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### Guidelines

## **EAU Guidelines on Urinary Incontinence**

Joachim W. Thüroff<sup>a,\*</sup>, Paul Abrams<sup>b</sup>, Karl-Erik Andersson<sup>c</sup>, Walter Artibani<sup>d</sup>, Christopher R. Chapple<sup>e</sup>, Marcus J. Drake<sup>b</sup>, Christian Hampel<sup>a</sup>, Andreas Neisius<sup>a</sup>, Annette Schröder<sup>a</sup>, Andrea Tubaro<sup>f</sup>

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#### **Abstract**

**Context:** The first European Association of Urology (EAU) guidelines on incontinence were published in 2001. These guidelines were periodically updated in past years.

**Objective:** The aim of this paper is to present a summary of the 2009 update of the EAU guidelines on urinary incontinence (UI).

**Evidence acquisition:** The EAU working panel was part of the 4th International Consultation on Incontinence (ICI) and, with permission of the ICI, extracted the relevant data. The methodology of the 4th ICI was a comprehensive literature review by international experts and consensus formation. In addition, level of evidence was rated according to a modified Oxford system and grades of recommendation were given accordingly.

**Evidence summary:** A full version of the EAU guidelines on urinary incontinence is available as a printed document (extended and short form) and as a CD-ROM from the EAU office or online from the EAU Web site (http://www.uroweb.org/guidelines/online-guidelines/).

The extent and invasiveness of assessment of UI depends on severity and/or complexity of symptoms and clinical signs and is different for men, women, frail older persons, children, and patients with neuropathy. At the level of *initial management*, basic diagnostic tests are applied to exclude an underlying disease or condition such as urinary tract infection. Treatment is mostly conservative (lifestyle interventions, physiotherapy, physical therapy, pharmacotherapy) and is of an empirical nature. At the level of *specialised management* (when primary therapy failed, diagnosis is unclear, or symptoms and/or signs are complex/severe), more elaborate assessment is generally required, including imaging, endoscopy, and urodynamics. Treatment options include invasive interventions and surgery.

**Conclusions:** Treatment options for UI are rapidly expanding. These EAU guidelines provide ratings of the evidence (guided by evidence-based medicine) and graded recommendations for the appropriate assessment and according treatment options and put them into clinical perspective.

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 $\label{lem:email} E-mail\ addresses: joachim.thueroff@unimedizin-mainz.de, irene.keenan@unimedizin-mainz.de (J.W.\ Th\"uroff).$ 

<sup>&</sup>lt;sup>a</sup> Department of Urology, Johannes Gutenberg University, Mainz, Germany

<sup>&</sup>lt;sup>b</sup> Bristol Urological Institute, Southmead Hospital, Bristol, UK

<sup>&</sup>lt;sup>c</sup> Wake Forest Institute for Regenerative Medicine, Winston-Salem, NC, USA

<sup>&</sup>lt;sup>d</sup> Department of Urology, Azienda Ospedaliera Universitaria Integrata, Verona, Italy

<sup>&</sup>lt;sup>e</sup> Department of Urology, Royal Hallamshire Hospital, Sheffield, UK

<sup>&</sup>lt;sup>f</sup>Department of Urology, University of Rome 'La Sapienza,' Rome, Italy

<sup>\*</sup> Corresponding author. Department of Urology, University Medical Centre, Johannes Gutenberg University, Langenbeckstrasse 1, 55131 Mainz, Germany. Tel. +49 6131 177183;

Fax: +49 6131 176415

#### 1. Introduction

The first International Consultation on Incontinence (ICI) in 1998 developed recommendations for assessment and treatment of incontinence based on review of evidence and consensus of international experts [1]. As an outflow of this process, recommendations for the management of incontinence were developed and presented in a specific structure of flow sheets (ie, algorithms), with recommendations for *initial management* and *specialised management* of urinary incontinence (UI) in children, men, women, patients with neuropathic bladder, and frail older patients [2]. These algorithms were, with permission of the ICI, adopted for the first European Association of Urology (EAU) guidelines on incontinence, presented in 2001 [3], and have been updated thereafter according to ICI-2 and ICI-3 consensus results.

For the ICI-4, literature review was comprehensive, including the results of ICI-1 through ICI-3. Additionally, the principles of evidence-based medicine were applied for analysis and rating of the relevant papers published in the literature, for which a modified Oxford system has been developed [4,5]. This approach applies levels of evidence (LoEs) to the body of analysed literature and, from there, derives grades of recommendation (GoRs) (Tables 1 and 2).

The 2009 update of the EAU guidelines on incontinence is based on the 4th ICI, held in July 2008 [6]. The 2009 EAU guidelines on incontinence are available as a printed document in an extended version with an exhaustive reference list and in a short form [7], as a CD-ROM version, and online at the EAU Web site (http://www.uroweb.org/guidelines/online-guidelines/).

### 2. Algorithms

The algorithms (Figs. 1–5), which continue to be the skeleton of the guidelines, are uniformly constructed to follow, from top to bottom, a chronologic pathway including assessment of the patient's history and symptoms, clinical assessment using appropriate studies and tests, and definition of the underlying pathophysiology as a basis for rational treatment decisions. To limit the number of diagnostic pathways in the algorithms, clinical presenta-

Table 1 - Level of evidence

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

<sup>\*</sup> Modified from Phillips et al [4] as described by Abrams et al [5].

Table 2 - Grade of recommendation

Grade	Nature of recommendations
Α	Based on clinical studies of good quality and consistency addressing the specific recommendations and including at least one randomised trial
В	Based on well-conducted clinical studies but without randomised clinical trials
С	Made despite the absence of directly applicable clinical studies of good quality
* Modif	ied from Phillips et al [4] as described by Abrams et al [5].

tions by history and symptoms that require a similar complexity of diagnostic evaluation have been grouped together.

For simplification, treatment options have been grouped under a few diagnoses (ie, "conditions") and their underlying pathophysiology, for which a terminology standardised by the International Continence Society (ICS) was used. As a rule, the least invasive treatment option is recommended first, proceeding in a stepwise escalation to more invasive treatment options when the former fails.

Extent and invasiveness of diagnostic evaluation and therapeutic interventions are grouped into two levels: initial management and specialised management. The level of initial management comprises measures generally required at the first patient contact with a health professional. Depending on the health care system and local or general service restrictions, this first contact may be with an incontinence nurse, a primary care physician, or a specialist.

The primary information about the patient's condition is established by medical history, by physical examination, and by applying readily available basic diagnostic tests to exclude an underlying disease or condition such as urinary tract infection (UTI). If treatment is instigated at this level of care, it will be mostly conservative and of an empirical nature. The level of specialised management applies to patients in whom a diagnosis could not be established at the initial management level, in whom empirical treatment failed, or in whom history and/or symptoms suggest a more complex or serious condition requiring more elaborate diagnostic evaluation and/or specific treatment options. At this level, urodynamic studies are usually required for establishing a diagnosis based on the underlying pathophysiology, and treatment options include invasive interventions and surgery.

