

Platinum Priority – Review – Female Urology – Incontinence

Editorial by Jean-Nicolas Cornu on pp. 71–72 of this issue

European Association of Urology Guidelines on the Diagnosis and Management of Female Non-neurogenic Lower Urinary Tract Symptoms. Part 1: Diagnostics, Overactive Bladder, Stress Urinary Incontinence, and Mixed Urinary Incontinence

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Abstract

Context: Female lower urinary tract symptoms (LUTS) are a common presentation in urological practice. Thus far, only a limited number of female LUTS conditions have been included in the European Association of Urology (EAU) guidelines compendium. The new non-neurogenic female LUTS guideline expands the remit to include these symptoms and conditions.

Objective: To summarise the diagnostic section of the non-neurogenic female LUTS guideline and the management of female overactive bladder (OAB), stress urinary incontinence (SUI), and mixed urinary incontinence (MUI).

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Evidence acquisition: New literature searches were carried out in September 2021 and evidence synthesis was conducted using the modified GRADE criteria as outlined for all EAU guidelines. A new systematic review (SR) on OAB was carried out by the panel for the purposes of this guideline.

Evidence synthesis: The important considerations for informing guideline recommendations are presented, along with a summary of all the guideline recommendations.

Conclusions: Non-neurogenic female LUTS are an important cause of urological dysfunction. Initial evaluation, diagnosis, and management should be carried out in a structured and logical fashion based on the best available evidence. This guideline serves to present this evidence to health care providers in an easily accessible and digestible format.

Patient summary: This report summarises the main recommendations from the European Association of Urology guideline on symptoms and diseases of the female lower urinary tract (bladder and urethra) not associated with neurological disease. We cover recommendations related to diagnosis of these conditions, as well as the treatment of overactive bladder, stress urinary incontinence, and mixed urinary incontinence.

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1. Introduction

The European Association of Urology (EAU) guidelines on non-neurogenic female lower urinary tract symptoms (FLUTS) have evolved from the previous guidelines on urinary incontinence (UI) [1] to incorporate the wider range of LUTS affecting women that were previously not considered in the EAU guidelines compendium. The wider scope of the subject area has resulted in a restructuring of the guidelines, which are now presented in a condition-based format.

Here we present a precis of the current version of these guidelines [2], specifically focusing on the sections on diagnostics, overactive bladder (OAB), stress urinary incontinence (SUI), and mixed urinary incontinence (MUI). The remaining topic areas will be covered in part 2 of this publication. Information on epidemiology is not presented here; rather, we consider the patient pathway from presentation through diagnostics to management of the specific symptom complexes. The best available evidence is summarised and the main recommendations from the full version of the guidelines are presented in a concise and easily digestible format.

2. Evidence acquisition

Owing to the expansion of the scope of these guidelines, a new literature search was carried out with expanded terminology and criteria. The full details of the search strategy are available online (<https://uroweb.org/wp-content/uploads/2021-EAU-Non-neurogenic-Female-LUTS-Guidelines-Search-Strategy.pdf>).

The EAU Guidelines Office uses a modified GRADE approach to evaluate the relevant literature pertaining to each topic area. High-quality systematic reviews (SRs) are referred to where available, and lower-quality evidence is evaluated when these are not available. For this guideline edition, new SRs on OAB and female bladder outlet obstruction (BOO) were carried out by the panel.

Evidence summary statements and assessment of the quality of the available evidence are reinforced by certainty ratings (from very low to high). Recommendations are then produced on the basis of these certainty ratings, the benefit-to-harm balance, and consideration of patient values and preferences, where feasible, to give an overall recommendation with a strength rating of “strong” or “weak”. It must be noted that the balance between “strong” and “weak” recommendations relates to these three factors rather than purely the evidence base for the intervention. Our panel recommendations are reinforced by the inclusion of patient representatives as part of the panel, who provide valuable input into the discussion around patient values and preferences.

3. Evidence synthesis

3.1. Diagnostics

3.1.1. History and physical examination

The value of a thorough medical history and physical examination remains undisputed despite the lack of high-level supporting evidence, which is reflected in the panel’s strong recommendation. History of non-neurogenic FLUTS should include an attempt to differentiate and quantify storage, voiding, and postmicturition symptoms, as well as sexual, gastrointestinal, and neurological symptoms. Urinary incontinence (UI) should be classified as urgency UI (UII), SUI, MUI (detailing the most bothersome component), or other forms of UI, such as overflow and continuous UI. All patients should be asked about any red flag symptoms (pain, haematuria, neurological symptoms or associated dysfunction, previous pelvic surgery or radiotherapy). Smoking status, comorbidities, and body mass index should also be recorded.

Clinical examination should include abdominal and genitourinary examination to assess for any palpable masses, pelvic floor muscle (PFM) tone and function, cough stress test for SUI, and vaginal oestrogenisation. A basic assessment for any pelvic organ prolapse (POP) should also be carried out.

3.1.2. Patient questionnaires

In general, questionnaires should be validated for the language in which they are being used and demonstrated to be sensitive to change [3]. The International Consultation on Incontinence Questionnaire-Female Lower Urinary Tract Symptoms (ICIQ-FLUTS), Questionnaire for Urinary Incontinence Diagnosis (QUID), 3 Incontinence Questions (3IQ), and ICIQ-short form (ICIQ-SF) have potential to discriminate UI types in women [4–6]. The Overactive Bladder-short form (OAB-SF) and Bladder Control Self-assessment Questionnaire (B-SAQ) have been developed to measure symptoms and bother in OAB. There is no evidence to indicate whether use of quality of life (QoL) or condition-specific questionnaires has an impact on the outcome of treatment. The recommendation on the use of questionnaires has been upgraded to “strong” on the basis of panel consensus.

3.1.3. Bladder diaries

The panel advocates consistent use of terminology in studies evaluating the tools variably described as micturition diary, frequency volume chart, bladder diary, and voiding diary. Consensus terminology is now well defined and should be widely accepted [7,8]. Moderate-quality observational studies have demonstrated that bladder diaries have satisfactory reproducibility [9,10], feasibility, reliability, and validity [11,12], and even therapeutic benefit [13]. The optimum diary duration appears to be guided by a balance between accuracy and compliance, with durations between 3 and 7 days routinely reported in the literature.

3.1.4. Urinalysis and urinary tract infections

Urinary tract infections (UTIs) are a common cause of FLUTS, and pre-existing FLUTS may be exacerbated by a UTI [14]. Urinalysis negative for nitrites and leucocyte esterase may exclude bacteriuria in women [15], and treatment of asymptomatic bacteriuria was not shown to be beneficial in the elderly [16].

3.1.5. Postvoid residual volume

There does not seem to be any consensus on what constitutes a significant postvoid residual volume (PVR) in women without neurological disease, and most studies investigating the topic assess mixed populations. The panel therefore suggests the additional use of bladder voiding efficiency (BVE), where $BVE = (\text{voided volume} / \text{voided volume} + \text{PVR}) \times 100$ [17]. The recommendations on PVR have been upgraded on the basis of potential harms in cases in which high PVR associated with UTI, upper tract dilatation, and renal insufficiency is missed.

3.1.6. Urodynamics

The utility of urodynamics in the diagnostic work-up of FLUTS is still unclear. Most of the evidence comes from observational studies, but a Cochrane review [18], SR and meta-analysis [19] and a randomised controlled trial (RCT) [20] have addressed the question in relation to SUI. Overall, preoperative urodynamics made no difference to cure rates or complication rates.

