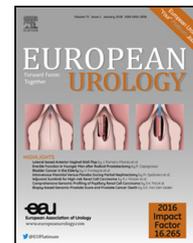


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European Association of Urology



Guidelines

EAU Guidelines on Assessment and Nonsurgical Management of Urinary Incontinence

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Abstract

Context: The European Association of Urology guidelines on urinary incontinence (UI) have been updated in cyclical fashion with successive major chapters being revised each year. The sections on assessment, diagnosis, and nonsurgical treatment have been updated as of mid-2016.

Objective: We present a condensed version of the full guideline on assessment and nonsurgical management of UI, with the aim of improving accessibility and increasing their dissemination.

Evidence acquisition: Our literature search was updated from the previous cut-off of July 2010 up to April 2016. Evidence synthesis was carried out by a pragmatic review of current systematic reviews and any newer subsequent high-quality studies, based on Population, Intervention, Comparator, and Outcome questions. Appraisal was conducted by an international panel of experts, working on a strictly nonprofit and voluntary basis, to develop concise evidence statements and action-based recommendations using modified Oxford and GRADE criteria.

Evidence synthesis: The guidelines include algorithms that summarise the suggested pathway for standard, uncomplicated patients with UI and are more useable in daily practice. The full version of the guideline is available at <http://uroweb.org/guideline/urinary-incontinence/>.

Conclusions: These updated guidelines provide an evidence-based summary of the assessment and nonsurgical management of UI, together with a clear clinical algorithm and action-based recommendations. Although these guidelines are applicable to a standard patient, it must be remembered that therapy should always be tailored to individual patients' needs and circumstances.

Patient summary: Urinary incontinence is a very common condition which negatively impacts patient's quality of life. Several types of incontinence exist and since the treatments will vary, it is important that the diagnostic evaluation establishes which type is present. The diagnosis should also identify patients who need rapid referral to an appropriate specialist. These guidelines aim to provide sensible and practical evidence-based guidance on the clinical problem of urinary incontinence.

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1. Introduction

We present a precis of the 2017 European Association of Urology guideline on the assessment and nonsurgical management of urinary incontinence (UI). This paper, and the guidelines on which it is based [1], are written by urologists for urologists and include practical, evidence-based guidance on the care of people with non-neurogenic UI. Information on the epidemiology of UI is not covered here, rather we provide a summary of the current best evidence for each aspect of assessment, diagnosis, and conservative management, followed by a set of recommendations based on this evidence and reinforced by panel consensus. A management algorithm is provided at the end to aid clinical decision making and delivery of high-quality care.

We recognise that not all management options are available at all centres and hence these guidelines were designed to help the treating urologist weigh the pros and cons of various options and thus arrive at the optimal solution for each individual patient.

2. Evidence acquisition

Consensus methods of creating guidelines are always fraught with difficulty. The European Association of Urology guidelines office therefore made a deliberate decision some years ago to adopt more rigorous and robust methods of guideline development to promote quality and maintain objectivity. These methods are constantly under review and evolving with the best international research and statistical methods. For the current iteration of the guideline each broad topic was subdivided based on a clear clinical question structured around the Patient, Intervention, Comparator, and Outcome format. These questions guided the search strategy and subsequent study selection process. Where existing, good quality systematic reviews were identified, these were considered without reference to the individual source studies and only newer high-quality studies beyond the cut-off date of the systematic reviews were considered separately.

The search was updated from the cut-off date of the previous guideline update (July 2010) to April 2016 and included Medline, EMBASE, and the Cochrane library. English language articles only were considered. A total of 5721 articles were identified and these were screened by two independent reviewers. Data extraction was then carried out for the relevant studies, either by guideline associates or panel members, and synthesised by a senior panel member to arrive at a set of evidence statements for each topic. The recommendations were then constructed by the entire panel at consensus meetings. A detailed search strategy is available online: <https://uroweb.org/guideline/urinary-incontinence/?type=appendices-publications>.

For the 2017 update of the guideline, the grade of recommendations has been changed from the old system of “A,” “B,” and “C” to “strong” or “weak” recommendations. This is based on a modified GRADE [2] system that has been adopted across the Guidelines Office in 2017 (details of

which are outlined in the full version of the Guidelines Book [3] and online (<http://uroweb.org/guidelines/>).

3. Evidence synthesis

Diagnostic tests for UI have been investigated for diagnostic accuracy, reproducibility, reliability, and prognostic value.