## 3. Epidemiology<sup>1</sup>

There is a wide range of published prevalences for UI, and this is explained by differences in the definition of UI, in epidemiologic methodology, and in demographic characteristics among the studies. However, recent prospective studies have provided data on the incidence of UI and its

<sup>&</sup>lt;sup>1</sup> This section of the guidelines is based on the recommendations of the ICI committee 1 chaired by Ian Milsom.

natural history (progression, regression, and resolution) [8–11].

The literature on incidence and remission of UI is still scarce, particularly among men. However, the annual incidence of UI in women ranges from 2% to 11%, with the highest incidence occurring during pregnancy. Rates of complete remission of UI range from 0% to 13%, with the highest remission rates after pregnancy. The annual incidence of overactive bladder (OAB) ranges from 4% to 6%, with annual remission rates of OAB ranging from 2% to 3% [10].

Involuntary urine loss has been reported to occur in 5–69% of women and in 1–39% of men. The wide range of published prevalences of UI reflects differences in broadness of definition of UI (from UI occurring once during the last 12 mo to UI occurring several times per day or week), in methodology (telephone interviews, mailed questionnaires, patient examinations), and in demographics of the studied population. Generally, UI is twice as common in women as in men. Limited data from twin studies suggest that there is a substantial genetic component to UI, especially in stress UI (SUI) [12,13].

#### 3.1. Risk factors in women

Pregnancy and vaginal delivery are relevant risk factors that become less important with increasing age. Contrary to previous popular belief, menopause per se does not appear to be a risk factor for UI, and there is conflicting evidence regarding hysterectomy. Diabetes mellitus is a risk factor in most studies. Oral oestrogen substitution and body mass index are important modifiable risk factors for UI. Although a mild loss of cognitive function is not a risk factor for UI, it increases the impact of UI. Smoking, diet, depression, UTIs, and exercise are not risk factors.

#### 3.1.1. Pelvic organ prolapse

Women who present with UI as their primary symptom may also have pelvic organ prolapse (POP), which may be symptomatic or asymptomatic. SUI and POP have familial transmission patterns mediated by either genetic or environmental factors (LoE: 2). The decision as to whether the prolapse should be treated surgically at the same time as UI is determined by the symptoms and bother that the prolapse produces for the patient and the influence that the prolapse surgery may have on the outcome of the surgery for the incontinence. Hence, assessment of UI should include assessment for POP, and, if present, treatment of POP should be considered within the management strategy of UI, specifically if surgical intervention is required. POP has a prevalence of 5-10% based on the finding of a mass bulging in the vagina. Childbirth carries an increased risk for POP later in life, the risk of which increases with the number of children. It is unclear whether caesarean section (CS) prevents the development of POP, although most studies suggest that CS carries less risk than vaginal delivery for subsequent pelvic floor morbidity. Several studies suggest that hysterectomy and other pelvic surgeries increase the risk of POP. Further research is needed.

#### 3.2. Risk factors in men

Risk factors for UI in men include increasing age, lower urinary tract symptoms (LUTS), UTI, functional and cognitive impairment, neurologic disorders, and prostatectomy.

#### 3.3. Overactive bladder

The prevalence of OAB ranges in adult males from 10% to 26% and in adult females from 8% to 42%. It increases with age and often is associated with other LUTS. Several common chronic conditions, such as depression, constipation, neurologic conditions, and erectile dysfunction, have been significantly associated with OAB, even after adjusting for significant confounders, such as age, gender, and country [14].

### 4. Pharmacotherapy<sup>2</sup>

Many drugs have been developed for treatment of UI (Tables 3 and 4). Although drugs may be efficacious in some patients, they frequently are not continued indefinitely because of side effects. Thus, drugs may be considered as an adjunct to conservative therapy [15].

## 4.1. Drugs used in the treatment of OAB/urgency urinary incontinence

The clinical relevance of efficacy of antimuscarinic drugs relative to placebo has been widely discussed [16]. However, recent large meta-analyses of the most widely used antimuscarinic drugs have clearly shown that these drugs provide a significant clinical benefit [17–19]. None of the commonly used antimuscarinic drugs (darifenacin, fesoterodine, oxybutynin, propiverine, solifenacin, tolterodine, and trospium) are an ideal first-line treatment for *all* OAB/detrusor overactivity (DO) patients. Optimal treatment should be individualised, considering the patient's comorbidities and concomitant medications and the pharmacologic profiles of different drugs [19].

## 4.2. Drugs used in the treatment of stress urinary incontinence

Factors that may contribute to urethral closure include the tone of urethral smooth and striated muscles and the passive properties of the urethral lamina propria, particularly its vasculature. The relative contribution of these factors to intraurethral pressure is still under debate. However, there is evidence that a substantial part of urethral tone is mediated through stimulation of  $\alpha$ -adrenoreceptors in the urethral smooth muscle by noradrenaline [20,21]. A contributory factor to SUI, mainly in elderly women with a lack of

<sup>&</sup>lt;sup>2</sup> This section of the guidelines is based on the recommendations of the ICI committee 8 chaired by Karl-Erik Andersson.

Table 3 – Drugs used in the treatment of overactive bladder (OAB)/ urgency urinary incontinence (UUI)

Drug	LoE	GoR
Antimuscarinic drugs		
Atropine, hyoscyamine	3	С
Darifenacin	1	Α
• Propantheline	2	В
• Solifenacin	1	Α
• Tolterodine	1	Α
• Trospium	1	Α
Drugs acting on membrane channels		
Calcium antagonists	2	
• K*-channel openers	2	
Drugs with mixed actions		
Oxybutynin	1	Α
Propiverine	1	Α
Dicyclomine	3	C
• Flavoxate	2	
Antidepressants		
Duloxetine	2	С
Imipramine	3	С
α-Adrenoreceptor antagonists		
Alfuzosin	3	С
Doxazosin	3	C
• Prazosin	3	C
Terazosin	3	С
Tamsulosin	3	С
β-Adrenoreceptor antagonists		
• Terbutaline (β-2)	3	С
• Salbutamol (β-2)	3	C
• YM-178 (β-3)	2	В
PDE5-Is (for male LUTS/OAB)		
• Sildenafil, taladafil, vardenafil	2	В
COX inhibitors		
• Indomethacin	2 2	C C
Flurbiprofen	2	C
Toxins		
Botulinum toxin (neurogenic),	2	Α
injected into bladder wall		
Botulinum toxin (idiopathic),      inicated into bladder well	3	В
injected into bladder wall  • Capsaicin (neurogenic), intravesical	2	С
Resiniferatoxin (neurogenic), intravesical	2	C
	2	Č
Other drugs		
Baclofen, intrathecal	3	С
Hormones		
Oestrogen	2	С
• Desmopressin, for nocturia (nocturnal polyuria),	1	Α
but care should be taken because of the risk		
of hyponatraemia, especially in the elderly		

LoE = level of evidence; GoR = grade or recommendation;  $K^+$  = potassium; LUTS/OAB = lower urinary intract symptoms/overactive bladder; PDE5-I = phosphodiesterase type 5 inhibitor; COX inhibitor = cyclo-oxygenase inhibitor.

oestrogen, may be deterioration of the mucosal coaptation. Pharmacologic treatment of SUI aims to increase the urethral closure by increasing the tone in the urethral smooth and striated muscles. Several drugs may contribute to such an increase [22,23]. Their clinical use is limited by efficacy and/ or side effects (Table 4).

