



## Recommendations

## Therapeutic management of erectile dysfunction: The AFU/SFMS guidelines

Prise en charge thérapeutique de la dysfonction érectile :  
les recommandations AFU/SFMS

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## ARTICLE INFO

## Keywords:

Erectile dysfunction  
PDE5 inhibitors  
Alprostadil  
Penile implants  
Sexual medicine

## ABSTRACT

**Context:** Erectile dysfunction (ED) is a common sexual disorder. In France, recent evidence-based guidelines are lacking.

**Aim:** To provide practice guidelines on ED therapeutic management.

**Evidence acquisition:** Publications indexed in PubMed/Medline<sup>®</sup> between January 1999 and October 2023, were reviewed. For each clinical question, a level of evidence was attributed to the conclusions. These conclusions and the working group arguments were used to develop and grade (A-C) the recommendations.

**Recommendations:** ED management must be personalized. Phosphodiesterase 5 inhibitors (PDE5I) are recommended as first-line treatment (A). In patients with severe ED, a combination of PDE5I may be proposed as first- or second-line treatment (Expert Agreement, EA). Extra-cavernous or intra-urethral injections of alprostadil may be offered as first-line alternative to PDE5I or as second-line treatment (B). In case of unsatisfactory response to PDE5I or alprostadil alone, the combination of a PDE5I with intra-cavernosal or intra-urethral alprostadil may be proposed (EA). Vacuum therapy can be offered to all patients (B). Low-intensity extracorporeal shockwave therapy may be proposed to patients with mild or moderate ED, alone or in combination with PDE5I (B). Penile implants are

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indicated for patients with ED who are refractory or intolerant to pharmacological or mechanical treatments, or if they wish a permanent solution (B). Revascularization surgery may be offered to patients without comorbidities following pelvic trauma and ED with isolated arterial insufficiency (B). In addition to pharmaceutical, mechanical and/or surgical treatments, it is suggested to always consider educational interventions and counseling, lifestyle modifications and management of co-morbidities and curable causes.

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## R É S U M É

### Mots clés:

Dysfonction érectile  
Inhibiteurs de la PDE5  
Alprostadil  
Implants péniens  
Médecine sexuelle

**Contexte:** La dysfonction érectile (DE) est un trouble sexuel courant. En France, il n'existe pas de recommandations récentes fondées sur des preuves.

**Objectif:** Fournir des recommandations pratiques sur la prise en charge thérapeutique de la dysfonction érectile.

**Acquisition de preuves:** Les publications indexées dans PubMed/Medline® entre janvier 1999 et octobre 2023 ont été analysées. Pour chaque question clinique, un niveau de preuve a été attribué aux conclusions. Ces conclusions et les arguments du groupe de travail ont été utilisés pour élaborer et classer les recommandations (A-C).

**Recommandations:** La prise en charge de la dysfonction érectile doit être personnalisée. Les inhibiteurs de la phosphodiesterase 5 (IPDE5) sont recommandés comme traitement de première intention (A). Chez les patients présentant une dysfonction érectile sévère, une association d'IPDE5 peut être proposée comme traitement de première ou de deuxième intention (Accord d'experts, AE). Les injections extra-caverneuses ou intra-urétrales d'alprostadil peuvent être proposées comme alternative de première ligne aux IPDE5 ou comme traitement de seconde ligne (B). En cas de réponse insatisfaisante à la IPDE5 ou à l'alprostadil seul, l'association d'une IPDE5 à l'alprostadil intra-caverneux ou intra-urétral peut être proposée (AE). Le traitement par vacuum peut être proposé à tous les patients (B). La thérapie par ondes de choc extracorporelles de faible intensité peut être proposée aux patients présentant une dysfonction érectile légère ou modérée, seule ou en association avec un IPDE5 (B). Les implants péniens sont indiqués pour les patients souffrant de dysfonction érectile qui sont réfractaires ou intolérants aux traitements pharmacologiques ou mécaniques, ou qui souhaitent une solution permanente (B). La chirurgie de revascularisation peut être proposée aux patients sans comorbidités à la suite d'un traumatisme pelvien et aux urgences présentant une insuffisance artérielle isolée (B). En plus des traitements pharmaceutiques, mécaniques et/ou chirurgicaux, il est suggéré de toujours envisager des interventions et des conseils éducatifs, des modifications du mode de vie et la prise en charge des comorbidités et des causes curables.

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## 1. Introduction

Erectile dysfunction (ED) is defined by ICD-11 as the inability or marked limitation to achieve or maintain a penile erection of sufficient duration or rigidity for sexual activity [1]. It occurs despite the sexual activity desire and adequate sexual stimulation, is episodic or persistent for at least several months, and is associated with clinically significant distress. ED is a common sexual disorder that mainly affects > 40-year-old men. A study carried out in four countries in three continents showed that the overall prevalence of moderate to severe ED was 9% in the 40–44 years group, 12% in the 45–49 years group, 18% in the 50–54 years group, 29% in the 55–59 years group, 38% in the 60–64 years group, and 54% in the 65–70 years group [2]. Therefore, ED is a major health problem in the ageing male population.

Like for all sexual dysfunctions, ED requires the precise assessment of the contributing factors based on the biopsychosocial model of health in order to propose the most appropriate management for each patient/couple. In France, the first-line ED management is currently based on the 2005 guidelines of the Association française d'urologie (AFU; French Association of Urology) and of the Association interdisciplinaire post-universitaire de sexologie (Interdisciplinary Post-University Association of Sexology) to general practitioners [3] that were updated in 2010 [4], 2013 [5] and 2018 [6]. However, they are not based on a well-defined guideline development methodology. Moreover, substantial advances in understanding the erection physiology and ED pathophysiology have led to therapeutic developments. Several treatments are currently under study for patients with complex ED, such as platelet-rich plasma (PRP), cell therapies, other pharmacological agents, venous embolization, shockwave therapy.

