

## Erectile Dysfunction

Kevan R. Wylie, MD, FRCPsych DSM, and Anna Machin

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Dr. Wylie is consultant psychiatrist and consultant in sexual medicine and Ms. Machin is student doctor at the University of Sheffield in England.

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Please direct all correspondence to: Kevan R. Wylie, MD, FRCPsych DSM, Consultant in Sexual Medicine and Consultant Psychiatrist, Porterbrook Clinic, 75 Osborne Rd, Sheffield S11 9BF, UK; Tel: 44-114-271-8674; Fax: 44-114-271-8693; E-mail: [k.r.wylie@sheffield.ac.uk](mailto:k.r.wylie@sheffield.ac.uk).

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## Focus Points

- Erectile dysfunction can be a sentinel marker for diabetes mellitus, cardiovascular disease, and hypogonadic states.
  - Major depressive disorder and anxiety often contribute to erectile dysfunction.
  - Multifactorial interventions are often required for maximal resolution of symptoms.
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## Abstract

*Erectile dysfunction is a common condition and is recognized as an important marker for underlying vascular and other disease states. A thorough evaluation with selected investigations will allow the clinician to offer a range of effective therapies and interventions. The evidence for psychologic interventions is described along with a description of other treatment options. Integrated assessment and therapeutic options allow for high success and patient satisfaction.*

## Introduction

Erectile dysfunction is defined as the inability to achieve or maintain an erection sufficient for sexual activity. The effect of erectile dysfunction on patients and their partners can be devastating. Routinely addressing patient sexual health is feasible for primary care physicians (PCPs), and a brief patient questionnaire is an excellent tool for PCPs to initiate communication on the topic.<sup>1</sup>

A cross-sectional, population-based, nationally representative survey in a general community setting

estimated the overall prevalence of erectile dysfunction as 22%.<sup>2</sup> Using targeted phone lists to create equivalent representation among Hispanic (n=676), Caucasian (n=901), and African-American (n=596) males  $\geq 40$  years of age, the survey found prevalence rates of 21.9% for Caucasian men, 24.4% for African-American men, and 19.9% for Hispanic men, with the odds ratio rising with increased age.

For all racial groups, probability of erectile dysfunction increased with diabetes, hypertension, and moderate-to-severe lower urinary tract symptoms (LUTS). For Hispanic men, moderate LUTS, hypertension, major depressive disorder (MDD), and an age  $\geq 60$  years increased erectile dysfunction probability. In Caucasian men, probability increased for patients with diabetes and those  $\geq 70$  years of age. Severe LUTS increased probability of erectile dysfunction for African-American men. Probability decreased overall in patients who exercise and had college experience versus those who only had a high school education. Probability decreased in Hispanic men with high school or college-level education, and in African-American men who exercised and had high-quality relationships. Alcohol intake was also associated with high probability of erectile dysfunction in the African-American population.

Components in the etiology of erectile dysfunction is multifactorial. Common vascular diseases associated with erectile dysfunction are atherosclerosis, heart disease, hypertension, hyperlipidemia, and diabetes mellitus. Endothelial dysfunction is recognized as the common denominator. As endothelium is present throughout the arterial tree, dysfunction at one point that is symptomatic of erectile dysfunction may be a marker for silent problems elsewhere (such as in the coronary arteries).

Thus, a patient with erectile dysfunction is a vascular patient until proven otherwise.<sup>3-5</sup> Erectile dysfunction may precede a chronic or acute presentation of chest pain by an average of 3 years. Men with these common vascular conditions are nearly four times more likely to develop complete erectile dysfunction.<sup>6</sup> Venous-occlusive disorder, previously called venous leak, is the other main vascular etiology for erectile dysfunction.

Neurologic conditions associated with erectile dysfunction are multiple sclerosis, diabetes mellitus, alcoholic neuropathy, spinal cord injury, and Parkinson's disease. Endocrine problems include low testosterone, high prolactin, and thyroid dysfunction. Common psychiatric disorders include anxiety, MDD, and drug and alcohol dependence. Surgical procedures, especially those performed on the rectum and prostate, may affect sexual function. Medications, particularly cardiovascular and psychiatric, can have a profound effect on erectile function.