Table 4 – Drugs used in the treatment of stress urinary incontinence (SUI)

Drug	LoE	GoR
Duloxetine	1	В
Midodrine	2	С
Clenbuterol	3	С
Oestrogen	2	NR
Methoxamine	2	NR
Imipramine	3	NR
Ephedrine	3	NR
Norephedrine (phenylpropanolamine)	3	NR
LoE = level of evidence; GoR = grade of recommendation; NR = no recommendation possible.		

### 4.3. Hormonal treatment of urinary incontinence

#### 4.3.1. Oestrogens

Oestrogen deficiency is an aetiologic factor in the pathogenesis of several conditions. However, oestrogen treatment, either alone or combined with a progestogen, has achieved only poor results in UI. The current evidence (LoE: 1) against the treatment of UI with oestrogen is based on studies originally designed to assess the use of oestrogens for preventing cardiovascular events. The evidence is derived from secondary analyses of questionnaires with selfreported symptoms of urinary leakage in these studies. Nevertheless, these large randomised controlled trials (RCTs) revealed a worsening of preexisting UI (stress and urgency) and an increased new incidence of UI, with either oestrogen monotherapy or oestrogen combined with a progestogen. It should be noted, however, that most patients were taking combined equine oestrogen, which may not be representative of all oestrogens and all routes of administration.

A systematic review of the effects of oestrogen on symptoms suggestive of OAB concluded that oestrogen therapy may be effective in alleviating OAB symptoms and local administration may be the most beneficial route of administration [24]. It is possible that urinary urgency, frequency, and urgency incontinence are symptoms of urogenital atrophy in older postmenopausal women [25]. There is good evidence that low-dose (local) vaginal oestrogen therapy may reverse the symptoms and cytologic changes of urogenital atrophy. However, oestrogens (with or without progesterone) should not be used to treat UI because no evidence shows that they have a direct effect on the lower urinary tract.

#### 4.3.2. Desmopressin

Desmopressin (DDVAP) was found to be well tolerated and resulted in a significant improvement compared to placebo in reducing nocturnal voids/UI and increasing the hours of undisturbed sleep. Quality of life (QoL) also improved. However, hyponatraemia is one of the main clinically important side effects of DDVAP administration. Hyponatraemia can lead to a range of adverse events from mild headache, nausea, vomiting, and anorexia to loss of consciousness, seizures, and death. The risk of hyponatraemia has been reported in a meta-analysis to be about 7.6% [26] and seems to increase with age, cardiac disease, and a high 24-h urine volume [27].

<sup>\*</sup> Assessments have been done according to the Oxford modified system (see Tables 1 and 2).

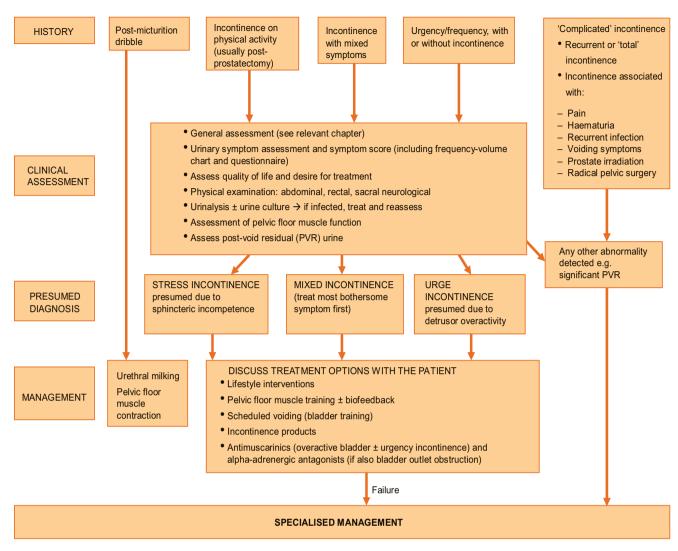


Fig. 1 - Algorithm for initial management of urinary incontinence in men.

### 5. Incontinence in men<sup>3</sup>

#### 5.1. Initial management of urinary incontinence in men (Fig. 1)

#### 5.1.1. Assessment

Initial assessment in men aims to identify and exclude patients with *complicated* incontinence, who need to be referred for specialised management. Complicated incontinence comprises patients with recurrent incontinence after failed previous surgery, with total UI, and/or with associated symptoms such as pain, haematuria, recurrent UTI, voiding symptoms, and/or a history of previous pelvic radiotherapy or radical pelvic surgery.

The remaining patients with a history of UI can be stratified into four main groups of symptoms suitable for initial management: (1) postmicturition dribble, (2) incon-

tinence on physical activity, (3) incontinence with mixed stress and urgency symptoms, and (4) urgency or frequency with or without incontinence.

#### 5.1.2. Management

Conservative management is the main approach to UI in men at the initial care level (Table 5) and is often considered to be simple and of low cost. The term *conservative management* describes any treatment that does not involve pharmacologic or surgical intervention. However, for conditions such as OAB, conservative strategies are often combined with drug treatment.

Many conservative management interventions require a change of behaviour, which is not easy either to initiate or to maintain. Most patients with mild to moderate symptoms wish to try less invasive treatments first. However, patients with complicated or severe symptoms may need to be referred directly for specialised management.

For men with postmicturition dribble, no further assessment is generally required. However, the patient should be told how to exert a strong pelvic floor muscle

<sup>&</sup>lt;sup>3</sup> This section of the guidelines is based on the recommendations of the ICI committees 5, 6, 7, 12 and 13 chaired by David Staskin, Gordon Hosker, David Vodusek, Andrea Tubaro, Jean Hay-Smith and Sender Herschorn.

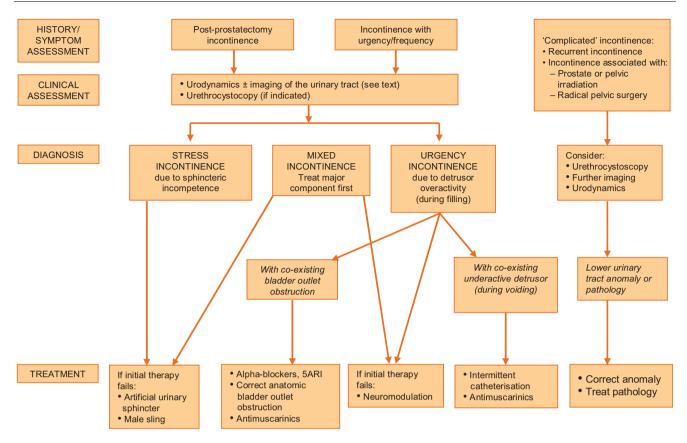


Fig. 2 – Algorithm for specialised management of urinary incontinence in men. 5-ARI = 5-alpha-reductase inhibitors.

contraction after voiding or to manually compress the bulbous urethra directly after micturition (GoR: B).