In this context, the AFU Comité d'andrologie et de médecine sexuelle (AFU-CAMS; AFU andrology and sexual medicine committee) and AFU Comité des pratiques professionnelles (AFU professional practice committee), together with the Société francophone de médecine sexuelle (SFMS; Francophone Society of Sexual Medicine) Scientific Committee,

were asked to analyze the available literature and to develop clinical practice guidelines on ED therapeutic management. The main objective was to ensure that all patients with ED and their partners benefit from relevant information and optimal treatment.

## 2. Evidence acquisition

This systematic review was performed following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [7].

### 2.1. Bibliographic strategy

A systematic search was performed in PubMed/Medline® to identify reports published in French or English between January 1999 and January 2023 (Table S1). The search was based on the PICOS criteria: (1) population (P): “erectile dysfunction”, “impotence”, “erection failure”, “male sexual dysfunction”, “penile erection”; (2) intervention (I): according to the clinical questions; (3) compared intervention (C): other interventions; (4) outcome (O): international index of erectile dysfunction (IIEF), erection hardness score (EHS), side effects, and acceptability; (5) study design (S): meta-analysis, randomized controlled trial, prospective non-randomized study, or retrospective study.

This search was supplemented by bibliographic monitoring (up to October 2023), consultation of the websites of international organizations (e.g., European Association of Urology, American Urological Association), search of systematic reviews in the Cochrane Library, and suggestions from the working group members, particularly on studies not indexed in Medline® at the time of the bibliographic search.

The inclusion and exclusion criteria were defined before the literature search. Studies were included if they assessed treatment(s) in adult patients with symptoms suggestive of ED not induced by a medical or surgical procedure, without age limit.

Publications deemed ineligible were studies on: (i) ED associated with prostate cancer and its treatments; (ii) ED secondary to pelvic surgery; (iii) ED associated with pelvic surgery; (iv) ED in patients with renal failure or renal transplantation; (v) patients with lower urinary tract symptoms; (vi) patients receiving antipsychotics or antidepressants; (vii) patients with Peyronie's disease or priapism. These populations will be evaluated in future dedicated guidelines. Other excluded publications were: (i) cost-benefit studies because they are largely dependent on each country healthcare system; (ii) clinical practice studies; (iii) animal or in vitro studies; (iv) case reports, general reviews, editorials, letters and comments. The methodologist (D.K.) selected the publications using these criteria after reading the abstract. The working group validated the selection. The developed recommendations had to address twelve clinical questions classified according to the PICOS criteria.

## 2.2. Project methodology

The project was carried out by a working group that included urologists from the AFU-CAMS and physicians qualified in sexual medicine from the SFMS. The recommendations were developed following the clinical practice recommendation method, based on the systematic review and the experts' judgment [8]. The methodological quality of the selected studies was analyzed using a dedicated grid. This allowed assigning levels of evidence (LOE) to each study and then to their evidence-based conclusions after taking into account the consistency of their results.

These conclusions and the working group members' arguments were used to developing the recommendations

- by default the formulated recommendation is the clinical attitude unanimously recognized as the reference by the experts;
- if a clinical attitude was judged acceptable on the basis of the literature data and expert opinion, but was not unanimously recognized as the reference, it is indicated that it can be discussed/proposed;
- in the absence of expert consensus, no recommendation is formulated.

The classification of conclusions by LOE (LOE1 is the highest; LOE4 the lowest) and the recommendation grading (grade A is the highest; grade C the lowest; Expert Agreement [EA] in the absence of data) are based on the grid proposed by the Haute Autorité de santé (French National Authority for Health) [8].

In December 2023, the document was reviewed using the Appraisal of Guidelines for Research and Evaluation II [9] instrument [9] by 34 independent experts from all medical and surgical specialties involved in ED management (22 urologists, 3 sexologists, 3 vascular physicians, 2 cardiologists, 2 endocrinologists, 2 general practitioners, and 2 patient representatives). Their comments were incorporated in the final version of the guideline in January 2024.

The full document, including the project rationale, methodology, detailed study analysis, conclusions, recommendations and review process, can be consulted on the Urofrance website (link to be completed).

## 3. Results

The study selection is outlined in the PRISMA flow diagram (Fig. 1). In total, 1468 publications were screened for eligibility by reading the title/abstract and 112 met the inclusion criteria. After full-text reading and inclusion of other publications identified by bibliographic monitoring or suggested by the working group, 220 studies were retained. Fig. 2 summarizes recommendations for ED management.

### 3.1. Question 1: lifestyle factors

The following reports were selected:

- 7 recommendations [10–16];
- 6 systematic reviews or meta-analyses [17–22];
- prospective studies [23–26].

#### 3.1.1. Conclusions based on data analysis

ED risk is higher in patients who smoke compared with patients who stopped smoking or never smoke (LOE2).