3.1. History and physical examination

In the absence of high-level evidence, the expert panel give a *strong* recommendation to taking a patient’s medical history and conducting a thorough physical examination as this is considered fundamental to clinical care. A list of the most important recommendations is summarised in Table 1.

Reasons for specialist referral include haematuria, pain, recurrent urinary tract infection (UTI), previous pelvic radiotherapy, abnormal digital rectal examination, and suspicion of voiding dysfunction. Table 1 lists the important features of history taking and physical examination for the assessment of UI.

3.2. Questionnaires

Although some questionnaires can discriminate different types of UI [4,5], are sensitive to change and can be used to quantify treatment outcomes, there is no evidence that the use of questionnaires improves the management of UI. However, questionnaires may help to quantify symptoms and will often be used in the context of research studies. Many health questionnaires and patient-reported outcome measures were developed and tested in patients with lower urinary tract symptoms but not specifically for UI and should therefore be used with caution in these populations (Table 2).

Table 1 – Recommendation for history taking and physical examination

Recommendations	Strength rating
History taking is an integral component of initial patient evaluation.	Strong
Physical examination is an important component of initial patient evaluation.	Strong
<ul style="list-style-type: none"> Abdominal examination to exclude urinary retention and pelvic masses. Perineal examination including external genitalia, vaginal or rectal examination, pelvic floor contraction, examination of the dermatomes innervated by sacral roots. Assessment of oestrogen status in women. 	

Table 2 – Recommendation on the use of questionnaires

Recommendations	Strength rating
Use a validated and appropriate questionnaire when standardised assessment is needed.	Strong

3.3. Voiding diaries

Voiding diaries (variably referred to as frequency voiding charts or micturition diaries) proved to be reliable to measure 24-h and night-time urine volume, day- and night-time frequency, mean voided volume, urgency, and UI episodes. The use of voiding diaries for 3–7 d, and particularly the recently validated one [6], is strongly recommended, and a behavioural therapeutic effect can be observed with more extended use (Table 3) [7].

3.4. Urinalysis and investigation for UTI

UTI may worsen or cause symptoms of UI and should be treated before further assessment of UI [8]. Asymptomatic bacteriuria does not cause UI and its treatment does not improve symptoms in elderly nursing home residents with established UI [9]. For recommendations, see Table 4.

3.5. Postvoid residual measurement

Higher postvoid residual urine volume (PVR) has been observed in patients with lower urinary tract dysfunction but elevated PVR is not a risk factor for UI, except for the problem of overflow incontinence in men with bladder outlet obstruction (BOO). There is no evidence to support the evaluation of PVR in all patients with UI. Measurement of PVR, if performed, should be with ultrasonography as this proved to be accurate and less invasive than catheterisation [10–15]. For recommendations, see Table 5.

3.6. Urodynamics

Urodynamic tests are performed to provide an objective assessment of lower urinary tract symptoms. They are also known to be used for predicting treatment outcomes, and provide information that may be useful when discussing different treatment options with patients. However, symptoms may not always be reproduced during a urodynamic test, and in these situations data should be interpreted with caution. The diagnostic accuracy of urodynamic tests can be

Table 5 – Recommendations on measuring postvoid residual

Recommendations	Strength rating
When measuring PVR, use ultrasound.	Strong
Measure PVR in patients with UI who have voiding symptoms, especially those being considered for surgical treatment.	Strong
Measure PVR when assessing patients with complicated UI.	Strong
PVR should be measured in patients receiving treatments that may cause or worsen voiding dysfunction.	Strong

PVR = post void residual urine volume; UI = urinary incontinence.

affected by technical issues relative to the equipment and methodological problems associated with test performance. Therefore, use of appropriate equipment and trained personnel in carrying out and interpreting the studies, as is dictated by good urodynamic practice recommendations [16], is of paramount importance.

3.6.1. Variability

There is limited and conflicting evidence regarding the variability of urodynamic studies [17,18]. Measures of urethral function do not correlate with UI severity [19] and conflicting data about its reproducibility have been reported [20,21].

3.6.2. Test accuracy

Accuracy of urodynamics for the diagnosis of UI and assessment of its severity remains questionable [22,23]. Measurement of urethral function is considered to be of questionable significance [24,25] and the clinical utility of ambulatory urodynamics remains unclear [26,27].

Test-retest variability up to 15% has been measured for most urodynamic parameters, and is large enough to change the diagnostic category (normal vs abnormal) in selected patients. Results of urethral function tests are not always correlated with other urodynamic tests or UI severity. Measures of Valsalva leak point pressures are not well standardised and a correlation between Valsalva leak point pressures with UI severity has been refuted [28].