For men with SUI, urgency, or mixed stress/urgency incontinence, initial management should include appropriate lifestyle advice, physical therapy, scheduled voiding, behavioural therapy, and medication. There is generally insufficient level 1 or 2 evidence, and most recommendations are essentially hypotheses requiring further testing in high-quality studies. If initial treatment is unsuccessful

Table 5 – Recommendations for initial management of urinary incontinence (UI) in men

Recommendations	GoR
Lifestyle interventions	NR
• Supervised pelvic-floor muscle training (PFMT) for	В
postprostatectomy stress UI	
• The use of biofeedback to assist PFMT is currently a	В
therapist/patient decision based on economics and preference	
<ul> <li>For men with postprostatectomy incontinence, adding</li> </ul>	В
electrical stimulation to a PFMT programme does not appear to	
be of benefit	
Scheduled voiding regimes	C
<ul> <li>When there is no evidence of significant postvoid residual</li> </ul>	Α
urine, antimuscarinic drugs for overactive bladder symptoms,	
with or without urgency incontinence	
$\bullet$ $\alpha$ -Adrenergic antagonists ( $\alpha$ -blockers) can be added if there is	C
also bladder outlet obstruction	
GoR = grade of recommendation; NR = no recommendation possible.	

after a reasonable period of time (eg, 8–12 wk), a specialist's advice is highly recommended.

## 5.2. Specialised management of urinary incontinence in men (Fig. 2)

#### 5.2.1. Assessment

The specialist may first decide to reinstitute initial management if previous therapy was inadequate. Patients with complicated incontinence referred directly to specialised management usually require additional testing (ie, cytology, urethrocystoscopy. or urinary tract imaging) to exclude any other underlying pathology. If these tests are normal, patients can be treated for incontinence by initial or specialised management options as appropriate. If symptoms suggestive of DO or of sphincteric incompetence persist, urodynamic studies are recommended to establish a diagnosis based on pathophysiologic findings (urodynamic diagnosis) (Table 6).

#### 5.2.2. Treatment

If initial management has failed and the incontinence is bothersome to the patient and affecting his QoL, invasive therapies may be considered.

5.2.2.1. Urinary incontinence after radical prostatectomy. The only group of men with UI that has been properly evaluated is those with UI after radical prostatectomy (RP). However,

Table 6 – Assessment for specialised management of urinary incontinence in men

#### General assessment

 Medical history and physical examination, urinalysis, postvoid residual urine, frequency/volume chart, pad test, and serum creatinine if renal disease is suspected

Further evaluation as required (LoE: 2-4, GoR: B-C)

- Cystourethroscopy to assess urethral integrity, sphincter appearance, stricture, and bladder pathology
- Imaging of the upper and lower urinary tract (ultrasound, cystourethrography, intravenous pyelogram)
- Urodynamic studies to assess sphincter and/or detrusor function
- Valsalva leak-point pressure to measure sphincter weakness
- Urethral pressure profile or retrograde perfusion sphincterometry may be performed if artificial urinary sphincter or slings are to be implanted
- Sphincter electromyography to investigate suspected neuropathy
- Multichannel pressure/flow video-urodynamic evaluation to assess detrusor function and characterise the underlying pathophysiology

definitions of continence after RP range from total control without any pad or leakage to no pad but loss of a few drops (ie, underwear staining) to none to one pad (ie, "safety pad") per day.

Reported risk factors for incontinence after RP include age at surgery, prostate size, comorbidities, nerve-sparing surgery, bladder neck stenosis, tumour stage (possibly related to surgical technique), and preoperative bladder and sphincter dysfunction. The risk is unrelated to the technique of prostatectomy (radical vs nerve sparing; open vs laparoscopic vs robotic), according to reports from centres of excellence.

5.2.2.2. Sphincter incompetence. For SUI due to sphincter incompetence, after a period of conservative management of at least 6–12 mo after RP, the artificial urinary sphincter (AUS) is the treatment of choice for patients with moderate to severe UI. In studies that report treatment results of UI after surgery for benign prostatic obstruction and prostate cancer together, the success rates for AUS range between 59% and 90% (none to one pad per day). Long-term success rates and high patient satisfaction seem to outweigh the need for periodic revisions in some patients. Until similar experience is seen with newer, less invasive treatments, the AUS remains the reference standard to which all other treatments must be compared (LoE: 2; GoR: B).

Recurrent incontinence after AUS implantation may result from alteration in bladder function, urethral atrophy, or mechanical malfunction. All or part of the prosthesis must be surgically removed if there is infection and/or erosion of components. Risk factors are surgery, radiotherapy, catheterisation, and endoscopy (LoE: 3, GoR: C). In patients with an implanted AUS, transurethral catheterisation or endoscopy requires special attention by prior opening and deactivation of the urinary sphincter to prevent harm to the urethra.

5.2.2.3. Mild to moderate stress urinary incontinence. Male slings are an alternative for men with mild to moderate SUI (radiotherapy is an adverse risk factor). The overall minimum success is 58%, with best results achieved in

patients with low to moderate leakage of urine who had not undergone radiotherapy (LoE: 3; GoR: C).

Bulking agents are a less effective option for some men with mild to moderate SUI. The early failure rate is about 50%, and any beneficial effects decrease with time (LoE: 3; GoR: C).

The implantation of compressive adjustable balloons is a new treatment option. Early high complication rates appear to have been resolved. However, more evidence is required before specific recommendations can be made (LoE: 3; GoR: C).

5.2.2.4. Urgency urinary incontinence. For urgency UI (UUI) due to refractory idiopathic DO, botulinum toxin A detrusor injection is a minimally invasive treatment with some efficacy that is currently used as an off-label medication for this indication. Other treatment options include neuromodulation or detrusor myectomy, which have both been successful in a few male patients. Augmentation cystoplasty with intestinal segments is potentially successful in controlling symptoms but may have side effects. Urinary diversion is a final option (LoE: 3; GoR: C).

5.2.2.5. Reduced bladder capacity. Augmentation cystoplasty has been successful in helping with reduced bladder capacity due to most aetiologies except radiotherapy cystitis (LoE: 3; GoR: C).

5.2.2.6. Detrusor underactivity. If incontinence is associated with poor bladder emptying due to detrusor underactivity, effective means should be used to ensure bladder emptying (eg, clean intermittent catheterisation [CIC]) (GoR: B–C).

