



Guidelines – Sexual Medicine

Guidelines on Male Sexual Dysfunction: Erectile Dysfunction and Premature Ejaculation

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Abstract

Context: Erectile dysfunction (ED) and premature ejaculation (PE) are the two most prevalent male sexual dysfunctions.

Objective: To present the updated version of 2009 European Association of Urology (EAU) guidelines on ED and PE.

Evidence acquisition: A systematic review of the recent literature on the epidemiology, diagnosis, and treatment of ED and PE was performed. Levels of evidence and grades of recommendation were assigned.

Evidence synthesis: ED is highly prevalent, and 5–20% of men have moderate to severe ED. ED shares common risk factors with cardiovascular disease. Diagnosis is based on medical and sexual history, including validated questionnaires. Physical examination and laboratory testing must be tailored to the patient's complaints and risk factors. Treatment is based on phosphodiesterase type 5 inhibitors (PDE5-Is), including sildenafil, tadalafil, and vardenafil. PDE5-Is have high efficacy and safety rates, even in difficult-to-treat populations such as patients with diabetes mellitus. Treatment options for patients who do not respond to PDE5-Is or for whom PDE5-Is are contraindicated include intracavernous injections, intraurethral alprostadil, vacuum constriction devices, or implantation of a penile prosthesis.

PE has prevalence rates of 20–30%. PE may be classified as *lifelong* (primary) or *acquired* (secondary). Diagnosis is based on medical and sexual history assessing intravaginal ejaculatory latency time, perceived control, distress, and interpersonal difficulty related to the ejaculatory dysfunction. Physical examination and laboratory testing may be needed in selected patients only.

Pharmacotherapy is the basis of treatment in lifelong PE, including daily dosing of selective serotonin reuptake inhibitors and topical anaesthetics. Dapoxetine is the only drug approved for the on-demand treatment of PE in Europe. Behavioural techniques may be efficacious as a monotherapy or in combination with pharmacotherapy. Recurrence is likely to occur after treatment withdrawal.

Conclusions: These EAU guidelines summarise the present information on ED and PE. The extended version of the guidelines is available at the EAU Web site (<http://www.uroweb.org/nc/professional-resources/guidelines/online/>).

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1. Introduction

Erectile dysfunction (ED; or impotence) and premature ejaculation (PE) are the two most prevalent complaints in male sexual medicine. The most recent summary of the European Association of Urology (EAU) guidelines on ED was published in 2006. The EAU's Guidelines Office decided to expand these guidelines to include PE. Therefore, the new guidelines include an update of the ED guidelines and a completely new section on PE based on a review of available scientific information, current research, and clinical practice in the field. (The extended version of the guidelines is available at the EAU Web site [<http://www.uroweb.org/nc/professional-resources/guidelines/online/>].) Levels of evidence and grades of recommendation also were assigned. The aim of this review is to present a summary of the 2009 update of the EAU guidelines on ED and PE.

2. Erectile dysfunction

2.1. Definition, epidemiology, and risk factors

ED is the persistent inability to attain and maintain an erection sufficient to permit satisfactory sexual performance [1]. ED affects physical and psychosocial health and has a significant impact on the quality of life (QoL) of sufferers and their partners and families. Epidemiologic studies of ED suggest that approximately 5–20% of men have moderate to severe ED [2]. The difference in reported incidences is probably due to differences in the methodology and in the age and socioeconomic status of the study populations.

ED shares common risk factors with cardiovascular disease, including lack of exercise, obesity, smoking, hypercholesterolaemia, and metabolic syndrome [3]. The risk of ED may be reduced by modifying these risk factors, particularly exercising or losing weight [4]. Another risk factor for ED is radical prostatectomy (RP) in any form (open, laparoscopic, or robotic) because of the risk of cavernosal nerve injury, poor oxygenation of the corpora cavernosa, and vascular insufficiency. Some 25–75% of men undergoing RP experience postoperative ED. Patients being considered for nerve-sparing RP, ideally, should be potent, and the cavernosal nerves must be preserved to ensure erectile function recovery after RP [5].

2.2. Diagnosis and work-up

2.2.1. Basic work-up

The basic work-up (minimal diagnostic evaluation) outlined in Fig. 1 must be performed in every patient with ED [6]. Because of the potential cardiac risks associated with sexual activity, the Second Princeton Consensus Conference [7] stratified patients with ED wanting to initiate or resume sexual activity into three risk categories. The low-risk group included asymptomatic patients with fewer than three risk factors for coronary artery disease (excluding male gender), mild or stable angina (evaluated and/or being treated), uncomplicated past myocardial infarction, left ventricular

Table 1 – Indications for specific diagnostic tests

Patients with primary erectile disorder (not caused by organic disease or psychogenic disorder) Young patients with a history of pelvic or perineal trauma who could benefit from potentially curative vascular surgery Patients with penile deformities (eg, Peyronie's disease, congenital curvature) that might require surgical correction Patients with complex psychiatric or psychosexual disorders Patients with complex endocrine disorders Specific tests may also be indicated at the request of the patient or his partner For medicolegal reasons (eg, penile prosthesis implant, sexual abuse)
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dysfunction or congestive heart failure (New York Heart Association class I), postsuccessful coronary revascularisation, controlled hypertension, and mild valvular disease. All other patients were included in intermediate- or high-risk categories and required a cardiology consultation prior to engaging in sexual activity (sexual activity for high-risk patients is not recommended).

