EAU GUIDELINES ON NON-NEUROGENIC MALE LUTS INCLUDING BENIGN PROSTATIC OBSTRUCTION

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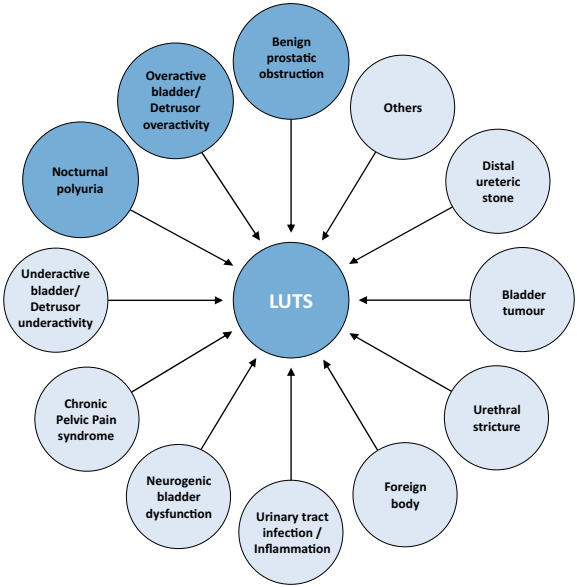
Introduction

The EAU Guidelines on Male Lower Urinary Tract Symptoms (LUTS) is a symptom-orientated guideline that mainly reviews LUTS secondary to benign prostatic obstruction (BPO), detrusor overactivity/overactive bladder (OAB), or nocturnal polyuria in men ≥ 40 years. The multifactorial aetiology of LUTS is illustrated in Figure 1.

Figure 1: Causes of male lower urinary tract symptoms (LUTS)



Diagnostic Evaluation

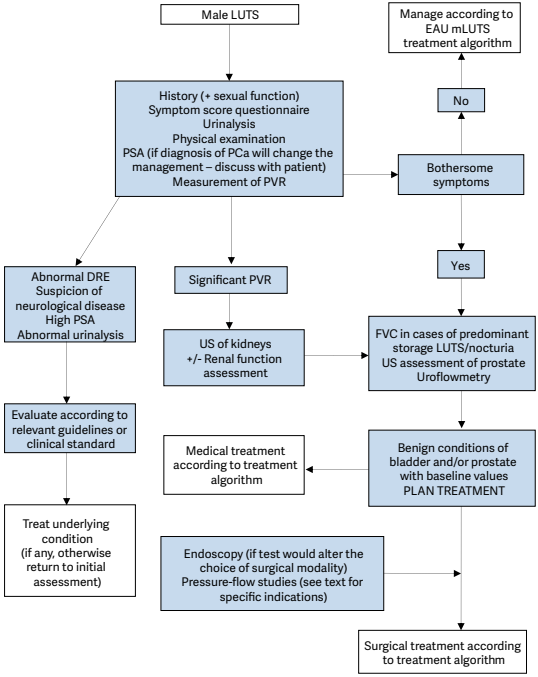
The high prevalence and the underlying multifactorial pathophysiology of male LUTS mean that an accurate assessment of LUTS is critical to provide best evidence-based care. Clinical assessment of LUTS aims to differentially diagnose and to define the clinical profile. A practical algorithm has been developed (Figure 2).

Recommendations for the diagnostic evaluation of male LUTS	Strength rating
Take a complete medical history from men with LUTS.	Strong
Use a validated symptom score questionnaire including bother and quality of life assessment during the assessment of male LUTS and for re-evaluation during and/or after treatment.	Strong
Use a bladder diary to assess male LUTS with a prominent storage component or nocturia.	Strong
Tell the patient to complete a bladder diary for at least three days.	Strong
Perform a physical examination including digital rectal examination in the assessment of male LUTS.	Strong
Urinalysis and prostate-specific antigen (PSA)	
Use urinalysis (by dipstick or urinary sediment) in the assessment of male LUTS.	Strong
Measure PSA if a diagnosis of prostate cancer will change management.	Strong
Measure PSA if it assists in the treatment and/or decision-making process.	Strong
Renal function, post-void residual and uroflowmetry	
Assess renal function if renal impairment is suspected based on history and clinical examination, or in the presence of hydronephrosis, or when considering surgical treatment for male LUTS.	Strong
Measure post-void residual in the assessment of male LUTS.	Weak