Psychological factors in the etiology of erectile dysfunction include obsessive personality traits; developmental factors include early sexual experiences and sexual trauma; and maintaining factors include poor body image, self-esteem, and confidence. Health problems, relationship problems, and life changes are also factors in the development of erectile dysfunction. Chronic health problems, vocational issues, and other contextual factors, such as children or elderly parents in the home and other factors which cause lack of privacy, are described by Althof and colleagues.<sup>7</sup>

## Assessment

Assessment involves a detailed medical, surgical, psychiatric, psychological, psychosexual, and relationship history.<sup>8</sup> In approximately two-thirds of cases, a combination of contributory factors will exist and the number of cases that are solely due to psychological or organic factors will be in the minority. The most frequently used questionnaire is the International Index of Erectile Function.<sup>9</sup> Scores from the index define erectile dysfunction as mild, moderate, or severe. A physical examination is an essential component of sexual dysfunction evaluation in every case. Examinations should focus mainly on the cardiovascular, gonadal, and neurologic systems, and initial investigations should include fasting glucose, lipid profile, and morning testosterone. When concurrent symptoms of low sexual desire are present, prolactin should also be measured.<sup>10</sup> Investigation by a specialist may be appropriate in some cases and could include nocturnal penile tumescence and rigidity monitoring (utilizing RigiScan), Doppler ultrasound of the cavernous arteries, and nerve conduction studies.

Evidence suggests that some men who have a predominantly psychogenic etiology for erectile dysfunction should be informed that an erection is possible using physiologic measurements. Evidence

of the occurrence of a normal erection is often sufficient for the patient to either begin psychological therapy or be sufficiently reassured that no serious physical causes are present.<sup>11</sup> In patients with a mixed etiology of erectile dysfunction, clinicians may find it necessary to facilitate an erection using an erectogenic agent or a vacuum device. When the cause is psychological in origin, production of an active erection that can be observed by the patient and his partner may be helpful in moving the “stuck couple system” forward, because the end goal for the couple—achieving and maintaining an erection—is confirmed as achievable using one or more treatment pathways.<sup>12</sup>

## Psychiatric Concerns

Erectile dysfunction and MDD often co-exist and can be compounding conditions. Sildenafil has been shown to be efficacious for erectile dysfunction in men with mild-to-moderate MDD. Treatment of erectile dysfunction improves depressive symptoms and quality of life.<sup>13</sup> Frequency of ejaculation and orgasm improved when compared to placebo in men with erectile dysfunction and MDD who were also taking a selective serotonin reuptake inhibitor (SSRI).<sup>14</sup> The added value of improving compliance with medication and avoiding reduction to a subtherapeutic dose of antidepressant is important to avoid the likelihood of depressive symptoms and drug-induced erectile dysfunction worsening MDD. For men with psychotic symptoms, many medications may also substantially impair sexual function.<sup>15</sup>

## Treatment Options

Physical treatment often provides the opportunity to explore psychological factors in detail with patients during the process of reviewing treatment effects. In addition, when psychological factors are believed to be maintaining the problem, reduction of performance and anticipatory anxiety by restoring sexual function using a physical treatment can often have a considerable impact in regenerating spontaneous sexual activity.

Except under certain contraindications, it is prudent for the patient to choose his preferred treatment. Clinical experience shows that this method is most likely to be effective, regardless of the most appropriate treatment being chosen given the considerable psychological contribution toward sexual function in most cases.

## Psychological Interventions

Many psychological interventions may be advantageous in even the most complex and organic cases. Couples therapy may be indicated where there is marked discord within the general relationship.<sup>16</sup> Psychotherapy aims to restore patient potency to an optimal level given the limits of physical well-being and life circumstances.<sup>17</sup> Literature suggests a wide variety of therapies from the simplicity of improving communication to a more complex program of combined psychotherapies, or a combination of psychotherapies and medical intervention.

## Communication and Negotiation

Fisher and colleagues<sup>18</sup> evaluated 449 men with erectile dysfunction, 429 partners of erectile dysfunction patients, and 389 PCPs using questionnaires. Some patients reported that they had communicated about erectile dysfunction on a high frequency, whereas others had either communicated about erectile dysfunction on a low frequency, or had not communicated about the condition. The authors reported positive responses regarding communicating about erectile dysfunction and negative responses regarding failing to communicate about erectile dysfunction. The authors

concluded that communication is important in the acceptance of erectile dysfunction and can have therapeutic value.

