EAU GUIDELINES ON SEXUAL AND REPRODUCTIVE HEALTH

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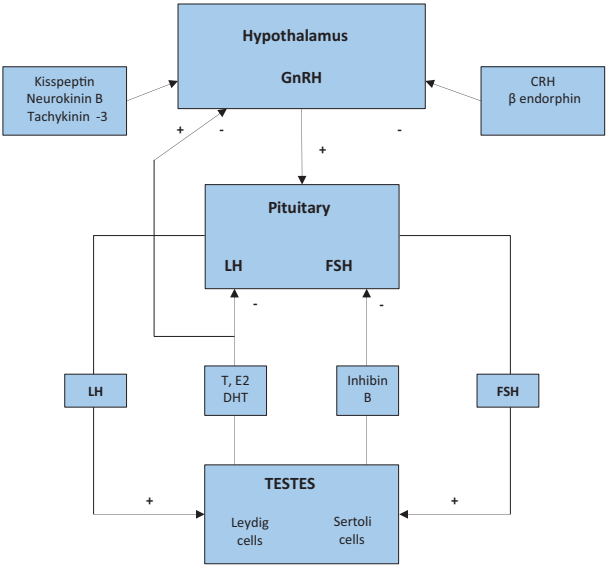
Introduction

This document presents a concise overview of the medical aspects relating to male sexual and reproductive health and combines the former guidelines on Male Sexual Dysfunction, Male Infertility and Male Hypogonadism.

Male Hypogonadism

Male Hypogonadism, also known as Testosterone Deficiency, is a disorder associated with decreased functional activity of the testes, with decreased production of androgens and/or impaired sperm production. It may adversely affect multiple organ functions and quality of life (QoL). The prevalence increases with age.

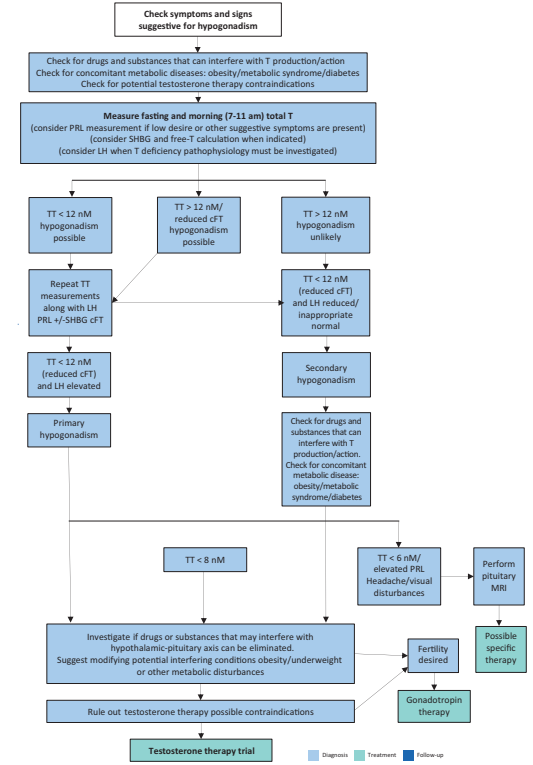
Figure 1: Physiology of testosterone production



GnRH = gonadotropin releasing hormone; LH = luteinising hormone; FSH = follicular stimulating hormone; T = testosterone; E2 = 7-β-estradiol; DHT = dehydroepiandrosterone; CRH = corticotrophin releasing hormone.

Diagnostic evaluation of Late-Onset Hypogonadism

Figure 2: Diagnostic evaluation of late-onset hypogonadism



TT = total testosterone; cFT = calculated free testosterone; PRL = prolactin; SHBG = sex hormone-binding globulin; LH = luteinising hormone; MRI = magnetic resonance imaging.

Recommendations for the diagnostic evaluation of late-onset hypogonadism

Recommendations	Strength rating
Diagnostic evaluation	
Check for concomitant diseases, drugs and substances that can interfere with testosterone production/action.	Strong
Measure total testosterone in the morning (07.00 and 11.00 hours) and in the fasting state, with a reliable laboratory assay.	Strong
Repeat total testosterone on at least two separate occasions when < 12 nmol/L and before starting testosterone therapy.	Strong
Use 12 nmol/L total testosterone (3.5 ng/mL) as a reliable threshold to diagnose late onset hypogonadism (LOH).	Strong
Measure sex hormone-binding globulin and free-testosterone calculation as indicated in section 3.4.4.	Strong
Analyse luteinising hormone and follicle-stimulating hormone serum levels to differentiate between the different types of hypogonadism.	Strong
Measure prolactin (PRL) levels if low sexual desire (or other suggestive signs/symptoms) and secondary hypogonadism is present.	Strong
Perform pituitary magnetic resonance imaging (MRI) in secondary hypogonadism, with elevated PRL or symptoms specific of a pituitary mass and/or presence of other anterior pituitary hormone deficiency.	Strong

Perform pituitary MRI in secondary severe hypogonadism (total testosterone < 6 nmol/L).	Weak

Recommendations for screening men for late-onset hypogonadism

Recommendations	Strength rating
Screen for late-onset hypogonadism (LOH) only in symptomatic men.	Strong
Do not use structured interviews and self-reported questionnaires for systematic screening for LOH as they have low specificity.	Strong

Recommendations for disease management

Recommendations for testosterone therapy outcome	Strength rating
Do not use testosterone therapy in eugonadal men.	Strong
Use testosterone therapy as first-line treatment in patients with symptomatic hypogonadism and mild erectile dysfunction (ED).	Strong
Use a combination of phosphodiesterase type 5 inhibitors and testosterone therapy in more severe forms of ED as it may result in better outcomes.	Weak
Use conventional medical therapies for severe depressive symptoms and osteoporosis.	Strong

Do not use testosterone therapy to reduce weight and enhance cardio-metabolic status.	Weak
Do not use testosterone therapy to improve cognition vitality and physical strength in ageing men.	Strong

Recommendations for late-onset hypogonadism choice of treatment	**Strength rating**
Treat, when indicated, organic causes of hypogonadism (e.g., pituitary masses, hyperprolactinemia, etc).	Strong
Improve lifestyle and reduce weight (e.g., obesity); withdraw, when possible, concomitant drugs that can impair testosterone production; treat co-morbidity before starting testosterone therapy.	Strong
Fully inform patients about expected benefits and adverse effects of any treatment option. Select the testosterone preparation in a joint decision process, only with fully informed patients.	Strong
The aim of testosterone therapy is to restore serum testosterone concentration to the therapeutic range for young men.	Weak
Use testosterone gels rather than long-acting depot administration when starting initial treatment, so that therapy can be adjusted or stopped in the case of treatment-related adverse effects.	Weak

Recommendations on risks factors in testosterone treatment	Strength rating
Fully counsel symptomatic hypogonadal men who have been surgically treated for localised prostate cancer (PCa) and who are currently without evidence of active disease considering testosterone therapy, emphasising the benefits and lack of sufficient safety data on long-term follow-up.	Weak
Restrict treatment to patients with a low risk for recurrent PCa (i.e., pre-operative PSA < 10 ng/mL; Gleason score < 7 [International Society for Urological Pathology grade 1]; cT1-2a)* and treatment should start after at least one year follow-up with PSA level < 0.01 ng/mL.	Weak
Advise patients that safety data on the use of testosterone therapy in men treated for breast cancer are unknown.	Strong
Assess cardiovascular risk factors before commencing testosterone therapy.	Strong
Assess men with known cardiovascular disease (CVD) for cardiovascular symptoms before testosterone therapy and with close clinical assessment and evaluation during treatment.	Strong
Treat men with hypogonadism and pre-existing CVD, venous-thromboembolism or chronic cardiac failure, who require testosterone therapy with caution, by careful clinical monitoring and regular measurement of haematocrit (not exceeding 54%) and testosterone levels.	Weak

Exclude a family history of venous-thromboembolism before starting testosterone therapy.	Strong
Monitor testosterone, haematocrit at three, six and twelve months after testosterone therapy initiation, and thereafter annually. A haematocrit > 54% should require testosterone therapy withdrawal and phlebotomy. Re-introduce testosterone therapy at a lower dose once the haematocrit has normalised and consider switching to topical testosterone preparations.	Strong
Evaluate patients with polycythaemia vera and those with a higher risk of developing elevated haematocrit every three months during the first year of testosterone therapy, and at least every six months thereafter.	Strong
Evaluate total PSA in PCa survivors at three, six and twelve months during the first year of testosterone therapy, and annually thereafter.	Strong