Perform uroflowmetry in the initial assessment of male LUTS.	Weak
Perform uroflowmetry prior to medical or invasive treatment.	Strong
Imaging and urethrocystoscopy	
Perform ultrasound of the upper urinary tract in men with LUTS.	Weak
Perform imaging of the prostate when considering medical treatment for male LUTS, if it assists in the choice of the appropriate drug.	Weak
Perform imaging of the prostate when considering surgical treatment.	Strong
Perform urethrocystoscopy in men with LUTS prior to minimally invasive/surgical therapies if the findings may change treatment.	Weak
Pressure-flow studies (PFS)	
Perform PFS only in individual patients for specific indications prior to invasive treatment or when further evaluation of the underlying pathophysiology of LUTS is warranted.	Weak
Perform PFS in men who have had previous unsuccessful (invasive) treatment for LUTS.	Weak
Perform PFS in men considering invasive treatment who cannot void > 150 mL.	Weak
Perform PFS when considering surgery in men with bothersome predominantly voiding LUTS and Q_{max} > 10 mL/s.	Weak

Perform PFS when considering invasive therapy in men with bothersome, predominantly voiding LUTS with a post-void residual > 300 mL.	Weak
Perform PFS when considering invasive treatment in men with bothersome, predominantly voiding LUTS aged > 80 years.	Weak
Perform PFS when considering invasive treatment in men with bothersome, predominantly voiding LUTS aged < 50 years.	Weak
Non-invasive tests in diagnosing bladder outlet obstruction	
Do not offer non-invasive tests, as an alternative to PFS, for diagnosing bladder outlet obstruction in men.	Strong

Figure 2: Assessment algorithm of LUTS in men aged 40 years or older



DRE = digital-rectal examination; FVC = frequency volume chart; LUTS = lower urinary tract symptoms; PCa = prostate cancer; PSA = prostate specific antigen; PVR = post-void residual; US = ultrasound.
Note: Readers are strongly recommended to read the full text that highlights the current position of each test in detail.

Disease Management

Conservative and pharmacological treatment

Watchful waiting is suitable for mild-to-moderate uncomplicated LUTS. It includes education, re-assurance, lifestyle advice, and periodic monitoring.

Recommendations for the conservative and pharmacological management of male LUTS	Strength rating
Conservative management	
Offer men with mild/moderate symptoms, minimally bothered by their symptoms, watchful waiting.	Strong
Offer men with LUTS lifestyle advice and self-care information prior to, or concurrent with, treatment.	Strong
Pharmacological management	
Offer α1-blockers to men with moderate-to-severe LUTS.	Strong
Use 5α-reductase inhibitors (5-ARIs) in men who have moderate-to-severe LUTS and an increased risk of disease progression (e.g. prostate volume > 40 mL).	Strong
Counsel patients about the slow onset of action of 5-ARIs.	Strong
Use muscarinic receptor antagonists in men with moderate-to-severe LUTS who mainly have bladder storage symptoms.	Strong
Do not use antimuscarinic overactive bladder medications in men with a post-void residual (PVR) volume > 150 mL.	Weak
Use beta-3 agonists in men with moderate-to-severe LUTS who mainly have bladder storage symptoms.	Weak