2.2.2. Specific examinations and tests

Although most patients with ED can be managed within the primary care setting, some circumstances, presented in Table 1, require specific diagnostic testing [1]. Specific diagnostic tests are presented in Table 2. Nocturnal penile tumescence and rigidity testing using Rigiscan should take place for at least two nights. A functional erectile mechanism is indicated by an erectile event of $\geq 60\%$ rigidity recorded on the tip of the penis lasting for ≥ 10 min [8]. The intracavernous injection test provides limited information about vascular status; however, duplex ultrasound provides a simple (albeit intrusive) way of assessing vascular status. Further vascular investigation is unnecessary if duplex ultrasound is normal, as indicated by a peak systolic blood flow >30 cm/s and a resistance index >0.8 . If the ultrasound is abnormal, however, arteriography and dynamic infusion cavernosometry and cavernosography should be performed only in patients who are potential candidates for vascular reconstructive surgery [9].

A summary of recommendations for the diagnostic work-up of ED is presented in Table 3.

2.3. Treatment of erectile dysfunction

Only certain types of ED have the potential to be cured with specific treatments. For psychogenic ED, psychosexual therapy may be given either alone or with another

Table 2 – Specific diagnostic tests

Nocturnal penile tumescence and rigidity using Rigiscan Vascular studies <ul style="list-style-type: none"> • Intracavernous vasoactive drug injection • Duplex ultrasound of the cavernous arteries • Dynamic infusion cavernosometry and cavernosography • Internal pudendal arteriography Neurologic studies (eg, bulbocavernosus reflex latency, nerve-conduction studies) Endocrinologic studies Specialised psychodiagnostic evaluation
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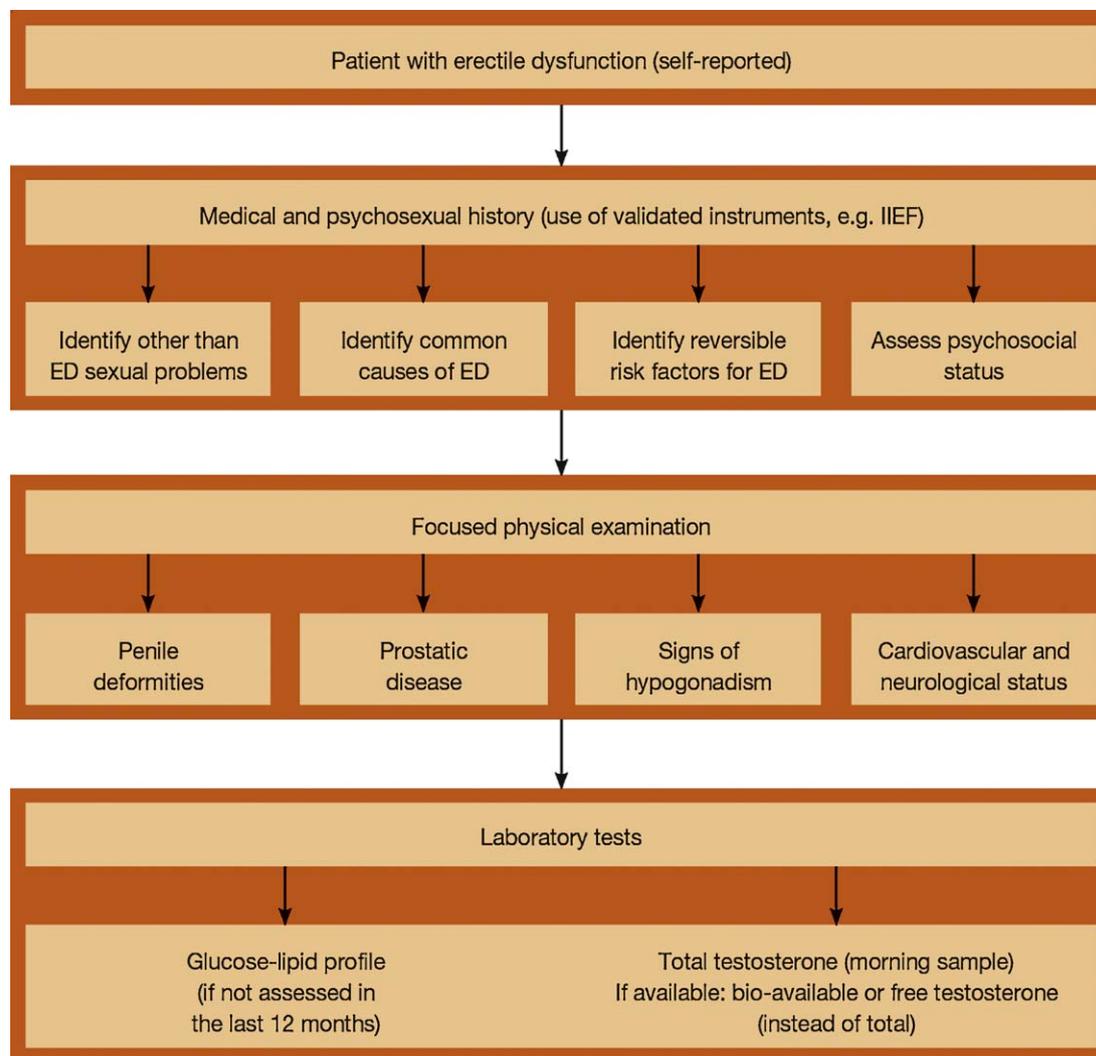


Fig. 1 – Basic diagnostic work-up in patients with erectile dysfunction.
ED = erectile dysfunction; IIEF = International Index of Erectile Function.

therapeutic approach, but this therapy takes time and has had variable results [10].