The presence of preoperative detrusor overactivity (DO) did not predict overall treatment failure following surgery for SUI [21], nor did DO have any predictive value for treat-

ment response in studies on fesoterodine, onabotulinum toxin, or sacral nerve stimulation for OAB symptoms [22–25].

Although pressure-flow studies are capable of discriminating BOO from detrusor underactivity (DU) as a cause of voiding dysfunction, post hoc analysis of two high-quality surgical trials of tension-free vaginal tape (TVT), Burch colposuspension, and autologous fascial slings showed that no preoperative urodynamic parameter predicted postoperative voiding dysfunction in a selected population of women with low preoperative PVR [26,27].

There is no consistent correlation between results for urethral function tests (eg, urethral pressure profilometry) and subsequent success or failure of SUI surgery [21,28].

The recommendations on urodynamics have been formulated taking into consideration the inconsistency in the evidence on their predictive value, while recognising their utility in cases of diagnostic difficulty.

3.1.7. Pad testing

Two SRs assessed the utility of pad testing for UI [29,30]. It has been shown that pad tests have high diagnostic accuracy, but variation in standardisation of the parameters used (bladder volume and degree of provocation) reduces their utility in daily clinical practice. Tests of shorter duration and standardised exercise protocols have higher specificity but lower sensitivity, whereas tests of longer duration are more reproducible and sensitive, but standardisation of activity levels remains difficult. These tests may therefore be more useful in the research setting than in routine practice.

3.1.8. Imaging

In cases of suspected LUTS/UI caused by an upper urinary tract (UUT) anomaly or ureterovaginal fistula, UUT imaging (intravenous urography or computed tomography) may be indicated [31].

Ultrasonography can be used to assess PFMs and their function, where indicated.

There is no consensus on the relationship between OAB and increased bladder wall thickness (BWT) or detrusor wall thickness (DWT) [32], and there is no evidence that BWT/DWT imaging improves management of OAB. DWT was also not associated with any urodynamic parameters that may indicate BOO [33].

There is large variation in magnetic resonance imaging (MRI) interpretation between observers [34] and little evidence to support its clinical usefulness in the management of LUTS/UI in general, although its utility for diagnosing urethral diverticula is recognised.

In general, there is no indication to carry out imaging investigations in the basic evaluation of FLUTS. The imaging component of video urodynamics is a special case for which the additional anatomical information obtained may be beneficial. Specific instances in which imaging modalities add value are discussed in the relevant disease sections.

Recommendations for the overall diagnosis of LUTS are provided in Table 1.

Table 1 – Recommendations for diagnostics.

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
Use a validated and appropriate questionnaire as part of the standardised assessment of female LUTS.	Strong
Ask patients with LUTS to complete a bladder diary as part of the standardised assessment of female LUTS.	Strong
Use a bladder diary with a duration of ≥ 3 d.	Strong
Perform urinalysis as a part of the initial assessment of patients with LUTS.	Strong
If UTI is present with LUTS, reassess the patient after treatment.	Strong
Do not routinely treat asymptomatic bacteriuria in elderly patients to improve UI.	Strong
Measure 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 volume efficiency as an additional parameter when measuring PVR volume.	Weak
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 SUI.	Strong
Do not routinely carry out urodynamics when offering first-line treatment to patients with uncomplicated OAB symptoms.	Strong
Perform urodynamics if the findings may change the choice of invasive treatment.	Weak
Do not use urethral pressure profilometry or leak point pressure to grade the severity of UI as these are primarily tests of urethral function.	Strong
When pad test is performed, use a standardised duration and activity protocol.	Strong
Use a pad test when quantification of UI is required, especially to assess response to treatment.	Weak
Do not routinely carry out imaging of the UUT or LUT as part of the assessment of LUTS.	Strong
LUT = lower urinary tract; LUTS = lower urinary tract symptoms; OAB = overactive bladder; PVR = postvoid residual; SUI = stress urinary incontinence; UI = urinary incontinence; UTI = urinary tract infection; UUT = upper urinary tract.	

3.2. Overactive bladder

OAB is defined by the International Continence Society (ICS) as “urinary urgency, usually accompanied by frequency and nocturia, with or without UI, in the absence of UTI or other obvious pathology” [35]. It is generally classified as wet or dry OAB according to the presence or absence of associated UI. As outlined in Section 3.1, a thorough baseline assessment should be carried out to classify the type and severity of symptoms and elucidate any signs of UI, associated POP, concomitant UTI, current anticholinergic burden, associated neurological dysfunction, or genitourinary symptoms of menopause.

3.2.1. Conservative management

3.2.1.1. Medication adjustment and containment. There is no evidence to suggest that improving any comorbid medical condition improves OAB symptoms, although it is recommended practice to review any new medication that is associated with the development or worsening of OAB symptoms. Of the containment devices, pads offer effective control of leakage [36] and an indwelling catheter or clean-

intermittent catheterisation is also useful in select patients [37,38].

3.2.1.2. Caffeine reduction. A recent review of 14 interventional and 12 observational studies showed that a reduction in caffeine intake may reduce symptoms of urgency, but the certainty of the evidence was low, with significant heterogeneity [39].

3.2.1.3. Modification of fluid intake. One RCT showed that a reduction in fluid intake by 25% improved symptoms in patients with OAB but not UI [40]. Personalised fluid advice compared to generic advice made no difference to continence outcomes in individuals receiving anticholinergics for OAB according to an RCT comparing drug therapy alone to drug therapy with behavioural advice [41].

3.2.1.4. Weight loss. There is evidence that the prevalence of both UI and SUI increases proportionately with body mass index [42], but this evidence base is largely related to SUI.

3.2.1.5. Smoking cessation. The effect of smoking cessation on LUTS was described as uncertain in a health technology assessment review [43].

3.2.1.6. Behavioural and physical therapies. Two SRs [44,45] confirmed a positive effect on continence for prompted voiding in comparison to standard care [45]. Three SRs on the effect of bladder training compared to standard care confirmed that bladder training is more effective than no treatment in improving UI [43,46,47]. An SR of 11 RCTs [48] in women with OAB compared the efficacy of PFM training (PFMT) to inactive control, usual care, other lifestyle modification, or other intervention. PFMT significantly reduced OAB symptoms (frequency and UI) in five RCTs, while the remaining six reported no significant difference. Substantial heterogeneity in protocols precluded meaningful comparisons.

Results from studies on percutaneous tibial nerve stimulation (PTNS) in women with refractory UI are consistent, showing that PTNS improves UI in women without adequate improvement with, or who cannot tolerate, antimuscarinic therapy [49,50]. An SR commissioned by this panel (currently in preparation) showed that PTNS techniques were more effective than antimuscarinics in reducing UI episodes (mean difference -0.67 , 95% confidence interval -1.31 to -0.02 ; $p = 0.04$; low certainty of evidence) with no significant difference in reducing mean symptoms score, frequency episodes, or urgency episodes.

3.2.2. Pharmacological management

Anticholinergic (antimuscarinic) drugs are currently the first-line pharmacological treatment for OAB; however, evaluation of cure or improvement of OAB is made harder by the lack of standard definitions. In general, SRs note that the overall treatment effect of drugs is usually small but greater than that of placebo (Table 2). A network meta-analysis of 128 RCTs comparing anticholinergics with placebo or other anticholinergics revealed that all anticholinergics except for imidafenacin led to a significant cure or

Table 2 – Summary of cure and discontinuation rates for anticholinergic drugs from RCTs [47].