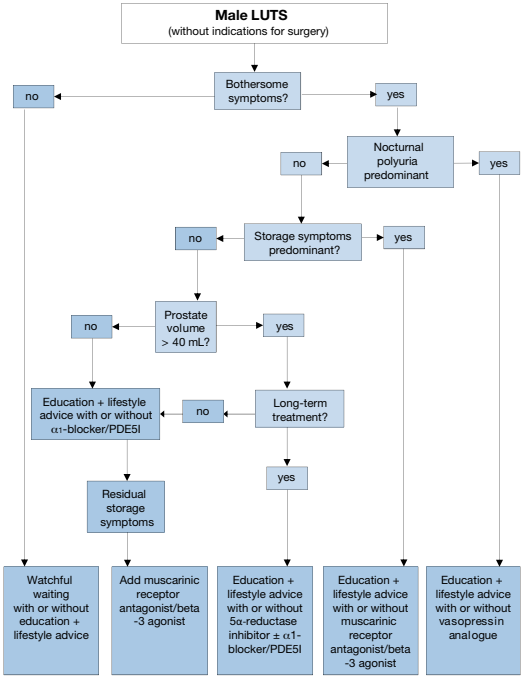
Use phosphodiesterase type 5 inhibitors in men with moderate-to-severe LUTS with or without erectile dysfunction.	Strong
Offer hexane extracted *Serenoa repens* (HeSR) to men with LUTS who want to avoid any potential adverse events especially related to sexual function.	Weak
Inform the patient that the magnitude of efficacy of HESr may be modest.	Strong
Offer combination treatment with an α1-blocker and a 5-ARI to men with moderate-to-severe LUTS and an increased risk of disease progression (e.g. prostate volume > 40 mL).	Strong
Use combination treatment of a α1-blocker with a muscarinic receptor antagonist in patients with moderate-to-severe LUTS if relief of storage symptoms has been insufficient with monotherapy with either drug.	Strong
Do not prescribe combination treatment in men with a PVR volume > 150 mL.	Weak
Use combination treatment of a α1-blocker with mirabegron in patients with persistent storage LUTS after treatment with α1-blockers monotherapy.	Weak

Summary conservative and/or medical treatment

First choice of therapy is behavioural modification, with or without pharmacological treatment. A flowchart illustrating conservative and pharmacological treatment choices according to evidence-based medicine and patients' profiles is provided in Figure 3.

Figure 3: Treatment algorithm of male LUTS using medical and/or conservative treatment options.

Treatment decisions depend on results assessed during initial evaluation. Note that patients' preferences may result in different treatment decisions.



PDE5I = phosphodiesterase type 5 inhibitor.
Note: Readers are strongly recommended to read the full text that highlights the current position of each treatment in detail.

Surgical treatment

Prostate surgery is usually required when patients have experienced recurrent or refractory urinary retention, overflow incontinence, recurrent urinary tract infections, bladder stones or diverticula, treatment-resistant visible haematuria due to BPH/BPE, or dilatation of the upper urinary tract due to BPO, with or without renal insufficiency (absolute operation indications, need for surgery). Surgery is usually needed when patients have had insufficient relief of LUTS or post-void residual after conservative or pharmacological treatments (relative operation indications). Surgical management is divided by surgical approach into: resection; enucleation; vaporisation; alternative ablative techniques; and non-ablative techniques.

Recommendations for surgical treatment of male LUTS

Recommendations for resection of the prostate	Strength rating
Offer bipolar- or monopolar-transurethral resection of the prostate to surgically treat moderate-to-severe LUTS in men with prostate size of 30-80 mL.	Strong
Offer laser resection of the prostate using Tm:YAG laser (ThuVARP) as an alternative to TURP.	Weak
Offer transurethral incision of the prostate to surgically treat moderate-to-severe LUTS in men with prostate size < 30 mL, without a middle lobe	Strong

Recommendations for enucleation of the prostate	
Offer open prostatectomy in the absence of bipolar transurethral enucleation of the prostate and holmium laser enucleation of the prostate to treat moderate-to-severe LUTS in men with prostate size > 80 mL.	Strong
Offer bipolar transurethral (plasmakinetic) enucleation of the prostate to men with moderate-to-severe LUTS as an alternative to transurethral resection (TURP) of the prostate.	Weak
Offer laser enucleation of the prostate using Ho:YAG laser (HoLEP) to men with moderate-to-severe LUTS as an alternative to TURP or open prostatectomy.	Strong
Offer enucleation of the prostate using the Tm:YAG laser (ThuLEP, ThuVEP) to men with moderate-to-severe LUTS as an alternative to TURP, holmium laser enucleation or bipolar transurethral (plasmakinetic) enucleation.	Weak
Offer Tm:YAG laser enucleation of the prostate to patients receiving anticoagulant or antiplatelet therapy.	Weak
Offer 120-W 980 nm, 1,318 nm or 1,470 nm diode laser enucleation of the prostate to men with moderate-to-severe LUTS as a comparable alternative to bipolar transurethral (plasmakinetic) enucleation or bipolar transurethral resection of the prostate (B-TURP).	Weak