For posttraumatic arteriogenic ED in young patients, surgical penile revascularisation has a 60–70% long-term success rate [11].

For hormonal causes of ED, testosterone replacement therapy is effective but should be used only after other

endocrinologic causes for testicular failure have been excluded. Although some data suggest that testosterone administration does not cause prostate cancer, it is currently contraindicated in men with a history of prostate carcinoma or with symptoms of prostatism. Close follow-up is necessary, including digital rectal examination, serum prostate-specific antigen testing, and haematocrit assessment as

Table 3 – Recommendations for the diagnostic work-up of erectile dysfunction (ED)

Recommendations	LE	GR
Clinical use of a validated questionnaire related to ED may help assess all sexual function domains and the effect of a specific treatment modality.	3	B
Physical examination is needed in the initial assessment of ED to identify underlying medical conditions associated with ED.	4	B
Routine laboratory tests, including glucose-lipid profile and total testosterone, are required to identify and treat any reversible risk factors and modifiable lifestyle factors.	4	B
Specific diagnostic tests are indicated by only a few conditions.	4	B

LE = level of evidence; GR = grade of recommendation.

well as monitoring of the development of hepatic or prostatic disease [12].

Although there is some debate, the use of pro-erectile drugs following RP seems important in achieving erectile function following surgery. Several trials have shown higher rates of recovery of post-RP erectile function in patients receiving any phosphodiesterase type 5 inhibitor (PDE5-I) or intracavernosal injections (therapeutic or prophylactic). Rehabilitation should start as soon as possible following RP [5].

Most men with ED will be treated with options that are not cause specific [1]. This approach requires a structured treatment strategy that depends on efficacy, safety, invasiveness, and cost as well as patient and partner satisfaction. The choice of treatment options must consider the effects on patient and partner satisfaction and other QoL factors as well as efficacy and safety. A treatment algorithm for ED is given in Fig. 2.

A summary of recommendations for the treatment of ED is presented in Table 4.

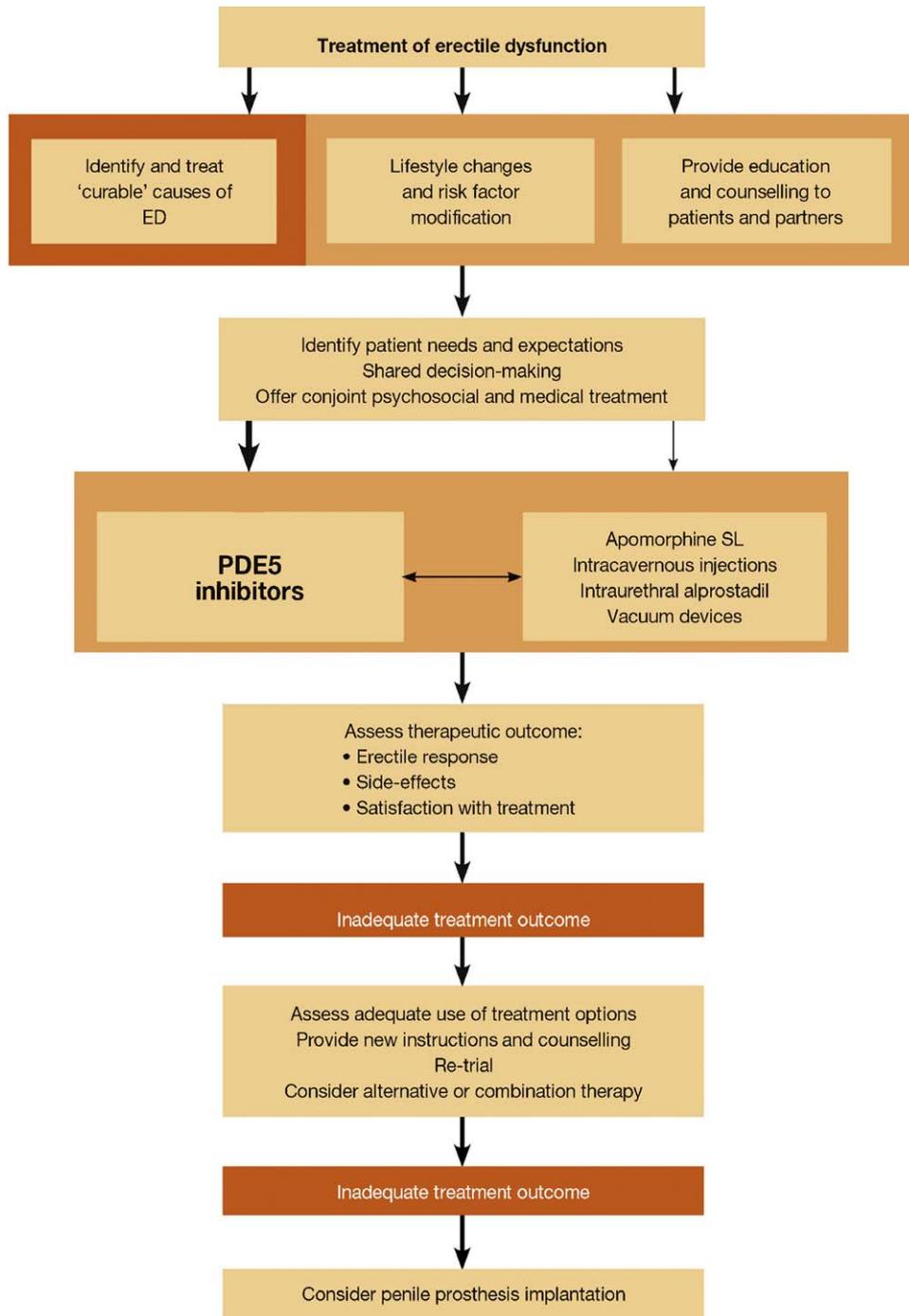


Fig. 2 – Treatment algorithm for erectile dysfunction (ED). PDE5 = phosphodiesterase type 5.

