistula formation and foreign body granuloma formation.

4.9.4.3 Success rate and complications

Transvaginal urethral diverticulectomy has a high success rate (defined by being dry) of 84-98%, with a reoperation rate of 2-13% after primary repair during a mean follow-up of twelve to 50 months [744, 747, 764, 782]. The resolution of symptoms after surgery has been reported to reach 68.8% but less than half of studies comment on symptom improvement [783].

One case series reported a recurrence rate of 33% in U-shaped and of 60% in circumferential diverticula within one year [751], one study found a 10.7% recurrence rate in 122 women undergoing diverticulectomy, with a higher risk of recurrence in those with proximal or multiple diverticula or after previous pelvic surgery [784] or radiation. Recurrent urethral diverticulum following initial successful urethral diverticulectomy may occur as a

result of a new infection or traumatic insult such as childbirth, a new urethral diverticulum, or recurrence of the original lesion. Recurrence may be due to incomplete removal of the urethral diverticulum, inadequate closure of the urethra, residual dead space (circumferential diverticula), or other technical factors. Repeat urethral diverticulectomy represents a unique challenge due to altered anatomy, scarring, and difficulty identifying proper anatomical planes.

One case series reported that storage symptoms decreased significantly post-operatively from 60% to 16% following surgery for urethral diverticulum [764]. Other series with long-term follow-up, however, have demonstrated rates of post-operative urgency of 54% [784], and *de novo* UUI in 36% of patients [776]. Such post-operative symptoms indicate persistence of urethral diverticulum, recurrence of urethral diverticulum, or *de novo* OAB syndrome or urethral obstruction.

Stress urinary incontinence can be worsened or occur *de novo* after diverticulectomy. This is most likely due to sphincteric damage from the dissection or scarification preventing urethral closure. *De novo* SUI (10.6% of women) seems to be more common in proximal and large (> 30 mm) diverticula [764]. However, a retrospective review noted at least some *de novo* SUI in 49% of patients following urethral diverticulectomy; most of which was minor and did not require additional therapy [785]. Only 10% of these individuals underwent subsequent SUI surgery. Treatment for SUI after diverticulectomy is not well described in the literature. The most commonly reported operation is an autologous pubovaginal sling [775] followed by retropubic suspension [776]. However, there are two reported cases of synthetic mesh sling to treat SUI, without mesh complications [751, 764], but this is controversial.

Early common post-operative complications include UTI (0-39%), *de novo* SUI (3.8-33%), and *de novo* urinary retention (0-9%), especially in the setting of concomitant placement of an autologous pubovaginal sling [744, 747, 764, 782]. Delayed complications such as urethral stricture are reported in 0-5.2% of cases [744, 747, 776, 782]. Urethro-vaginal fistula is a devastating complication presenting in 0.9-8.3% of cases [786]. A distal fistula located beyond the sphincteric mechanism can present with split urinary stream or vaginal voiding and may not require repair. However, a fistula located anywhere from the mid-urethra to the bladder neck may result in UI. These patients should undergo repair with consideration of an adjuvant tissue flap, such as a Martius flap, to aid in closure. The timing of the fistula repair is not well defined, with a delay of three to six months after the initial repair being a good balance between patient discomfort and optimal tissue quality. Rare complications include: distal urethral necrosis, bladder injury, urethral injury, ureteric injury, and vaginal scarring or narrowing with consequent dyspareunia [786].

4.9.4.4 Pathological findings

Most urethral diverticula are lined with squamous cells, urothelium or columnar epithelium [747, 787, 788]. In a meta-analysis, there was a high prevalence of chronic or acute inflammation (68.6%) and the most commonly reported lesions were nephrogenic metaplasia, which occurred in 8% of cases. Diverticula may undergo neoplastic alterations (6%), including invasive adenocarcinoma [789], followed by squamous cell carcinoma in 0.7%. It is unknown if the diverticulum forms first and then transform into a malignancy or if the malignancy develops first. These malignancies are treated in a similar fashion to urethral cancer in women.

*4.9.5 **Summary of evidence and recommendations for urethral diverticulum***

Summary of evidence	**LE**
Magnetic resonance imaging has the best sensitivity and specificity for the diagnosis of urethral diverticulum.	3
Surgical removal of symptomatic urethral diverticulum provides good long-term results; however, women should be counselled of the risk of recurrence and *de novo* SUI.	3

Recommendations	**Strength rating**
Use magnetic resonance imaging for diagnosis and characterisation of urethral diverticula, with urethroscopy, voiding cystourethrogram and ultrasound where necessary.	Weak
Offer surgical removal of symptomatic urethral diverticulum.	Weak
Surgeons and other healthcare professionals involved in urethral diverticulum treatment should have appropriate training, skills, and experience to select an appropriate procedure for each patient.	Weak

If conservative management is adopted, warn patients of the small (1-6%) risk of cancer developing within the diverticulum.	Weak
Carefully question and investigate patients for coexisting voiding dysfunction and urinary incontinence (UI).	Strong
Following appropriate counselling, address bothersome stress urinary incontinence at the time of urethral diverticulectomy with concomitant non-synthetic sling.	Weak
Counsel patients regarding the possibility of *de novo* or persistent LUTS including UI, despite technically successful urethral diverticulectomy.	Strong

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6. CONFLICT OF INTEREST

All members of the Non-neurogenic Female LUTS Panel have provided disclosure statements of all relationships that they have that might be perceived as a potential source of a conflict of interest. This information is publicly accessible through the European Association of Urology website: https://uroweb.org/guideline/non-neurogenic-female-luts/.

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