Recommendations for vaporisation of the prostate	
Offer bipolar transurethral vaporisation of the prostate as an alternative to transurethral resection of the prostate to surgically treat moderate-to-severe LUTS in men with a prostate volume of 30-80 mL.	Weak
Offer 80-W 532-nm Potassium-Titanyl-Phosphate (KTP) laser vaporisation of the prostate to men with moderate-to-severe LUTS with a prostate volume of 30-80 mL as an alternative to TURP.	Strong
Offer 120-W 532-nm Lithium Borat (LBO) laser vaporisation of the prostate to men with moderate-to-severe LUTS with a prostate volume of 30-80 mL as an alternative to TURP.	Strong
Offer 180-W 532-nm LBO laser vaporisation of the prostate to men with moderate-to-severe LUTS with a prostate volume of 30-80 mL as an alternative to TURP.	Strong
Offer laser vaporisation of the prostate using 80-W KTP, 120- or 180-W LBO lasers for the treatment of patients receiving antiplatelet or anticoagulant therapy with a prostate volume < 80 mL.	Weak
Recommendations for alternative ablative techniques	
Offer Aquablation* to patients with moderate-to-severe LUTS and a prostate volume of 30-80 mL as an alternative to TURP.	Weak
Inform patients about the risk of bleeding and the lack of long-term follow-up data.	Strong

Offer prostatic artery embolisation (PAE)* to men with moderate-to-severe LUTS who wish to consider minimally invasive treatment options and accept less optimal outcomes compared with TURP.	Weak
Perform PAE only in units where the work up and follow up is performed by urologists working collaboratively with trained interventional radiologists for the identification of PAE suitable patients.	Strong
Recommendations for non-ablative techniques	
Offer Prostatic urethral lift (Urolift®) to men with LUTS interested in preserving ejaculatory function, with prostates < 70 mL and no middle lobe.	Strong
Do not offer intraprostatic Botulinum toxin-A injection treatment to patients with male LUTS.	Strong

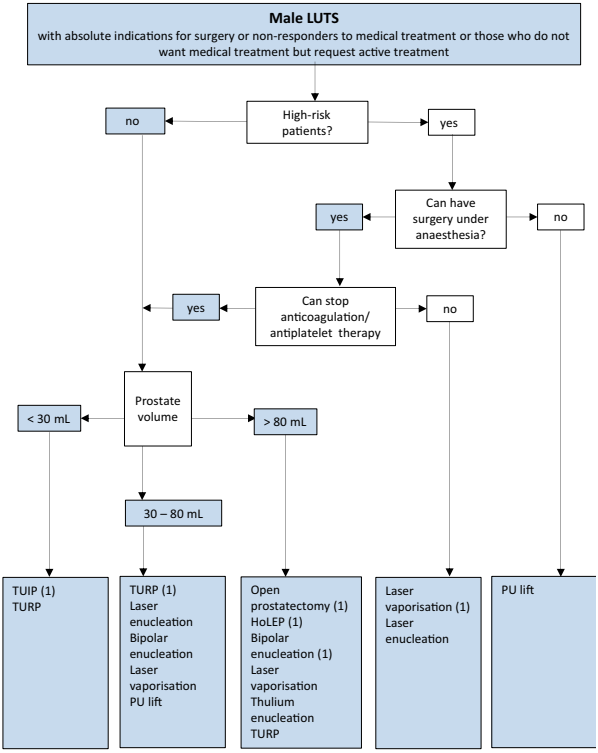
**Technique remains under investigation*

Summary surgical treatment

The choice of the surgical technique depends on prostate size, co-morbidities, ability to undergo anaesthesia, patient's preference/willingness to accept surgery-associated side effects, availability of the surgical armamentarium, and experience of the surgeon. Figure 4 illustrates surgical treatment choices according to the patient's profile.

