

GUIDELINES ON MALE SEXUAL DYSFUNCTION: Erectile Dysfunction and Premature Ejaculation

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Definition, Epidemiology and Risk factors

Erectile dysfunction (ED) is the persistent inability to attain and maintain an erection sufficient to permit satisfactory sexual performance. Although ED is a benign disorder, it affects physical and psychosocial health and has a significant impact on the quality of life (QoL) of sufferers and their partners and families. A recent review of epidemiological studies of ED suggests that approximately 5-20% of men have moderate to severe ED. The difference in reported incidences is probably due to differences in methodology and in the ages and socio-economic status of the study populations.

Erectile dysfunction shares common risk factors with cardiovascular disease including lack of exercise, obesity, smoking, hypercholesterolaemia, and the metabolic syndrome. The risk of ED may be reduced by modifying these risk factors,

particularly taking exercise or losing weight. 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. About 25-75% of men undergoing RP experience post-operative ED. Patients being considered for nerve-sparing radical prostatectomy (NSRP) should ideally be potent and the cavernosal nerves must be preserved to ensure erectile function recovery after RP.

Diagnosis and work-up

Basic work-up

The basic work-up (minimal diagnostic evaluation) outlined in Figure 1 must be performed in every patient with ED.

Due to the potential cardiac risks associated with sexual activity, the 2nd Princeton Consensus Conference stratified patients with erectile ED wanting to initiate, or resume, sexual activity into three risk categories (Fig. 2). The low-risk group included asymptomatic patients with less 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 dysfunction or congestive heart failure (NYHA class I), post-successful coronary revascularisation, controlled hypertension, and mild valvular disease. All other patients were included in an intermediate- or high-risk category and required a cardiology consultation.

Specific examinations and tests

Although most patients with ED can be managed within the sexual care setting, some circumstances require specific diagnostic testing:

- 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 (e.g. 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 medico-legal reasons (e.g. penile prosthesis implant, sexual abuse).

Specific diagnostic tests include:

- nocturnal penile tumescence and rigidity (NTPR) using Rigiscan®;
- vascular studies:
 - intracavernous vasoactive drug injection;
 - duplex ultrasound of the cavernous arteries;
 - dynamic infusion cavernosometry/cavernosography (DICC);
 - internal pudendal arteriography;
- neurological studies (e.g. bulbocavernosus reflex latency, nerve conduction studies);

- endocrinological studies;
- specialised psychodiagnostic evaluation.

The NPTR should take place for at least two nights. A functional erectile mechanism is indicated by an erectile event of at least 60% rigidity recorded on the tip of the penis, lasting for 10 min or longer.

The intracavernous injection test provides limited information about vascular status. However, Duplex ultrasound provides a simple 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 ultrasound is abnormal, however, arteriography and DICC should be performed only in patients who are potential candidates for vascular reconstructive surgery.

Recommendations for the Diagnostic Work-up		
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 4 B
only a few conditions.

LE = level of evidence; GR = grade of recommendation; ED = erectile dysfunction.

Figure 1. Minimal diagnostic evaluation (basic work-up) in patients with erectile dysfunction