**As for EAU risk groups for biochemical recurrence of localised or locally advanced prostate cancer (see EAU Prostate Cancer Guidelines, 2024).*

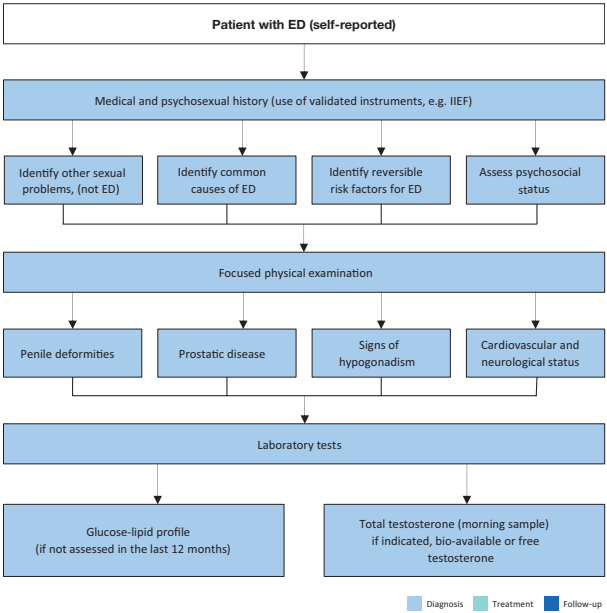
Erectile dysfunction

Erectile dysfunction (ED) is defined as the persistent inability to attain and maintain an erection sufficient to permit satisfactory sexual performance. Erectile dysfunction may affect physical and psychosocial health and may have a significant impact on the QoL of sufferers and their partners. There is increasing evidence that ED can also be an early

manifestation of coronary artery and peripheral vascular disease; therefore, ED should not be regarded only as a QoL issue, but also as a potential warning sign of CVD.

Diagnostic evaluation

Figure 3: Minimal diagnostic evaluation (basic work-up) in patients with erectile dysfunction



ED = erectile dysfunction; IIEF = International Index of Erectile Function.

Table 1: Cardiac risk stratification (based on 2nd and 3rd Princeton Consensus)

Low-risk category	Intermediate-risk category	High-risk category
Asymptomatic, < 3 risk factors for CAD (excluding sex)	≥ 3 risk factors for CAD (excluding sex)	High-risk arrhythmias
Mild, stable angina (evaluated and/or being treated)	Moderate, stable angina	Unstable or refractory angina
Uncomplicated previous MI	Recent MI (> 2, < 6 weeks)	Recent MI (< 2 weeks)
LVD/CHF (NYHA class I or II)	LVD/CHF (NYHA class III)	LVD/CHF (NYHA class IV)
Post-successful coronary revascularisation	Non-cardiac sequelae of atherosclerotic disease (e.g., stroke, peripheral vascular disease)	Hypertrophic obstructive and other cardiomyopathies
Controlled hypertension		Uncontrolled hypertension
Mild valvular disease		Moderate-to-severe valvular disease

CAD = coronary artery disease; CHF = congestive heart failure; LVD = left ventricular dysfunction; MI = myocardial infarction; NYHA = New York Heart Association.

Table 2: Indications for specific diagnostic tests

Primary ED (not caused by acquired organic disease or psychogenic disorder).
Young patients with a history of pelvic or perineal trauma, who could benefit from potentially curative revascularisation surgery or angioplasty.
Patients with penile deformities which might require surgical correction (e.g., Peyronie's disease, congenital penile curvature).
Patients with complex psychiatric or psychosexual disorders.
Patients with complex endocrine disorders.
Specific tests may be indicated at the request of the patient or their partner.
Medico-legal reasons (e.g., implantation of penile prosthesis to document end stage ED, sexual abuse).

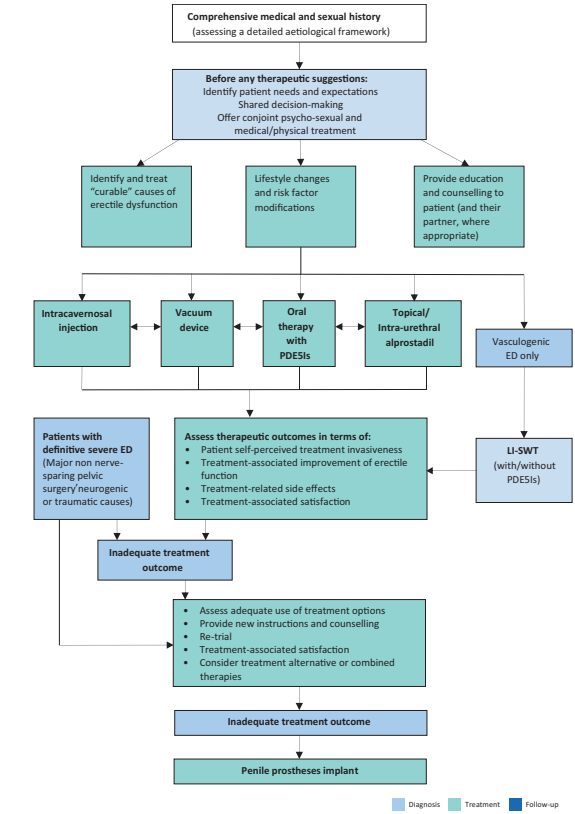
Table 3: Specific diagnostic tests

Nocturnal Penile Tumescence and Rigidity (NTPR) using Rigiscan®
Vascular studies: - Intracavernous vasoactive drug injection - Penile dynamic duplex ultrasonography - Penile dynamic infusion cavernosometry and cavernosography - Internal pudendal arteriography
Specialised endocrinological studies
Specialised psycho-diagnostic evaluation

Recommendations for the diagnosis of erectile dysfunction	Strength rating
Take a comprehensive medical and sexual history in every patient presenting with erectile dysfunction (ED). Take a targeted psychosexual history, including life stressors, cultural aspects, and cognitive factors regarding patient sexual performance.	Strong
Use a validated questionnaire related to ED to assess all sexual function domains (e.g., International Index of Erectile Function) and the effect of a specific treatment modality.	Strong
Include a focused physical examination in the initial assessment of men with ED to identify underlying medical conditions and comorbid genital disorders that may be associated with ED.	Strong
Evaluate laboratory tests, including glucose and lipid profile and total testosterone, to identify and treat any reversible risk factors and lifestyle factors that can be modified.	Strong
Include specific diagnostic tests in the initial evaluation of ED in the presence of the conditions presented in Table 1.	Strong

Disease management

Figure 4: Management algorithm for erectile dysfunction



ED = erectile dysfunction; PDE5Is = phosphodiesterase type 5 inhibitors; LI-SWT = low-intensity shockwave treatment.

Table 4: Summary of the key pharmacokinetic data for the four PDE5Is currently EMA-approved to treat erectile dysfunction*

Parameter	Sildenafil, 100 mg	Tadalafil, 20 mg	Vardenafil, 20 mg	Avanafil, 200 mg
C_{max}	560 µg/L	378 µg/L	18.7 µg/L	5.2 µg/L
T_{max} (median)	0.8-1 hours	2 hours	0.9 hours	0.5-0.75 hours
T1/2	2.6-3.7 hours	17.5 hours	3.9 hours	6-17 hours
AUC	1,685 µg.h/L	8,066 µg.h/L	56.8 µg.h/L	11.6 µg.h/L
Protein binding	96%	94%	94%	99%
Bio-availability	41%	NA	15%	8-10%

** Fasted state, higher recommended dose. Data adapted from EMA statements on product characteristics.*

C_{max} = maximal concentration; T_{max} = time-to-maximum plasma concentration; T1/2 = plasma elimination halftime; AUC = area under curve or serum concentration time curve.