5.2.2.7. Bladder outlet obstruction. If incontinence is due to bladder outlet obstruction (BOO), then the obstruction should be relieved first (GoR: B–C). Pharmacologic treatment options for UI and proven outlet obstruction are  $\alpha$ -blockers or  $5\alpha$ -reductase inhibitors (GoR: C). There is increasing evidence for the safety of antimuscarinic agents for OAB symptoms in men with outlet obstruction when combined with an  $\alpha$ -blocker (GoR: B).

#### 6. Incontinence in women<sup>4</sup>

# 6.1. Initial management of urinary incontinence in women (Fig. 3)

## 6.1.1. Assessment

Initial assessment aims to identify and exclude patients with complicated incontinence, who require referral for specialised management. Complicated incontinence comprises patients with recurrent incontinence after failed previous surgery and/or patients with associated symptoms such as pain, haematuria, recurrent UTI, voiding symptoms, and/or a history of previous pelvic radiotherapy, radical pelvic surgery, or suspected fistula.

<sup>&</sup>lt;sup>4</sup> This section of the guidelines is based on the recommendations of the ICI committees 5, 6, 7, 12 and 14 chaired by David Staskin, Gordon Hosker, David Vodusek, Andrea Tubaro, Jean Hay-Smith and Tony Smith.

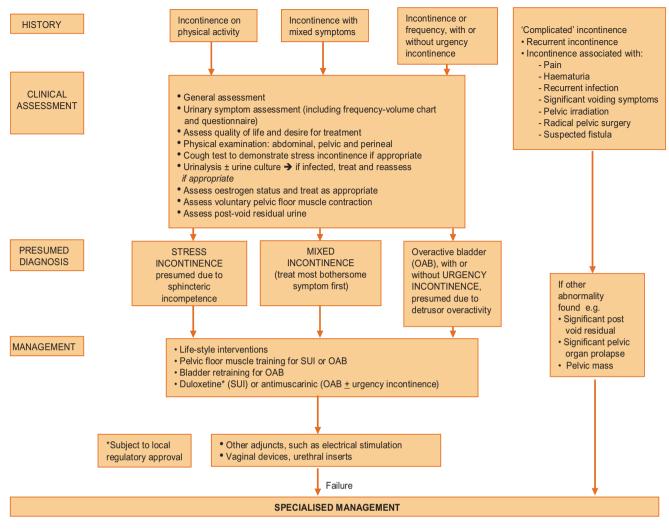


Fig. 3 – Algorithm for initial management of urinary incontinence in women. SUI = stress urinary incontinence.

The remaining patients with a history of UI can be stratified into three main groups of symptoms suitable for initial management: (1) incontinence on physical activity, (2) incontinence with mixed urgency and stress symptoms, and (3) urgency or frequency with or without incontinence.

Routine physical examination includes abdominal, pelvic, and perineal examinations. Women should perform a stress test (eg, cough and strain) to detect leakage secondary to sphincter incompetence. Any POP or urogenital atrophy must be assessed. It is also important to assess voluntary pelvic floor muscle function by vaginal or rectal examination before starting pelvic floor muscle training (PFMT). Postvoid residual urine (PVR) should be assessed when UI is associated with voiding difficulties and/or POP.

#### 6.1.2. Management

For women with SUI, UUI, or mixed UI, initial management includes appropriate lifestyle advice, physical therapy, scheduled voiding, behavioural therapy, and medication (Table 7; Fig. 3). Some recommendations are based on a good and consistent level of evidence. However, many other

recommendations are based on insufficient evidence and are essentially hypotheses requiring further testing in high-quality studies.

## 6.2. Specialised management of urinary incontinence in women (Fig. 4)

## 6.2.1. Assessment

Women with complicated incontinence requiring specialised management usually require additional testing (ie, cytology, urethrocystoscopy, or urinary tract imaging) to exclude any other underlying pathology. If these tests reveal no further pathology, the patient should be treated for UI by initial or specialised management options, as appropriate.

Women who have failed initial management and are bothered by their symptoms and an impaired QoL are likely to request further treatment. If initial management has been exhausted, interventional therapy may be indicated. Urodynamic testing to diagnose the type of UI is highly recommended prior to intervention if the results are likely to influence the choice of treatment. It may also be helpful

Table 7 - Recommendations for initial management of urinary incontinence (UI) in women

Treatment	GoR
Lifestyle interventions	
• For morbidly and moderately obese women, weight loss helps to reduce UI symptoms	A
Caffeine intake reduction may benefit UI symptoms	В
<ul> <li>A decrease in fluid intake should only be tried in patients with abnormally high fluid intakes, as a decrease in fluids may lead to UTIs, constipation, or dehydration</li> </ul>	С
Crossing the legs and bending forward can help to reduce leakage during coughing or other provocations	С
	C
Pelvic floor muscle training (PFMT): general considerations	
• PFMT should be offered as first-line conservative therapy to women with stress, urgency, or mixed UI	Α
• Provide the most intensive PFMT programme possible (ie, amount of exercise and of health professional supervision) within service	Α
constraints, as health professional or supervised programmes are more effective than self-directed programmes; in addition, greater health	
professional contact is better than less  • The addition of biofeedback to the PFMT programme does not appear to be of benefit:	
- clinic biofeedback	Α
- home-based biofeedback	В
	ь
Vaginal cones (VC)	
VC may be offered to women with SUI or MUI	В
• VC can be offered as first-line conservative therapy to those who can and are prepared to use them	В
• VC may be inappropriate due to side effects and discomfort	NR
• VC and EStim seem equally effective in SUI and MUI, but the usefulness of VC and EStim is limited because of side effects and discomfort	В
Electrical stimulation	
EStim may be offered to women with SUI, UUI, or MUI	
• For treating SUI, 6 mo of EStim, 50 Hz twice daily at home, may be better than no treatment	С
• Low-intensity home-based EStim daily for 6 mo may be better than 16 sessions of maximal clinic-based EStim	С
• For treating UUI secondary to DO, 9 wk of EStim, 4–10 Hz twice daily at home, might be better than no treatment	C
Addition of EStim to a biofeedback-assisted PFMT programme does not appear to add benefit	C
• EStim may have limited usefulness because some women cannot use it (due to contraindications), have difficulty using it, or dislike it	NR
Magnetic stimulation (MStim)	
• MStim should only be used as part of a clinical trial as its benefit has not been established	NR
Bladder training (BT)	
BT is an appropriate first-line treatment for UUI in women	Α
BT may be as effective as antimuscarinic drugs for treating UUI	В
Some patients may prefer BT because it does not produce the adverse events associated with drug therapy	5
Addition of a brief written instruction for BT, in addition to drug therapy, has no benefit	В
• For women with symptoms of SUI or MUI, a combination of PFMT/BT may be better than PFMT alone in the short term	В
• Clinicians and researchers should refer to the operant conditioning and educational literature to explain their choice of training parameters	NR
or approach	
• Clinicians should provide the most intensive BT supervision possible within service constraints	В
Timed voiding	
• Timed voiding with a 2-h voiding interval may be beneficial as a sole intervention for women with mild UI and infrequent voiding patterns	С
GoR = grade of recommendation; UTI = urinary tract infection; SUI = stress urinary incontinence; MUI = mixed urinary incontinence; EStim =	electrical

GoR = grade of recommendation; UTI = urinary tract infection; SUI = stress urinary incontinence; MUI = mixed urinary incontinence; EStim = electrical stimulation; NR = not possible to make recommendation; UUI = urge urinary incontinence; DO = detrusor overactivity.

to test urethral function by urethral pressure profile or leak-point pressure measurement during urodynamic testing.