Drug	Studies	Patients	RR (95% CI) (of curing UI)	NNT (95% CI) (to achieve 1 cure of UI)
Cure of incontinence				
Fesoterodine	2	2465	1.3 (1.1–1.5)	8 (5–17)
Oxybutynin (includes IR)	4	992	1.7 (1.3–2.1)	9 (6–16)
Propiverine (includes IR)	2	691	1.4 (1.2–1.7)	6 (4–12)
Solifenacin	5	304	1.5 (1.4–1.6)	9 (6–17)
Tolterodine (includes IR)	4	3404	1.2 (1.1–1.4)	12 (8–25)
Trospium (includes IR)	4	2677	1.7 (1.5–2.0)	9 (7–12)
Discontinuation due to adverse events				
			RR (95% CI) (of discontinuation)	NNT (95% CI) (for 1 discontinuation)
Darifenacin	7	3138	1.2 (0.8–1.8)	
Fesoterodine	4	4433	2.0 (1.3–3.1)	33 (18–102)
Oxybutynin (includes IR)	5	1483	1.7 (1.1–2.5)	16 (8–86)
Propiverine (includes IR)	2	1401	2.6 (1.4–5)	29 (16–77)
Solifenacin	7	9080	1.3 (1.1–1.7)	78 (39–823)
Tolterodine (includes IR)	10	4466	1.0 (0.6–1.7)	
Trospium (includes IR)	6	3936	1.5 (1.1–1.9)	56 (30–228)

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

improvement in OAB symptoms [51]. There is limited evidence that patients who do not respond to first-line anticholinergic treatment respond to a higher dose or a different anticholinergic agent [52,53].

No single anticholinergic has been shown to have superior cure, improvement, or QoL characteristics compared to others.

Three SRs assessing the clinical effectiveness of mirabegron [54–56] revealed that mirabegron at doses of 25, 50, and 100 mg/d results in significantly greater reductions in UI episodes, urgency episodes, and micturition frequency in comparison to placebo, with no difference in the rate of common adverse events [55]. One SR showed that mirabegron is as efficacious as most anticholinergics in reducing UUI episodes [57]. 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 placebo. An RCT in patients who had an inadequate response to solifenacin monotherapy 5 mg demonstrated that combination treatment with mirabegron 50 mg had a higher chance of achieving a clinically meaningful improvement in UI in comparison to dose escalation of solifenacin [58].

Two SRs of largely retrospective cohort studies showed a consistent association between long-term anticholinergic use and cognitive dysfunction [59,60].

The association of LUTS with genitourinary syndrome of menopause (GSM) should be considered [61]. GSM is a new term that describes various menopausal symptoms and signs associated with physical changes in 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. Evidence from a SR suggests benefit from vaginal oestrogen therapy in GSM [62].

3.2.3. Surgical management

3.2.3.1. *Bladder wall injection of botulinum toxin A.* Data from an SR [63,64] have shown that onabotA injections are more effective than antimuscarinics for cure of UUI (27% vs 13%), while resulting in higher rates of urinary retention (5% vs 0%) and UTI (33% vs 13%).

3.2.3.2. *Sacral nerve stimulation.* A 2018 review of trials including sacral nerve stimulation (SNS) with ≥ 6 mo of follow-up revealed cure rates of 43–56% [65]. Adverse events occurred in 50% of implanted cases, with surgical revision necessary in 33–41% [66,67]. A large RCT reported similar efficacy between SNS and onabotA injections at 2 yr, although satisfaction rates and treatment endorsement were higher with onabotA [68].

3.2.3.3. *Augmentation/clam cystoplasty.* The evidence on augmentation/clam cystoplasty is of low quality and from mixed populations (including neurogenic DO), showing continence and satisfaction rates of approximately 58% at 5 yr [69]. The risk of malignant transformation remains very low and almost exclusively occurs beyond 10 yr after the original cystoplasty [70].

Recommendation for the management of OAB are provided in Table 3.

3.3. Stress urinary incontinence

SUI is defined as involuntary loss of urine on effort or physical exertion and can be broadly classified as uncomplicated or complicated SUI. Complicated SUI refers to SUI associated with 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; or significant associated OAB/UUI.

The panel recognises the role of urodynamics in evaluation of SUI and has incorporated a separate recommendation for these cases, as shown in Table 4.

3.3.1. Conservative management

Evidence from SRs and RCTs suggests that weight loss improves UI in obese women.

A Cochrane SR 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 (56% vs 6%) [71].

3.3.2. Pharmacological management

3.3.2.1. *Oestrogen therapy.* A Cochrane SR looked at the use of oestrogen therapy in postmenopausal women, with 17 studies focusing on SUI [72] and reporting improvement in the short term. Vaginal oestrogen therapy can be given as

Table 3 – Recommendations for OAB.

Recommendation	Strength rating
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.	Weak
Ensure that women with 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 wet OAB, either for temporary symptom control or when other treatments are not feasible.	Strong
Offer prophylactic antibiotics to patients with recurrent UTI who perform CISC or have an indwelling catheter, after discussion regarding the risk of increasing antimicrobial resistance.	Strong
Encourage overweight and obese adults with OAB/UI to lose weight and maintain weight loss.	Strong
Advise adults with OAB that reducing caffeine intake may improve symptoms of urgency and frequency, but not incontinence.	Strong
Review the type and amount of fluid intake in patients with OAB.	Weak
Provide smoking cessation strategies to patients with OAB who smoke.	Strong
Offer prompted voiding for adults with OAB who are cognitively impaired.	Strong
Offer bladder training as first-line therapy to adults with OAB/UI.	Strong
Ensure that PFMT programmes are as intensive as possible.	Strong
Consider PTNS as an option for improvement of OAB/UI in women who have not benefited from anticholinergic medication.	Strong
Offer anticholinergic drugs or mirabegron to adults with OAB for whom conservative treatment fails.	Strong
Consider extended release formulations of anticholinergic drugs whenever possible.	Strong
If an anticholinergic treatment proves ineffective, consider dose escalation or offering an alternative anticholinergic formulation, or mirabegron, or a combination.	Strong
Encourage early review (of efficacy and adverse effects) for patients on anticholinergic medication for OAB.	Strong
Long-term anticholinergic treatment should be used with caution in elderly women, especially those who are at risk of or who have pre-existing cognitive dysfunction.	Strong
Assess the anticholinergic burden and associated comorbidity in patients being considered for anticholinergic therapy for OAB syndrome.	Weak
Offer vaginal oestrogen therapy to women with LUTS and associated symptoms of GSM.	Weak
Offer bladder wall injections of onabotulinum toxin A (100 U) to patients with OAB/UI refractory to conservative therapy or drug treatment.	Strong
Warn patients of the limited duration of response, risk of UTI, and possible prolonged need for CISC before treatment with onabotulinum toxin A.	Strong
Offer repeat injections of onabotulinum toxin, 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 SNS to patients who have OAB/UI refractory to anticholinergic therapy.	Strong
Offer life-long surveillance to women who have a SNS implant to monitor for lead displacement, malfunction, and battery wear.	Strong
Offer augmentation cystoplasty to patients with OAB/UI for whom all other treatment options have failed and who have been warned about the possible small risk of malignancy.	Weak
Inform patients undergoing augmentation cystoplasty of the high risk of CISC (ensure they are willing and able to do so) and that they need lifelong surveillance.	Strong
Do not offer detrusor myectomy as a treatment for UI.	Weak
Only offer urinary diversion to patients for whom less-invasive therapies for the treatment of OAB/UI have failed who will accept a stoma and have been warned about the possible small risk of malignancy.	Weak

CISC = clean intermittent self catheterisation; GSM = genitourinary syndrome of menopause; LUTS = lower urinary tract symptoms; OAB = overactive bladder; PFMT = pelvic floor muscle training; PTNS = percutaneous tibial nerve stimulation; SNS = sacral nerve stimulation; UI = urinary incontinence; UTI = urinary tract infection; UII = urge urinary incontinence.

conjugated equine oestrogen, oestriol or oestradiol in vaginal pessaries, vaginal rings, or creams.