Farre and colleagues<sup>19</sup> stress the importance of communication by suggesting that psychiatrists should perform a “general intervention” in patients with erectile dysfunction. This should include reassurance, the provision of appropriate sexual information, and the modification or correction of any sexual myths that the patient may hold.

## Education

Studies have proposed that education can enhance the effect of erectile dysfunction therapies or could be used as a sole treatment.<sup>20-22</sup> One study<sup>20</sup> compared the effect of sildenafil versus sildenafil and psychoeducation in 83 couples. The 60–90-minute psychoeducation workshop had a behavioral motivational theme and was accompanied by written educational material, which contained goals for treatment, a communication homework assignment, referral sources, and references for self-improvement books. The authors found that despite there being no difference in treatment outcome (eg, increase in potency) between the two groups, couples who took the psychoeducation workshop reported a higher level of satisfaction with treatment and increased communication about sex than couples in the medication-only group.

## Psychodynamic Therapy

Psychodynamic therapy is typically used for individual patients rather than couples, and seeks to find past experiences related to causation. In particular, psychodynamic therapists would examine the possibility of an unresolved Oedipal complex in patients with erectile dysfunction.<sup>17</sup> Optale and colleagues<sup>23</sup> combined psychodynamic psychotherapy with virtual reality in an attempt to treat erectile dysfunction. Therapy consisted of 12 sessions of 1-hour duration over the course of 25 weeks. The first session involved acoustic therapy, the second session used psychotherapy, and sessions 3–12 alternated between acoustic therapy and virtual reality experiences. Virtual reality consisted of scenarios developed to arouse memories and emotions within the patient, which could be discussed with the therapist afterward. The process aimed to rebuild sexual identity, which the authors hypothesized was initially acquired in the early years of life. The patients' partners were also offered three sessions to identify problems. Of 50 study patients with erectile dysfunction solely due to psychogenic causes, erectile dysfunction improved or was resolved in 76% of patients. Forty-five percent of the 60 patients with erectile dysfunction of mixed causation found improvement in their symptoms or remission. These results remained after 6 months.

## Cognitive Therapy

Cognitive therapists perform either singles or couples therapy to tackle faulty scripts or beliefs that interfere with erectile response, and replace them with more adaptive cognitive strategies.<sup>17</sup>

## Behavioral Therapy

Behavioral therapists aim to eliminate performance anxiety and increase confidence to treat erectile dysfunction.<sup>17</sup> In one study, 37 men with erectile dysfunction were evaluated.<sup>24</sup> Along with their partners, 23 of the men completed six sessions of couples therapy consisting of Modified Modern Sex Therapy and Behavioral Systems Couple Therapy. The study found improvement in 20 of the couples whom completed therapy (14 couples had excellent or moderate outcomes) and no improvement in three couples.

O'Donoghue<sup>22</sup> suggested that therapists must explain the origins of erectile dysfunction to the couple through simple education. Use of techniques established by Masters and Johnson<sup>25</sup> in 1970 (including banning of sexual intimacy, nongenital sensate focus, genital sensate focus, and vaginal penetration) are encouraged. The study also highlighted several potential limitations to this treatment method, including situational erectile dysfunction, single men, unwilling or embarrassed partners, and religions that forbid masturbation.

Stravynski and colleagues<sup>26</sup> studied 69 single men and compared interpersonal difficulties-orientated therapy, sexual dysfunction-orientated therapy, a combination of the two therapies, and assessment only. Patients who received therapy had 19 sessions of 90-minute duration. Interpersonal difficulties-orientated therapy was based on social skills training that consisted of behavior-modification techniques (eg, description of desired behavior, modeling, role rehearsal, self monitoring, and discussion). Sexual dysfunction-orientated therapy involved masturbation exercises, instruction in sensate focus, stop-start and squeeze techniques, sensory awareness exercises, sexual misconception discussion and correction, and practice in disclosing sexual inadequacy fears. Outcomes were superior for patients who received interpersonal difficulties-orientated therapy alone or in combination with other therapies than patients who received sexual dysfunction-orientated therapy alone. The authors concluded that treatments focusing on interpersonal difficulties had better efficacy than those focusing on sexual dysfunction in single men. Maurice<sup>27</sup> provides an excellent summary of some of these interventions within clinical scenarios.