3.6.3. Clinical benefit

Urodynamics may change the way patients with UI are managed but there is no evidence that this may improve the outcome of conservative treatment [29]. For example, the finding of detrusor overactivity (DO) has no predictive value for the outcome of antimuscarinic treatment [30,31] and although urodynamics may change the clinical diagnosis of patients with UI in up to 56% of patients,

Table 3 – Recommendations about the use of voiding diaries

Recommendations	Strength rating
Ask patients with urinary incontinence to complete a voiding diary when standardised assessment is needed.	Strong
Use a diary duration of at least 3 d.	Strong

Table 4 – Recommendations on the use of urinalysis and urine culture

Recommendations	Strength rating
Perform urinalysis as a part of the initial assessment of a patient with UI.	Strong
If a symptomatic UTI is present with UI, reassess the patient after treatment.	Strong
Do not routinely treat asymptomatic bacteriuria in elderly patients to improve UI.	Strong

UI = urinary incontinence; UTI = urinary tract infection.

the type of treatment offered, and the success of stress UI (SUI) surgery is not influenced by urodynamics [32–35]. Clearly, the lack of correlation between the urodynamic finding of DO and the outcome of antimuscarinic treatment may also be due to the limited efficacy of antimuscarinics to cure UI. No consistent correlation was found between the results of urethral function tests and success or failure of SUI surgery [36–40].

The diagnosis of DO has been associated with postoperative urge UI (UUI) following SUI surgery, but not associated with midurethral sling treatment failure [40]. Low preoperative urinary flow rates are correlated with, but not predictive of, voiding dysfunction [36–39]. Also, in women with normal voiding prior to surgery, the presence of abnormal pressure flow values does not predict postoperative voiding dysfunction following SUI surgery [41]. The clinical benefit of urodynamics in men with postprostatectomy UI remains uncertain [42,43].

In conclusion, although it seems reasonable to perform urodynamics before irreversible treatments such as surgery, the evidence of any clinical benefit or prognostic value remains inconsistent, particularly in patients with uncomplicated forms of incontinence. Table 6 shows recommendations for urodynamic assessment.

3.7. Pad test

Pad tests of different durations and with various exercise schedules have been used to quantify the amount of urine loss. Although the test is sensitive to change [45] and

good specificity was shown, sensitivity for symptoms of SUI, and mixed urinary incontinence (MUI) is rather low [46,47]. Overall, the clinical benefit of quantifying the amount of UI is uncertain as is the predictive value for treatment outcomes [46,48]. No pad test schedule is shown to be superior to another. For recommendations, see Table 7.

3.8. Imaging

The use of imaging in patients with UI has been advocated to investigate the anatomical abnormalities underlying the condition. As a research tool it has been used both before and after treatment to investigate the relationship between anatomy, symptoms, and function at the level of the central nervous system, bladder, and pelvic floor muscles.

X-ray imaging has mainly been replaced by ultrasound and magnetic resonance techniques. Imaging of bladder neck/urethral mobility in patients with UI proved inconclusive [49]. Magnetic resonance offers global imaging of pelvic floor structures but evidence of its clinical utility is lacking, particularly in uncomplicated UI [50,51]. Ultrasound imaging of midurethral slings postoperatively has shown some correlation with clinical outcomes [52,53]. Imaging of urethral volume and membranous urethral length has been proposed in female patients with SUI and in male patients undergoing radical prostatectomy but the relation with treatment outcomes remains weak [54–57].

Measures of bladder/detrusor wall thickness has been advocated to diagnose BOO in men and DO in women but standardisation remains poor and at the current time there is little evidence for clinical benefit.

Imaging in the field of UI seems to be limited to clinical research. For recommendation, see Table 8.

3.9. Conservative treatment

3.9.1. Simple clinical interventions

3.9.1.1. Treatment of comorbidity and adjustment of medication. UI, especially in the elderly, has been associated with multiple comorbid conditions including: cardiac failure, chronic renal failure, diabetes, chronic obstructive pulmonary disease, neurological disease including stroke and multiple sclerosis, general cognitive impairment, sleep disturbances, for example, sleep apnoea, depression, and metabolic syndrome. It is possible that improvement of associated diseases may reduce the severity of urinary symptoms.

There is a higher prevalence of UI in women with type 2 diabetes; however, one study showed no correlation between earlier treatment of type 1 diabetes mellitus and the prevalence of UI in later life versus conventional treatment [58].