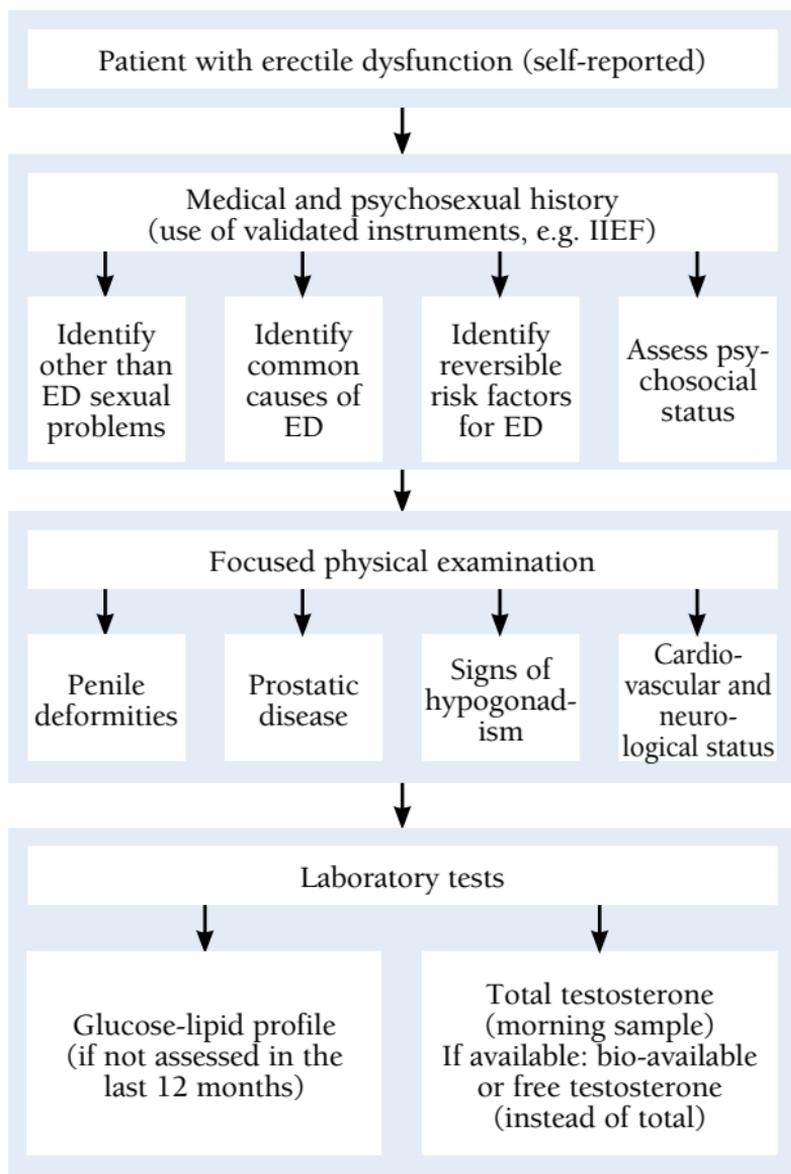
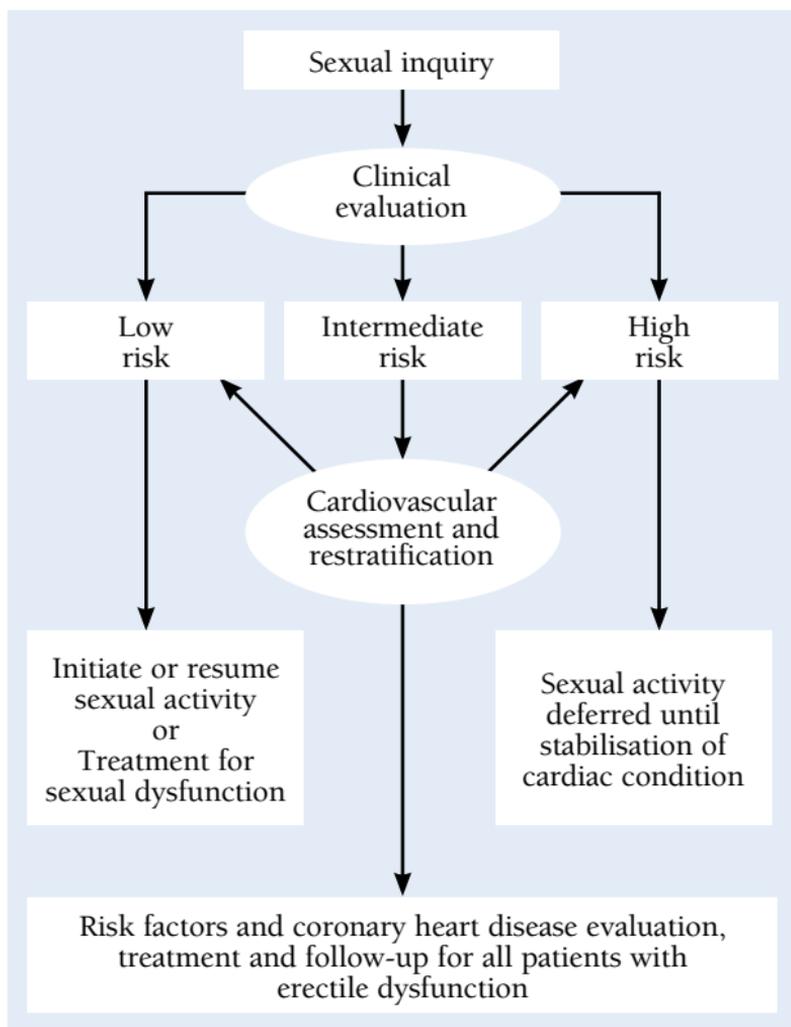