3.3.2.2. Duloxetine. An SR showed significant efficacy for duloxetine compared to placebo in women with SUI, but with a higher risk of adverse events [73].

Table 4 – Recommendations for the diagnosis of SUI.

Recommendation	Strength rating
Do not routinely carry out urodynamic tests when offering treatment for uncomplicated SUI.	Strong
Perform preoperative urodynamic tests 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.	Weak
Use a pad test with a standardised duration and activity protocol.	Strong
Use a standardised pad test when quantification of SUI is required, especially to assess response to treatment.	Weak

POP = pelvic organ prolapse; SUI = stress urinary incontinence.

3.3.3. Surgical management

Concerns regarding the use of polypropylene mesh are legitimate and legislation on its use varies between countries in Europe. The ESTER SR and network meta-analysis [74] is a high-quality review comparing the different surgical modalities for treatment of SUI. Individual rankograms for all surgical interventions were created, which give the probabilities of an intervention being ranked 1 (the highest) to 9 (the lowest) for each outcome. A surface under the cumulative ranking (SUCRA) score is then given, which is

Table 5 – SUCRA curve values for the number of women cured as outcome, adapted from the ESTER meta-analysis [74].

Procedure	Number of women cured (%)
Traditional sling operations	89.4
Retropubic MUS operations	89.1
Open colposuspension	76.7
Transobturator MUS operations	64.1
Laparoscopic colposuspension	48.9
Single-incision sling operations	39.8
Bladder-neck needle suspension	26.9
Anterior vaginal repair	12.5

MUS = mid-urethral sling; SUCRA = surface under the cumulative ranking.

a numerical representation of the overall ranking as a single number associated with each intervention. We report this figure for each intervention for comparative purposes (Table 5) while acknowledging that the ESTER review is limited by only reporting follow-up of 1 yr.

3.3.3.1. Other considerations. A Cochrane SR [75] on open colposuspension revealed a subjective cure rate of 70% at 5 yr. A subanalysis from this review revealed better effectiveness for autologous fascial slings compared to open colposuspension at 1–5 yr.

Bulking agents were not included as a comparator in ESTER. An SR of 23 studies using Macroplastique showed that 75% of patients experienced improvement and 43% were dry at <6 mo, and 64% experienced improvement and 36% were cured at >18 mo [76]. In a more recent RCT comparing TVT to Bulkamid, the objective cure rate was 95% versus 64% [77].

A long-term cohort study of retropubic TVT showed an objective cure rate of 89.9% and a subjective cure rate of 76.1% at 10 yr. Overall, 82.6% of patients reported high satisfaction with their surgery [78]. However, another 10-yr follow-up study from an RCT reported a dry rate of 31.7% following TVT, and 50.8% following autologous fascial sling [79]. A long-term prospective study on transobturator slings showed that the objective and subjective cure rates were

78.9% and 62.6%, respectively, at 145 mo, with no significant deterioration in SUI cure rates over time [80].

The retropubic approach for mid-urethral sling (MUS) was associated with a significantly higher rate of bladder perforation than transobturator MUS (5% vs 0.2%), but groin pain was more frequent after transobturator MUS than retropubic MUS (6.3% vs 1.3%). The rate of tape/mesh exposure or extrusion was similar between retropubic and transobturator MUS (2.1% vs 2.4%; odds ratio 1.10) [73].

Adjustable compression devices and artificial urinary sphincters are used in select patients in some countries but lack high-quality studies to support their use. Other surgical modalities, such as the Vesair intravesical pressure-attenuating balloon, should only be offered as part of a well-regulated research trial.

3.3.3.2. Shared decision-making. The panel recognises that a shared decision-making approach is paramount when any treatments are proposed, but feels that there should be a particular emphasis on the topic area of surgical treatment for SUI. A number of different options are available for patients that vary in both efficacy and safety profile. Consequently, the amount of information given to patients considering surgery for SUI is substantial. The panel unequivocally advises adherence to the fundamental principles of the shared decision-making process, which include:

Table 6 – Recommendations for the management of SUI.

Recommendation	Strength rating
Encourage overweight and obese women with LUTS/SUI to lose weight and maintain weight loss.	Strong
Offer incontinence pads and/or containment devices for management of SUI, either for temporary symptom control or when other treatments are not feasible.	Strong
Offer supervised intensive PFMT, lasting at least 3 mo, as first-line therapy to all women with SUI or MUI (including elderly women and prenatal 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 complications from invasive surgery for SUI.	Strong
Do not offer electrical stimulation with surface electrodes (skin, vaginal, anal) alone for treatment of SUI.	Strong
Offer vaginal oestrogen therapy to postmenopausal women with SUI and symptoms of vulvovaginal atrophy.	Strong
Offer duloxetine (where licensed) to select patients with SUI who are unresponsive to other conservative treatments and who want to avoid invasive treatment, counselling carefully about the risk of adverse events.	Strong
Duloxetine should be initiated and withdrawn using dose titration because of the high risk of adverse events.	Strong
Offer patients who have explored/failed conservative treatment options 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. The outcomes must be monitored in a registry or as part of a well-regulated research trial.	Strong
Offer colposuspension (open or laparoscopic) to women seeking surgical treatment for SUI following a thorough discussion of the risks and benefits relative to other surgical modalities.	Strong
Offer autologous sling placement to women seeking surgical treatment for SUI following a thorough discussion of the risks and benefits relative to other surgical modalities.	Strong
Offer urethral bulking agents to women seeking surgical treatment for 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 with other surgical procedures, repeat injections are likely, and the long-term durability and safety are not established.	Strong
Do not offer autologous fat and hyaluronic acid as urethral bulking agents owing to the higher risk of adverse events.	Strong
Offer an MUS to women seeking surgical treatment for SUI following a thorough discussion of the risks and benefits relative to other surgical modalities.	Strong
Inform women that long-term outcomes for MUS inserted via 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 a single-incision sling that long-term efficacy remains uncertain.	Strong
Inform obese women with SUI about the higher risks associated with surgery, together with the lower probability of benefit.	Weak
Inform older women with SUI about the higher risks associated with surgery, together with the likelihood of a lower probability of benefit.	Weak
Inform women receiving an artificial urinary sphincter or adjustable compression 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

LUTS = lower urinary tract symptoms; MUS = mid-urethral sling; MUI = mixed urinary incontinence; PFMT = pelvic floor muscle training; SUI = stress urinary incontinence.