Table 5: Common adverse events of the four PDE5Is currently EMA-approved to treat erectile dysfunction*

Adverse event	Sildenafil	Tadalafil	Vardenafil	Avanafil, 200mg
Headache	12.8%	14.5%	16%	9.3%
Flushing	10.4%	4.1%	12%	3.7%
Dyspepsia	4.6%	12.3%	4%	uncommon

Nasal congestion	1.1%	4.3%	10%	1.9%
Dizziness	1.2%	2.3%	2%	0.6%
Abnormal vision	1.9%		< 2%	None
Back pain		6.5%		< 2%
Myalgia		5.7%		< 2%

** Adapted from EMA statements on product characteristics.*

Recommendations for treatment of erectile dysfunction	**Strength rating**
Fully inform patients of the mechanism of action and the ways in which phosphodiesterase type 5 inhibitors (PDE5Is) should be taken, as incorrect use/ inadequate information is the main causes of a lack of response to PDE5Is.	Strong
Direct the patient to Cognitive Behaviour Therapy as a psychological approach (include the partner), when indicated, combined with medical treatment to maximise treatment outcomes.	Strong
Discuss with patients undergoing active treatment for prostate cancer about the risk of sexual changes other than erectile dysfunction (ED), including sexual desire reduction, changes in orgasm, anejaculation, Peyronie's like disease and penile size changes.	Strong

Initiate lifestyle changes and risk factor modification prior to, or at the same time as, initiating ED treatments.	Strong
Use PDE5Is as first-line therapy for the treatment of ED.	Strong
Use intracavernous injections as an alternative first-line therapy in those in whom PDE5I are contra-indicated or as second-line therapy in men who fail to respond to PDE5I.	Strong
Use topical/intra-urethral alprostadil as an alternative first-line therapy in well-informed patients who: • do not wish to have or are not suitable for oral vasoactive therapy; • do not wish to have intracavernous injections; • in patients who prefer a less-invasive therapy.	Weak
Use low intensity shockwave treatment (LI-SWT) with/without PDE5Is in patients • with mild vasculogenic ED; • as an alternative therapy in well-informed patients who do not wish to have or are not suitable for oral vasoactive therapy; • who are vasculogenic ED patients that are poor responders to PDE5Is.	Weak
Use vacuum erection devices in well-informed patients requesting non-invasive, drug-free management of ED.	Weak

Implant a penile prosthesis if other treatments fail or depending upon patient preference. Patients should be fully informed of the benefits an harms associated with the procedure.	Strong
Start pro-erectile treatments at the earliest opportunity after radical prostatectomy/ pelvic surgery and other curative treatments for prostate cancer.	Weak

Disorders of ejaculation

Ejaculation is a complex physiological process, which is composed of emission and expulsion and is mediated by interwoven neurological and hormonal pathways. Any condition that interferes with these pathways may cause a wide range of ejaculatory disorders.

Table 6: Spectrum of ejaculatory disorders

Premature ejaculation	Retrograde ejaculation
Retarded or delayed ejaculation	Anorgasmia
Anejaculation	Haemospermia
Painful ejaculation	

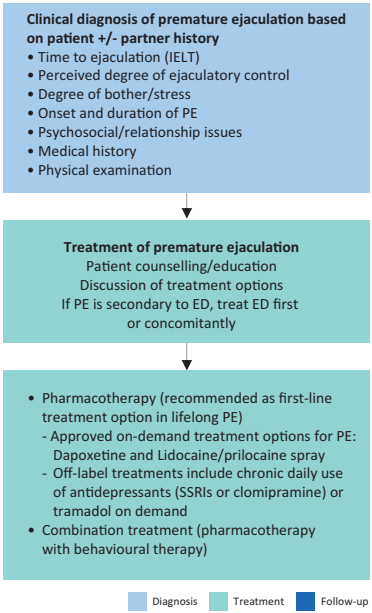
Diagnostic evaluation

Recommendations for the diagnostic evaluation of premature ejaculation	Strength rating
Perform the diagnosis and classification of premature ejaculation (PE) based on medical and sexual history, which should include assessment of intravaginal ejaculatory latency time (IELT) (self-estimated), perceived control, distress and interpersonal difficulty due to the ejaculatory dysfunction.	Strong
Use either stopwatch-measured IELT or self-estimated IELT in clinical practice.	Weak
Use patient-reported outcomes in daily clinical practice.	Weak
Include physical examination in the initial assessment of PE to identify anatomical abnormalities that may be associated with PE or other sexual dysfunctions, particularly erectile dysfunction.	Strong
Do not perform routine laboratory or neuro-physiological tests. They should only be directed by specific findings from history or physical examination.	Strong

Disease management

Recommendations for the treatment of premature ejaculation	Strength rating
Treat erectile dysfunction (ED), other sexual dysfunction or genitourinary infection (e.g., prostatitis) first.	Strong
Use either dapoxetine or the lidocaine/prilocaine spray as first-line treatments for lifelong premature ejaculation (PE).	Strong
Use off-label oral treatment with daily selective serotonin re-uptake inhibitor (SSRIs) or daily/on-demand clomipramine as a viable alternative for second-line treatments.	Strong
Use off-label tramadol with caution as a viable on-demand third-line treatment alternative to on-demand/daily antidepressants (SSRIs or clomipramine).	Strong
Use PDE5Is alone or in combination with other therapies in patients with PE (without ED).	Strong
Use psychological/behavioural therapies in combination with pharmacological treatment in the management of acquired PE.	Weak
Use hyaluronic acid injection with caution as a treatment option for PE compared to other more established treatment modalities.	Weak
Do not perform dorsal neurectomy because more safety data are warranted.	Weak

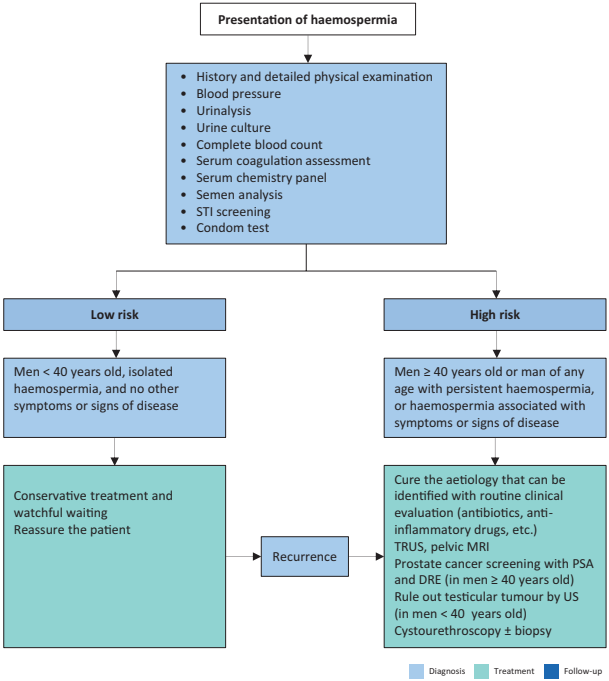
Figure 5: Management of premature ejaculation*



**Adapted from Lue et al., 2004.*
ED = erectile dysfunction; PE = premature ejaculation; IELT = intravaginal ejaculatory latency time; SSRI = selective serotonin receptor inhibitor.

Recommendations for the investigation and management of haemospermia	Strength rating
Perform a full medical and sexual history with detailed physical examination.	Strong
Screen men aged ≥ 40 years with persistent haemospermia for prostate cancer.	Weak
Screen men aged < 40 years with persistent haemospermia for STIs.	Weak
Use non-invasive imaging modalities (TRUS and MRI) in men aged ≥ 40 years or men of any age with persistent or refractory haemospermia.	Weak
Use invasive methods such as cystoscopy and vesiculoscopy when non-invasive methods are inconclusive or in patients with recurrent haemospermia.	Weak

Figure 6: Management algorithm for haemospermia



STI = sexually transmitted infections; PSA = prostate-specific antigen; DRE = digital rectal examination; US = ultrasonography; TRUS = transrectal ultrasonography; MRI = magnetic resonance imaging.

Low Sexual Desire

It has always been a challenge to define sexual desire because of its complex nature and the fact it can be conceptualised in many different ways. According to the ICD-10, lack or loss of sexual desire should be the principal problem with no other sexual problems accompanying it such as ED. In the Diagnostic and Statistical Manual of Mental Disorders (DSM-V), male hypoactive sexual desire disorder was defined as *"the persistent or recurrent deficiency (or absence) of sexual or erotic thoughts or fantasies and desire for sexual activity"*. The judgment of deficiency is made by the clinician, taking into account other factors that may affect sexual function, such as age and socio-cultural factors in an individual's life. According to the fourth International Consultation on Sexual Medicine (ICSM-IV), the definition of male hypoactive sexual desire disorder was proposed as a *"persistent or recurrent deficiency or absence of sexual or erotic thoughts or fantasies and desire for sexual activity (clinical principle)"*.