Figure 4: Treatment algorithm of bothersome LUTS refractory to conservative/medical treatment or in cases of absolute operation indications.

The flowchart is stratified by the patient's ability to have anaesthesia, cardiovascular risk, and prostate size.



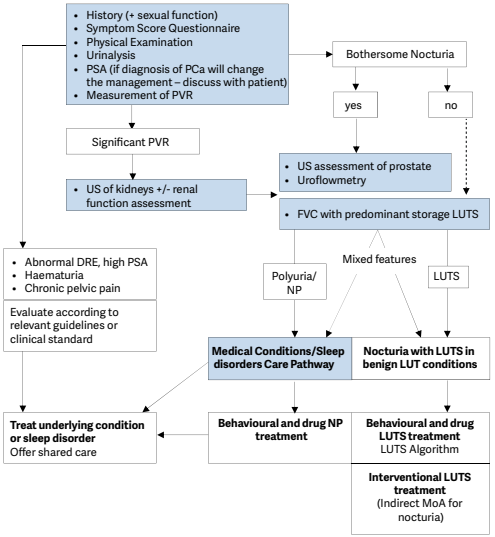
Laser vaporisation includes GreenLight, thulium, and diode laser vaporisation; Laser enucleation includes holmium and thulium laser enucleation.
HoLEP = holmium laser enucleation; PU = prostatic urethral; TUIP = transurethral incision of the prostate; TURP = transurethral resection of the prostate.

Management of Nocturia in Men with LUTS

Diagnostic assessment

Evaluation is outlined in Figure 5.

Figure 5: Evaluation of nocturia in non-neurogenic male LUTS



Assessment must establish whether the patient has polyuria, LUTS, sleep disorder or a combination. Therapy may be driven by the bother it causes, but non-bothersome nocturia may warrant assessment with a frequency volume chart, (indicated by the dotted line), depending on history and clinical examination since potential presence of a serious underlying medical condition must be considered.
DRE = digital rectal examination; NP = nocturnal polyuria; MoA = mechanism of action; PVR = post-void residual; PSA = prostate-specific antigen; US = ultrasound; FVC = frequency volume chart.

Medical conditions and sleep disorders shared care pathway

Table 1: Shared care pathway for nocturia, highlighting the need to manage potentially complex patients using relevant expertise for the causative factors.

UROLOGICAL CONTRIBUTION	*SHARED CARE*	*MEDICAL CONTRIBUTION*
Diagnosis of LUTD • Urological/ LUTS evaluation • Nocturia symptom scores • Bladder diary		**Diagnosis of conditions causing NP** • Evaluate patient's known conditions • Screening for sleep disorders • Screening for potential causes of polyuria*

Conservative management Behavioural therapy • Fluid/sleep habits advice • Drugs for storage LUTS • Drugs for voiding LUTS • ISC/ catherisation • Leg elevation • Weight loss **Interventional therapy** • Therapy of refractory storage LUTS • Therapy of refractory voiding LUTS	**Conservative management** • Antidiuretic • Diuretics • Drugs to aid sleep	**Management** • Initiation of therapy for new diagnosis • Optimised therapy of known conditions * Potential causes of polyuria NEPHROLOGICAL DISEASE • Tubular dysfunction • Global renal dysfunction CARDIOVASCULAR DISEASE • Cardiac disease • Vascular disease ENDOCRINE DISEASE • Diabetes insipidus/mellitus • Hormones affecting diuresis/natriuresis NEUROLOGICAL DISEASE • Pituitary and renal innervation • Autonomic dysfunction RESPIRATORY DISEASE • Obstructive sleep apnoea BIOCHEMICAL • Altered blood oncotic pressure

Recommendations for treatment of nocturia	Strength rating
Treat underlying causes of nocturia, including behavioural, systemic condition(s), sleep disorders, lower urinary tract dysfunction, or a combination of factors.	Weak
Discuss behavioural changes with the patient to reduce nocturnal urine volume and episodes of nocturia, and improve sleep quality.	Weak