PRISMA 2020 flow diagram for new systematic reviews which included searches of databases, registers and other sources

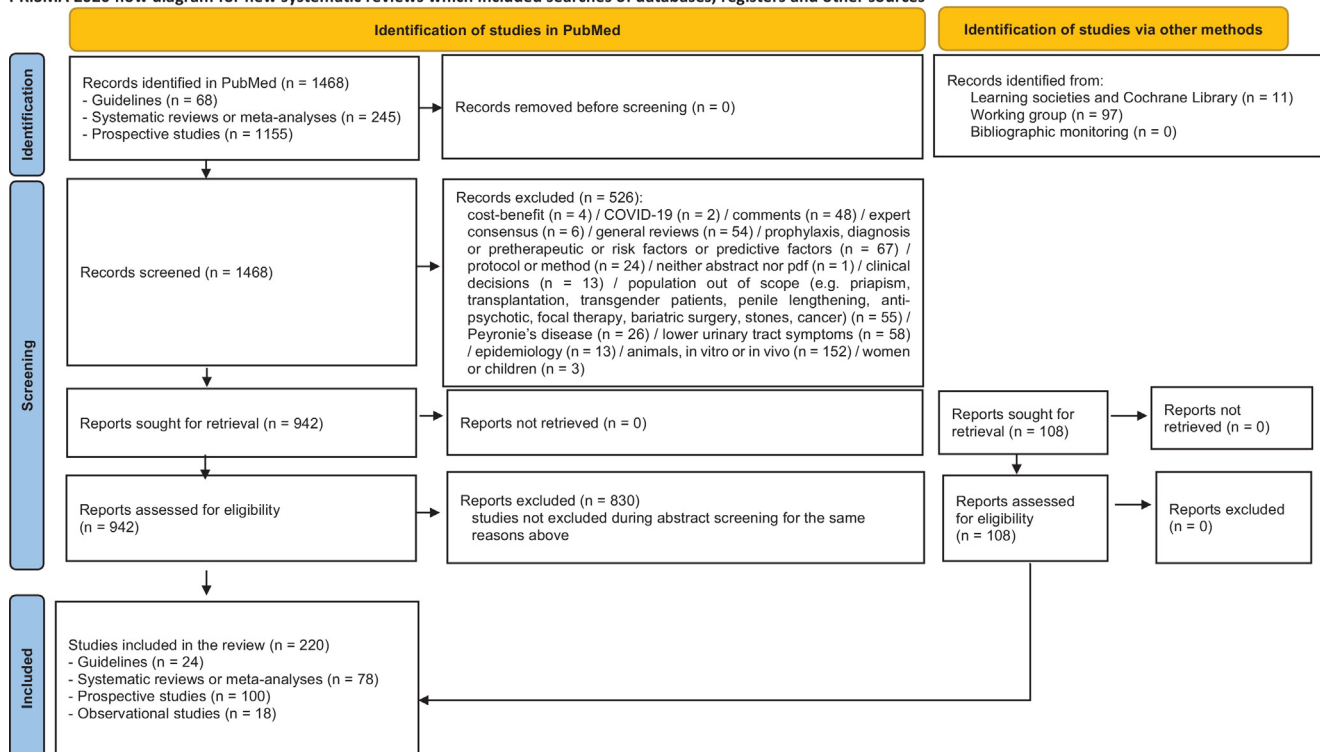


Fig. 1. Flowchart of study selection.