Table 7: The list of common causes of low sexual desire in men

Androgen deficiency	Post-traumatic stress syndrome
Hyperprolactinaemia	Renal failure
Anger and anxiety	Coronary disease and heart failure
Depression	Ageing
Relationship conflict	HIV infection
Stroke	Body-building and eating disorders
Antidepressant therapy	Erectile dysfunction
Epilepsy	Prostatitis/chronic pelvic pain syndrome

Psychological intervention

Findings on treatment efficacy for psychological intervention are scarce. Accordingly, recommendations must be interpreted with caution. Psychological interventions with a focus on cognitive and behavioural strategies may be beneficial for low sexual desire (LSD) in men, as well as mindfulness treatments. Since both members of a couple may experience age-related changes concurrently and interdependently, it could be helpful to address the sexual health needs of the aging couple (including LSD) as a whole rather than treating the individual patient.

Disease management

Recommendations for the treatment of low sexual desire	Strength rating
Perform the diagnosis and classification of low sexual desire (LSD) based on medical and sexual history, which could include validated questionnaires.	Weak
Include physical examination in the initial assessment of LSD to identify anatomical abnormalities that may be associated with LSD or other sexual dysfunctions, particularly erectile dysfunction.	Weak
Perform laboratory tests to rule out endocrine disorders.	Strong
Modulate chronic therapies which can negatively impact toward sexual desire.	Weak
Provide testosterone therapy if LSD is associated with signs and symptoms of testosterone deficiency.	Strong

Penile curvature

Congenital penile curvature (CPC) results from disproportionate development of the tunica albuginea of the corporal bodies and is not associated with urethral malformation. In the majority of the cases curvature is ventral but can be lateral and rarely dorsal.

Diagnostic evaluation

Taking a medical and sexual history is usually sufficient to establish the diagnosis of CPC. Patients usually present after reaching puberty as the curvature becomes more apparent with erections, and a severe curvature can make intercourse difficult or impossible. Physical examination during erection (autophotograph or after intracavernosal injection of vasoactive drugs) is useful to document curvature and exclude other pathologies.

Disease management

The definitive treatment for this disorder remains surgical and can be deferred until after puberty. Surgical treatments for CPC generally share the same principles as in Peyronie's disease (PD). Nesbit's procedure with excision of an ellipse of the tunica albuginea is the optimum surgical treatment but many other techniques have been described and employed. Plication techniques are widely used including techniques producing a de-rotation of the corporal bodies. Most of the time, dissection and mobilisation of the penile dorsal neurovascular bundle are required in order to avoid loss of sensation and ischaemia to the glans penis.

Recommendation for the treatment of congenital penile curvature	Strength rating
Use the Nesbit procedure or plication techniques with or without neurovascular bundle dissection (medial/lateral) for satisfactory curvature correction.	Strong

Peyronie's disease

The aetiology of Peyronie's disease (PD) is unknown. However, repetitive microvascular injury or trauma to the tunica albuginea is still the most widely accepted hypothesis to explain the aetiology. Abnormal wound healing leads to the remodelling of connective tissue into a fibrotic plaque. Penile plaque formation can result in curvature which, if severe, may impair penetrative sexual intercourse. The most commonly associated comorbidity and risk factors are diabetes, hypertension, dyslipidaemia, ischaemic cardiopathy, autoimmune diseases, ED, smoking, excessive consumption of alcohol, low testosterone and pelvic surgery (e.g., radical prostatectomy).

Two phases of the disease can be distinguished. The first is the active inflammatory phase, which may be associated with painful erections and a palpable nodule or plaque in the tunica of the penis; typically, but not invariably, a penile curvature begins to develop. The second is the fibrotic phase with the formation of hard, palpable plaques that can calcify, with stabilisation of the disease and development of the penile deformity.

Diagnostic evaluation

The aim of the initial evaluation is to obtain information on the presenting symptoms and their duration (e.g., pain on erection, palpable nodules, deformity, length and girth and erectile function). It is important to obtain information on the distress caused by the symptoms and the potential risk factors for ED and PD.

Recommendations for diagnosis of Peyronie's disease	Strength rating
Undertake a medical and sexual history of patients with Peyronie's disease (PD), include duration of the disease, pain on erection, penile deformity, difficulty in vaginal/anal intromission due to disabling deformity and erectile dysfunction (ED).	Strong
Perform a physical examination, including assessment of palpable plaques, stretched or erect penile length, degree of curvature (self-photography, vacuum-assisted erection test or pharmacological-induced erection) and any other related diseases (e.g., Dupuytren's contracture, Ledderhose disease) in patients with PD.	Strong
Use the intracavernous injection (IC) method in the diagnostic work-up of PD to provide an objective assessment of penile curvature with an erection.	Weak

Use the PD specific questionnaire especially in clinical trials, but mainstream usage in daily clinical practice is not mandatory.	Weak
Do not use ultrasound (US), computed tomography or magnetic resonance imaging to assess plaque size and deformity in routine clinical practice.	Weak
Use penile Doppler US in the case of diagnostic evaluation of ED, to evaluate penile haemodynamic and vascular anatomy, and to assess location and calcification of plaques, especially prior to grafting surgery.	Weak

Disease management

Non-operative treatment

Table 8: Conservative treatments for Peyronie's disease

Oral treatments
Nonsteroidal anti-inflammatory drugs (NSAIDs)
Phosphodiesterase type 5 inhibitors (PDE5Is)
Intralesional treatments
Verapamil
Nicardipine
Clostridium collagenase
Interferon α2B
Hyaluronic acid
Botulinum toxin

Topical treatments
H-100 gel
Other
Traction devices
Multimodal treatment
Extracorporeal shockwave treatment
Vacuum Erection Device

Recommendations for non-operative treatment of Peyronie's disease	Strength rating
Offer conservative treatment to patients not fit for surgery or when surgery is not acceptable to the patient.	Strong
Fully counsel patients regarding all available treatment options and outcomes before starting any treatment.	Strong
Do not offer oral treatment with vitamin E, potassium para-aminobenzoate (potaba), tamoxifen, pentoxifylline, colchicine and acetyl esters of carnitine to treat Peyronie's disease (PD).	Strong
Use nonsteroidal anti-inflammatory drugs to treat penile pain in the acute phase of PD.	Strong
Use extracorporeal shockwave treatment (ESWT) to treat penile pain in the acute phase of PD.	Weak
Use phosphodiesterase type 5 inhibitors to treat concomitant erectile dysfunction or if the deformity results in difficulty in penetrative intercourse in order to optimise penetration.	Weak

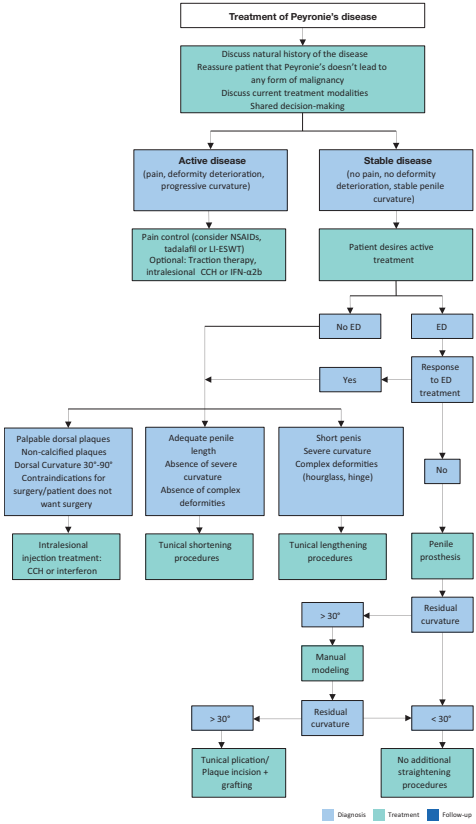
Offer intralesional therapy with interferon alpha-2b to patients with stable curvature dorsal or lateral > 30^0 seeking a minimal invasive procedure.	Weak
Offer intralesional therapy with Collagenase *Clostridium Histolyticum* to patients with stable PD and dorsal or lateral curvature > 30^0, who request non-surgical treatment, although the placebo effects are high.	Strong
Do not offer intralesional treatment with steroids to reduce penile curvature, plaque size or pain.	Strong
Do not use intralesional platelet-rich plasma or hyaluronic acid, either alone or in combination with oral treatment, to reduce penile curvature, plaque size or pain outside the confines of a clinical trial.	Strong
Do not offer ESWT to improve penile curvature and reduce plaque size.	Strong
Offer penile traction devices to reduce penile deformity or as part of a multimodal therapy approach.	Weak