A systematic assessment for POP is highly recommended. The Pelvic Organ Prolapse Quantification method should be used in research studies and can also be used outside the research setting. Coexisting symptomatic POP should be treated.

### 6.2.2. Treatment

6.2.2.1. Stress urinary incontinence. If urodynamic SUI is confirmed, the following treatment options may be recommended for patients with some bladder-neck and urethral mobility: (1) full range of nonsurgical treatments, (2) retropubic suspension procedures, and (3) bladder neck/suburethral sling operations.

If surgery for SUI is indicated, various confounding variables determining the success of surgery have to be considered (Table 8). Surgical approaches to UI in women are listed in Table 9. The true incidence of complications associated with surgery for UI is not known due to a lack of standards of reporting and definitions. In addition, there is a discrepancy between academic and community practice. However, there appears to be a low incidence of most complications, making it difficult to perform power calculations for RCTs. National registries provide some information about the level of complications. Complications are less likely with proper surgical training (LoE: 2–3) and skills can be maintained by performing at least 20 cases annually for each primary procedure, according to the UK National Institute of Health and Clinical Excellence. It may be helpful to correct symptomatic POP at the same time. For patients with intrinsic sphincteric deficiency, sling procedures, injectable bulking agents, and the AUS may be considered.

6.2.2.2. Idiopathic detrusor overactivity. Urgency incontinence (eg, OAB) secondary to idiopathic DO may be treated by neuromodulation or bladder augmentation. Botulinum toxin

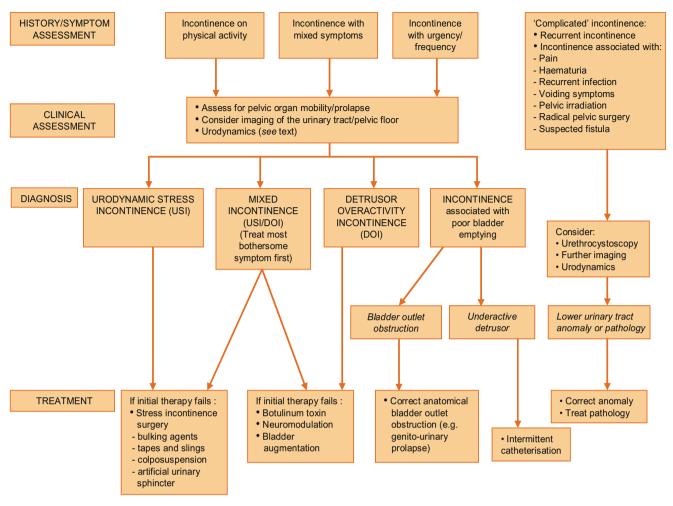


Fig. 4 – Algorithm for specialised management of urinary incontinence in women.

injection can be used to treat idiopathic DO unresponsive to other therapies (GoR: C). Botulinum toxin for detrusor injections is currently being used off-label for this indication.

6.2.2.3. Voiding dysfunction. Patients with voiding dysfunction leading to significant PVR may have BOO or detrusor underactivity. POP is a common cause of voiding dysfunction.

## Table 8 – Possible confounding variables for the success of surgery for stress urinary incontinence in women

- Age
- Physical activity
- Medical illness
- Psychiatric illness
- Obesity
- Parity
- Previous incontinence surgery
- Hysterectomy during anti-incontinence procedure
- Race
- Severity and duration of symptoms
- Overactive bladder
- Urethral occlusive forces
- Surgical factors

## 6.2.3. Outcome measures

Until a universal outcome tool has been established, multiple outcome measures must be used, including (1) symptoms and a separate bother questionnaire; (2) clinically important outcomes (pad use, reoperation rates, use of anticholinergics, CIC, and recurrent UTIs); (3) complications; (4) a QoL tool with minimal clinically important difference

Table 9 – Recommendations for surgical treatment of stress urinary incontinence in women

Surgical procedure	GoR
Anterior colporrhaphy     Transvaginal BNS (needle)	NR NR
Burch procedure: open     Burch procedure: laparoscopic (by experienced	A B
laparoscopic surgeon only)  • Paravaginal repair  • MMK urethroplasty	NR NR
BN sling: autologous fascia     Suburethral slings (TVT)	A A
Urethral bulking agents	В

GoR = grade of recommendation; NR = no recommendation possible; BNS = bladder-neck suspension; MMK = Marshall-Marchetti-Krantz; BN = bladder neck; TVT = tension-free vaginal tape.

and Global Impression Index; and (5) health-economic outcome.

## 7. Urinary incontinence in frail older persons<sup>5</sup>

Healthy older persons should be offered a range of treatment options similar to those offered younger persons. Frail older persons, however, require a different approach. Their evaluation must address the potential role of comorbidity, current medications (prescribed, over the counter, and/or naturopathic), and functional and/or cognitive impairment in both causation and subsequent management of the patient's UI. Studies and intervention in frail older people should consider the degree of bother to the patient and/or the caregiver, the goals for care, the level of cooperation, and the overall prognosis and life expectancy. Effective management to meet the goals of care should be possible for most frail older persons.

#### 7.1. Assessment

Because frail older persons have a very high prevalence of UI, active case finding and screening for UI should be done in this population (GoR: A). The history should identify comorbid conditions and medications likely to cause or worsen UI.

The mnemonic DIAPPERS (delirium, infection, atrophic vaginitis, pharmaceuticals, psychological condition, excess urine output, reduced mobility, stool impaction) includes some comorbid conditions and factors to be considered. Two alterations from the original mnemonic should be noted: (1) Atrophic vaginitis does not by itself cause UI and should not be treated solely for the purpose of decreasing UI alone (GoR: B), and (2) the current consensus criteria for diagnosis of UTIs are both poorly sensitive and nonspecific in nursing-home residents (LoE: 2).

The patient and/or the caregiver should be asked directly about (1) the degree of bother of UI (GoR: B), (2) goals for UI care (dryness, specific decrease in symptom severity, QoL, reduction of comorbidity, decreased care burden) (GoR: B), and (3) the likely level of cooperation with management (GoR: C). It is also important to consider the patient's overall prognosis and remaining life expectancy (GoR: C).