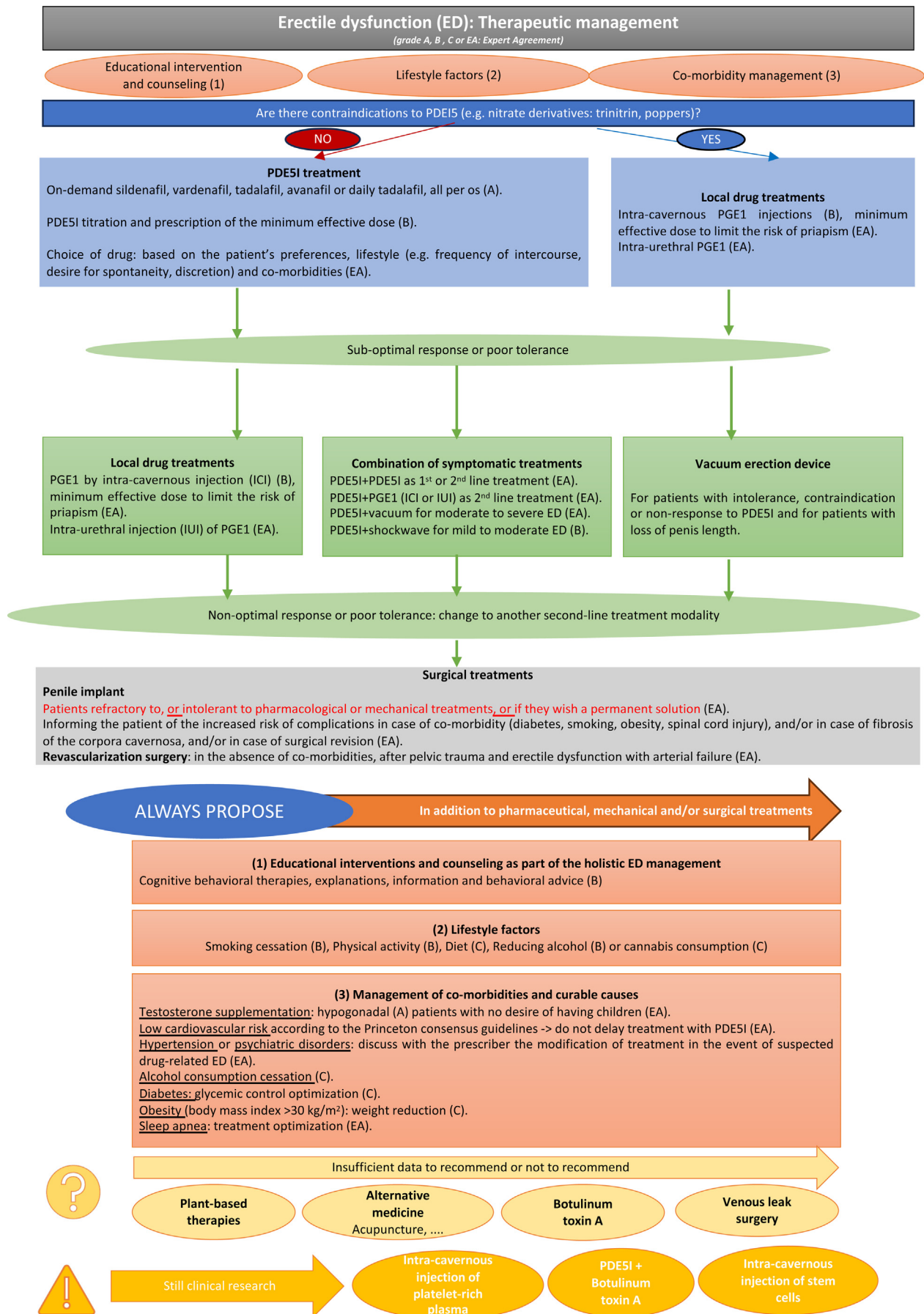


Fig. 2. Algorithm: strategy for ED management.



Smoking cessation improves erectile function (LOE2).

The relationship between alcohol and erectile function is not linear: low alcohol consumption (< 3 standard units/day and < 8 standard units/week) has a beneficial effect, whereas higher consumption sharply increases ED risk (LOE2).

Lack of physical activity increases ED risk (LOE2).

Regular physical activity improves erectile function (LOE2).

The main gain is observed with aerobic exercise of moderate to high intensity for 150–180 minutes per week (LOE2).

A healthy diet (particularly of the Mediterranean type) seems to reduce ED risk (LOE3).

Cannabis use seems to be associated with an increased risk of ED (LOE3).

The literature on the link between ED and the use of other psychoactive products is too scarce to reach any conclusion.

For public health reasons, the working group strongly recommends smoking and alcohol cessation, despite the moderate LOE (LOE2).

### 3.1.2. Recommendations

Lifestyle and diet are an integral part of ED management and should be considered in the context of the personalized management after a shared decision with the patient.

R1. In patients with ED, smoking cessation is recommended (grade B).

R2. In patients with ED, it is recommended to look for excessive alcohol intake (grade B) and to advise moderation.

R3. In patients with ED, regular physical activity (aerobic, 150–180 minutes/week) is recommended (grade B).

R4. In patients with ED, it is suggested to follow a healthy diet (Mediterranean type) (grade C).

R5. In patients with ED, it is suggested to screen for cannabis use (grade C) and to recommend its cessation.

## 3.2. Question 2: phytotherapies

The following reports were selected:

- recommendations [10,14,15,27,28];
- 8 systematic reviews or meta-analyses [29–36];
- randomized studies [37–42];
- 2 prospective non-randomized studies [43,44].

### 3.2.1. Conclusions based on data analysis

Several phytotherapies have been proposed for ED treatment (e.g., ginseng, Pycnogenol<sup>®</sup>, Tribulus terrestris, Lepidium meyenii, L-arginine, maca root, E-MA-H and E-MA-HP, VigRX Plus, Cappra<sup>®</sup>, saffron, Ecklonia bicyclis); however, as the literature data are discordant, it is impossible to conclude on their efficacy.

Phytotherapies also open the door to self-medication using products bought on the Internet, with a composition often unverifiable, sometimes including phosphodiesterase 5 inhibitors (PDE5I), with the risk of overdosing and consumption despite contraindications.

### 3.2.2. Recommendations

R6. It is not possible to recommend the use of phytotherapies for ED.

## 3.3. QUESTION 3: Alternative and complementary therapies

The following reports were selected:

- 6 systematic reviews or meta-analyses [30,35,45–48];
- 2 randomized studies [49,50];
- prospective non-randomized studies [51–53].

### 3.3.1. Conclusions based on data analysis

Many alternative or complementary treatments of ED have been proposed and tested (acupuncture, functional electrical stimulation and pelvic floor muscle strengthening, low-frequency magnetic pulses,

dynamic creative image synthesis). For all these treatments, evidence was insufficient to conclude on their effectiveness in ED management.

### 3.3.2. Recommendations

R7. It is not possible to recommend or to not recommend alternative or complementary therapies for ED management.

## 3.4. Question 4: comorbidity management

The following reports were selected:

- 12 recommendations [10,11,13–16,27,54–59] and one synthesis of existing recommendations [60];
- 30 meta-analyses [61–87];
- 18 prospective randomized and non-randomized studies [88–105];
- 1 retrospective study [106].

### 3.4.1. Conclusions based on data analysis

**3.4.1.1. Testosterone deficiency.** In patients with ED and testosterone deficiency, testosterone supplementation improves erectile function (LOE1). It should be noted that testosterone supplementation carries a risk of spermatogenesis arrest due to the negative feedback by exogenous testosterone on pituitary gonadotropin secretion.

In eugonadal patients with ED, testosterone supplementation does not improve erectile function (LOE1).

With testosterone supplementation, erectile function improvement is observed only after 3–6 months of treatment (LOE3).

**3.4.1.2. Cardiovascular diseases.** ED predicts the risk of cardiovascular events (coronary heart disease, stroke and all-cause mortality) (LOE2).

Some antihypertensive drugs can negatively affect erectile function, depending on their class (LOE1).

Angiotensin II receptor antagonists and nebivolol are the least likely to cause ED (LOE1).

ED appears to be a cause of non-adherence to antihypertensive treatment (LOE4).

PDE5I improve adherence to antihypertensive treatments (LOE4).

**3.4.1.3. Psychiatric disorders.** There is a bidirectional association between depression and ED (LOE2).

Most antidepressants may impair erectile function (LOE1).

**3.4.1.4. Alcohol misuse.** Excessive alcohol intake (> 3 drinks/day) is associated with ED (LOE4).

In patients with alcohol misuse, alcohol cessation improves erectile function after 3 months (LOE4).