Figure 2. Treatment algorithm according to cardiac risk (2nd Princeton Consensus Conference)



Treatment of ED

Only certain types of ED have the potential to be cured with specific treatments:

- Psychogenic ED: psychosexual therapy may be given either alone or with another therapeutic approach, but takes time and has had variable results.
- Post-traumatic arteriogenic ED in young patients: surgical penile revascularisation has a 60-70% long-term success rate.
- Hormonal causes of ED: testosterone replacement therapy is effective, but should only be used after other endocrinological causes for testicular failure have been excluded. Currently, it is contraindicated in men with a history of prostate carcinoma or with symptoms of prostatism. Close follow-up is necessary, including digital rectal examination (DRE), serum prostate serum antigen (PSA) and haematocrit assessment, as well as monitoring the development of hepatic or prostatic disease.

The use of pro-erectile drugs following RP is very important in achieving erectile function after surgery. Several trials have shown higher rates of recovery of post-RP erectile function in patients receiving any phosphodiesterase type 5 (PDE5) inhibitor or intracavernosal injections (therapeutic or prophyllactic). Rehabilitation should start as soon as possible following RP.

Most men with ED will be treated with treatment options that are not cause-specific. This approach requires a structured treatment strategy that depends on efficacy, safety, invasiveness, and cost, as well as patient and partner satis-

faction. 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 Figure 3.

First-line Therapy

Oral pharmacotherapy

Three potent selective PDE5 inhibitors have been approved by the European Medicines Agency (EMA) for the treatment of ED. 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™)

Sildenafil, launched in 1998, was the first PDE5 inhibitor available. It is effective after 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 and adapted according to patient response and side-effects. Efficacy may last for up to 12 h.

In pre-marketing studies, after 24 weeks 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.

Tadalafil (Cialis™)

Tadalafil 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 and is adapted according to patient response and side-effects.

In pre-marketing, dose-response studies, improved erections were reported after 12 weeks of treatment by 67% and 81% of men taking 10 mg and 20 mg of tadalafil, respectively, compared to 35% of men taking placebo. The results were confirmed in post-marketing studies. Tadalafil also improved erections in difficult-to-treat subgroups.

Vardenafil (Levitra™)

Vardenafil was licensed for ED in 2003. It is effective after 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 and 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 pre-marketing, dose-response studies, improved erections after 12 weeks of treatment were reported by 66%, 76% and 80% of men taking 5 mg, 10 mg and 20 mg of vardenafil, respectively, compared to 30% of men taking placebo. Efficacy was confirmed in post-marketing studies. Vardenafil also improved erections in difficult-to-treat subgroups.

Choice of, or preference for, different PDE5 inhibitors

The choice of a PDE5 inhibitor depends on the frequency of intercourse (occasional use or regular therapy, 3-4 times

weekly) and the patient's personal experience of the agent. Patients need to know whether a drug is short- or long-acting, possible disadvantages, and how to use it.

On-demand or chronic use of PDE5 inhibitors

Although PDE5 inhibitors were introduced as on-demand treatment, in 2008, tadalafil was also approved for continuous, everyday use in 2.5 and 5 mg doses. Two studies assessing daily use of 5 and 10 mg tadalafil for 12 weeks and daily use of 2.5 and 5 mg tadalafil for 24 weeks, showed that daily dosing was well tolerated and significantly improved erectile function. Similar results have been found in diabetic patients. However, these studies lacked an on-demand treatment arm. Daily tadalafil provides an alternative to on-demand dosing for couples that 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 effect after its discontinuation. This was confirmed in another study of chronic sildenafil in men with type 2 diabetes. In contrast, another RCT found that once-daily dosing of vardenafil, 10 mg/day, did not offer any sustainable effect after cessation of treatment compared to on-demand vardenafil in patients with mild-to-moderate ED.

Adverse events

Common adverse events include headache, flushing, dizziness, dyspepsia, and nasal congestion. Sildenafil and vardenafil

fil have been associated with visual abnormalities in less than 2% of patients, while tadalafil has been associated with back pain/myalgia in 6% of patients. However, adverse events are generally mild in nature, self-limited by continuous use, and the dropout rate due to adverse events is similar to placebo.