Surgical treatment

Recommendations for the surgical treatment of Peyronie's disease	Strength rating
Perform surgery only when Peyronie's disease (PD) has been stable for at least three months (without pain or deformity deterioration), which is usually the case after twelve months from the onset of symptoms, and intercourse is compromised due to the deformity.	Strong
Assess penile length, curvature severity, erectile function (including response to pharmacotherapy in case of erectile dysfunction [ED]) and patient expectations prior to surgery.	Strong
Use tunical shortening procedures as the first treatment option for congenital penile curvature and for PD with adequate penile length and rigidity, less severe curvatures and absence of complex deformities (hourglass or hinge). The type of procedure used is dependent on surgeon and patient preference, as no procedure has proven superior to its counterparts.	Weak

Use tunical lengthening procedures for patients with PD and normal erectile function, with adequate penile length, severe curvature or presence of complex deformities (hourglass or hinge). The type of graft used is dependent on the surgeon and patient factors, as no graft has proven superior to its counterparts.	Weak
Do not use the sliding technique as there is a significant risk of life changing complications (e.g., glans necrosis).	Strong
Do not use synthetic grafts in PD reconstructive surgery.	Strong
Use penile prosthesis implantation, with or without any additional straightening procedures (modelling, plication, incision or excision with or without grafting), in PD patients with ED not responding to pharmacotherapy.	Strong

Figure 7 : Treatment algorithm for Peyronie's disease



ED = erectile dysfunction; LI-ESWT= low-intensity extracorporeal shockwave treatment; CCH = collagenase Clostridium histolyticum; NSAIDs = nonsteroidal anti-inflammatory drugs.

Penile size abnormalities and dysmorphophobia

Short penis condition represents both a diagnostic and treatment challenge. To date there is no consensus on standard penis size. Disorders of penile size include: micropenis; adult acquired buried penis; small penis anxiety syndrome; and penile dysmorphic disorder related to body dysmorphic disorder.

Table 9: Classification of the clinical conditions underlying a short penis condition or dysmorphophobia in the adult

Group name	Etiology	Definition	Pathogenesis	Prevalence, %
False penile shortness	Acquired	Reduced exposure of the penile shaft in the presence of normal penile size	Adult acquired buried penis	NA
Intrinsic penile shortness	Congenital	Small penis due to an incomplete genital development secondary to a congenital condition	· Hypogonadotropic hypogonadism · Genetic syndromes · Bladder exstrophy-epispadias complex	0.9 - 2.1

Intrinsic penile shortness	Acquired	Shortening/ shrinking of the corpora cavernosa due to an acquired pathological process	· Peyronie's Disease · Radical prostatectomy · Radical cystectomy · Radiation therapy · Low flow priapism · Multiple penile operations (e.g., urethral surgery or PP infection) · Penile traumatic event (traumatic or surgical amputation for penile cancer)	NA
Body dysmorphic disorder	Acquired	Perceived defect or flaw in the individual's physical appearance followed by significant distress or impairment in important areas of the individual's life	· Penile Dysmorphic Disorder	1.8 – 9.5

Recommendations for classification of short penile size	Strength rating
Perform a detailed genital examination in all men and particularly in men with BMI > 30, lichen sclerosis or penile cancer history and complaints of urinary/sexual difficulties or poor cosmesis to exclude the presence of an adult acquired buried penis (AABP) condition.	Strong
Use classification systems to classify AABP clinical presentation and surgical management.	Weak
Inquire on the presence of body dysmorphic disorder/penile dysmorphic disorder in patients with normal-sized penis complaining of short penile size.	Strong

Diagnosis

Recommendations for diagnosis of short penile size	Strength rating
Take a comprehensive medical and sexual history in every patient presenting complaining of short penile size.	Strong
Use stretched penile length measurements (skin junction-to-glans tip or dorsally from the pubic bone-to-glans tip) to define penile length.	Weak
Measure flaccid and erect measurements to assess penile length in detail.	Weak

Measure penile girth in every patient presenting complaining of a short penile size.	Weak
Use validated questionnaires to screen for body dysmorphic disorder (BDD) in cases of a normal-sized penis.	Weak
Use validated questionnaires (e.g., IIEF-15, BAPS) to assess baseline sexual function and beliefs concerning penile size.	Weak
Refer patients with BDD for mental health counselling.	Strong

Management

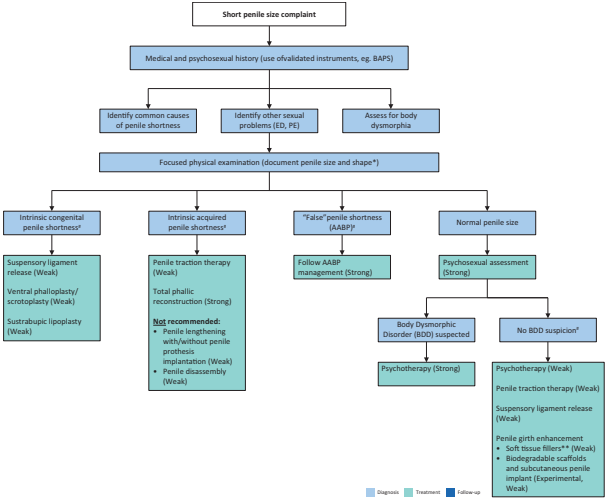
Recommendations for non-surgical management of short penile size	**Strength rating**
Consider psychotherapy when psychopathological comorbidities are detected, or when aversive relationship dynamics may underlie the request for penile augmentation.	Strong
Consider the use of penile traction therapy as a conservative treatment to increase penile length.	Weak
Do not use vacuum erection devises to increase penile length.	Weak
Use endocrinological therapies to restore penile size in boys with micropenis or disorders of sex development.	Strong
Do not use testosterone therapy or other hormonal therapies to increase penile size in men after puberty.	Strong

Recommendations surgical treatment	Strength rating
Adult acquired buried penis (AABP)	
Extensively counsel patients on the benefits and complications of AABP surgery.	Strong
Initiate lifestyle changes and modification of risk factors, particularly weight loss, to minimise AABP surgical complications and to optimise surgical outcomes.	Strong
Surgical reconstructive techniques may be considered to address AABP.	Weak
Congenital intrinsic penile shortness	
Perform penile reconstruction surgery for AABP in high volume centres.	Strong
Use suspensory ligament release (SLR), ventral phalloplasty and suprapubic lipoplasty/liposuction/lipectomy to address penile lengthening.	Weak
Extensively discuss possible complications related to SLR, ventral phalloplasty and suprapubic lipoplasty/liposuction/ lipectomy.	Strong
Use total phallic reconstruction to restore genital anatomy in patients affected by congenital micropenis.	Weak
Acquired penile shortness	
Do not recommend penile prosthesis implantation, penile disassembly or sliding technique to patients seeking penile lengthening options.	Strong
Use total phallic reconstruction to restore genital anatomy in genetic males with penile inadequacy due to traumatic loss.	Weak

Penile girth enhancement

Recommendations	Strength rating
Counsel patients extensively regarding the risks and benefits of penile girth enhancement techniques.	Strong
Do not use silicone, paraffin and petroleum jelly (Vaseline) to address penile girth enhancement.	Strong
Use hyaluronic acid, soft tissue fillers and autologous fat injection to address penile girth enhancement.	Weak
Do not use hyaluronic acid, soft tissue fillers and autologous fat injection can be utilised to address penile girth enhancement in men with penile dysmorphic disorder.	Weak
Do not use grafts in penile girth enhancement as they are considered experimental.	Strong
Do not use biodegradable scaffolds and subcutaneous penile implant (Penuma®) to address penile girth enhancement as they are considered experimental.	Strong

Figure 8: Management of short penile size



* *Penile length should be measured stretched both from penopubic skin junction-to-glans tip (STT) and from the pubic bone-to-glans tip (BTT).*

\# *There is lack of evidence to recommend one treatment over another.*

** *Hyaluronic acid (HA), poly-l-lactic acid (PLA), hydroxyethyl methacrylate, polymethylmethacrylate (PMMA), polyalkylamide hydrogel (PAAG) and calcium hydroxyapatite are considered as injectable materials for penile girth enhancement. Although the level of evidence is low, there is more evidence for HA, PLA and PMMA. Do not use silicone, paraffin or Vaseline (Strong evidence against). Strength of recommendations is depicted between brackets where appropriate.*

Priapism

Priapism is a persistent erection in the absence of sexual stimulation that fails to subside. It can be divided into ischaemic, non-ischaemic and stuttering priapism.