**3.4.1.5. Diabetes.** In patients with diabetes, ED prevalence is > 50% (LOE4).

Improving glycemic control appears to improve erectile function (LOE3).

Antidiabetic drugs appear to improve erectile function (LOE2).

**3.4.1.6. Obesity.** ED prevalence is higher in men with obesity (LOE4).

Weight loss, particularly after bariatric surgery, appears to improve erectile function (LOE2).

**3.4.1.7. Sleep apnea syndrome.** The results on positive airway pressure therapy in patients with ED linked to obstructive sleep apnea are inconclusive.

### 3.4.2. Recommendations

**3.4.2.1. Testosterone deficiency.** R8. Testosterone supplementation should be offered to hypogonadal patients with ED (grade A).

R9. In men with testosterone deficiency, testosterone supplementation and symptomatic ED treatment should be combined at least in the first few months of treatment (grade EA).

R10. Testosterone supplementation is not recommended in eugonadal men (testosterone > 12 nmol/L) with ED (grade A).

R11. Testosterone supplementation is not recommended for men with ED who wish to become fathers (grade EA).

R12. In patients receiving neuroleptic drugs, hypogonadism with hyperprolactinemia should be investigated as a possible drug adverse effect (grade EA).

**3.4.2.2. Cardiovascular diseases.** R13. According to the Princeton IV consensus guidelines, PDE5I treatment should not be delayed in patients with low cardiovascular risk (grade EA).

R14. In patients with suspected drug-related ED, a possible change of antihypertensive drug should be discussed with the prescriber (grade EA).

**3.4.2.3. Psychiatric disorders.** R15. In patients with ED, it is recommended to look for and treat a depressive syndrome (grade B).

R16. In patients with a psychiatric disorder and suspected drug-induced ED, the possibility of modifying the treatment should be discussed with the prescriber (grade EA).

**3.4.2.4. Alcohol misuse.** R17. In patients with alcohol misuse and ED, alcohol consumption cessation is recommended (grade C).

**3.4.2.5. Diabetes.** R18. In patients with diabetes, glycemic control should be optimized to improve erectile function (grade C).

**3.4.2.6. Obesity.** R19. In patients with obesity (body mass index > 30 kg/m<sup>2</sup>), weight loss is suggested to improve erectile function (grade C).

**3.4.2.7. Sleep apnea syndrome.** R20. In patients with ED, sleep apnea syndrome management should be optimized (grade EA).

### 3.5. Question 5: educational interventions and counseling

The following reports were selected:

- recommendations [10,15,27]
- 2 systematic reviews or meta-analyses [107,108]
- 2 randomized studies [109,110]

**Table 1**

Explanations, information and behavioral advice.

|                                                                                                                                                                                              |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Explain to the patients and their partners                                                                                                                                                   |
| – The physiology of erection                                                                                                                                                                 |
| – How anxiety inhibits erection                                                                                                                                                              |
| – The difference between desire and erection                                                                                                                                                 |
| – The fact that erection is a reflex phenomenon and by its very nature unstable                                                                                                              |
| – The involvement of many interacting factors: physiological, psychological, relational, sexual and contextual                                                                               |
| – Negative conditioning linked to repeated failure that in turn leads to failure                                                                                                             |
| – PDE5I mode of action to explain the need of stimulation                                                                                                                                    |
| – The time to PDE5I onset of action when taken “on demand”                                                                                                                                   |
| – PDE5I duration of action of few hours once the efficacy level has been reached                                                                                                             |
| – The importance of regular treatment in the case of daily treatment with PDE5I                                                                                                              |
| – The mode of action of intra-cavernous injections and how they are administered during one or more dedicated consultations                                                                  |
| Inform the patients and their partners about                                                                                                                                                 |
| – The frequency of erectile dysfunction                                                                                                                                                      |
| – The link between erectile dysfunction and cardiovascular pathologies                                                                                                                       |
| Advise the patients and their partner                                                                                                                                                        |
| – To remove the guilt from self-eroticism                                                                                                                                                    |
| – Not to focus on their erection                                                                                                                                                             |
| – Not to rush for fear of losing their erection                                                                                                                                              |
| – Not to reduce sexuality to the fact of having or not having an erection. Encourage them to develop non-penetrative sexuality                                                               |
| – To talk to their partner about how, together, they can reverse the balance between relaxation-pleasure and anxiety-avoidance                                                               |
| – To give a few intra-cavernous injections outside a sexual context, to get used to the gesture and adapt the dosage when injections are indicated                                           |
| – For the intra-urethral route, the importance of instilling the product at the right temperature and inserting the tip correctly into the meatus when intra-urethral treatment is indicated |

### 3.5.1. Conclusions based on data analysis

ED can be improved by providing appropriate information on the physiological and psychological processes involved in the sexual response in a way that can be understood by the patient and partner, from a biopsychosocial perspective (LOE2).

Cognitive-behavioral therapies, as a psychological approach (including the partner), optimize ED management (LOE1).

Sex therapy, alone or in combination with other ED treatments, appears to improve erectile function (LOE2).

### 3.5.2. Recommendations

R21. All patients with ED should receive information on the physiological and psychological processes involved in the sexual response that can be easily understood and from a biopsychosocial perspective (grade B).

R22. The working group proposes a practical information sheet and behavioral advice (Table 1) to be given to the patients and their partners (grade EA).

R23. Cognitive-behavioral therapies are recommended as a psychological approach (including for the partner) (grade A).

R24. Sex therapy is an integral part of ED management and is recommended to improve erectile function (grade B).