Table 6 – Recommendations on the use of urodynamics

Recommendations (NB: concerning only neurologically intact adults with urinary incontinence)	Strength rating
When performing urodynamics in patients with UI adhere to good urodynamic practice standards as described by the International Continence Society [44]: <ul style="list-style-type: none"> • attempt to replicate the patient’s symptoms; • check recordings for quality control; • interpret results in the context of the clinical problem; • remember there may be physiological variability within the same individual. 	Strong
Do not routinely carry out urodynamics when offering treatment for uncomplicated SUI.	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 severity of incontinence.	Strong

SUI = stress urinary incontinence; UI = urinary incontinence.

Table 7 – Recommendations on the use of pad tests

Recommendations	Strength rating
Use a pad test of standardised duration and activity protocol.	Strong
Use a pad test when quantification of UI is required.	Weak

UI = urinary incontinence.

Table 8 – Recommendation on the use of imaging

Recommendation	Strength rating
Do not routinely carry out imaging of the upper or lower urinary tract as part of the assessment of UI.	Strong

UI = urinary incontinence.

Our literature review failed to identify any studies addressing whether adjustment of specific medications could alter existing symptoms of UI. Also, there is little evidence relating to the occurrence or worsening of UI in relation to prescription of any specific drugs. For recommendations, see [Table 9](#).

3.9.2. Constipation

Several studies have shown strong associations between constipation and UI [59–62] and also prolapse and UI [63]. Constipation can be improved by behavioural, physical, and medical treatments (eg, assisted toileting or altering fluid intake). For recommendation, see [Table 10](#).

3.9.3. Containment

Containment is important for people with UI when active treatment does not cure the problem, when it is not available or not possible, or if the risks of treatment outweigh benefits. Types of containment include absorbent pads, urinary catheters, external collection devices, penile clamps for men, and intravaginal devices for women. Detailed literature summaries can be found in the current international consultation on urological diseases monograph [64] and in European Association of Urological Nurses guidance documents [65,66]. A useful resource for health care professionals and patients can be found at: www.continenceproductadvisor.org.

There is evidence that pads are effective in containing urine, hinge-type penile clamps are more effective than circular clamps in controlling SUI in men, and vaginal devices may improve SUI in women in selective groups. See [Table 11](#) for recommendations on containment devices.

3.10. Lifestyle interventions

3.10.1. Caffeine reduction

Many drinks contain caffeine, particularly tea, coffee, and cola. Anecdotal reports of urinary symptoms being

Table 11 – Recommendations on containment devices

Recommendations	Strength rating
Ensure that adults with UI and/or their carers are informed regarding available treatment options before deciding on containment alone.	Strong
Offer incontinence pads and/or containment devices for management of UI.	Strong
UI = urinary incontinence.	

aggravated by excessive caffeine intake has focused attention on whether caffeine reduction may improve UI. The evidence shows that reduction of caffeine intake does not improve UI, but reduction in caffeine intake may improve symptoms of urgency and frequency [67–71].

3.10.2. Physical exercise

Regular physical activity may strengthen the pelvic floor musculature and possibly decrease the risk of developing UI, especially SUI. However, it is also possible that heavy physical exercise may aggravate UI (eg, female athletes may experience UI during intense physical activity but not during common activities). Strenuous physical activity does not predispose to UI for women later in life but moderate exercise is associated with lower rates of UI in middle-aged or older women [72–78].

3.10.3. Fluid intake

Modification of fluid intake, particularly restriction, is a strategy commonly used by people with UI to relieve symptoms. Advice on fluid intake given by health care professionals should be based on 24-h fluid intake and urine output measurements. From a general health point of view, it should be advised that fluid intake should be sufficient to avoid thirst and that low or high 24-h urine output should be investigated. A reduction in fluid intake by 25% improved symptoms in patients with overactive bladder (OAB) but not UI [79]. Another randomised controlled trial (RCT) comparing drug therapy alone to drug therapy with behavioural advice also showed no difference in continence outcomes [80].

3.10.4. Obesity and weight loss

Being overweight or obese has been identified as a risk factor for UI in many epidemiological studies [81,82]. There is evidence that the prevalence of both UI and SUI increases proportionately with rising body mass index [83]. The proportion of patients who undergo surgery for incontinence who are overweight or obese is higher than that of the general population [84]. Current evidence shows that nonsurgical and surgical weight loss in overweight and obese women improves UI. In addition, weight loss in obese adults with diabetes mellitus reduces the risk of developing UI.