Ischaemic (low-flow or veno-occlusive) priapism

Ischaemic priapism is a persistent erection marked by rigidity of the corpora cavernosa and by little or no cavernous arterial inflow. Ischaemic priapism is the most common subtype of priapism, accounting for > 95% of all episodes.

Diagnostic evaluation

Table 10: Key points when taking the history of priapism

Duration of erection
Presence and severity of pain
Previous episodes of priapism and methods of treatment
Current erectile function, especially the use of any erectogenic therapies prescription or nutritional supplements
Medications and recreational drug use
Sickle cell disease, haemoglobinopathies, hypercoagulable states, vessel vasculitis
Trauma to the pelvis, perineum or penis

Table 11: Key findings in priapism

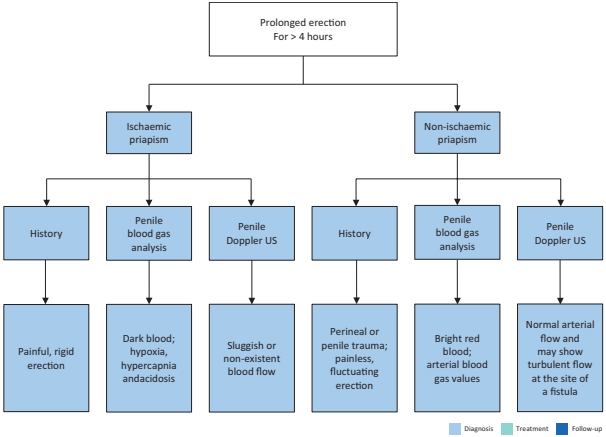
	Ischaemic priapism	Non-ischaemic priapism
Corpora cavernosa fully rigid	Typically	Seldom
Penile pain	Typically	Seldom
Abnormal penile blood gas	Typically	Seldom
Haematological abnormalities	Sometimes	Seldom
Recent intracavernosal injection	Sometimes	Sometimes
Perineal trauma	Seldom	Typically

Table 12: Typical blood gas values

Source	pO_2 (mmHg)	pCO_2 (mmHg)	pH
Normal arterial blood (room air) (similar values are found in arterial priapism)	> 90	< 40	7.40
Normal mixed venous blood (room air)	40	50	7.35
Ischaemic priapism (first corporal aspirate)	< 30	> 60	< 7.25

pCO_2, partial pressure of carbon dioxide; pO_2, partial pressure of oxygen.

Figure 9: Differential diagnosis of priapism



US = ultrasound.

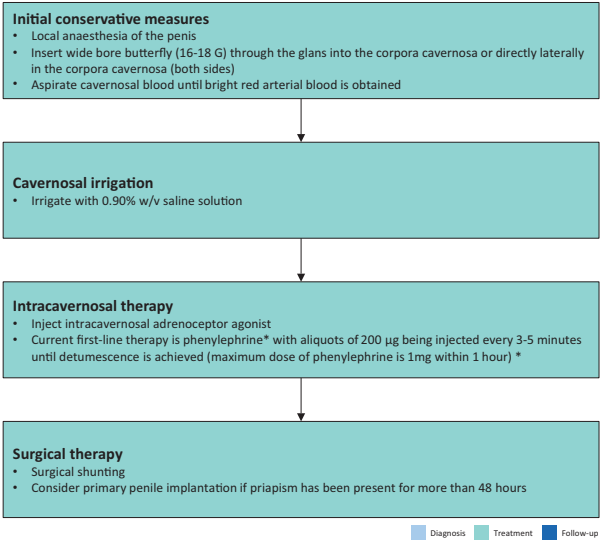
Recommendations for the diagnosis of ischaemic priapism	**Strength rating**
Take a comprehensive history to establish the diagnosis which can help to determine the priapism subtype.	Strong
Include a physical examination of the genitalia, perineum and abdomen in the diagnostic evaluation.	Strong

Include a full blood count, white blood cell count with blood cell differential, platelet count and coagulation profile for laboratory testing. Perform directed further laboratory testing depending upon history and clinical and laboratory findings. Perform a complete evaluation of all possible causes of priapism in children.	Strong
Perform a haemoglobinopathy screen in patients with low flow priapism who are at high risk of sickle cell disease or thalassemia.	Strong
Analyse the blood gas parameters from blood aspirated from the penis to differentiate between ischaemic and non-ischaemic priapism.	Strong
Perform colour duplex ultrasound of the penis and perineum before aspiration to differentiate between ischaemic and non-ischaemic priapism.	Strong
Use magnetic resonance imaging of the penis in cases of prolonged ischaemic priapism or refractory priapism, and as an adjunct to predict smooth muscle viability.	Weak

Disease management of ischaemic priapism

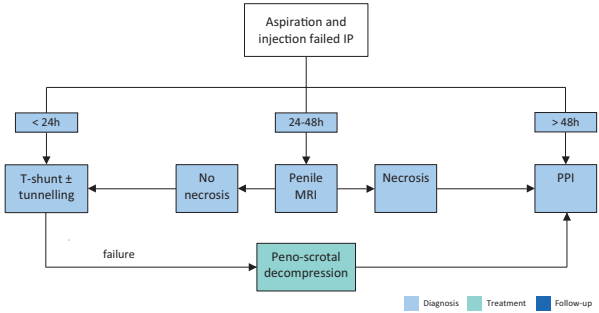
The treatment is sequential and physicians should move on to the next stage if treatment fails.

Figure 10: Medical and surgical management of ischaemic priapism



(*) Dose of phenylephrine should be reduced in children. It can result in significant hypertension and should be used with caution in men with cardiovascular disease. Monitoring of pulse and blood pressure is advisable in all patients during administration and for one hour afterwards. Its use is contraindicated in men with a history of cerebro-vascular disease and significant hypertension.

Figure 11: Algorithm on surgical management of priapism



MRI = Magnetic resonance imaging; PPI = penile prosthesis implantation; IP = ischaemic priapism.

Recommendations for the treatment of ischaemic priapism	**Strength rating**
Start management of ischaemic priapism as early as possible (within four to six hours) and follow a stepwise approach.	Strong
Decompress the corpus cavernosum by penile aspiration and washout until fresh red blood is obtained as first treatment step.	Strong
Replace blood aspiration with intracavernous injection of a sympathomimetic drug as the first step in priapism secondary to intracavernous injections of vasoactive agents.	Strong
Perform intracavernous injection of a sympathomimetic drug in priapism that persists despite aspiration.	Strong

Repeat aspiration and intracavernous injection of a sympathomimetic drug in cases that persist despite prior aspiration and intracavernous injection of a sympathomimetic drug, before considering surgical intervention.	Strong
Treat ischaemic priapism associated with sickle cell disease in the same fashion as idiopathic ischaemic priapism. Do not use exchange transfusion as a primary treatment. Provide other supportive measures (intravenous hydration, oxygen administration with alkalisation with bicarbonate, blood exchange transfusions), but do not delay initial treatment to the penis.	Strong
Proceed to surgical treatment only when blood aspiration and intracavernous injection of sympathomimetic drugs have failed.	Strong
Perform distal shunt surgical procedures first and combine them with tunnelling if necessary.	Weak
Use proximal procedures in cases of distal shunt failure (< 48 hours) or in patients who do not wish to proceed with immediate penile implant insertion.	Weak
Discuss implantation of a penile prosthesis in cases of delayed presentation (> 48 hours) and in cases refractory to injection therapy and distal shunting.	Weak

Delay implantation of a penile prosthesis if a shunt has been performed, to minimise the risk of infection and erosion of the implant.	Strong
Decide on which type of implant to insert based on: • patient suitability; • surgeons' experience; and • availability and cost of equipment. If a malleable penile prosthesis is implanted it can be exchanged later for an inflatable penile implant.	Strong

Priapism in special situations

Stuttering (recurrent or intermittent) priapism

Stuttering priapism is similar to ischaemic priapism in that it is low-flow and ischaemic and, if left untreated, can result in significant penile fibrosis, with Sickle Cell Disease being the most common cause.

Recommendations for treatment of stuttering priapism	Strength rating
Manage each acute episode according to the treatment recommendation for ischaemic priapism.	Strong
Use hormonal therapies (mainly gonadotropin-receptor hormone agonists or antagonists) and/or anti-androgens for the prevention of future episodes in patients with frequent relapses. Do not use them before sexual maturation is reached.	Weak

Initiate treatment with phosphodiesterase type 5 inhibitors only when the penis is in its flaccid state.	Weak
Use digoxin, α-adrenergic agonists, baclofen, gabapentin or terbutaline only in patients with frequent and uncontrolled relapses.	Weak
Use intracavernous self-injections of sympathomimetic drugs at home for treatment of acute episodes on an interim basis until ischaemic priapism has been alleviated.	Weak

Non-ischaemic (high-flow or arterial) priapism

Non-ischaemic priapism is significantly less common than the ischaemic type, comprising only 5% of all priapism cases. A comprehensive history is also mandatory in the diagnosis of non-ischaemic priapism and follows the same principles as described in Table 11.