- Full participation from the patient;
- Delivery of factual information regarding benefits and risks of any particular treatment, adapted to the specific situation of the patient if possible;
- Delivery of information about the experience and expertise of the health care provider/institution carrying out 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 documentation of individual patient preferences;
- Patient opportunity to consider and confirm any decisions made; and
- Clinician assistance with implementation of the final decision.

Recommendations for the management of SUI are provided in [Table 6](#).

3.4. Mixed urinary incontinence

The term MUI may refer to equal stress and urgency symptoms, stress-predominant symptoms, urgency-predominant symptoms, urodynamic SUI (USUI or USI) with DO, or USUI with clinical urgency symptoms but no DO [81]. The challenge with this broad definition is that it leads to inconsistencies when evaluating treatment options and outcomes.

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.

3.4.1. Conservative management

PFMT appears to be less effective for MUI than for SUI alone, and the addition of bladder training may provide additional benefit [82].

Table 7 – Recommendations for the diagnosis and management of MUI.

Recommendation	Strength rating
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
Treat the most bothersome symptom first in patients with MUI.	Weak
Offer bladder training as a first-line therapy to adults with MUI.	Strong
Offer supervised intensive PFMT, lasting at least 3 mo, as a first-line therapy to all women with MUI (including elderly and postnatal women).	Strong
Offer anticholinergic drugs or $\beta 3$ agonists to patients with urgency-predominant MUI.	Strong
Offer duloxetine (where licensed) to select patients with stress-predominant MUI unresponsive to other conservative treatments and who want to avoid invasive treatment, counselling carefully about the risk of adverse events.	Weak
Warn women that surgery for MUI is less likely to be successful than surgery for SUI alone.	Strong
Inform women with MUI that one single treatment may not cure UI; it may be necessary to treat other components of the incontinence problem as well as the most bothersome symptom.	Weak
PFMT = pelvic floor muscle training; MUI = mixed urinary incontinence; SUI = stress urinary incontinence; UI = urinary incontinence.	

3.4.2. Pharmacological management

Tolterodine and solifenacin have been assessed in RCTs in MUI patients, with results showing improvement of the UUI component [83–85]. Duloxetine has also shown efficacy in improving incontinence and QoL in all MUI subgroups in an RCT versus placebo [86]. However, adverse event rates were high at 61.3% and the discontinuation rate was 15.7%.

3.4.3. Surgical management

Few RCTs on surgical management of SUI report separate outcomes for MUI subgroups. Post hoc analyses show poorer results for participants with preoperative urgency or DO, but these results are conflicting [87,88]. In a study of 1113 women treated with transobturator TVT, SUI was cured equally in stress-predominant and urgency-predominant MUI. However, women with stress-predominant MUI had significantly better overall outcomes than women with urgency-predominant MUI [89].

In contrast to studies examining older surgical methods, more recent studies (generally small case series) have reported that UUI symptoms improve in 30–85% of women with MUI after MUS surgery [90].

Recommendations for MUI diagnosis and management are provided in [Table 7](#).

4. Conclusions

Non-neurogenic FLUTS comprise a broad subject area, much of which has not previously been covered in the EAU guidelines compendium. This article provides an overview of the management pathway from general diagnostics in FLUTS through to treatment of OAB, SUI, and MUI. A related article will similarly outline the management of underactive bladder, female BOO, nocturia, POP related to LUTS, urinary fistula, and urethral diverticulum.

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References

- [1] Burkhard FC, Bosch JH, Cruz F, et al. EAU guidelines on urinary incontinence in adults. Arnhem, The Netherlands: European Association of Urology; 2017. https://uroweb.org/wp-content/uploads/14-Urinary-Incontinence_2017_webV2.pdf.
- [2] Harding CK, Lapitan MC, Arlandis S, et al. EAU guidelines: non-neurogenic female lower urinary tract symptoms. Arnhem, The Netherlands: European Association of Urology; 2021. <https://uroweb.org/guideline/non-neurogenic-female-luts/>.
- [3] US Department of Health and Human Services. FDA guidance for industry. Patient-reported outcome measures: use in medical product development to support labeling claims. Silver Spring, MD: US FDA; 2009. <https://www.fda.gov/media/77832/download>.
- [4] Farrell SA, Bent A, Amir-Khalkhali B, et al. Women's ability to assess their urinary incontinence type using the QUID as an educational tool. *Int Urogynecol J* 2013;24:759–62. <https://doi.org/10.1007/s00192-012-1925-6>.
- [5] Hess R, Huang AJ, Richter HE, et al. Long-term efficacy and safety of questionnaire-based initiation of urgency urinary incontinence treatment. *Am J Obstet Gynecol* 2013;209(244):e1–9. <https://doi.org/10.1016/j.ajog.2013.05.008>.