### 3.6. Question 6: oral therapy with PDE5I

The following reports were selected:

- 6 recommendations [6,10,12,15,111–113];
- 15 meta-analyses [114–128];
- prospective randomized studies [129–132];
- 2 prospective non-randomized studies [133,134].

### 3.6.1. Conclusions based on data analysis

Studies on the place of oral drugs in ED treatment reported concordant findings.

PDE5I are effective as first-line treatment of ED (LOE1).

The different PDE5I included in the analysis (sildenafil, vardenafil, tadalafil, avanafil) are equivalent in terms of efficacy and safety (LOE1).

Due to the discordant results, no conclusion could be drawn on the difference in efficacy between daily versus on-demand tadalafil.

Yohimbine, when administered alone, is not effective for ED management (LOE2).

### 3.6.2. Recommendations

The working group recalls the 2024 Princeton IV consensus guidelines that recommend a cardiology consultation in the presence of more than two cardiovascular risk factors before prescribing PDE5I [135]:

- PDE5I are contraindicated in patients with unstable angina, decompensated heart disease or untreated symptomatic rhythm disorder, or in association with nitrate derivatives (e.g., trinitrine, poppers);
- a PDE5I can be prescribed after treatment of the heart disease, infarction or stroke with heart function stabilized for > 6 weeks.

R25. PDE5I are recommended as first-line ED treatment (grade A).

R26. It is recommended to gradually increase PDE5I doses and to prescribe the minimum effective dose to limit adverse effects (grade B).

R27. The choice between daily tadalafil and on-demand PDE5I should be based on the patient's informed choice, lifestyle (e.g., intercourse frequency, desire for spontaneity, discretion) and existing comorbidities (lower urinary tract symptoms) (grade EA).

R28. It is not recommended to prescribe yohimbine alone for ED management (grade B).

### 3.7. Question 7: local drug delivery

The following reports were selected:

- recommendations [10,12,15,111];
- systematic reviews or meta-analyses [136–138];
- 9 randomized studies [139–147];
- prospective non-randomized studies [148–152].

#### 3.7.1. Conclusions based on data analysis

Alprostadil (prostaglandin E1, PGE1) is the only molecule available in France for intra-cavernous or intra-urethral administration.

Alprostadil by intra-cavernous injection is effective for ED management with low morbidity and good satisfaction rates (LOE2).

Alprostadil by the intra-urethral route is less effective than by the intra-cavernous route (LOE2). Intra-urethral administration appears to be more effective than administration via the urethral meatus (LOE3).

Studies are heterogeneous in terms of products and doses used.

In all published studies, the introduction of PGE1 (alprostadil) (intra-cavernous or intra-urethral administration) was associated with therapeutic patient education and a titration phase.

#### 3.7.2. Recommendations

R29. When prescribing local PGE1 (intra-cavernous or intra-urethral administration), patients should receive also therapeutic education (Table 1) (grade EA).

R30. It is recommended to inform patients of the risk of post-intra-cavernous injection priapism and the steps to be taken (grade EA).

R31. It is recommended to gradually increase the doses of PGE1 dose by intra-cavernous injection in order to prescribe the minimum effective dose and limit adverse events (grade EA).

R32. Alprostadil by intra-cavernous injection can be proposed as first-line alternative to PDE5I or as second-line treatment of ED (grade B).

R32. Intra-urethral PGE1 can be offered as first-line alternative to PDE5I or as second-line treatment of ED (grade EA).

R33. Regular follow-up is recommended to optimize the therapeutic response, assess tolerance, and check the administration modality (grade EA).

### 3.8. Question 8: combining symptomatic treatments

The following reports were selected:

- 2 recommendations [10,15];
- 2 meta-analyses [10,153];
- randomized studies [154–157];
- 2 prospective non-randomized studies [158,159];

- cohort studies [160–164];
- retrospective studies [165–167].

#### 3.8.1. Conclusions based on data analysis

In patients with severe ED, the combination two PDE5I seems to be superior to a single PDE5I, without increasing the risk of adverse effects (LOE2).

In patients with ED and unsatisfactory response to a PDE5I on-demand, the combination of one PDE5I with intra-urethral alprostadil might improve the therapeutic response with a good tolerability profile (LOE3).

In patients with ED and unsatisfactory response to a PDE5I on-demand, the combination of one PDE5I with alprostadil by intra-cavernous injection might improve the therapeutic response with a good tolerability profile (LOE2).

In patients with diabetes and moderate to severe ED, the combination of one PDE5I with a vacuum erection device is superior to PDE5I alone, without increasing the risk of adverse effects (LOE2). It also potentiates the vacuum erection device effect (LOE2).

Data on the benefits of combining a vacuum erection device with a local treatment (intra-cavernous or intra-urethral) are inconclusive.

In patients with ED and unsatisfactory response to a PDE5I alone, the combination of low-intensity extracorporeal shockwave therapy (LI-SWT) with PDE5I appears to improve the response (LOE4).

In patients with ED, data on the efficacy of combining botulinum toxin A with a PDE5I, compared with botulinum toxin A alone, are inconclusive.

#### 3.8.2. Recommendations

R34. In patients with severe ED, a combination of two PDE5I can be proposed as first- or second-line therapy (grade EA).

R35. In patients with ED and unsatisfactory response to PDE5I alone or alprostadil (intra-urethral or intra-cavernous) alone, the combination of one PDE5I with alprostadil (intra-urethral or intra-cavernous) may be proposed (grade EA).

R36. In patients with moderate to severe ED, the PDE5I and vacuum erection device combination may be proposed (grade EA).

R37. In patients with moderate to severe ED, the combination of vacuum erection device and local treatment may be proposed (grade EA).

R38. To date, the combination of botulinum toxin A with a PDE5I should be considered only in the context of research protocols (grade EA).