Table 4 – Recommendations for the treatment of erectile dysfunction (ED)

Recommendations	LE	GR
Lifestyle changes and risk factor modification must precede or accompany ED treatment.	1b	A
Pro-erectile treatments must be given at the earliest opportunity after radical prostatectomy.	1b	A
If a curable cause of ED is found, treat the cause first.	1b	B
PDE5-Is are first-line therapy.	1a	A
Daily administration of PDE5-Is may improve results and restore erectile function.	1b	A
Inadequate/incorrect prescription and poor patient education are the main causes of a lack of response to PDE5-Is.	3	B
Testosterone replacement restores efficacy in hypogonadic nonresponders to PDE5-Is.	1b	B
Apomorphine can be used in mild to moderate ED, psychogenic ED, or in patients with contraindications to PDE5-Is.	1b	B
A vacuum constriction device can be used in patients with stable relationship.	4	C
Intracavernous injection is second-line therapy.	1b	B
Penile implant is third-line therapy.	4	C

LE = level of evidence; GR = grade of recommendation; PDE5-I = phosphodiesterase type 5 inhibitor.

2.3.1. First-line therapy

2.3.1.1. Oral pharmacotherapy. Three potent selective PDE5-Is have been approved by the European Medicines Agency for the treatment of ED [13]. They are not initiators of erection and require sexual stimulation for an erection to occur. Efficacy is defined as rigidity sufficient for vaginal penetration.

Sildenafil (Viagra), launched in 1998, was the first PDE5-I available. It is effective 30–60 min from administration. A heavy fatty meal may reduce or prolong absorption. It is administered in 25-, 50-, and 100-mg doses. The recommended starting dose is 50 mg, which is adapted according to patient response and side-effects. Efficacy may last for up to 12 h. In premarketing studies, after 24 wk of treatment in a dose-response study, improved erections were reported by 56%, 77%, and 84% of men taking 25, 50, and 100 mg of sildenafil, respectively, compared with 25% of men taking placebo. The efficacy of sildenafil in almost every subgroup of patients with ED has been well established in pre- and postmarketing studies.

Tadalafil (Cialis) was licensed for ED in 2003. It is effective from 30 min after administration, but its peak efficacy occurs after about 2 h. Efficacy is maintained for up to 36 h. Its efficacy is not affected by food. It is administered in 10- and 20-mg doses. The recommended starting dose is 10 mg, which is adapted according to patient response and side-effects. In premarketing dose-response studies, improved erections were reported after 12 wk of treatment by 67% and 81% of men taking 10 mg and 20 mg of tadalafil, respectively, compared with 35% of men taking placebo. The results were confirmed in postmarketing studies. Tadalafil also improved erections in difficult-to-treat subgroups.

Vardenafil (Levitra) was licensed for ED in 2003. It is effective 30 min from administration. A fatty meal (>57% in fat) reduces its effect. It is administered in 5-, 10-, and 20-mg doses. The recommended starting dose is 10 mg, which is adapted according to the response and side-effects. In vitro, it is 10-fold more potent than sildenafil; however, this does not necessarily mean greater clinical efficacy. In premarketing dose-response studies, improved erections after 12 wk of treatment were reported by 66%, 76%, and 80% of men taking 5 mg, 10 mg, and 20 mg of vardenafil, respectively, compared with 30% of men taking placebo.

Efficacy was confirmed in postmarketing studies. Vardenafil also improved erections in difficult-to-treat subgroups.

2.3.1.1.1. Choice of or preference for different phosphodiesterase type 5 inhibitors. The choice of a PDE5-I depends on the frequency of intercourse (occasional use or regular therapy, three to four times weekly) and the patient's personal experience with the agent. Consideration should be given to which drug better fits the patient's premorbid sexual script with his partner to optimise response. Patients need to know whether a drug is short or long acting, its possible disadvantages, and how to use it.

2.3.1.1.2. On-demand or chronic use of phosphodiesterase type 5 inhibitors. Although PDE5-Is were initially introduced as on-demand treatment, in 2008, tadalafil was also approved for continuous, everyday use in 2.5- and 5-mg doses. Two studies [14,15] assessing daily use of 5- and 10-mg tadalafil for 12 wk and daily use of 2.5- and 5-mg tadalafil for 24 wk showed that daily dosing was well tolerated and significantly improved erectile function. Similar results have been found in diabetic patients [16]. These studies, however, lacked an on-demand treatment arm. Daily tadalafil provides an alternative to on-demand dosing for couples who prefer spontaneous rather than scheduled sexual activity or who have frequent sexual activity. Daily dosing overcomes the requirement for dosing and sexual activity to be temporally linked. Other studies have shown that chronic but not on-demand tadalafil treatment improved endothelial function, with sustained effects after its discontinuation. This finding was confirmed in another study of chronic sildenafil use in men with type 2 diabetes [17]. In contrast, a randomised clinical study found that once-daily dosing of vardenafil at 10 mg/d did not offer any sustainable effect after cessation of treatment compared with on-demand vardenafil in patients with mild to moderate ED [18].