Offer desmopressin to decrease nocturia due to nocturnal polyuria in men < 65 years of age.	Weak
Offer low dose desmopressin for men > 65 years of age with nocturia at least twice per night due to nocturnal polyuria.	Weak
Screen for hyponatremia at baseline, day three and day seven, one month after initiating therapy and periodically during treatment. Measure serum sodium more frequently in patients > 65 years of age and in patients at increased risk of hyponatremia.	Strong
Discuss with the patient the potential clinical benefit relative to the associated risks from the use of desmopressin, especially in men > 65 years of age.	Strong
Offer α1-adrenergic antagonists for treating nocturia in men who have nocturia associated with LUTS.	Weak
Offer antimuscarinic drugs for treating nocturia in men who have nocturia associated with overactive bladder.	Weak
Offer 5α-reductase inhibitors for treating nocturia in men who have nocturia associated with LUTS and an enlarged prostate (> 40 mL).	Weak
Do not offer phosphodiesterase type 5 inhibitors for the treatment of nocturia.	Weak

Management of male urinary incontinence

Urinary incontinence (UI) is defined as an unintentional loss of urine and is reported to have a prevalence of 11% in men aged

60 to 64 years old to 31% in men ≥ 85 years and to affect up to 32% of men with LUTS.

Table 2: Epidemiology and pathophysiology overview of male urinary incontinence

Type	*Definition*	*Causes and associated factors*	*Pathophysiology*	*Clinical presentation*
Stress UI: prevalence < 10%	Urine loss during movement or efforts or in general during increased abdominal pressure.	• Benign Prostatic Obstruction surgery • Neurogenic condition • Pelvic surgery • Radical prostatectomy • Urethral surgery	Sphincter deficiency	**Symptoms:** UI during physical activity, exercises, e.g. during coughing, sneezing, no leakage during sleep, no nocturnal enuresis **Voiding diary/Pad test:** with activity **Cough stress test:** leakage can coincide with coughing

Urgency UI: prevalence 40-80%	Urine loss concomitant or immediately following an urgency episode.	• Ageing process • Anorectal dysfunction/ GI disorders • Behavioural factors (fluid intake and caffeine consumption) • Chronic BPO • Idiopathic • Intrinsic bladder diseases (cystitis, fibrosis, interstitial cystitis) • Metabolic syndrome • Neurogenic conditions • UTIs	• Detrusor overactivity (Neurogenic or not) • Urothelial stimulation • Increased afferent signalling • Others (pelvic organ cross talk, bladder wall ischemia; etc.)	**Symptoms:** urgency, usually associated with, increased frequency and nocturia **Voiding diary:** urgency, frequency and nocturia
Mixed UI: prevalence 10-30%	Any combination of SUI and UUI.	Causes of both SIU and UUI	Combination of SUI and UUI	**Symptoms:** UI equally as often with physical activity as with a sense of urgency **Voiding diary:** varies **Cough stress test:** may show leakage with coughing

Recommendations for the diagnostic evaluation of male UI

Recommendations	Strength rating
Take a complete medical history including symptoms and comorbidities, medications, and a focused physical examination in the evaluation of men with urinary incontinence (UI).	Strong
Use a validated symptom score questionnaire, bladder diary and pad-test to assess UI.	Strong
Measure post-void residual in the assessment of UI.	Strong
Perform urodynamics for UI when considering invasive treatment.	Weak

Recommendations for conservative treatment of male UI

Recommendations for simple clinical interventions for male UI	Strength rating
Offer lifestyle advice that may improve UI to patients; however, patients should be informed that the evidence for these interventions is lacking.	Weak
Review any medication associated with the development or worsening of UI.	Weak
Use pads and/or penile sheaths as a palliative option for the management of UI.	Weak

Recommendations for behavioural and physical therapies for male UI	
Implement prompted voiding for patients with UI where appropriate.	Strong
Offer bladder training as a complementary treatment for UI.	Weak
Offer pelvic floor muscle training alone or in combination with biofeedback and/or electrostimulation to men undergoing radical prostatectomy to speed recovery from UI.	Weak