### 3.9. Question 9. External vacuum erection devices

The following reports were selected:

- 2 international recommendations [10,15];
- prospective randomized studies [156,164,168,169];
- 2 prospective non-randomized studies [159,170].

#### 3.9.1. Conclusions based on data analysis

Vacuum treatment for ED improves the patients' sexuality (LOE3).

The combination with a PDE5I potentiates the vacuum device effect (LOE2).

The vacuum device also improves penile length in traction (LOE2).

#### 3.9.2. Recommendations

R39. A vacuum erection device can be proposed to all patients with ED, particularly to those who are unresponsive, intolerant or with contraindications to pharmacological treatments (grade EA).

R40. The vacuum erection device can be proposed to patients with ED and loss of penile length (grade EA).

### 3.10. Question 10: emergent and regenerative therapies

The following reports were selected:

- recommendations [10,15,171];
- 8 meta-analyses [172–179];
- randomized studies [154,180–183];
- 12 prospective studies [184–195].

### 3.10.1. Conclusions based on data analysis

In patients with mild to moderate ED with a vascular component and responding to PDE5I, LI-SWT improves the IIEF and EHS scores (LOE1) with few adverse effects (LOE2), but the clinical benefit is uncertain.

Intra-cavernous injection of different types of stem cells has been evaluated in a small number of patients with ED, not allowing to conclude on their efficacy.

In patients with ED, intra-cavernous injection of PRP is an emerging treatment. Studies are discordant on the significance of the short-term IIEF score improvement. Few adverse events have been reported (LOE3). The injected volume seems to be a predictor of treatment efficacy.

In patients with PDE5I-refractory ED, botulinum toxin A might improve erectile function (LOE2) with few adverse effects (LOE2).

### 3.10.2. Recommendations

R41. In patients with mild to moderate ED, LI-SWT may be proposed, alone or in combination with PDE5I (grade B).

R42. Patients should be informed that the long-term (> 6 months) efficacy and risks of LI-SWT have not been evaluated (grade EA).

R43. Several LI-SWT sessions are necessary, but the literature data do not allow recommending a specific protocol (grade EA).

R44. In patients with ED, intra-cavernous stem cell injections should be offered only in the context of clinical trials after failure of first- and second-line treatments and before penile implant insertion.

R45. To date, data are insufficient to recommend intra-cavernous injections of PRP for the routine ED management (grade EA).

R46. Patients should be informed that the long term (> 6 months) efficacy and risks of PRP intra-cavernous injections have not been evaluated (grade EA).

R47. Several injections seem necessary, but the literature data do not allow recommending PRP intra-cavernous injections outside the framework of clinical trials after the failure of first- and second-line treatments (grade EA).

R48. Currently, data are insufficient to recommend botulinum toxin A for ED.

#### 3.10.2.1. Regulatory data.

- The use of stem cells is subject to strict regulations (European Regulation 2007 No. 1349/2007) that impose specific constraints in terms of quality control, administration modality, and traceability. Currently, cell therapies can only be prepared in specialized, accredited hospitals (mainly the “Établissement français du sang” in France).
- PRP is not subject to the constraints of the 2007 European regulation (No. 1349/2007) concerning innovative therapeutic drugs, making it use easier.

### 3.11. Question 11: integrative care, sexological care combined with the medical treatment

The following reports were selected:

- recommendations [10,15,196];
- meta-analyses [197–199];
- 9 randomized studies [169,200–207].

#### 3.11.1. Conclusions based on data analysis

The combination of cognitive-behavioral approaches and other treatments optimizes erectile function (LOE1).

Offering some explanations and advice (Table 1) when prescribing drugs for ED improves the treatment results (LOE2).

#### 3.11.2. Recommendations

R49. It is recommended to combine cognitive-behavioral approaches with other ED treatments in a biopsychosocial approach, whatever the ED etiology (grade B).

R50. All drug prescriptions must be accompanied by explanations, information and behavioral advice (grade B).

R51. The working group proposes a practical information sheet and behavioral advice (Table 1) to be given to patients with ED and their partners (grade EA).

### 3.12. Question 12: surgical management

The following reports were selected:

- recommendations [10,15,208,209];
- 8 systematic reviews or meta-analyses [210–217];
- prospective studies [218–220];
- 9 retrospective studies [221–229].

#### 3.12.1. Conclusions based on data analysis

The mean time between ED onset and penile implant insertion is 56 months (75 months in patients with diabetes).

More than 80% of patients and partners reported satisfaction about the penile implant and 50% of them would have liked to have undergone this procedure earlier (LOE4).

The quality of sexual life with an inflatable penile implant is improved by psychosexual counselling before and after the penile implant placement (LOE2).

Currently, two types of inflatable (2 or 3 pieces) and malleable implants are available.

Several surgical approaches are available, none of which has been shown to be superior to the others: infrapubic approach, penoscrotal approach, subcoronal approach (LOE non applicable, systematic review).

The classic implant complication is infection (1–3% of patients after first surgery). The infection rate is lower when using implants with antibiotic coating (LOE2).

However, some populations are at higher risk of complications: patients with diabetes, with obesity (body mass index > 30 kg/m<sup>2</sup>), with spinal cord injuries, undergoing revision surgery, associated surgical procedures, and with fibrosis of the corpora cavernosa (LOE2). Active smoking increases the risk of surgical site infection. Immunosuppression, besides a CD4-positive T cell count < 300, increases the risk in patients with HIV. Immunosuppressed patients on corticosteroids are slightly more at risk of surgical complications, such as site infection and poor healing, but studies remain small and sometimes contradictory.

Satisfaction and complications were comparable in patients with different implant types (LOE non applicable, systematic review).