Cardiovascular safety

Clinical trials and post-marketing data of all PDE5 inhibitors have demonstrated no increase in myocardial infarction rates. No PDE5 inhibitor has adversely affected total exercise time or time to ischaemia during exercise testing in men with stable angina. In fact, they may improve exercise tests.

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

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

Alpha-blocker interactions

All PDE5 inhibitors appear to interact with alpha-blockers, which under some conditions may result in orthostatic hypotension. 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 alpha-blocker. The use of vardenafil with an alpha-blocker is not recommended. However, co-administration of vardenafil with tamsulosin is not associated with clinically significant hypotension. Tadalafil is contraindicated in patients taking alpha-blockers, except for tamsulosin.

Dosage adjustments

Lower doses of PDE5 inhibitors may be required in patients taking ketoconazole, itraconazole, erythromycin, clarithromycin, and HIV protease inhibitors (ritonavir, saquinavir). Higher doses of PDE5 inhibitors 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.

Management of non-responders to PDE5 inhibitors

The two main reasons why patients fail to respond to a PDE5 inhibitor are either incorrect drug use or inefficacy of the drug. Physicians should check that the patient is using a licensed medication and that the medication has been properly prescribed and correctly used (adequate sexual stimulation, dosage, and enough time between taking the medication and attempt at intercourse).

Provided a patient is using a PDE5 inhibitor appropriately, there are several ways of improving efficacy. They include modification of associated risk factors, treatment of associated hypogonadism, changing to another PDE5 inhibitor, or continuous use of a PDE5 inhibitor. There is limited evi-

dence to support using these interventions.

Vacuum constriction devices

A vacuum constriction device (VCD) applies a 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 is more acceptable to older patients. Efficacy, defined by an erection satisfactory for intercourse, is as high as 90%. Satisfaction rates range between 27% and 94%. Long-term use of VCDs decreases to 50-64% after 2 years. Most men who discontinue use of VCDs do so within 3 months. The adverse effects associated with vacuum therapy are penile pain, numbness, and delayed ejaculation and occur in less than 30% of patients.

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 5-40 µg doses. 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 described, with most dropouts occurring within the first 2-3 months. Complications of intracavernous alprostadil include penile pain (50% of patients after 11% of

injections), prolonged erections (5%), priapism (1%), and fibrosis (2%). Drug combinations (mainly the three-drug combination of alprostadil + papaverine + 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 doctor to avoid any damage to the intracavernous muscle, as this will result in permanent impotence. 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. However, if the penis then becomes rigid again, phenylephrine should be injected into the intracavernous muscle, starting at 200 µg every 5 min and increasing to 500 µg if necessary. If this problem occurs, the dosage of the next intracavernosal injection is usually reduced.

Prostaglandin E1 may be administered intraurethraly as a semi-solid pellet (125-1000 µg). 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%).

Third-line Therapy (Penile Prosthesis)

Surgical implantation of a penile prosthesis may be considered in patients who fail pharmacotherapy or who want a permanent solution. Prosthesis are either malleable (semi-rigid) or inflatable (two- or three-piece). Most patients pre-

for 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.

The two main complications of penile prosthesis implantation are mechanical failure (less than 5% after 5-year follow-up with currently available three-piece prostheses) and infection. 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 re-implantation after 6-12 months. However, 82% success rates have been achieved using salvage therapy, involving removal and re-implantation immediately following copious irrigation of the corpora with a multi-antibiotic solution. Although diabetes is considered to be a main risk factor for infection, this is not supported by current data.