Recommendations for the diagnosis of non-ischaemic priapism	Strength rating
Take a comprehensive history to establish the diagnosis, which can help to determine the priapism subtype.	Strong
Include a physical examination of the genitalia, perineum and abdomen in the diagnostic evaluation.	Strong
Include a neurological examination if neurogenic non-ischaemic priapism is suspected.	Strong

Include complete blood count, with white blood cell differential, and coagulation profile for laboratory testing.	Strong
Analyse the blood gas parameters from blood aspirated from the penis to differentiate between ischaemic and non-ischaemic priapism.	Strong
Perform colour duplex ultrasound of the penis and perineum to differentiate between ischaemic and non-ischaemic priapism.	Strong
Perform selected pudendal arteriography when embolisation is planned for non-ischaemic priapism.	Strong

Recommendations for the treatment of non-ischaemic priapism	**Strength rating**
Perform definitive management for non-ischaemic priapism at the discretion of the treating physician as it is not a medical emergency.	Weak
Manage non-ischaemic priapism conservatively with the use of site-specific perineal compression as the first step. Consider androgen deprivation therapy only in adults.	Weak
Perform selective arterial embolisation when conservative management has failed.	Strong
Perform the first selective arterial embolisation using temporary material.	Weak

Repeat selective arterial embolisation with temporary or permanent material for recurrent non-ischaemic priapism following selective arterial embolisation.	Weak
Reserve selective surgical ligation of a fistula as a final treatment option when repeated arterial embolisations have failed.	Weak

Male infertility

'Infertility is the inability of a sexually active, non-contraceptive couple to achieve spontaneous pregnancy in one year' (World Health Organization 2000).

Diagnostic evaluation

A focused evaluation of the male patient must always be undertaken and should include: a medical and reproductive history; physical examination; semen analysis – with strict adherence to World Health Organization (WHO) reference values for human semen characteristics, and hormonal evaluation. Other investigations (e.g., genetic analysis and imaging) may be required depending on the clinical features and findings on semen analysis.

Semen analysis

A comprehensive andrological examination is always indicated if the semen analysis shows abnormalities when compared to reference values (Table 14).

Table 13: Lower reference limits (5th centiles and their 95% CIs) for semen characteristics

Parameter	2010 Lower reference limit (95% CI)	2021 Lower reference limit (95% CI)
Semen volume (mL)	1.5 (1.4-1.7)	1.4 (1.3-1.5)
Total sperm number (10^6/ejaculate)	39 (33-46)	39 (35-40)
Sperm concentration (10^6/mL)	15 (12-16)	16 (15-18)
Total motility (PR + NP, %)	40 (38-42)	42 (40-43)
Progressive motility (PR, %)	32 (31-34)	30 (29-31)
Vitality (live spermatozoa, %)	58 (55-63)	54 (50-56)
Sperm morphology (normal forms, %)	4 (3.0-4.0)	4 (3.9-4.0)
Other consensus threshold values		
pH	> 7.2	> 7.2
Peroxidase-positive leukocytes (10^6/mL)	< 1.0	< 1.0
Tests for antibodies on spermatozoa		
MAR test (motile spermatozoa with bound particles, %)	< 50	No evidence-based reference values. Each laboratory should define its normal reference ranges by testing a sufficiently large number of normal fertile men.

Immunobead test (motile spermatozoa with bound beads, %)	< 50	No evidence-based reference limits.
Accessory gland function		
Seminal zinc (µmol/ejaculate)	≥ 2.4	≥ 2.4
Seminal fructose (µmol/ejaculate)	≥ 13	≥ 13
Seminal neutral α-glucosidase (mU/ejaculate)	≥ 20	≥ 20

CIs = confidence intervals; MAR = mixed antiglobulin reaction; NP = non-progressive; PR = progressive (a+b motility).

** Distribution of data from the population is presented with one-sided intervals (extremes of the reference population data). The lower 5th percentile represents the level under which only results from 5% of the men in the reference population were found.*

Recommendations for the diagnostic work-up of male infertility

Recommendations	Strength rating
Include a parallel assessment of the fertility status, including ovarian reserve, of the female partner during the diagnosis and management of the infertile male, since this might determine decision making in terms of timing and therapeutic strategies (e.g., assisted reproductive technology (ART) versus surgical intervention).	Strong
Examine all men seeking medical help for fertility problems, including men with abnormal semen parameters.	Strong

Take a complete medical reproductive and family history, assessment of lifestyle and behaviour risk factors, physical examination and semen analysis.	Weak
Counsel infertile men or men with abnormal semen parameters on the associated health risks.	Weak
Assess testicular volume with a Prader's orchidometer or testicular ultrasound (US).	Weak
Perform semen analyses according to the latest edition of the WHO Manual for the Examination and Processing of Human Semen Perform at least two consecutive semen analyses if the baseline analysis was abnormal.	Strong
Do not routinely use reactive oxygen species (ROS) testing in the diagnosis and management of the male partner of an infertile couple.	Weak
Perform sperm DNA fragmentation (SDF) testing in the assessment of couples with recurrent pregnancy loss from natural conception and failure of ART or men with unexplained infertility.	Strong
Consider the use of testicular sperm for ICSI in patients with high SDF in ejaculated sperm as experimental.	Weak
Perform hormonal evaluation including serum total testosterone and Follicle Stimulating Hormone/Luteinising Hormone at least in all cases of oligozoospermia and azoospermia.	Strong

Offer standard karyotype analysis and genetic counselling to all men with azoospermia and oligozoospermia (spermatozoa < 5 million/mL) for diagnostic purposes.	Strong
Provide long-term endocrine follow-up and appropriate medical treatment to men with Klinefelter syndrome.	Strong
Perform Y-chromosome microdeletion testing in men with sperm concentrations of ≤ 1 million sperm/mL. Consider it in men with sperm concentrations of < 5 million sperm/mL	Strong
Inform men with Yq microdeletion and their partners who wish to proceed with intra-cytoplasmic sperm injection (ICSI) that microdeletions will be passed to sons.	Strong
Do not perform testicular sperm extraction in patients with complete deletions that include the AZFa and AZFb regions.	Strong
Test men with structural abnormalities of the vas deferens (unilateral or bilateral absence with no renal anomalies) and their partners for cystic fibrosis transmembrane conductance regulator gene mutations.	Strong
Provide genetic counselling in all couples with a genetic abnormality found on clinical or genetic investigation and in patients who carry a (potential) inheritable disease.	Strong
Perform scrotal US in patients with infertility, as there is a higher risk of testis cancer.	Weak

Discuss invasive diagnostic modalities (e.g., US-guided testicular biopsy with frozen section versus radical orchidectomy versus surveillance) in infertile men with US-detected indeterminate testicular lesions, especially if additional risk factors for malignancy are present in a multidisciplinary team setting.	Weak
Perform transrectal US if a partial or complete distal obstruction is suspected.	Strong

Special Conditions and Relevant Clinical Entities

Crytorchidism

Cryptorchidism is the most common congenital abnormality of the male genitalia; at one year of age nearly 1% of all full-term male infants have cryptorchidism. Approximately 30% of undescended testes are non-palpable and may be located within the abdominal cavity.

Recommendations	Strength rating
Do not use hormonal treatment for cryptorchidism in post-pubertal men.	Strong
Perform simultaneous testicular biopsy, for the detection of intratubular germ cell neoplasia in situ (formerly carcinoma in situ), if undescended testes are corrected in adulthood.	Strong
Offer adult men with unilateral undescended testis and normal hormonal function/spermatogenesis orchidectomy.	Strong

Offer adult men with unilateral or bilateral undescended testis with biochemical hypogonadism and or spermatogenic failure (i.e., infertility) unilateral or bilateral orchidopexy, if technically feasible.	Weak

Germ cell malignancy and male infertility

Testicular germ cell tumour (TGCT) is the most common malignancy in Caucasian men aged 15-40 years, and affects approximately 1% of sub-fertile men. Overall, sperm, cryopreservation is considered standard practice in all patients with cancer and not only those with testicular cancer. As such, it is important to stress that all men with cancer must be offered sperm cryopreservation prior to the therapeutic use of gonadotoxic agents or ablative surgery which may impair spermatogenesis or ejaculation (i.e., chemotherapy; radiation therapy; retroperitoneal surgery). Men with TGCT have decreased semen quality, even before cancer treatment.