2.3.1.1.3. Adverse events. Common adverse events include headache (10–16%), flushing (5–12%), dyspepsia (4–12%), nasal congestion (1–10%), and dizziness (2–3%) [13]. Sildenafil and vardenafil have been associated with visual abnormalities in <2% of patients, while tadalafil has been

associated with back pain/myalgia in 6% of patients. Adverse events are generally mild in nature and self-limited by continuous use, and the dropout rate due to adverse events is similar to that seen with placebo.

2.3.1.1.4. Cardiovascular safety. Clinical trials and postmarketing data of all PDE5-Is have demonstrated no increase in myocardial infarction rates [17]. No PDE5-I has adversely affected total exercise time or time to ischemia during exercise testing in men with stable angina. In fact, they may improve exercise tests.

Nitrates are totally contraindicated with all PDE5-Is due to unpredictable hypotension. The duration of interaction between organic nitrates and PDE5-Is varies according to the PDE5-I and nitrate. If a patient develops angina while using a PDE5-I, other antiangina agents may be used instead of nitroglycerine or until the appropriate time has passed (24 h for sildenafil or vardenafil and 48 h for tadalafil) [17].

In general, the adverse event profile of the PDE5-I is not worsened, even when the patient is on multiple antihypertensive agents.

2.3.1.1.5. α -Blocker interactions. The concomitant use of PDE5-Is with α -blockers may result in orthostatic hypotension under some conditions. The labelling for sildenafil currently includes a precaution advising that 50 or 100 mg (not 25 mg) of sildenafil should not be taken within 4 h of taking an α -blocker. The use of vardenafil with an α -blocker is not recommended; however, coadministration of vardenafil with tamsulosin is not associated with clinically significant hypotension. Tadalafil is contraindicated in patients taking α -blockers, except for tamsulosin [17]. Generally, the patient should be stable in his α -blocker therapy before using a PDE5-I. The long-acting α -blockers (doxazosin, terazosin) should be avoided in this concomitant use. Alfuzosin and tamsulosin are the preferred α -blockers.

2.3.1.1.6. Dosage adjustments. Lower doses of PDE5-Is may be required in patients taking ketoconazole, itraconazole, erythromycin, clarithromycin, and HIV protease inhibitors (ritonavir, saquinavir) [13]. Higher doses of PDE5-Is may be necessary in patients taking rifampicin, phenobarbital, phenytoin, or carbamazepine. Kidney or hepatic dysfunction may require dose adjustments. In patients with hypogonadism, androgen supplementation improves erectile response.

2.3.1.1.7. Management of nonresponders to phosphodiesterase type 5 inhibitors. The two main reasons that patients fail to respond to a PDE5-I are either incorrect drug use or inefficacy of the drug [13]. Physicians should check that the patient is using a licensed medication and that the medication has been properly prescribed and correctly used (ie, that there is adequate sexual stimulation and dosage and enough time between taking the medication and an attempt at intercourse).

Provided that a patient is using a PDE5-I appropriately, efficacy can be improved in several ways, including modification of associated risk factors, treatment of

associated hypogonadism, changing to another PDE5-I, or continuous use of a PDE5-I. Limited evidence supports using these interventions [19]. Additionally, an accumulating body of evidence supports the use of psychosexual educational counselling in combination with pharmaceutical treatments to further optimise response.

2.3.1.2. Vacuum constriction devices. A vacuum constriction device (VCD) applies negative pressure to the penis to draw venous blood into the penis, which is then retained by application of a visible constricting band at the base of the penis. This method seems more acceptable to older patients [20]. Efficacy, defined by an erection satisfactory for intercourse, is as high as 90%. Satisfaction rates range between 27% and 94% [20]. After 2 yr, only 50–64% of men continue to use VCDs. Most men who discontinue use of VCDs do so within 3 mo. The adverse effects associated with vacuum therapy are penile pain, numbness, and delayed ejaculation; these effects occur in <30% of patients.

2.3.2. Second-line therapy

Patients not responding to oral drugs may be offered intracavernous injections. Alprostadil (Caverject, Edex/Viridal) is the only drug approved for intracavernous treatment of ED. It is the most efficacious monotherapy for intracavernous treatment using 5- to 40- μ g doses [21]. Erection appears after 5–15 min and lasts according to the dose injected. The patient should be enrolled in an office-based training programme (one or two visits) to learn the correct injection process. Efficacy rates are about 70%, with reported sexual activity after 94% of injections and satisfaction rates of 87–93.5% in patients and 86–90.3% in partners. Dropout rates of 41–68% have been reported, with most dropouts occurring within the first 2–3 mo [22].

Complications of intracavernous alprostadil include penile pain (50% of patients after 11% of injections), prolonged erections (5%), priapism (1%), and fibrosis (2%) [13]. Drug combinations (mainly the three-drug combination of alprostadil plus papaverine plus phentolamine) may increase efficacy by up to 90%. Fibrosis was found to be more common (5–10%) if papaverine was used (depending on total dose). After 4 h of erection, patients are advised to consult their doctors to avoid any damage to the intracavernous tissue, as this will result in permanent impotence [21]. A 19-gauge needle is used to aspirate blood and decrease the intracavernous pressure. This simple technique is usually sufficient to make the penis flaccid. If the penis then becomes rigid again, phenylephrine should be injected into the intracavernous muscle, starting at 200 μ g every 5 min and increasing to 500 μ g if necessary. If this problem occurs, the dosage of the next intracavernosal injection is usually reduced.