- [6] ICIQ Development Group. International Consultation on Incontinence Questionnaire Female Lower Urinary Tract Symptoms Modules (ICIQ-FLUTS). Bristol, UK: Bristol Urological Institute; 2014. <https://icq.net/icq-fluts>.
- [7] Abrams P, Cardozo L, Fall M, et al. The standardisation of terminology of lower urinary tract function: report from the Standardisation Sub-committee of the International Continence Society. *Neurourol Urodyn* 2002;21:167–78. <https://doi.org/10.1002/nau.10052>.
- [8] Haylen BT, Freeman RM, Swift SE, et al. An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint terminology and classification of the complications related directly to the insertion of prostheses (meshes, implants, tapes) and grafts in female pelvic floor surgery. *Neurourol Urodyn* 2011;30:2–12. <https://doi.org/10.1002/nau.21036>.
- [9] Brown JS, McNaughton KS, Wyman JF, et al. Measurement characteristics of a voiding diary for use by men and women with overactive bladder. *Urology* 2003;61:802–9. [https://doi.org/10.1016/s0090-4295\(02\)02505-0](https://doi.org/10.1016/s0090-4295(02)02505-0).
- [10] Nygaard I, Holcomb R. Reproducibility of the seven-day voiding diary in women with stress urinary incontinence. *Int Urogynecol J Pelvic Floor Dysfunct* 2000;11:15–7. <https://doi.org/10.1007/pl00004021>.
- [11] Bright E, Cottrell N, Drake M, Abrams P. Developing and validating the International Consultation on Incontinence Questionnaire bladder diary. *Eur Urol* 2014;66:294–300. <https://doi.org/10.1016/j.eururo.2014.02.057>.
- [12] Jimenez-Cidre MA, Lopez-Fando L, Esteban-Fuertes M, et al. The 3-day bladder diary is a feasible, reliable and valid tool to evaluate the lower urinary tract symptoms in women. *Neurourol Urodyn* 2015;34:128–32. <https://doi.org/10.1002/nau.22530>.
- [13] Burgio KL, Locher JL, Goode PS, et al. Behavioral vs drug treatment for urge urinary incontinence in older women: a randomized controlled trial. *JAMA* 1998;280:1995–2000. <https://doi.org/10.1001/jama.280.23.1995>.
- [14] Arinzon Z, Shabat S, Peisakh A, Berner Y. Clinical presentation of urinary tract infection (UTI) differs with aging in women. *Arch Gerontol Geriatr* 2012;55:145–7. <https://doi.org/10.1016/j.archger.2011.07.012>.
- [15] Buchsbaum GM, Albushies DT, Guzik DS. Utility of urine reagent strip in screening women with incontinence for urinary tract infection. *Int Urogynecol J Pelvic Floor Dysfunct* 2004;15:391–3. <https://doi.org/10.1007/s00192-004-1192-2>.
- [16] Ouslander JG, Schapira M, Schnelle JF, et al. Does eradicating bacteriuria affect the severity of chronic urinary incontinence in nursing home residents? *Ann Intern Med* 1995;122:749–54. <https://doi.org/10.7326/0003-4819-122-10-199505150-00003>.
- [17] Abrams P. Bladder outlet obstruction index, bladder contractility index and bladder voiding efficiency: three simple indices to define bladder voiding function. *BJU Int* 1999;84:14–5. <https://doi.org/10.1046/j.1464-410x.1999.00121.x>.
- [18] Clement KD, Lapitan MCM, Omar MI, Glazener CMA. Urodynamic studies for management of urinary incontinence in children and adults CD003195. *Cochrane Database Syst Rev* 2013. <https://doi.org/10.1002/14651858.cd003195.pub3>.
- [19] Rachaneni S, Latthe P. Does preoperative urodynamics improve outcomes for women undergoing surgery for stress urinary incontinence? A systematic review and meta-analysis. *Br J Obstet Gynaecol* 2015;122:8–16. <https://doi.org/10.1111/1471-0528.12954>.
- [20] Nager CW, Brubaker L, Litman HJ, et al. A randomized trial of urodynamic testing before stress-incontinence surgery. *N Engl J Med* 2012;366:1987–97. <https://doi.org/10.1056/nejmoa1113595>.
- [21] Nager CW, Sirls L, Litman HJ, et al. Baseline urodynamic predictors of treatment failure 1 year after mid urethral sling surgery. *J Urol* 2011;186:597–603. <https://doi.org/10.1016/j.juro.2011.03.105>.
- [22] Nitti VW, Rovner ES, Bavendam T. Response to fesoterodine in patients with an overactive bladder and urgency urinary incontinence is independent of the urodynamic finding of detrusor overactivity. *BJU Int* 2010;105:1268–75. <https://doi.org/10.1111/j.1464-410x.2009.09037.x>.
- [23] Rovner E, Kennelly M, Schulte-Baukloh H, Zhou J, Haag-Molkenteller C, Dasgupta P. Urodynamic results and clinical outcomes with intradetrusor injections of onabotulinumtoxinA in a randomized, placebo-controlled dose-finding study in idiopathic overactive bladder. *Neurourol Urodyn* 2011;30:556–62. <https://doi.org/10.1002/nau.21021>.
- [24] Koldewijn EL, Rosier PF, Meuleman EJ, Koster AM, Debruyne FM, van Kerrebroeck PE. Predictors of success with neuromodulation in lower urinary tract dysfunction: results of trial stimulation in 100 patients. *J Urol* 1994;152:2071–5. [https://doi.org/10.1016/s0022-5347\(17\)32311-x](https://doi.org/10.1016/s0022-5347(17)32311-x).
- [25] South MM, Romero AA, Jamison MG, Webster GD, Amundsen CL. Detrusor overactivity does not predict outcome of sacral neuromodulation test stimulation. *Int Urogynecol J Pelvic Floor Dysfunct* 2007;18:1395–8. <https://doi.org/10.1007/s00192-007-0351-7>.
- [26] Abdel-Fattah M, Barrington JW, Arunkalaivanan AS. Pelvic pubovaginal sling versus tension-free vaginal tape for treatment of urodynamic stress incontinence: a prospective randomized