All patients must be screened for haematuria (GoR: C) because it is not known if treatment of otherwise asymptomatic bacteriuria and pyuria is beneficial (no recommendation possible). Such treatment may cause harm by increasing the risk of antibody resistance and causing severe adverse effects, such as *Clostridium difficile* colitis (GoR: C).

There is insufficient evidence to recommend a clinical stress test in frail older persons.

For frail older people with bothersome nocturia, assessment should focus on identifying the potential underlying causes, including (GoR: C) nocturnal polyuria, a primary sleep problem (including sleep apnoea), and

Table 10 – Recommendations for evaluation of frail older persons with urinary incontinence

Recommendations	GoR
Rectal examination for faecal loading or impaction	С
• Functional assessment (mobility, transfers, manual	Α
dexterity, ability to successfully toilet)	
Screening test for depression	В
• Cognitive assessment to assist in planning management	С
GoR = grade of recommendation.	

conditions resulting in a low voided volumes (eg, elevated PVR) (Table 10).

A bladder diary (frequency-volume chart) may be useful in the evaluation of patients with nocturia (GoR: C).

Wet checks can be used to assess UI frequency in long-term-care residents (GoR: C).

Measuring PVR volume may be useful in frail older persons with diabetes mellitus (especially if longstanding); with prior episodes of urinary retention; or with a history of high PVR, recurrent UTIs, medications that impair bladder emptying (eg, anticholinergics), chronic constipation, persistent or worsening UI despite treatment with antimuscarinics, and prior urodynamic study demonstrating detrusor underactivity and/or BOO (GoR: C).

Treatment of coexisting conditions (eg, constipation) and stopping anticholinergic drugs may reduce PVR. There is no consensus regarding what constitutes *high* PVR in any population. A period of catheterisation may be considered in patients with PVR >200–500 ml, in whom high PVR may be a major contributor to UI or bothersome frequency (GoR: C).

The most common types of UI in frail older persons are UUI, SUI, and mixed UI (in frail older women). Frail older persons with UUI often have concomitant detrusor underactivity with an elevated PVR in the absence of outlet obstruction, a condition called *detrusor hyperactivity with impaired contractility during voiding* (DHIC), although this is not part of ICS standardised terminology. There is no published evidence that antimuscarinics are less effective or cause retention in persons with DHIC (no recommendation possible).

## 7.2. Initial management of urinary incontinence in frail older persons (Fig. 5)

Initial management should be individualised and influenced by goals of care, treatment preferences, and estimated remaining life expectancy as well as by the most likely clinical diagnosis (GoR: C).

In some patients, it is important to recognise that contained UI (eg, managed with pads) may be the only possible outcome for UI that persists after treatment of contributing comorbidity and other factors. This is especially true for frail persons with no or minimal mobility (ie, require the help of at least two persons to transfer), advanced dementia (ie, unable to state their own name), and/or nocturnal UI. Conservative and behavioural therapies for UI include lifestyle changes (GoR: C), bladder

<sup>&</sup>lt;sup>5</sup> This section of the guidelines is based on the recommendations of the ICI committee 11 chaired by Catherine Dubeau.

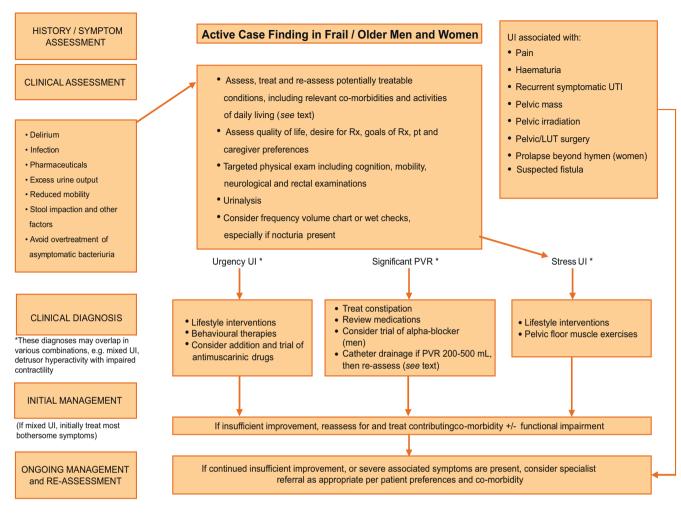


Fig. 5 – Algorithm for management of urinary incontinence (UI) in frail older persons. UTI = urinary tract infection; pt = patient; LUT = lower urinary tract; Rx = pharmacotherapy; PVR = postvoid residual.

training in fit or alert patients (GoR: B), and prompted voiding for frail and cognitively impaired patients (GoR: A).

For selected, cognitively intact, frail persons, pelvic muscle exercises may be considered, but they have not been well studied in this population (GoR: C).

Any drug treatment (Table 11) should be started with a low dose and titrated with regular review until the desired improvement has been achieved or there are adverse effects.

UI can usually be managed successfully using a combination of the above approaches. However, if initial management does not provide sufficient improvement in

UI, then the next step should be to reassess the patient for contributing comorbidity and/or functional impairment and to treat it.

## 7.3. Specialised management of urinary incontinence in frail older persons

Specialist referral should be considered when, in the initial assessment, a frail older person with UI has (1) other significant factors (eg, pain, haematuria); (2) UI symptoms that cannot be classified as urgency, stress, or mixed

Table 11 - Recommendations for drug therapy in frail older persons with urinary incontinence

Recommendations	GoR
<ul> <li>A trial of antimuscarinic drugs may be considered as an adjunct to conservative therapy of urgency urinary incontinence</li> <li>Similarly, alpha-blockers may be cautiously considered in frail men with suspected outlet obstruction from prostate disease</li> <li>Because DDAVP (vasopressin) carries a high risk of clinically significant hyponatraemia, it should NOT be used in frail older persons to treat nocturia or nocturnal polyuria</li> </ul>	A–C, depending on agent C A Not recommended
GoR = grade of recommendation.	

Table 12 - Recommendations for care of frail older patients prior to surgery

Recommendations	GoR
• Evaluation and treatment for any comorbidity, medications, and cognitive and/or functional impairment that may be contributing to urinary incontinence and/or could compromise the outcome of the planned surgery; for example, artificial sphincter should not be placed in men with dementia who cannot manage the device on their own	С
An adequate trial of conservative therapy followed by reassessment of the need for surgery	С
• A discussion with the patient and/or carer to make sure that the anticipated surgical outcome is consistent with the preferred goals of care in the context of the patient's remaining life expectancy	С
Urodynamic testing because the clinical diagnosis may be inaccurate	В
Preoperative assessment and perioperative care to establish risks for, and to minimise, common postoperative complications in the elderly, such as:	
– delirium and urinary tract infection	Α
– dehydration and falls	С
GoR = grade of recommendation.	

incontinence or other complicated comorbidity that the primary clinician is unable to address (eg, dementia, functional impairment); and 3) a response to initial management that is insufficient.