3.10.5. Smoking

Smoking cessation is now a generalised public health measure and has been shown to be weakly associated with improving urgency, frequency, and UI [67,85].

Table 9 – Recommendations on simple clinical interventions

Recommendations	Strength rating
Patients with UI who have associated conditions, should have appropriate treatment for those conditions in line with good medical practice.	Strong
Take a history of current medication use from all patients with UI.	Strong
Review any new medication associated with the development or worsening of UI.	Weak
UI = urinary incontinence.	

Table 10 – Recommendations on treatment of constipation

Recommendation	Strength rating
Adults with UI who also suffer from constipation should be given advice about bowel management in line with good medical practice.	Weak
UI = urinary incontinence.	

Table 12 – Recommendations on lifestyle interventions

Recommendations	Strength rating
Encourage obese adults with UI to lose weight and maintain weight loss.	Strong
Advise adults with UI that reducing caffeine intake may improve symptoms of urgency and frequency but not incontinence.	Strong
Review type and amount of fluid intake in patients with UI.	Weak
Provide smoking cessation strategies to patients with UI who smoke.	Strong
UI = urinary incontinence.	

For recommendations on lifestyle interventions, see [Table 12](#).

3.11. Behavioural and physical therapies

Approaches include prompted voiding, bladder training (BT), pelvic floor muscle training (PFMT), electrical stimulation, magnetic stimulation, and posterior tibial nerve stimulation.

3.11.1. Prompted voiding

Two systematic reviews (9 RCTs) confirmed a positive effect on continence outcomes for prompted voiding in comparison to standard care [86,87]. A Cochrane review of timed voiding reviewed two RCTs, finding inconsistent improvement in continence compared with standard care in cognitively impaired adults [88]. Prompted voiding, either alone or as part of a behavioural modification programme, has been shown to improve continence in elderly, care-dependent people.

3.11.2. Bladder training

There have been three systematic reviews that confirmed that BT is better than no treatment in women with UUI and MUI [22,89,90]. However, the effectiveness of BT diminishes after treatment cessation. There are no adverse events.

BT has been compared with other treatments for UI. In a review of seven RCTs in which BT was compared to drug therapy alone, only oxybutynin was shown to be effective in cure and improvement of UI (level of evidence: 2) [91]. The combination of BT with antimuscarinic drugs does not result in greater improvement of UI but may improve frequency and nocturia. BT is, however, better than pessary alone.

3.11.3. PFMT

3.11.3.1. Pelvic floor muscle therapy in women.

Meta-analysis showed that PFMT was effective for cure or improvement of incontinence, and improvement in quality of life (QoL). The effect applies in women with SUI, UUI, and MUI, though the effect in MUI is lower than in women with pure SUI. A Cochrane review comparing different approaches to delivery of PFMT (21 RCTs) concluded that increased intensity of delivery of therapy improves response and that there is no consistent difference between group therapy and individualised treatment sessions

[92]. Long-term adherence to treatment was poor and half of patients had progressed to surgery [93]. There is uncertain evidence about the additional value of BT or biofeedback to the effect of PFMT.

3.11.3.2. PFMT in postpartum period.

PFMT has been compared with several alternative therapies, alone or in combination, in a mixed treatment comparison [90]. This supported the general principle that greater efficacy was achieved by adding together different modalities of treatment and increasing intensity. PFMT for UI in the postpartum period was shown to increase the rate of cure after 12 mo [94].

3.11.3.3. Pelvic floor muscle therapy in men with stress urinary incontinence following radical prostatectomy.

A Cochrane review, carried out in 2015, concluded that there was no overall benefit at 12-mo postsurgery for men who received postoperative PFMT for the treatment of post-prostatectomy UI and that the benefits of conservative treatment of postprostatectomy UI remain uncertain [95]. A meta-analysis within this review showed that a greater proportion of men were dry from between 3 mo and 12 mo suggesting that PFMT may speed recovery of continence.

3.11.3.4. Preventive value of PFMT.

It has been shown that PFMT reduces the risk of incontinence in late pregnancy and up to 6-mo postpartum [94] and that preoperative PFMT speeds recovery of continence in men undergoing radical prostatectomy [96].

3.11.4. Electrical stimulation (surface electrodes)

Most evidence on electrical stimulation (ES) refers to women with SUI and is inconsistent about whether it alone can improve UI. Two health technology assessments and three systematic reviews were found [97] that included studies of low quality with a lack of consistency in the parameters used for ES and outcome measures. It was not possible to conclude whether ES is more effective than sham stimulation and whether ES adds to the benefit of PFMT alone.