- three-year follow-up study. *Eur Urol* 2004;46:629–35. <https://doi.org/10.1016/j.eururo.2004.07.013>.
- [27] Lemack GE, Krauss S, Litman H, et al. Normal preoperative urodynamic testing does not predict voiding dysfunction after Burch colposuspension versus pubovaginal sling. *J Urol* 2008;180:2076–80. <https://doi.org/10.1016/j.juro.2008.07.027>.
- [28] van Brummen HJ, Heintz APM, van der Vaart CH. The association between overactive bladder symptoms and objective parameters from bladder diary and filling cystometry. *Neurourol Urodyn* 2004;23:38–42. <https://doi.org/10.1002/nau.10162>.
- [29] Al Afraa T, Mahfouz W, Campeau L, Corcos J. Normal lower urinary tract assessment in women: I. Uroflowmetry and post-void residual, pad tests, and bladder diaries. *Int Urogynecol J* 2012;23:681–5. <https://doi.org/10.1007/s00192-011-1568-z>.
- [30] Krhut J, Zachoval R, Smith PP, et al. Pad weight testing in the evaluation of urinary incontinence. *Neurourol Urodyn* 2014;33:507–10. <https://doi.org/10.1002/nau.22436>.
- [31] Khullar V, Amarenco G, Doumouchsis SK. Imaging, neurophysiological testing and other tests. In: Abrams P, Cardozo L, Wagg A, Wein A, editors. *Incontinence*, 6th ed.. Bristol, UK: International Continence Society; 2017. p. 671–804. , https://www.ics.org/publications/ici_6/Incontinence_6th_Edition_2017_eBook_v2.pdf.
- [32] Antunes-Lopes T, Cruz CD, Cruz F, Sievert KD. Biomarkers in lower urinary tract symptoms/overactive bladder: a critical overview. *Curr Opin Urol* 2014;24:352–7. <https://doi.org/10.1097/mou.0000000000000064>.
- [33] Lekskulchai O, Dietz HP. Is detrusor hypertrophy in women associated with voiding dysfunction? *Aust N Z J Obstet Gynaecol* 2009;49:653–6. <https://doi.org/10.1111/j.1479-828x.2009.01070.x>.
- [34] Lockhart ME, Fielding JR, Richter HE, et al. Reproducibility of dynamic MR imaging pelvic measurements: a multi-institutional study. *Radiology* 2008;249:534–40. <https://doi.org/10.1148/radiol.2492072009>.
- [35] Haylen BT, de Ridder D, Freeman RM, et al. An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for female pelvic floor dysfunction. *Neurourol Urodyn* 2010;29:4–20. <https://doi.org/10.1002/nau.20798>.
- [36] Brazzelli M, Shirran E, Vale L. Absorbent products for containing urinary and/or fecal incontinence in adults. *J Wound Ostomy Continence Nurs* 2002;29:45–54. <https://doi.org/10.1067/mjw.2002.120870>.
- [37] Geng V, Cobussen-Boekhorst H, Farrell J, et al. Catheterisation. Indwelling catheters in adults – urethral and suprapubic – evidence-based guidelines for best practice in urological health care. Arnhem, The Netherlands: European Association of Urology Nurses; 2012. <https://nurses.uroweb.org/guideline/catheterisation-indwelling-catheters-in-adults-urethral-and-suprapubic/>.
- [38] Prieto J, Murphy C, Moore KN, Fader M. Catheter designs, techniques and strategies for intermittent catheterisation: what is the evidence for preventing symptomatic UTI and other complications? A Cochrane systematic review. *Eur Urol Suppl* 2014;13:. [https://doi.org/10.1016/S1569-9056\(14\)60751-Xe762](https://doi.org/10.1016/S1569-9056(14)60751-Xe762).
- [39] Le Berre M, Presse N, Morin M, et al. What do we really know about the role of caffeine on urinary tract symptoms? A scoping review on caffeine consumption and lower urinary tract symptoms in adults. *Neurourol Urodyn* 2020;39:1217–33. <https://doi.org/10.1002/nau.24344>.
- [40] Hashim H et al.. How should patients with an overactive bladder manipulate their fluid intake? *BJU Int* 2008;102:62. , <https://pubmed.ncbi.nlm.nih.gov/18284414>.
- [41] Zimmern P, Litman HJ, Mueller E, Norton P, Goode P. Urinary Incontinence Treatment Network. Effect of fluid management on fluid intake and urge incontinence in a trial for overactive bladder in women. *BJU Int* 2010;105:1680–5. <https://doi.org/10.1111/j.1464-410x.2009.09055.x>.
- [42] Chen CC, Gatmaitan P, Koeppe S, et al. Obesity is associated with increased prevalence and severity of pelvic floor disorders in women considering bariatric surgery. *Surg Obes Relat Dis* 2009;5:411–5. <https://doi.org/10.1016/j.soard.2008.10.006>.
- [43] Imamura M, Abrams P, Bain C, et al. Systematic review and economic modelling of the effectiveness and cost-effectiveness of non-surgical treatments for women with stress urinary incontinence. *Health Technol Assess* 2010;14:1–188. <https://doi.org/10.3310/hta14400>.
- [44] Eustice S, Roe B, Paterson J. Prompted voiding for the management of urinary incontinence in adults CD002113. *Cochrane Database Syst Rev* 2000. <https://doi.org/10.1002/14651858.cd002113>.
- [45] Flanagan L, Roe B, Jack B, et al. Systematic review of care intervention studies for the management of incontinence and promotion of continence in older people in care homes with urinary incontinence as the primary focus (1966–2010). *Geriatr Gerontol Int* 2012;12:600–11. <https://doi.org/10.1111/j.1447-0594.2012.00875.x>.
- [46] NICE guidance – urinary incontinence and pelvic organ prolapse in women: management. *BJU Int* 2019;123:777–803. <https://doi.org/10.1111/bju.14763>.
- [47] Shamlivan T, Wyman J, Kane RL. *Nonsurgical treatments for urinary incontinence in adult women: diagnosis and comparative effectiveness*. Rockville, MD: Agency for Healthcare Research and Quality; 2012. PMID: 22624162.
- [48] Bo K, Fernandes ACNL, Duarte TB, Brito LGO, Ferreira CHJ. Is pelvic floor muscle training effective for symptoms of overactive bladder in women? A systematic review. *Physiotherapy* 2020;106:65–76. <https://doi.org/10.1016/j.physio.2019.08.011>.
- [49] Finazzi-Agro E, Petta F, Sciobica F, Pasqualetti P, Musco S, Bove P. Percutaneous tibial nerve stimulation effects on detrusor overactivity incontinence are not due to a placebo effect: a randomized, double-blind, placebo controlled trial. *J Urol* 2010;184:2001–6. <https://doi.org/10.1016/j.juro.2010.06.113>.
- [50] Peters KM, Carrico DJ, Perez-Marrero RA, et al. Randomized trial of percutaneous tibial nerve stimulation versus sham efficacy in the treatment of overactive bladder syndrome: results from the SUmIT trial. *J Urol* 2010;183:1438–43. <https://doi.org/10.1016/j.juro.2009.12.036>.
- [51] Herbison P, McKenzie JE. Which anticholinergic is best for people with overactive bladders? A network meta-analysis. *Neurourol Urodyn* 2019;38:525–34. <https://doi.org/10.1002/nau.23893>.
- [52] Chapple C, Schneider T, Haab F, et al. Superiority of fesoterodine 8 mg vs 4 mg in reducing urgency urinary incontinence episodes in patients with overactive bladder: results of the randomised, double-blind, placebo-controlled EIGHT trial. *BJU Int* 2014;114:418–26. <https://doi.org/10.1111/bju.12678>.
- [53] Kaplan SA, Cardozo L, Herschorn S, et al. Efficacy and safety of fesoterodine 8 mg in subjects with overactive bladder after a suboptimal response to tolterodine ER. *Int J Clin Pract* 2014;68:1065–73. <https://doi.org/10.1111/ijcp.12464>.
- [54] Chapple CR, Cardozo L, Nitti VW, Siddiqui E, Michel MC. Mirabegron in overactive bladder: a review of efficacy, safety, and tolerability. *Neurourol Urodyn* 2014;33:17–30. <https://doi.org/10.1002/nau.22505>.
- [55] Cui Y, Zong H, Yang C, Yan H, Zhang Y. The efficacy and safety of mirabegron in treating OAB: a systematic review and meta-analysis of phase III trials. *Int Urol Nephrol* 2014;46:275–84. <https://doi.org/10.1007/s11255-013-0509-9>.
- [56] Wu T, Duan X, Cao CX, Peng CD, Bu SY, Wang KJ. The role of mirabegron in overactive bladder: a systematic review and meta-analysis. *Urol Int* 2014;93:326–37. <https://doi.org/10.1159/000361079>.
- [57] Maman K, Aballea S, Nazir J, et al. Comparative efficacy and safety of medical treatments for the management of overactive bladder: a systematic literature review and mixed treatment comparison. *Eur Urol* 2014;65:755–65. <https://doi.org/10.1016/j.eururo.2013.11.010>.
- [58] MacDiarmid S, Al-Shukri S, Barkin J, et al. Mirabegron as add-on treatment to solifenacin in patients with incontinent overactive bladder and an inadequate response to solifenacin monotherapy. *J Urol* 2016;196:809–18. <https://doi.org/10.1016/j.juro.2016.03.174>.
- [59] Cai X, Campbell N, Khan B, Callahan C, Boustani M. Long-term anticholinergic use and the aging brain. *Alzheimers Dement* 2013;9:377–85. <https://doi.org/10.1016/j.jalz.2012.02.005>.
- [60] Campbell N, Boustani M, Limbil T, et al. The cognitive impact of anticholinergics: a clinical review. *Clin Interv Aging* 2009;4:225–33. <https://doi.org/10.2147/cia.s5358>.
- [61] Rogers RG, Pauls RN, Thakar R, et al. An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for the assessment of sexual health of women with pelvic floor dysfunction. *Neurourol Urodyn* 2018;37:1220–40. <https://doi.org/10.1002/nau.23508>.
- [62] Biehl C, Plotsker O, Mirkin S. A systematic review of the efficacy and safety of vaginal estrogen products for the treatment of