The type of specialist will depend on local resources and the reason for referral. Surgical specialists could include urologists or gynaecologists. Patients with functional impairment could be referred to a geriatrician or a physical therapist. Continence nurse specialists may be helpful for homebound patients. The decision to refer a patient should take into account the goals of care, the patient's or caregiver's desire for invasive therapy, and the estimated life expectancy.

Age itself is not a contraindication to incontinence surgery (GoR: C). However, before surgery is considered in this group, all patients should be subjected to the items mentioned in Table 12.

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Study concept and design: Thüroff, Abrams, Andersson, Artibani, Chapple, Drake, Hampel, Neisius, Schröder, Tubaro.

Acquisition of data: Thüroff, Abrams, Andersson, Artibani, Chapple, Drake, Hampel, Neisius, Schröder, Tubaro.

Analysis and interpretation of data: Thüroff, Abrams, Andersson, Artibani, Chapple, Drake, Hampel, Neisius, Schröder, Tubaro.

Drafting of the manuscript: Thüroff.

Critical revision of the manuscript for important intellectual content: Thüroff, Abrams, Andersson, Artibani, Chapple, Drake, Hampel, Neisius, Schröder. Tubaro.

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### References

- Abrams P, Khoury S, Wein A, editors. Incontinence: 1st International Consultation on Incontinence. Plymouth, UK: Health Publications; 1999.
- [2] Thüroff JW, Abrams P, Artibani W, et al. Clinical guidelines for the management of incontinence. In: Abrams P, Khoury S, Wein A, editors. Incontinence: 1st International Consultation on Incontinence. Plymouth, UK: Health Publications; 1999. p. 933–43.
- [3] Hampel C, Hohenfellner M, Abrams P, et al. EAU guidelines on incontinence. Plymouth, UK: Health Publications Ltd; 2001.
- [4] Phillips B, Ball C, Sackett D, et al. Oxford Centre for Evidence-based Medicine levels of evidence (March 2009). Centre for Evidence Based Medicine Web site. http://www.cebm.net/index.aspx? o=1025. Updated September 16, 2010.
- [5] Abrams P, Khoury S, Grant A. Evidence-based medicine overview of the main steps for developing and grading guideline recommendations. In: Abrams P, Cardozo L, Khoury S, Wein A, editors. Incontinence: 3rd International Consultation on Incontinence. Paris, France: Health Publications; 2005. p. 10–1.
- [6] Abrams P, Cardozo L, Wein A, Khoury S. Incontinence: 4th International Consultation on Incontinence; Paris, France: Health Publications; 2009.
- [7] Schröder A, Abrams P, Andersson K-E, et al. EAU guidelines on urinary incontinence. European Association of Urology Web site. http://www.uroweb.org/guidelines/online-guidelines/.

- [8] Offermans MP, Du Moulin MF, Hamers JP, Dassen T, Halfens RJ. Prevalence of urinary incontinence and associated risk factors in nursing home residents: a systematic review. Neurourol Urodyn 2009;28:288–94.
- [9] Botlero R, Davis SR, Urquhart DM, Shortreed S, Bell RJ. Age-specific prevalence of, and factors associated with, different types of urinary incontinence in community-dwelling Australian women assessed with a validated questionnaire. Maturitas 2009;20:134–9.
- [10] Wennberg A-L, Molander U, Fall M, Edlund C, Peeker R, Milsom I. A longitudinal population-based survey of urinary incontinence, overactive bladder, and other lower urinary tract symptoms in women. Eur Urol 2009;55:783–91.
- [11] Long RM, Giri SK, Flood HD. Current concepts in female stress urinary incontinence. Surgeon 2008;6:366–72.
- [12] Altman D, Forsman M, Falconer C, Lichtenstein P. Genetic influence on stress urinary incontinence and pelvic organ prolapse. Eur Urol 2008;54:918–23.
- [13] Rohr G, Kragstrup J, Gaist D, Christensen K. Genetic and environmental influences on urinary incontinence: a Danish populationbased twin study of middle-aged and elderly women. Acta Obstet Gynecol Scand 2004;83:978–82.
- [14] Irwin DE, Milsom I, Reilly K, et al. Overactive bladder is associated with erectile dysfunction and reduced sexual quality of life in men. J Sex Med 2008;5:2904–10.
- [15] Andersson K-E, Appell R, Cardozo L, et al. Pharmacological treatment of urinary incontinence. In: Abrams P, Khoury S, Wein A, editors. Incontinence: 3rd International Consultation on Incontinence. Paris, France: Health Publications; 2005. p. 809–54.
- [16] Herbison P, Hay-Smith J, Ellis G, Moore K. Effectiveness of anticholinergic drugs compared with placebo in the treatment of overactive bladder: systematic review. Br Med J 2003;326:841–4.

- [17] Chapple C, Khullar V, Gabriel Z, Dooley JA. The effects of antimuscarinic treatments in overactive bladder: a systematic review and meta-analysis. Eur Urol 2005;48:5–26.
- [18] Novara G, Galfano A, Secco S, et al. Systematic review and metaanalysis of randomized controlled trials with antimuscarinic drugs for overactive bladder. Eur Urol 2008;54:740–64.
- [19] Chapple CR, Khullar V, Gabriel Z, Muston D, Bitoun CE, Weinstein D. The effects of antimuscarinic treatments in overactive bladder: an update of a systematic review and meta-analysis. Eur Urol 2008;54: 543–62
- [20] Andersson KE. Pharmacology of lower urinary tract smooth muscles and penile erectile tissues. Pharmacol Rev 1993;45:253–308.
- [21] Andersson KE, Wein AJ. Pharmacology of the lower urinary tract: basis for current and future treatments of urinary incontinence. Pharmacol Rev 2004;56:581–631.
- [22] Andersson KE. Current concepts in the treatment of disorders of micturition. Drugs 1988;35:477–94.
- [23] Zinner N, Gittelman M, Harris R, Susset J, Kanelos A, Auerbach S, Trospium Study Group. Trospium chloride improves overactive bladder symptoms: a multicenter phase III trial. J Urol 2004;171:2311–5.
- [24] Cardozo L, Lose G, McClish D, Versi E. A systematic review of the effects of estrogens for symptoms suggestive of overactive bladder. Acta Obstet Gynecol Scand 2004;83:892–7.
- [25] Robinson D, Cardozo LD. The role of estrogens in female lower urinary tract dysfunction. Urology 2003;62(Suppl 1):45–51.
- [26] Weatherall M. The risk of hyponatremia in older adults using desmopressin for nocturia: a systematic review and meta-analysis. Neurourol Urodyn 2004;23:302–5.
- [27] Rembratt A, Norgaard JP, Andersson KE. Desmopressin in elderly patients with nocturia: short-term safety and effects on urine output, sleep and voiding patterns. BJU Int 2003;91:642–6.