A Cochrane review of ES in men with UI (6 RCTs) concluded that there was some evidence that ES enhanced the effect of PFMT and was also more effective than sham stimulation in the short term. There were, however, more adverse effects (pain or discomfort) with ES [98].

3.11.5. Magnetic stimulation

There is no consistent evidence for the efficacy of magnetic stimulation for the cure or improvement of UI (level of evidence: 2a), although there are no reports of adverse events (level of evidence: 1b). Eight RCTs were found, but they were mostly of poor quality. The techniques of electromagnetic stimulation were poorly standardised and involved different devices, modes of delivery, and stimulation parameters [99,100]. Blinding was difficult to achieve, which resulted in a high risk of bias in some trials. There was a lack of evidence for effectiveness in men with UI.

Table 13 – Recommendations on behavioural and physical therapies

Recommendations	Strength rating
Offer prompted voiding for adults with UI who are cognitively impaired.	Strong
Offer bladder training as a first-line therapy to adults with UUI or MUI.	Strong
Offer supervised PFMT, lasting at least 3 mo, as a first-line therapy to all women with SUI or MUI (including the elderly and postnatal).	Strong
Offer instruction on PFMT to men undergoing radical prostatectomy to speed recovery from UI.	Strong
PFMT programmes should be as intensive as possible.	Strong
Do not offer electrical stimulation with surface electrodes (skin, vaginal, anal) alone for the treatment of stress UI.	Strong
Do not offer magnetic stimulation for the treatment of UI or overactive bladder in adult women.	Strong
Consider PTNS as an option for improvement of UUI in women who have not benefited from antimuscarinic medication.	Strong

MUI = mixed urinary incontinence; PFMT = pelvic floor muscle training; PTNS = percutaneous tibial nerve stimulation; SUI = stress urinary incontinence; UI = urinary incontinence; UUI = urge urinary incontinence.

3.11.6. Posterior (percutaneous) tibial nerve stimulation

Compared with sham treatment, percutaneous tibial nerve stimulation (PTNS) was shown to improve but not cure UUI in some women who have not benefited from antimuscarinic medication or who are not able to tolerate these drugs [101,102]. PTNS is no more effective than tolterodine for the improvement of UUI in women [101], but there are insufficient data to determine the effectiveness of PTNS in men. No serious adverse events have been reported.

For recommendations on behavioural and physical therapies, see Table 13.

3.12. Drug treatment

3.12.1. Drugs for treatment of OAB/UUI

Antimuscarinic (anticholinergic) drugs and mirabegron (the first clinically available beta-3 agonist) are the mainstays of drug treatment for UUI. Antimuscarinic drugs are an early treatment option for adults with UUI, whereas mirabegron has only been available since 2013.

3.12.1.1. Antimuscarinics (Table 14).

Available antimuscarinic drugs differ in muscarinic receptor affinity, pharmacokinetic properties, for example, lipid solubility and half-life, and their formulation. Seven systematic reviews of individual antimuscarinic drugs versus placebo were reviewed (summarised in Table 14) [90,103–108]. Cure of UI was deemed to be the most important outcome measure. Every study of antimuscarinic versus placebo with cure of UI as an outcome measure shows superiority compared with placebo, but the absolute size of effect is small. There is limited evidence that one antimuscarinic drug is superior to another for cure or

improvement of UUI. Dose escalation of antimuscarinic drugs may be adequate in selected patients to cure or improve UUI but with a higher risk of side effects.

On balance, immediate release formulations tend to be associated with more side effects compared with extended release (ER) formulations. Dry mouth is the commonest side effect, though constipation, blurred vision, fatigue, and cognitive dysfunction may occur [90].

A transdermal delivery system and gel developed for oxybutynin gives a further alternative formulation. Safety profile is good but data on cure of UUI with transdermal delivery system formulation were not found.

The question of drug versus conservative treatment of UUI was also addressed. However, no consistent evidence was found to show superiority of antimuscarinic drug therapy over conservative therapy. Likewise, insufficient evidence exists as to the benefit of adding PFMT to drug treatment for treatment of UUI.