- genitourinary syndrome of menopause. *Menopause* 2019;26:431–53. <https://doi.org/10.1097/gme.0000000000001221>.
- [63] Visco AG, Brubaker L, Richter HE, et al. Anticholinergic therapy vs. onabotulinumtoxinA for urgency urinary incontinence. *N Engl J Med* 2012;367:1803–13. <https://doi.org/10.1056/nejmoa1208872>.
- [64] Drake MJ, Nitti VW, Ginsberg DA, et al. Comparative assessment of the efficacy of onabotulinumtoxinA and oral therapies (anticholinergics and mirabegron) for overactive bladder: a systematic review and network meta-analysis. *BJU Int* 2017;120:611–22. <https://doi.org/10.1111/bju.13945>.
- [65] Tutolo M, Ammirati E, Heesakkers J, et al. Efficacy and safety of sacral and percutaneous tibial neuromodulation in non-neurogenic lower urinary tract dysfunction and chronic pelvic pain: a systematic review of the literature. *Eur Urol* 2018;73:406–18. <https://doi.org/10.1016/j.eururo.2017.11.002>.
- [66] van Kerrebroeck PE, van Voskuilen AC, Heesakkers JPFA, et al. Results of sacral neuromodulation therapy for urinary voiding dysfunction: outcomes of a prospective, worldwide clinical study. *J Urol* 2007;178:2029–34. <https://doi.org/10.1016/j.juro.2007.07.032>.
- [67] Amundsen CL, Richter HE, Menefee SA, et al. OnabotulinumtoxinA vs sacral neuromodulation on refractory urgency urinary incontinence in women: a randomized clinical trial. *JAMA* 2016;316:1366–74. <https://doi.org/10.1001/jama.2016.14617>.
- [68] Amundsen CL, Komesu YM, Chermansky C, et al. Two-year outcomes of sacral neuromodulation versus onabotulinumtoxinA for refractory urgency urinary incontinence: a randomized trial. *Eur Urol* 2018;74:66–73. <https://doi.org/10.1016/j.eururo.2018.02.011>.
- [69] Awad SA, Al-Zahrani HM, Gajewski JB, Bourque-Kehoe AA. Long-term results and complications of augmentation ileocystoplasty for idiopathic urge incontinence in women. *Br J Urol* 1998;81:569–73. <https://doi.org/10.1046/j.1464-410x.1998.00549.x>.
- [70] Biarreau X, Chartier-Kastler E, Roupêt M, Phé V. Risk of malignancy after augmentation cystoplasty: a systematic review. *Neurourol Urodyn* 2016;35:675–82. <https://doi.org/10.1002/nau.22775>.
- [71] Dumoulin C, Cacciari LP, Hay-Smith EJC. Pelvic floor muscle training versus no treatment, or inactive control treatments, for urinary incontinence in women CD005654. *Cochrane Database Syst Rev* 2018. <https://doi.org/10.1002/14651858.cd005654.pub4>.
- [72] Cody JD, Jacobs ML, Richardson K, Moehrer B, Hextall A. Oestrogen therapy for urinary incontinence in post-menopausal women CD001405. *Cochrane Database Syst Rev* 2012. <https://doi.org/10.1002/14651858.cd001405.pub3>.
- [73] Li J, Yang L, Pu C, Tang Y, Yun H, Han P. The role of duloxetine in stress urinary incontinence: a systematic review and meta-analysis. *Int Urol Nephrol* 2013;45:679–86. <https://doi.org/10.1007/s11255-013-0410-6>.
- [74] Brazzelli M, Javanbakht M, Imamura M, et al. Surgical treatments for women with stress urinary incontinence: the ESTER systematic review and economic evaluation. *Health Technol Assess* 2019;23:1–306. <https://doi.org/10.3310/hta23140>.
- [75] Lapitan MC, Cody JD. Open retropubic colposuspension for urinary incontinence in women. *Cochrane Database Syst Rev* 2016;2016:CD002912. <https://doi.org/10.1002/14651858.cd002912.pub6>.
- [76] Ghoniem GM, Miller CJ. A systematic review and meta-analysis of Macroplastique for treating female stress urinary incontinence. *Int Urogynecol J* 2013;24:27–36. <https://doi.org/10.1007/s00192-012-1825-9>.
- [77] Itkonen Freitas AM, Mentula M, Rahkola-Soisalo P, Tulokas S, Mikkola TS. Tension-free vaginal tape surgery versus polyacrylamide hydrogel injection for primary stress urinary incontinence: a randomized clinical trial. *J Urol* 2020;203:372–8. <https://doi.org/10.1097/jju.0000000000000517>.
- [78] Svanngren R, Staff AC, Schiøtz HA, Western K, Kulseng-Hanssen S. Long-term follow-up of the retropubic tension-free vaginal tape procedure. *Int Urogynecol J* 2013;24:1271–8. <https://doi.org/10.1007/s00192-013-2058-2>.
- [79] Khan ZA, Nambiar A, Morley R, Chapple CR, Emery SJ, Lucas MG. Long-term follow-up of a multicentre randomised controlled trial comparing tension-free vaginal tape, xenograft and autologous fascial slings for the treatment of stress urinary incontinence in women. *BJU Int* 2015;115:968–77. <https://doi.org/10.1111/bju.12851>.
- [80] Natale F, Illiano E, Marchesi A, La Penna C, Costantini E. Transobturator tape: over 10 years follow-up. *Urology* 2019;129:48–53. <https://doi.org/10.1016/j.urology.2019.03.003>.
- [81] Chughtai B, Laor L, Dunphy C, Lee R, Te A, Kaplan S. Diagnosis, evaluation, and treatment of mixed urinary incontinence in women. *Rev Urol* 2015;17:78–83. <https://doi.org/10.3909/riu0653>.
- [82] Kaya S, Akbayrak T, Gursen C, Beksac S. Short-term effect of adding pelvic floor muscle training to bladder training for female urinary incontinence: a randomized controlled trial. *Int Urogynecol J* 2015;26:285–93. <https://doi.org/10.1007/s00192-014-2517-4>.
- [83] Khullar V, Hill S, Laval KU, Schiøtz HA, Jonas U, Versi E. Treatment of urge-predominant mixed urinary incontinence with tolterodine extended release: a randomized, placebo-controlled trial. *Urology* 2004;64:269–74. <https://doi.org/10.1016/j.jurology.2004.02.029>.
- [84] Kreder Jr KJ, Brubaker L, Mainprize T. Tolterodine is equally effective in patients with mixed incontinence and those with urge incontinence alone. *BJU Int* 2003;92:418–21. <https://doi.org/10.1046/j.1464-410x.2003.04363.x>.
- [85] Kelleher C, Cardozo L, Kobashi K, Lucente V. Solifenacin: as effective in mixed urinary incontinence as in urge urinary incontinence. *Int Urogynecol J Pelvic Floor Dysfunct* 2006;17:382–8. <https://doi.org/10.1007/s00192-005-0023-4>.
- [86] Bent AE, Gousse AE, Hendrix SL, et al. Duloxetine compared with placebo for the treatment of women with mixed urinary incontinence. *Neurourol Urodyn* 2008;27:212–21. <https://doi.org/10.1002/nau.20471>.
- [87] Richter HE, Diokno A, Kenton K, et al. Predictors of treatment failure 24 months after surgery for stress urinary incontinence. *J Urol* 2008;179:1024–30. <https://doi.org/10.1016/j.juro.2007.10.074>.
- [88] Richter HE, Litman HJ, Lukacz ES, et al. Demographic and clinical predictors of treatment failure one year after midurethral sling surgery. *Obstet Gynecol* 2011;117:913–21. <https://doi.org/10.1097/aog.0b013e31820f3892>.
- [89] Kulseng-Hanssen S, Husby H, Schiøtz HA. Follow-up of TVT operations in 1,113 women with mixed urinary incontinence at 7 and 38 months. *Int Urogynecol J Pelvic Floor Dysfunct* 2008;19:391–6. <https://doi.org/10.1007/s00192-007-0449-y>.
- [90] Sung VW, Borello-France D, Dunivan G, et al. Methods for a multicenter randomized trial for mixed urinary incontinence: rationale and patient-centeredness of the ESTEEM trial. *Int Urogynecol J* 2016;27:1479–90. <https://doi.org/10.1007/s00192-016-3031-7>.