Prostaglandin E1 may be administered intraurethraly as a semisolid pellet (125–1000 μ g) [23]. A band placed at the base of the penis improves the resulting rigidity. The clinical success rate is lower than with intracavernosal injections, but about 70% of patients are satisfied or very satisfied with treatment. Side-effects include local

pain (29–41%), dizziness (1.9–14%), and urethral bleeding (5%).

2.3.3. Third-line therapy (penile prostheses)

Surgical implantation of a penile prosthesis may be considered in patients who fail pharmacotherapy or who want a permanent solution. Prostheses are either malleable (semirigid) or inflatable (two or three piece). Most patients prefer the three-piece inflatable devices because erections are more “natural,” but these implants are much more expensive. Satisfaction rates of 70–87% are reported from patients after appropriate consultation [24].

The two main complications of penile prosthesis implantation are mechanical failure (<5% after 5-yr follow-up with currently available three-piece prostheses) and infection [25]. With antibiotic prophylaxis, the infection rate is 2–3% and may be further reduced by using an antibiotic-impregnated or hydrophilic-coated implant. Infection requires removing the prosthesis, antibiotic administration, and reimplantation after 6–12 mo; however, an 82% success rate has been achieved using salvage therapy, involving removal and reimplantation immediately following copious irrigation of the corpora with a multiantibiotic solution [24]. Although diabetes is considered to be a main risk factor for infection, this association is not supported by current data.

3. Premature ejaculation

3.1. Definition, epidemiology, and risk factors

There has been difficulty in gaining consensus about how best to define PE. The Second International Consultation on Sexual and Erectile Dysfunction has defined PE as “ejaculation with minimal stimulation and earlier than desired, before or soon after penetration, which causes bother or distress, and over which the sufferer has little or no voluntary control” [26]. The International Society for Sexual Medicine has adopted a completely new definition, and the first evidence-based definition, for *lifelong* PE: “Premature ejaculation is a male sexual dysfunction characterised by ejaculation which always or nearly always occurs prior to or within about one minute of vaginal penetration; and inability to delay ejaculation on all or nearly all vaginal penetrations; and negative personal consequences, such as distress, bother, frustration and/or the avoidance of sexual intimacy” [27]. All definitions have taken into account the time to ejaculation, the inability to control or delay ejaculation, and the negative consequences (bother/distress) from PE.

PE may be classified as *lifelong* (primary) or *acquired* (secondary) [28]. Lifelong PE is characterised by onset from the first sexual experience and remains a problem throughout life. Ejaculation occurs too quickly, either before vaginal penetration or <1–2 min afterwards. Acquired PE is characterised by a gradual or sudden onset, with ejaculation being normal before onset of the problem. Time to ejaculation is short but not usually as fast as in lifelong PE [27].

PE is a common male sexual dysfunction, with prevalence rates of 20–30% [29,30]. Limited data suggest that the prevalence of lifelong PE, defined as intravaginal ejaculatory

latency time (IELT) <1–2 min, is about 2–5% [31]. The aetiology of PE is unknown, with little data to support suggested biological and psychological hypotheses, including anxiety, penile hypersensitivity, and serotonin receptor dysfunction [26]. In contrast to ED, the prevalence of PE is not affected by age [29,30]. Risk factors for PE are generally unknown. PE has a detrimental effect on self-confidence and on relationship with the partner. It may cause mental distress, anxiety, embarrassment, and depression; however, most men with PE do not seek help [30].

3.2. Diagnostic work-up

Diagnosis of PE is based on the patient's medical and sexual history [32]. The history should classify PE as lifelong or acquired and determine whether PE is situational (under specific circumstances or with a specific partner) or consistent. Special attention should be given to the length of time of ejaculation, degree of sexual stimulus, impact on sexual activity and QoL, and drug use or abuse. It is also important to distinguish PE from ED.

The use of IELT alone is not sufficient to define PE because there is significant overlap between men with and without PE [33]. In everyday clinical practice, self-estimated IELT is sufficient. Diagnosis should be multidimensional and should assess IELT, perceived control, distress, and interpersonal difficulty due to ejaculatory dysfunction. The need to assess PE objectively has produced several questionnaires, such as the Premature Ejaculation Diagnostic Tool (PEDT) [34]. Other questionnaires used to characterise PE and determine treatment effects include the Premature Ejaculation Profile (PEP) [31], the Index of Premature Ejaculation (IPE) [35], and the Male Sexual Health Questionnaire Ejaculatory Dysfunction (MSHQ-EJD) [36]. Currently, their role is optional in everyday clinical practice.

Physical examination includes a brief examination of the vascular, endocrine, and neurologic systems to identify underlying medical conditions associated with PE or other sexual dysfunctions, such as chronic illness, endocrinopathy, autonomic neuropathy, Peyronie's disease, urethritis, or prostatitis. Laboratory or physiologic testing should be directed by specific findings from history or physical examination and is not routinely recommended [32].

A summary of recommendations for the diagnosis of PE is presented in Table 5.

3.3. Treatment of premature ejaculation

In many relationships, PE causes few if any problems [28]. In such cases, treatment should be limited to psychosexual counselling. Before beginning treatment, it is essential to discuss patient expectations thoroughly. ED or other sexual dysfunction or genitourinary infection (eg, prostatitis) should be treated first or at the same time as PE.

Various behavioural techniques have demonstrated benefit in treating PE. In lifelong PE, behavioural techniques are not recommended for first-line treatment [27]. They are time intensive, require the support of a partner, and can be difficult to do.