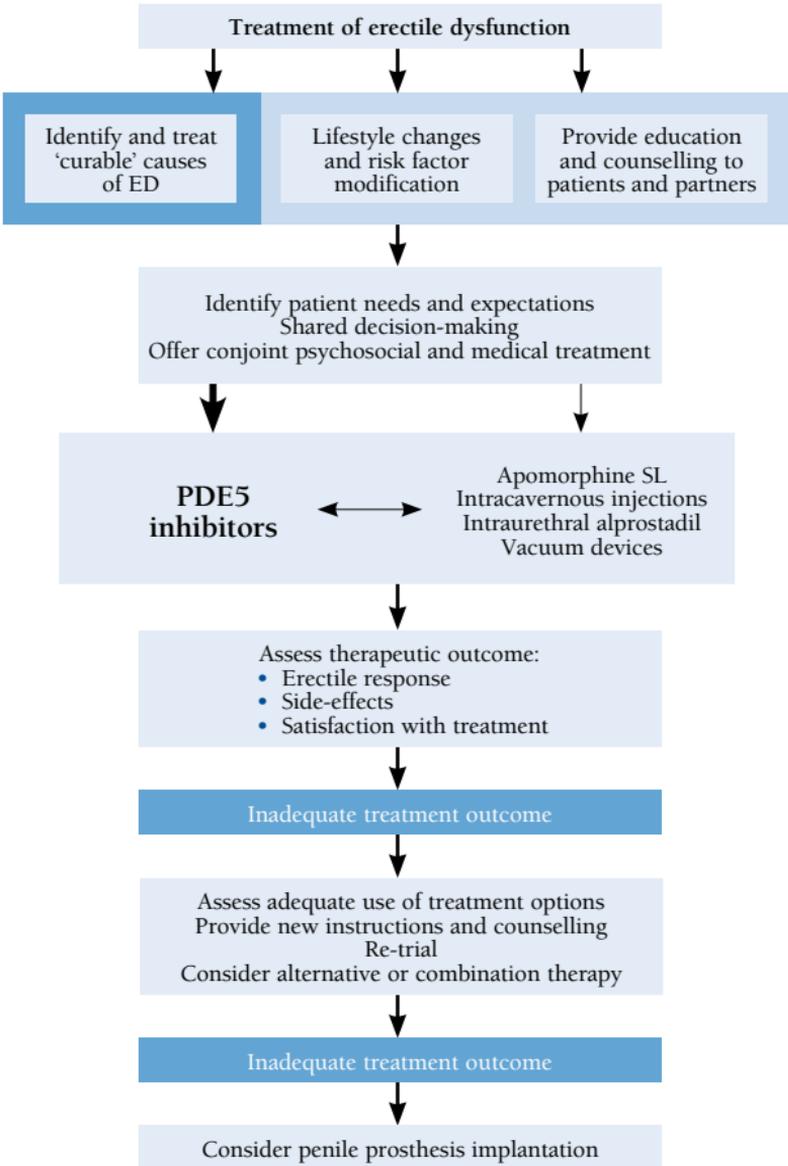
Recommendations for ED Treatment

Recommendations	LE	GR
Lifestyle changes and risk factor modification must precede or accompany ED treatment.	1b	A
Pro-erectile treatments have to 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 inhibitors are first-line therapy.	1a	A
Daily administration of PDE5 inhibitors 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 inhibitors.	3	B
Testosterone replacement restores efficacy in hypogonadic non-responders to PDE5 inhibitors.	1b	B
Apomorphine can be used in mild-to-moderate ED, psychogenic ED, or in patients with contraindications to PDE5 inhibitors.	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

PDE5 inhibitor = phosphodiesterase type 5 inhibitor.

Figure 3. Treatment algorithm for ED



PDE5 inhibitor = phosphodiesterase type 5 inhibitor.

PREMATURE EJACULATION

Definition, Epidemiology and Risk Factors

There has been difficulty in gaining consensus on how best to define premature ejaculation (PE). The two most widely accepted definitions are:

- 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’*.
- The International Society for Sexual Medicine (ISSM) has adopted a completely new definition of lifelong PE, which is the first evidence-based definition: *‘Premature ejaculation is a male sexual dysfunction characterized 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’*.

Thus, PE may be classified as ‘lifelong’ (primary) or ‘acquired’ (secondary). Lifelong PE is characterised by onset from the first sexual experience and remains a problem during life. Ejaculation occurs too fast 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.

Premature ejaculation is the most common male sexual dysfunction, with prevalence rates of 20-30%. Limited data sug-

gest that the prevalence of lifelong PE, defined as intravaginal ejaculatory latency time (IELT) < 1-2 min, is about 2-5%.

The aetiology of PE is unknown, with little data to support suggested biological and psychological hypotheses, including anxiety, penile hypersensitivity, and serotonin receptor dysfunction. In contrast to erectile dysfunction, the prevalence of PE is not affected by age. Risk factors for PE are generally unknown.

Premature ejaculation has a detrimental effect on self-confidence and relationship with the partner. It may cause mental distress, anxiety, embarrassment, and depression. However, most men with PE do not seek help.