## Creative-Dynamic Image Synthesis

Creative-dynamic image synthesis has its base in neurolinguistic programming and utilizes emotions, memories, words, and drawing to overcome problems.<sup>28</sup> Sommer and colleagues<sup>28</sup> compared creative-dynamic image synthesis, oral yohimbine, and placebo in 69 erectile dysfunction patients where no organic cause for erectile dysfunction had been identified. Patients in image synthesis attended sessions alone and were asked to draw a picture representing their impotence and then a picture representing their aggression. Afterward, patients were asked to integrate these two pictures using memory, emotion, and self-induced trance and draw a corresponding picture. With the therapists' guidance, patients then applied three to four powerful positive key phrases to this picture. This completed image was to be taken home by the patient and focused on three times a day to help overcome erectile dysfunction. The authors claimed that this process could be performed within 4–15 sessions. At 6 months post-therapy, potency was found to be increased by 75% in patients who performed image synthesis compared to 55% in patients who took oral yohimbine and 30% for those taking placebo.

## Humanistic Therapy

Kleinplatz<sup>29</sup> proposed the use of experiential psychotherapy. In this therapy model, patients attend alone and describe a strong experience or memory. The therapist encourages the patient to welcome feelings that this experience or memory may arouse in an attempt bring the experience "into reach." The aim of therapy is for the patient to "become" the experience, thus becoming what is deeper within them, which is a process called actualization. The goal for this method is for the client to change dramatically by this process and for the original problems to cease to exist.

## Systemic Therapy

Systemic therapists find that erectile dysfunction is often related to a couple's emotional relationship. Atwood and colleagues<sup>30</sup> discussed tools that a systemic therapist may use to treat erectile dysfunction, but stated that medical interventions should be used if indicated. The authors said that systemic therapists should use a curious, respecting, empathic, understanding, and hopeful approach to explore a couple's meaning systems as well as provide a calm and safe environment for any crisis

that may arise. The therapist should also work on building communication between the couple, allowing empowerment, anger diffusion, and time to discuss any guilt or ambivalence present. Homework tasks are an essential feature of this therapeutic approach, with bibliotherapy being a good start for education. Couples could try to “connect and caress,” brainstorm activities, and have “date nights.” Sensate focus can also be used. Other important areas for discussion include the “loss of the erectile dysfunction” and “future focus.”

Hawton<sup>31</sup> highlighted the importance of a systemic approach by describing that in many men with erectile dysfunction there is significant sexual dysfunction in the partner that predates the onset of his symptoms.

## Integrated Therapies

Rosen<sup>32</sup> presented a combined cognitive-behavioral approach in erectile dysfunction treatment that uses bibliotherapy, education, cognitive restructuring, and script adaptation to overcome unrealistic expectations and sexual ignorance. Self-hypnosis and fantasy training procedures are also indicated, along with positive imagery training with or without masturbation. Rosen also noted the importance of interpersonal and systemic approaches in the management of sexual dysfunction. The use of a combined approach is supported by other studies.<sup>20,33</sup>

Giommi and colleagues<sup>21</sup> advocated an integrative approach with a focus on cognitive-behavioral therapy (CBT) and counseling. They found that sexual psychotherapy should be short, motivational, and active in producing a change in thought and behavior. They suggested several questions that a therapist should ask during the initial meeting with the couple, including which areas of sexuality are or are not present in the relationship, what does erectile dysfunction inhibit, and what does it protect. Counseling should be educational and provide simple explanations of male and female sexuality as well as finding areas where possible changes can be made.

## Integrated Therapies and Medical Treatments

Several studies support the use of psychotherapy combined with medical interventions.<sup>17,19,31,34,35</sup>

Farre and colleagues<sup>19</sup> stated that CBT should be used with adjuvant pharmacologic intervention. Initially, the pharmacologic agents should be used to help overcome the effects of anxiety and quickly begin psychotherapy. Agents should be reduced as self-confidence is gained.

Melnik and Abdo<sup>36</sup> studied 30 men with erectile dysfunction who were randomly allocated to receive group psychotherapy and sildenafil, sildenafil only, or group psychotherapy only. The weekly psychotherapy was time limited and theme based. The authors found an improvement in erectile function in all three groups. However, improvement was only significant in patients who received group psychotherapy either alone or with sildenafil. There was no statistical difference between patients receiving therapy and combination treatment, suggesting that psychotherapy was the major factor that improved erectile function.