3.12.2. Mirabegron

Mirabegron has been evaluated in industry-sponsored trials [109–112] and in three systematic reviews [109,110,113]. It is licensed in Europe in a dose of 50 mg and in some non-European countries in doses of 25 mg and 50 mg. Mirabegron results in a significantly greater reduction in UUI episodes, urgency episodes, and micturition-frequency/d compared with placebo. The mirabegron dry rate in most of these trials is between 43% and 50% and 35% and 40% for placebo. Similar improvement in frequency of incontinence episodes/d and micturitions/d was found in people who had and had not previously tried antimuscarinic agents. One systematic review showed that mirabegron is similarly efficacious to most antimuscarinics in reducing UUI

Table 14 – Summary of systematic review findings on antimuscarinics for UI

Drug	No. of studies	Patients	Relative risk (95% CI; of curing UI)	No. needed to treat (95% CI; to achieve one 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	6,304	1.5 (1.4–1.6)	9 (6–17)
Tolterodine (includes IR) =	4	3,404	1.2 (1.1–1.4)	12 (8–25)
Trospium (includes IR)	4	2,677	1.7 (1.5–2.0)	9 (7–12)

CI = confidence interval; IR = immediate release; UI = urinary incontinence.

episodes [114]. Posthoc analyses of RCTs showed that clinical improvement observed in parameters of OAB severity translates to an improvement in Health-related QoL and efficacy is maintained in patients with a more severe degree of UUI [115,116].

Evaluation of urodynamic parameters in men with combined BOO and OAB concluded that mirabegron 50 mg did not adversely affect voiding urodynamic parameters compared with placebo [117]. One RCT showed that a combination of mirabegron 50 mg and an alpha-blocker was superior to an alpha-blocker alone to treat storage symptoms in men [118].

The most common treatment associated adverse events in the mirabegron groups were hypertension (7.3%), nasopharyngitis (3.4%), and UTI (3%), with the overall rate similar to placebo [109,112,119]. Although mirabegron should not be offered to patients with severe uncontrolled hypertension, the cardiovascular safety of mirabegron was comparable with that of antimuscarinic agents in a recent systematic review [120].

3.12.3. Comparison between antimuscarinics and mirabegron

In a 12-mo, active-controlled RCT of mirabegron 50 mg versus tolterodine ER 4 mg, the improvement in efficacy seen at 12 wk was sustained at the 12-mo evaluation for both drugs. The reported dry rates at 12 mo were 43% and 45%, respectively [119]. One systematic review showed that mirabegron is as efficacious as most antimuscarinics in reducing UUI episodes [114]. UUI was a secondary endpoint in a study that compared mirabegron 50 mg and solifenacin 5 mg in OAB patients dissatisfied with previous antimuscarinic treatment due to the lack of efficacy. At the end of treatment, dry rate was similar in both arms—67.3% and 68.5%, respectively [121]. A RCT in patients who had inadequate response to solifenacin monotherapy 5 mg, demonstrated that combination treatment with mirabegron 50 mg had a higher chance of achieving clinically meaningful improvement in UI as compared with dose escalation to solifenacin 10 mg [122]. For recommendations on drugs for UUI, see Table 15.

3.12.4. OAB treatment in elderly patients

Antimuscarinic drugs are effective in elderly patients to cure or improve UUI. However, two recent longitudinal cohort studies showed a risk of deterioration in cognitive

function, alteration in central nervous system metabolism, and an association with brain atrophy with prolonged use of drugs with antimuscarinic effects [123,124]. These changes had not been revealed by short-term studies with most antimuscarinics approved for OAB. A 12-wk RCT with solifenacin 5 mg and fesoterodine 8 mg in vulnerable elderly patients did not show any significant deterioration of cognitive function [125,126]. Trospium does not cross the blood brain barrier in significant amounts in healthy individuals and also did not impair cognitive function [127,128]. In elderly volunteers, 2 wk of treatment with darifenacin had no effect on cognitive function [126]. There is, however, evidence that oxybutynin immediate release may cause/worsen cognitive dysfunction in adults [125,129–133].

When starting anticholinergics in elderly patients, the number of medications that have anticholinergic effects and their cumulative effects on mental function should be assessed objectively and monitored. The anticholinergic risk scale is a useful tool to aid with this [134].

Mirabegron 25 mg and 50 mg showed similar efficacy in UUI treatment in the population >65 yr and >75 yr when compared with the overall population [135] and should be considered to treat UUI in elderly patients if additional antimuscarinic load is to be avoided (Table 16).

3.12.5. Adherence and persistence in OAB treatment

In one RCT, equivalent adherence was observed for tolterodine and mirabegron at 12 mo (5.5% and 3.6%) [119]. However, adherence in real-life practice between the two classes of drugs seems to be different. Adherence to antimuscarinic treatment is low and decreases over time, most patients stopping antimuscarinic agents within the 1st 12 mo because of lack of efficacy, adverse events, and/or cost. Recent data from Canada and UK indicate that persistence on treatment is higher among patients medicated with mirabegron than with antimuscarinics [136].