Diagnostic Work-up

Diagnosis of PE is based on the patient's medical and sexual history. 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, as there is significant overlap between men with and without PE. In everyday clinical practice, self-estimated IELT is sufficient. The need to assess PE objectively has produced several questionnaires, such as the Premature Ejaculation Diagnostic Tool (PEDT). Other questionnaires used to characterise PE and determine treatment effects include the Premature

Ejaculation Profile (PEP), the Index of Premature Ejaculation (IPE), and the Male Sexual Health Questionnaire Ejaculatory Dysfunction (MSHQ-EjD). Currently, their role is optional in everyday clinical practice.

Physical examination includes a brief examination of the vascular, endocrine and neurological 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 physiological testing should be directed by specific findings from history or physical examination and is not routinely recommended.

Recommendations for diagnosis of PE		
Recommendations	LE	GR
Diagnosis and classification of PE is based on medical and sexual history.		
It should be multidimensional and 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 they 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 neurophysiological tests are not recommended. Additional tests should be directed by specific findings from history or physical examination.	3	C

IELT = intravaginal ejaculatory latency time.

Treatment of PE

In many relationships, PE causes few if any problems. In such cases, treatment should be limited to psychosexual counselling. Before beginning treatment, it is essential to discuss patient expectations thoroughly. Erectile dysfunction or other sexual dysfunction or genitourinary infection (e.g. 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. They are time-intensive, require the support of a partner, and can be difficult to do. Pharmacotherapy is the basis of treatment in lifelong PE but all medical treatments are off-label indications. Only chronic selective serotonin reuptake inhibitors (SSRIs) and on-demand topical anaesthetic agents have consistently shown efficacy in PE. A treatment algorithm for PE is presented in Figure 4.

Psychological/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). Masturbation before anticipation of sexual intercourse is another technique used by many younger men.

Overall, success rates of 50-60% have been reported short term. A double blind, randomised, crossover study showed that pharmacological treatment resulted in greater IELT prolongation than behavioural therapy. Furthermore, clinical experience suggests that improvements achieved with these techniques are generally not maintained long term.

Topical anaesthetic agents

Lidocaine-prilocaine cream (5%) is applied for 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 RCTs, lidocaine-prilocaine cream significantly increased the stopwatch-measured IELT compared to placebo. 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.

SS-cream is a topical anaesthetic agent made from the extracts of nine herbs. It is applied to the glans penis 1 h

before and washed off immediately prior to coitus. In a RCT, application of 0.2 g SS-cream significantly improved IELT and satisfaction compared to the placebo group. Mild local burning and mild pain were reported by 18.5% of patients. No adverse effects on sexual function or partner or systemic side-effects were observed.

Selective serotonin reuptake inhibitors

Daily selective serotonin reuptake inhibitors (SSRIs) are the first choice of treatment in PE, but are used off-label for PE. Commonly used SSRIs include paroxetine (20-40 mg/day), sertraline (25-200 mg/day), and fluoxetine (10-60 mg).

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. 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 weeks 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 and gradually improve after 2-3 weeks. 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.

Dapoxetine is a potent SSRI, which has been specially designed as an on-demand oral treatment for PE. An integrated analysis of two RCTs reported that dapoxetine, 30

and 60 mg, improved IELT significantly compared to placebo. 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. Common adverse events were nausea, diarrhoea, headache, and dizziness. The proportions of men with a two-category or greater increase in control and satisfaction with sexual intercourse (from a 5-point scale, 'very poor' to 'very good') with dapoxetine 30 and 60 mg were 36.3% and 44.5%, respectively (vs 15% with placebo). In another RCT, dapoxetine reduced the personal distress and interpersonal difficulty associated with PE. Dapoxetine has been approved (December 2008) for the on-demand treatment of PE in seven European countries (Sweden, Austria, Finland, Germany, Spain, Italy, and Portugal). This is currently the first and only drug approved for such an indication.

Phosphodiesterase type 5 inhibitors

Several recent studies have supported the therapeutic role of PDE5 inhibitors in PE. However, there is only one RCT comparing sildenafil to placebo. Although IELT was not significantly improved, sildenafil increased confidence, the perception of ejaculatory control and overall sexual satisfaction, reduced anxiety, and decreased the refractory time to achieve a second erection after ejaculation.

In two other RCTs, lidocaine-prilocaine monotherapy showed similar efficacy to that of combination with sildenafil, while the efficacy of sildenafil alone was similar to placebo. In another study, Sildenafil significantly improved IELT and satisfaction and reduced overall anxiety compared

to several SSRIs and the ‘pause-squeeze’ technique. Several open-label studies found that sildenafil combined with an SSRI is superior to SSRI monotherapy.