Table 5 – Recommendations for diagnosis of premature ejaculation (PE)

Recommendations	LE	GR
Diagnosis and classification of PE is based on medical and sexual history. It should be multidimensional and should assess IELT, perceived control, distress, and interpersonal difficulty due to the ejaculatory dysfunction.	1a	A
Clinical use of self-estimated IELT is adequate. Stopwatch-measured IELT is necessary in clinical trials.	2a	B
Patient-reported outcomes have the potential to identify men with PE. Further research is needed before patient-reported outcomes can be recommended for clinical use.	3	C
Physical examination may be necessary in initial assessment of PE to identify underlying medical conditions associated with PE or other sexual dysfunctions, particularly ED.	3	C
Routine laboratory or neurophysiologic tests are not recommended. Additional tests should be directed by specific findings from history or physical examination.	3	C

ED = erectile dysfunction; LE = level of evidence; GR = grade of recommendation; IELT = intravaginal ejaculatory latency time.

Pharmacotherapy is the basis of treatment in lifelong PE, but all medical treatments (except dapoxetine in some countries) are off-label indications. Only chronic selective serotonin reuptake inhibitors (SSRIs) and on-demand topical anaesthetic agents have consistently shown efficacy in PE.

A summary of recommendations for the treatment of PE is presented in Table 6 and a treatment algorithm is given in Fig. 3.

3.3.1. Psychological and behavioural strategies

Behavioural strategies mainly include the “stop-start” programme developed by Semans and its modification, the “squeeze” technique, proposed by Masters and Johnson (several modifications exist) [28]. Masturbation before anticipation of sexual intercourse is another technique used by many younger men.

Success rates of 50–60% have been reported in the short term [37]. A double-blind, randomised, crossover study showed that pharmacologic treatment resulted in greater IELT prolongation than behavioural therapy [38]. Furthermore, clinical experience suggests that improvements achieved with these techniques are generally not maintained in the long term [39]. However, there is emerging evidence that these behavioural psychosexual techniques can be combined with the pharmaceutical treatments described below to extend and optimise treatment effects [40].

3.3.2. Topical anaesthetic agents

Lidocaine-prilocaine cream (5%) is applied 20–30 min prior to intercourse. Prolonged application of a topical anaesthetic agent (30–45 min) may result in loss of erection due to numbness of the penis. A condom is required to avoid

diffusion of the topical anaesthetic agent into the vaginal wall, causing numbness in the partner. In two randomised clinical trials, lidocaine-prilocaine cream significantly increased the stopwatch-measured IELT compared to placebo [41,42]. No significant side-effects have been reported. An aerosol formulation of lidocaine 7.5 mg plus prilocaine 2.5 mg (Topical Eutectic Mixture for Premature Ejaculation [TEMPE]) is under evaluation and has shown similar results [43]. SS-cream is a topical anaesthetic agent made from the extracts of nine herbs. It is applied to the glans penis 1 h before intercourse and is washed off immediately prior to coitus. In a randomised clinical trial, application of 0.2 g of SS-cream significantly improved IELT and satisfaction compared with the placebo group [44]. Mild local burning and mild pain were reported by 18.5% of patients. No adverse effects on sexual function or on the partner were observed, and no systemic side-effects were observed.

3.3.3. Selective serotonin reuptake inhibitors

Daily SSRIs are the first choice of treatment in PE but are used off label. Commonly used SSRIs include paroxetine (20–40 mg/d), sertraline (25–200 mg/d), and fluoxetine (10–60 mg/d). Based on a systematic review and meta-analysis, SSRIs were expected to increase the geometric mean IELT by 2.6-fold to 13.2-fold [45]. Paroxetine was found to be superior to fluoxetine, clomipramine, and sertraline. Ejaculation delay may start a few days after drug intake, but it is more evident after 1–2 wk and may be maintained for several years. Common side-effects of SSRIs include fatigue, drowsiness, yawning, nausea, vomiting, dry mouth, diarrhoea, and perspiration; they are usually mild

Table 6 – Recommendations for premature ejaculation (PE) treatment

Recommendations	LE	GR
ED, other sexual dysfunction, or genitourinary infection (eg, prostatitis) should be treated first.	2a	B
Behavioural techniques can benefit PE; however, they are time intensive, require the support of a partner, and can be difficult to do.	3	C
Pharmacotherapy is the basis of treatment in lifelong PE	1a	A
Daily SSRIs are first-line, off-label, pharmacologic treatment for PE. The pharmacokinetic profiles of currently available SSRIs are not amenable to on-demand dosing.	1a	A
Dapoxetine is a short-acting SSRI that has been approved in Europe for the on-demand treatment of PE.	1a	A
Topical anaesthetic agents provide viable alternatives to SSRIs (off label).	1b	A
Recurrence is likely after treatment cessation.	1b	A
Behavioural therapy may augment pharmacotherapy to enhance prevention of relapse.	3	C

LE = level of evidence; GR = grade of recommendation; ED = erectile dysfunction; SSRIs = selective serotonin reuptake inhibitors.