Recommendations for the pharmacological management of male UI

Recommendations	**Strength rating**
Offer antimuscarinic drugs or mirabegron to adults with urge urinary incontinence who failed conservative treatment.	Strong
Offer duloxetine to men with stress urinary incontinence.	Weak
Inform patients about the possible adverse events of duloxetine and that its use is off label for this indication in Europe.	Strong

Recommendations for the surgical management of male UI

Recommendations for bulking agents	Strength rating
Do not offer bulking agents to men with post-prostatectomy urinary incontinence (PPI).	Weak
Recommendations for male slings	
Offer non-adjustable transobturator slings to men with mild-to-moderate* PPI.	Weak
Inform men that severe incontinence, prior pelvic radiotherapy or transurethral surgery, may worsen the outcome of non-adjustable male sling surgery.	Weak
Recommendations for compression devices	
Offer artificial urinary sphincter (AUS) to men with moderate-to-severe stress urinary incontinence.	Strong
Implantation of AUS or ProACT© for men should only be offered in expert centres.	Weak
Warn men receiving AUS or ProACT© that, although cure can be achieved there is a high risk of complications, mechanical failure, and the need for explantation.	Strong
Do not offer non-circumferential compression device (ProACT©) to men who have had pelvic radiotherapy.	Weak

Recommendations for the surgical management of male urge urinary incontinence

Recommendations for bladder wall injection of botulinum toxin.	**Strength rating**
Offer bladder wall injections of onabotulinum toxin A (100 U) to patients with overactive bladder/urgency urinary incontinence (UUI) refractory to medical therapy.	Weak
Warn patients of the limited duration of response, risk of urinary tract infection and the possible prolonged need for clean intermittent self-catheterisation (ensure that they are willing and able to do so).	Strong
Recommendation for sacral nerve stimulation	
Offer sacral nerve stimulation to patients who have UUI refractory to medical therapy and are willing to undergo surgical treatment.	Weak
Recommendations for cystoplasty	
Offer augmentation cystoplasty to patients with overactive bladder (OAB)/UUI who have failed all other treatment options and are able and willing to perform self-catheterisation.	Weak
Inform patients undergoing augmentation cystoplasty of the high risk of complications; the risk of having to perform clean intermittent self-catheterisation and the need for life-long surveillance.	Strong
Only offer urinary diversion to patients who have failed less invasive therapies for the treatment of OAB/UUI, who will accept a stoma.	Weak

Follow-up

Recommended follow-up strategy:

- Patients managed with watchful waiting should be reviewed at six months and then annually, provided symptoms do not deteriorate or absolute indications develop for surgical treatment.
- Patients receiving α1-blockers, muscarinic receptor antagonists, beta-3 agonists, phospodiesterase 5 inhibitors, or a combination should be reviewed four to six weeks after drug initiation. If patients gain symptomatic relief, without troublesome side effects, drug therapy may be continued. Patients should be reviewed at six months and then annually, provided symptoms do not deteriorate or absolute indications develop for surgical treatment.
- Patients receiving 5α-reductase inhibitors should be reviewed after twelve weeks and six months to determine their response and adverse events.
- Patients receiving desmopressin: serum sodium concentration should be measured at day three and seven and after one month and, if serum sodium concentration has remained normal, every three months subsequently; the follow-up sequence should be restarted after dose escalation.
- Patients after prostate surgery should be reviewed four to six weeks after catheter removal to evaluate treatment response and side effects. If patients have symptomatic relief and there are no side effects, further assessment is not necessary.

Recommendations for follow-up	Strength rating
Follow-up all patients who receive conservative, medical or surgical management.	Weak
Define follow-up intervals and examinations according to the specific treatment.	Weak

Readers are strongly recommended to read the full version of the Guidelines where the efficacy, safety and considerations for each treatment are presented.

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-94-92671-16-5) available to all members of the European Association of Urology at their website, http://www.uroweb.org/guidelines.