In a highly selected population (patients with venous leak who did not respond to pharmacological treatment), surgical and endovascular treatment might have a positive effect on penile rigidity (LOE3).

In a highly selected population (young patients with history of pelvic trauma), revascularization surgery is of interest, after Doppler evaluation and diagnosis of arterial insufficiency, for recovering erectile function with or without pharmacological treatment (LOE non applicable, systematic review).

#### 3.12.2. Recommendations

R52. Patients with ED and an organic component should be informed about the possible treatment options, including penile implants, following a discussion on their benefits and risks (grade EA).

R53. A penile implant is indicated for patients with ED who are refractory or intolerant to pharmacological or mechanical treatments, or if the patient wishes a permanent solution (grade EA).

R54. Before the penile implant insertion, the patient and if possible the partner must receive full information (different implant types, sexuality



with an implant, early and late complications, mechanical failure, revision rate and the procedure definitive nature) (grade EA).

R55. Patients with co-morbidities (diabetes, smoking, obesity, spinal cord injury) and/or fibrosis of the corpora cavernosa, and/or revision surgery should be informed about the increased risk of complications (grade EA).

R56. Patient preparation should include optimization, if possible with smoking cessation 1 month before surgery and optimal diabetes control (glycated hemoglobin ideally < 8.5%) (grade EA).

R57. Penile implants with antibiotic coating should be preferred (grade B).

R58. Revascularization surgery can be offered to patients without comorbidities after pelvic trauma and ED with isolated arterial insufficiency (grade EA).

R59. There is currently no standardized venous leak management.

## Disclosure of interest

The authors declare that they have no competing interest.

## Acknowledgements

The authors thank the Association française d'urologie (AFU) for facilitating this work. AFU mission is to promote urological research in all its forms and to enable the emergence of large-scale, interdisciplinary research programs.

The working group was coordinated by Eric Huyghe (urologist, Toulouse, CAMS). AFU members: Jean Pierre Graziana, Antoine Faix, Nadja Schoentgen, Astrid Boulenger de Hauteclouque, Hugo Dupuis, Ala Chebbi, Ismael Chelghaf, Aurélie Schirmann, Lucas Freton, Cyrille Guillot-Tantay, Cédric Lebâcle, Sabine Roux, Johann Barkatz, Ludovic Ferretti, Charlotte Methorst, William Akakpo, François-Xavier Madec. SFMS members: Carol Burte, Laure Grellet, Eric Huyghe, Jean Pierre Graziana, Antoine Faix, Charlotte Methorst.

This work brings together cooperating groups, scientific associations and researchers working on ED management in France and in French-speaking countries.

The authors would like to thank the following scientific societies and associations for their support: Association française d'urologie (AFU), Société francophone de médecine sexuelle (SFMS), Association interdisciplinaire post-universitaire de sexologie (AIUS), Association française des urologues en formation (AFUF), Société française de médecine vasculaire (SFMV), Société française de cardiologie (SFC), Société française d'endocrinologie (SFE), Société belge d'urologie, Société française de médecine générale (SFMG) and the Comité d'éthique pour la recherche (CER) as well as the following reviewers: 1- Aboyans Victor, cardiologist and vascular physician, SFC, Limoges; 2- Anastay Vassili, urologist, AFUF, Toulon; 3- Bachelot Anne, endocrinologist, SFE, Paris; 4- Beirnaert Jeanne, urologist, SBU, Brussels; 5- Berchiche William, urologist, AFUF, Marseille; 6- Boissier Romain, urologist, AFU, Marseille; 7- Bondil Pierre, urologist, AIUS, Chambéry; 8- Bonnin Christophe, vascular physician, SFMV, Nice; 9- Charra Clément, general practitioner, SFMG, Ladoix-Serrigny; 10- Chevrot Armand, urologist, AFU, Avignon; 11- Christin-Maitre Sophie, endocrinologist, SFE, Paris; 12- Culty Thibaut, urologist, AFU, Angers; 13- Cuzin Béatrice, urologist, SFMS, Lyon; 14- Degraeve Amandine, urologist, SBU, Namur; 15- Della-Negra Emmanuel, urologist, AFU, Plerin; 16- Frontczak Alexandre, urologist, AFU, Besançon; 17- Gas Jérôme, urologist, AFU, Montauban; 18- Kownator Serge, cardiologist, SFC, Thionville; 19- Leon Priscilla, urologist, AFU, Royan; 20- Lévy Stephan, urologist, AFUF, Toulouse; 21- Mahbouli Meriem, psychiatrist-sexologist, SFMS, Tunis; 22- Pauly Jean-Marc, general practitioner, SFMG, Rodemack; 23- Peyrottes Arthur, urologist, AFUF, Paris; 24- Richard Claire, urologist, AFU, Rennes; 25- Roumeguère Thierry, urologist, SBU, Brussels; 26- Roumigué Mathieu, urologist, AFU, Toulouse; 27- Salama Samuel, gynecologist

– andrologist – sexologist, AIUS, Neuilly-sur-Seine; 28- Seizilles de Mazancourt Emilien, urologist, AFUF, Paris; 29- Sitruk Jonas, vascular physician, SFMV, Paris; 30- Six Hubert, patient representative, Comité d'éthique pour la recherche (CER); 31- Staerman Frédéric, urologist, SFMS, Reims; 32- Vidart Adrien, urologist, AFU, Suresnes; 33- Waber Lakshmi, psychiatrist-psychotherapist-sexologist, SFMS, Geneva; 34- Wilisch Jonas, urologist, AFU, Lyon.

We are grateful to Dr Elisabetta Andermarcher for editing the manuscript.

## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.fjurol.2024.102842.

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