Recommendations	Strength rating
Advise men with testicular microcalcification (TM) to perform self-examination even without additional risk factors, as this may result in early detection of testicular germ cell tumour (TGCT).	Weak
Do not perform testicular biopsy, follow-up scrotal ultrasound (US), measure biochemical tumour markers, or abdominal or pelvic computed tomography, in men with isolated TM without associated risk factors (e.g., infertility, cryptorchidism, testicular cancer, and atrophic testis).	Strong

Offer testicular biopsy to infertile men with TM, who belong to one of the following higher risk groups: spermatogenic failure (infertility), bilateral TM, atrophic testes (< 12 mL), history of undescended testes and TGCT.	Weak
Perform inguinal surgical exploration with testicular biopsy or offer orchidectomy after multi-disciplinary team meeting and discussion with the patient, if there are suspicious findings on physical examination or US in patients with TM with associated lesions.	Strong
Manage men treated for TGCT in a multi-disciplinary team setting with a dedicated late-effects clinic and survivorship program, since they are at increased risk of developing hypogonadism, sexual dysfunction and cardiovascular risk.	Strong
Perform sperm cryopreservation prior to planned orchidectomy or before additional neoadjuvant or adjuvant oncological therapies.	Strong
Offer onco-testicular sperm extraction (onco-TESE) at the time of radical orchidectomy in men with testicular cancer and azoospermia or severe abnormalities in their semen parameters.	Strong

Varicocele

Varicocele is a common genital abnormality, which may be associated with the following andrological conditions:

- male subfertility;
- failure of ipsilateral testicular growth and development;
- symptoms of pain and discomfort;
- hypogonadism.

Recommendations	Strength rating
In adolescents offer surgery for varicocele associated with a persistent small testis (size difference of > 2 mL or 20%), which should be confirmed on two subsequent visits performed six months apart.	Strong
Do not treat varicocele in infertile men who have normal semen analysis and in men with a sub-clinical varicocele.	Strong
Treat infertile men with a clinical varicocele, abnormal semen parameters and otherwise unexplained infertility in a couple where the female partner has good ovarian reserve to improve fertility rates.	Strong
Varicocelectomy may be considered in men with raised DNA fragmentation with otherwise unexplained infertility or who have suffered from failed assisted reproductive techniques, including recurrent pregnancy loss, failure of embryogenesis and implantation.	Weak

Male accessory gland infections and infertility

Infections of the male urogenital tract are potentially curable causes of male infertility. The WHO considers urethritis, prostatitis, orchitis and epididymitis to be male accessory gland infections (MAGIs). Semen analysis clarifies whether the prostate is involved as part of a generalised MAGI and provides information regarding sperm quality. In addition, leukocyte analysis allows differentiation between inflammatory and non-inflammatory chronic pelvic pain syndrome.

Recommendations	Strength rating
Treat male accessory gland infections as it may improve sperm quality, although it does not necessarily improve the probability of conception.	Weak
Refer sexual partners of patients with accessory sex gland infections that are known or suspected to be caused by sexually transmitted diseases for evaluation and treatment.	Strong

Non-Invasive Male Infertility Management

Idiopathic male infertility and OATS

Oligo-astheno-teratozoospermia (OAT) is a clinical condition, with a reduced number of spermatozoa in the ejaculate, which is also characterised by a reduced motility and morphology; often referred to as OAT syndrome (OATS).

Recommendations	Strength rating
Inform infertile men about the detrimental effects of obesity, low physical activity, smoking and high alcohol intake on sperm quality and testosterone levels. Therefore, advise infertile men to improve life style factors to improve their chances of conception.	Strong
Do not routinely treat patients with idiopathic infertility with antioxidants, selective oestrogen receptor modulators (SERMs) or aromatase inhibitors (Ais).	Weak

Hormonal therapy

Recommendations	Strength rating
Induce spermatogenesis in men with congenital or acquired hypogonadotropic hypogonadism who wish to conceive by effective drug therapy (human chorionic gonadotropin (hCG); human menopausal gonadotropins; recombinant folliclestimulating hormone (FSH); highly purified FSH).	Strong
Use FSH treatment in men with idiopathic oligozoospermia and FSH values within the normal range to ameliorate spermatogenesis outcomes.	Weak
Do not treat idiopathic infertility with high dose FSH.	Weak

Do not start hormonal stimulation prior TESE in men with non-obstructive azoospermia (NOA) outside clinical trials.	Weak
Do not use testosterone therapy for the treatment of male infertility.	Strong
Provide testosterone therapy for symptomatic patients with primary and secondary hypogonadism who are not considering parenthood.	Strong
Offer dopamine agonist therapy in men with hyperprolactinemia to improve sperm quality.	Weak
Withdraw anabolic steroids in infertile men for six to twelve months before considering treatment with selective oestrogen receptor modulators or gonadotrophin therapy to induce spermatogenesis.	Weak

Invasive Male Infertility Management

Obstructive azoospermia

Obstructive azoospermia (OA) is the absence of spermatozoa in the sediment of a centrifuged sample of ejaculate due to obstruction. Obstructive azoospermia is less common than non-obstructive azoospermia (NOA) and occurs in 20-40% of men with azoospermia. Men with OA usually have a normal FSH, testes of normal size and epididymal enlargement or distension. Of clinical relevance, men with late maturation arrest may present with normal gonadotrophins and testis size and may be only be distinguished from OA at the time of surgical exploration. The vas deferens may be absent bilaterally (CBAVD) or unilaterally (CUAVD). Obstruction in primary infertile men is more frequently present at the epididymal level.

Recommendations	Strength rating
Perform microsurgical vasovasostomy or epididymovasostomy for azoospermia caused by epididymal or vasal obstruction in men with female partners of good ovarian reserve.	Strong
Use sperm retrieval techniques, such as microsurgical epididymal sperm aspiration (MESA), testicular sperm extraction (TESE) and percutaneous techniques (PESA and TESA) either as an adjunct to reconstructive surgery, or if the condition is not amenable to surgical repair, or when the ovarian reserve of the partner is limited or patient preference is not to undertake a surgical reconstruction and the couple prefer to proceed to ICSI treatment directly.	Strong

Non-obstructive azoospermia

Non-obstructive azoospermia (NOA) is defined as the absence of sperm in semen analysis after centrifugation, with usually a normal ejaculate volume. This finding should be confirmed on at least two consecutives semen analyses. The severe deficit in spermatogenesis observed in NOA patients is often a consequence of primary testicular dysfunction or may be related to a dysfunction of the hypothalamus-pituitary-gonadal (HPG) axis.

Recommendations	Strength rating
Confirm a diagnosis of non-obstructive azoospermia (NOA) in two consecutive semen analyses, when no sperm are found after centrifugation.	Strong
Perform a comprehensive assessment, including detailed medical history, hormonal profile, genetic tests and scrotal ultrasound to investigate the underlying aetiology and associated co-morbidity in patients with NOA.	Strong
Genetic counselling is mandatory in couples with genetic abnormalities prior to any assisted reproductive technology.	Strong
Perform surgery for sperm retrieval in men who are candidates for assisted reproductive technology (i.e., ICSI).	Strong
Do not perform surgery for spoerm retrieval in patients with complete AZFa and AZFb microdeletions, since the chance of sperm retrieval is zero.	Strong
Do not perform fine needle aspiration (FNA) and testicular sperm aspiration (TESA) in patients with NOA.	Strong
Do not perform FNA mapping as a prognostic procedure prior to definitive testicular sperm extraction (any type) in patients with NOA in routine clinical practice.	Weak
Use microdissection TESE as the treatment of choice to retrieve sperm in patients with NOA.	Weak

Do not consider pre-operative biochemical and clinical variables as sufficient and reliable predictors of sperm retrieval outcome at surgery in patients with NOA.	Weak
Do not routinely use medical therapy, e.g. hormonal stimulation in men with NOA and hypergonadotrophic hypogonadism before TESE (any type) to improve sperm recovery.	Weak

This short booklet is based on the more comprehensive EAU Guidelines (ISBN 978-94-92671-23-3), available on the EAU website: http://www.uroweb.org/guidelines/.