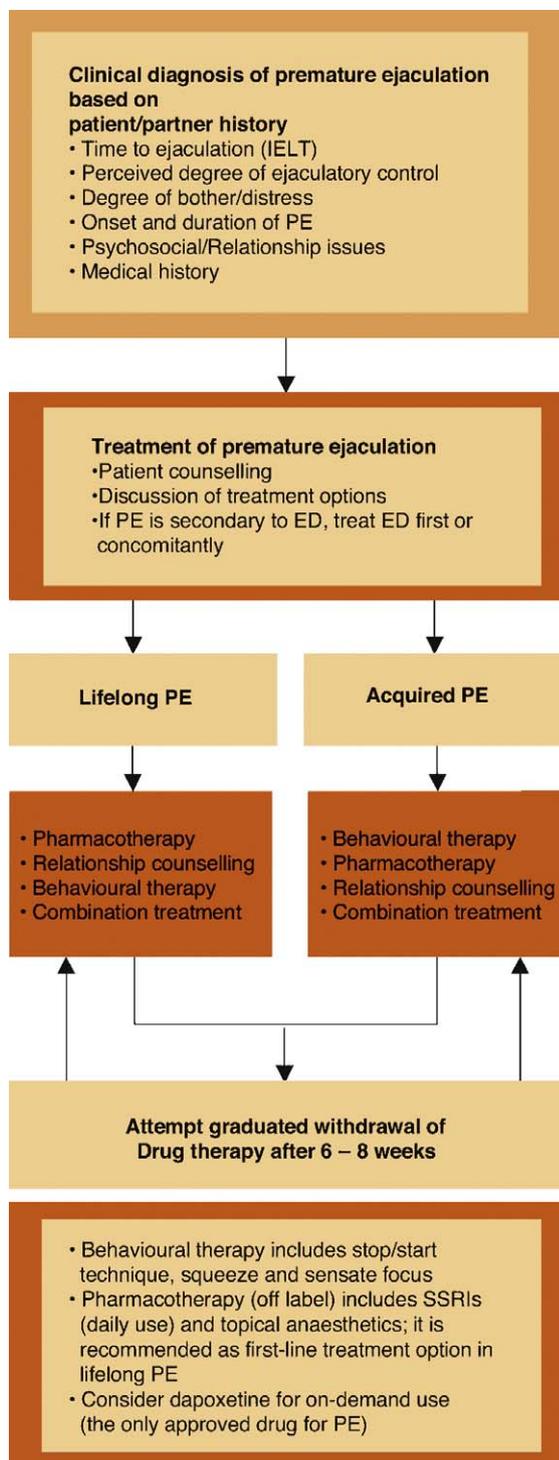


Fig. 3 – Management of premature ejaculation (PE) provided separately. IELT = intravaginal ejaculatory latency time; ED = erectile dysfunction; SSRIs = selective serotonin reuptake inhibitors.

and gradually improve after 2–3 wk. Decreased libido, anorgasmia, anejaculation, and ED have been also reported. On-demand treatment is inferior to daily dosing but may be combined with an initial trial of daily treatment or concomitant low-dose daily treatment to reduce adverse effects [46].

Dapoxetine is a potent SSRI that has been specially designed as an on-demand oral treatment for PE. An integrated analysis of two randomised clinical trials reported that dapoxetine, 30 and 60 mg, improved IELT significantly compared with placebo [47]. Improved ejaculation control was reported by 51% and 58% of patients in the 30-mg and 60-mg dosage groups, respectively. Both dapoxetine doses were effective on the first dose. In another randomised clinical trial, the mean average IELT increased from 0.9 min at baseline (all groups) to 1.9 min, 3.2 min, and 3.5 min with placebo and dapoxetine 30 mg and dapoxetine 60 mg, respectively [48]. The geometric mean IELT increased from 0.7 min at baseline to 1.1 min, 1.8 min, and 2.3 min, respectively ($p < 0.001$). The most common adverse events were nausea (16.5–30.6%), dizziness (7.7–13.4%), diarrhoea (3.9–11.3%), and headache (6.4–13.6%). However, these adverse events led to discontinuation in only 1.3%, 3.9%, and 8.2% of subjects with placebo, dapoxetine 30 mg, and dapoxetine 60 mg, respectively. Dapoxetine has been approved (December 2008) for the treatment of PE in seven European countries (Sweden, Austria, Finland, Germany, Spain, Italy, and Portugal).

3.3.4. Phosphodiesterase type 5 inhibitors

Several recent studies have supported the therapeutic role of PDE5-Is in PE; however, only one randomised clinical trial compares sildenafil to placebo [49]. Although IELT was not significantly improved, sildenafil increased confidence, the perception of ejaculatory control, and overall sexual satisfaction as well as reduced anxiety and decreased the refractory time to achieve a second erection after ejaculation.

In another randomised clinical trial, lidocaine-prilocaine monotherapy showed similar efficacy to that of combination with sildenafil, while the efficacy of sildenafil alone was similar to placebo [50]. In another study, sildenafil significantly improved IELT and satisfaction and reduced overall anxiety compared with several SSRIs and the “pause-squeeze” technique [38]. Several open-label studies found that sildenafil combined with an SSRI is superior to SSRI monotherapy.

4. Conclusions

ED and PE are the two most common male sexual dysfunctions. PDE5-Is are the first-line treatment option for ED, whereas SSRIs represent the most efficacious treatment option for PE. Physicians should identify patients' needs and expectations and adapt treatment accordingly. This summary of the EAU guidelines provides the framework for diagnosis and treatment of ED and PE in clinical practice.

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Study concept and design: Hatzimouratidis, Amar, Eardley, Giuliano, Hatzichristou, Montorsi, Vardi, Wespes.

Acquisition of data: Hatzimouratidis, Amar, Eardley, Giuliano, Hatzichristou, Montorsi, Vardi, Wespes.

Analysis and interpretation of data: Hatzimouratidis, Amar, Eardley, Giuliano, Hatzichristou, Montorsi, Vardi, Wespes.

Drafting of the manuscript: Hatzimouratidis.

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