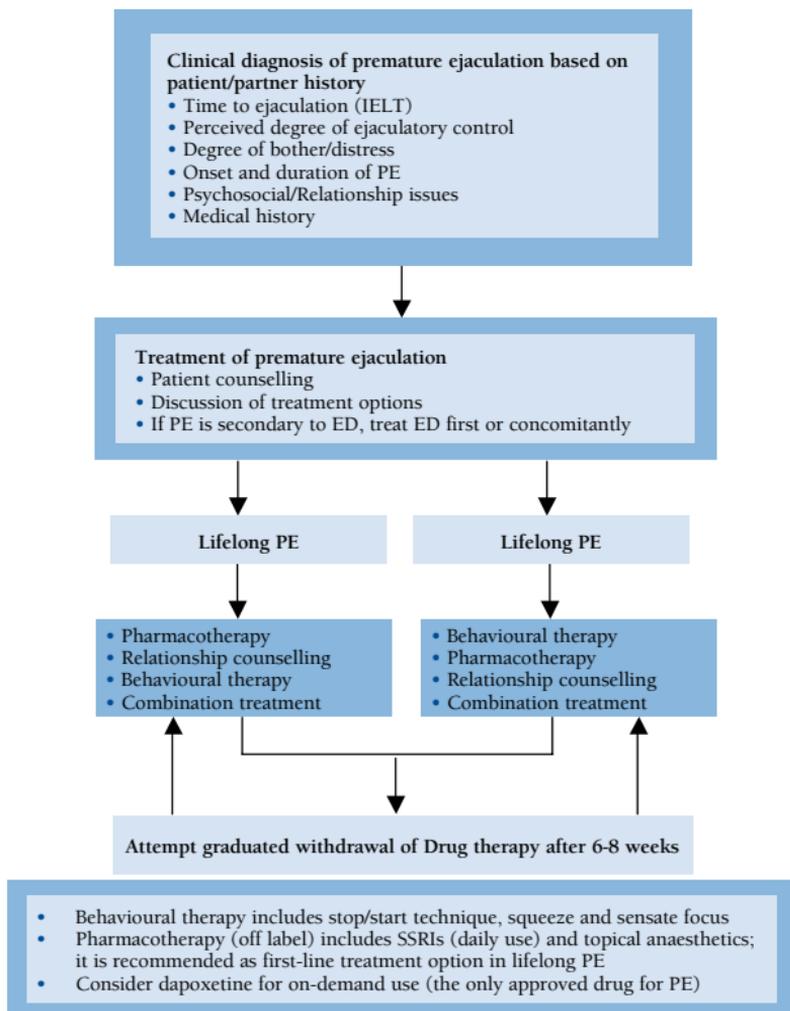
Recommendations for PE treatment		
Recommendations	LE	GR
Erectile dysfunction, other sexual dysfunction, or genitourinary infection (e.g. prostatitis) should be treated first.	2a	B
Behavioural techniques can benefit PE. However, they are time intensive, require the support of a partner, and can be difficult to do.	3	C
Pharmacotherapy is the basis of treatment in lifelong PE.	1a	A
Daily SSRIs are first-line, off-label, pharmacological treatment for PE. The pharmacokinetic profile of currently available SSRIs is not amenable to on-demand dosing.	1a	A
Dapoxetine, a short-acting SSRI, has already been approved for the on-demand treatment of PE in seven European countries.	1a	A
Topical anaesthetic agents provide viable alternatives to SSRIs (off-label).	1b	A
PDE5 inhibitors.	2B	C
Recurrence is likely after treatment cessation.	1b	A

Behavioural therapy may augment pharmacotherapy to enhance prevention of relapse. 3 C

SSRI = selective serotonin reuptake inhibitor; pm = on-demand administration.

This short booklet text is based on the more comprehensive EAU guidelines (ISBN 978-90-79754-09-0), available to all members of the European Association of Urology at their website - <http://www.uroweb.org/guidelines/online-guidelines/>.

Figure 4. Management of PE



PE = premature ejaculation; IELT = intravaginal ejaculatory latency time; ED = erectile dysfunction; SSRI = selective serotonin receptor inhibitor. Adapted from Lue et al. Summary of the recommendations on sexual dysfunctions in men. *J Sex Med* 2004;1:6-23.