3.13. Drugs for SUI

Duloxetine has been investigated for relief of SUI in adult women, and men for temporary improvement or when more effective options such as surgery cannot be used. In women, duloxetine 80 mg may be superior to PFMT alone [137]. A cure rate of 10% may be achieved with doses of 80 mg/d but with inconsistent data concerning QoL improvement [107,138,139]. In men with SUI after prostate surgery, RCTs suggest an earlier recovery of continence with duloxetine either alone [140], or in addition to PFMT [141,142].

Table 15 – Recommendations on drugs for UUI

Recommendations	Strength rating
Offer antimuscarinic drugs or mirabegron for adults with UUI who failed conservative treatment.	Strong
Consider extended release formulations of antimuscarinic drugs whenever possible.	Strong
If an antimuscarinic treatment proves ineffective, consider dose escalation or offering an alternative antimuscarinic formulation or mirabegron or a combination.	Strong
Encourage early review (of efficacy and side effects) of patients on antimuscarinic medication for UUI.	Strong
UUI = urge urinary incontinence.	

Table 16 – Recommendations on treatment of UUI in elderly patients

Recommendation	Strength rating
Long-term antimuscarinic treatment should be used with caution in elderly patients especially those who are at risk of, or have, cognitive dysfunction.	Strong
UUI = urge urinary incontinence.	

Table 17 – Recommendations on drugs for SUI

Recommendations	Strength rating
Offer duloxetine in selected patients with symptoms of SUI when surgery is not indicated.	Strong
Duloxetine should be initiated and withdrawn using dose titration because of high risk of adverse event.	Strong
SIU = stress urinary incontinence.	

All studies had a high patient withdrawal rate, which was caused by a lack of efficacy and high incidence of adverse events, including nausea and vomiting (40% or more of patients), dry mouth, constipation, dizziness, insomnia, somnolence, and fatigue [143,144]. For recommendations on drugs for SUI, see Table 17.

3.14. Desmopressin

One RCT compared desmopressin with placebo in women with daytime UI and improved continence was shown during the 1st 4 h after taking the drug [145]. No evidence was found demonstrating efficacy of desmopressin on nocturnal incontinence, despite its positive outcome on nocturnal polyuria. The use of desmopressin carries a risk of developing hyponatraemia, particularly in elderly patients, and should be used with caution in this group.

3.15. Drug treatment in MUI

Tolterodine ER and solifenacin were effective for improvement of UUI in women with MUI suggesting that the SUI component is not affected by the action of the antimuscarinic drug [146–149]. In one RCT of duloxetine versus placebo, 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 [150]. Duloxetine was found to have equal efficacy for SUI and MUI in an RCT (n = 553) following secondary analysis of respective subpopulations [151].

3.16. Intravaginal oestrogens

Vaginal oestrogen treatment with oestradiol and oestriol is not associated with the increased risk of thromboembolism,

Table 18 – Recommendations on vaginal oestrogen therapy

Recommendations	Strength rating
Offer long-term vaginal oestrogen therapy to postmenopausal women with UI and symptoms of vulvo-vaginal atrophy.	Strong
In women with a history of breast cancer, the treating oncologist should be consulted.	Weak
For women taking oral conjugated equine oestrogen as hormone replacement therapy who develop or experience worsening UI, discuss alternative hormone replacement therapies.	Strong
Advise women who are taking systemic oestradiol who suffer from UI that stopping the oestradiol is unlikely to improve their incontinence.	Strong
UI = urinary incontinence.	

endometrial hypertrophy, and breast cancer, and does not increase the risk of UI that is often seen with systemic administration [152–154]. Although primarily used to treat symptoms of vaginal atrophy in postmenopausal women, a Cochrane review found that vaginal oestrogen treatment improved symptoms of UI in the short term [152]. Local oestrogen was less likely to improve UI than PFMT but no differences in UI outcomes were observed for other comparisons. No adverse effects of vaginal administration of oestradiol over 2 yr were seen in one trial [155]. For recommendations, see Table 18.

4. Conclusions

Urinary incontinence is a common and distressing symptom with a potentially significant impact on patients' quality of life. Conservative management is an often over-looked and under-used management option, with a number of different modalities available. Clinicians should be aware of these options and tailor management according to individual needs and circumstances.

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