Another study examined integrating cognitive, behavioral, and psychodynamic approaches with pharmacotherapy.<sup>34</sup> Three methods were cognitive restructuring and insight therapy with the patient alone, improving communication and overcoming role conflicts and relationship problems with couples, and intervention with the partner alone. This latter method considered the partner’s subjective experience, sabotage attempts, and their degree of involvement.

A further study of 45 men with erectile dysfunction compared psychotherapy plus vacuum constriction device treatment to psychotherapy alone.<sup>35</sup> Patients and their partners received between three and six 40–50-minute sessions of psychotherapy, integrating relationship therapy with Masters and Johnson’s sex therapy. Behavioral, cognitive, systemic, and brief-dynamic techniques were used. The study concluded that the early addition of a vacuum constriction device to psychotherapy in men with erectile

dysfunction led to an improvement in treatment outcome.

## Pharmacologic and Non-Pharmacologic Interventions

First-line treatments for patients with erectile dysfunction with difficulty either attaining or maintaining erection are oral phosphodiesterase type 5 (PDE-5) inhibitors, such as sildenafil, tadalafil, and vardenafil. All three oral PDE-5 inhibitors require sexual activity to initiate the sexual arousal process. The overall effectiveness of these agents is approximately 80% in psychological cases and approximately 50% in organic cases. Sildenafil, the first PDE-5 inhibitor, has become well established as an initial treatment. Patients start with a 50 mg dose taken 1 hour before anticipated sexual activity. Sexual foreplay and activity are required for a full arousal response. Sildenafil is available in three doses and can be tailored up to 100 mg or down to 25 mg depending on clinical response and side effects. The most common side effects are headache (16%), facial flushing (10%), and dyspepsia (7%). A mild and transient disturbance of color vision with a blue hue alongside increased sensitivity to light is described by approximately 3% of men. Absorption is delayed by a full stomach. Sildenafil is a safe treatment for erectile disorder. It is contra-indicated in patients who are taking systemic or as-required nitrate medications (eg, glyceryl trinitrate sprays), as this causes intense and possibly fatal hypotension. Caution should also be taken when prescribing this and other agents in patients with cardiovascular disease, as moderate exercise may provoke untoward cardiac events.

Tadalafil has a different selectivity for PDE subtypes when compared with sildenafil and vardenafil. It has an extended plasma release, with a half-life of approximately 17.5 hours. This allows patients to have successful sexual intercourse for up to 24–36 hours after a dose of 20 mg (dosage can be 10 mg or 20 mg). Side effects are headache, dyspepsia, back pain, flushing, myalgia, and nasal congestion. Effects typically occur in <15% of patients and may not occur for the duration of action of this agent. There is no delay in absorption of food in the stomach and no alteration of color vision. In patients on nitrate medications, the same caution must be applied as with sildenafil.

Vardenafil has a profile similar to sildenafil and is available in 10 mg and 20 mg doses. It is well tolerated, with a low adverse-event profile, the most common being headache, flushing, dyspepsia, and rhinitis. Side effects occur in <15% of patients. A full review of all PDE-5 inhibitors is available elsewhere.<sup>37</sup> Other oral agents include apomorphine, which has been withdrawn from the market, and yohimbine, which is an unlicensed preparation and available on a named-patient basis only.

In the small number of patients in whom there is biochemical and/or clinical evidence of low testosterone, supplementation is appropriate and can be effective in restoring normal function.<sup>38</sup> However, the latter is not inevitable and concurrent erectogenic agents may be required. PDE-5 inhibitors may be ineffective where the testosterone levels are low.

For men where there is failure of sildenafil (or another PDE-5 inhibitor) therapy, medication optimization, counseling, and modification of associated risk factors can provide success. Failure may be due to lack of efficacy or side effects. Inadequate instructions, follow-up, suboptimal dosing, insufficient time, number of dose attempts, and insufficient clarity about safety issues or concerns for the patient are all important factors that the clinician must attend to.<sup>39</sup>

Second-line treatments include intra-urethral and intracavernosal agents as well as vacuum devices. Medicated Urethral System for Erection (MUSE) is a device containing a small intra-urethral pellet that is inserted into the end of the urethra to bring about penile erection. The normal starting dose is 250 µg and the dosage can be adjusted higher or lower depending on response. The most common side effect is a burning sensation and discomfort in the urethra. The erection takes approximately 10 minutes to evolve. Patient drop-out rate is high, which may reflect the need for skilled advice on how to make this agent effective and the relatively-intrusive nature of this treatment option. Other side effects include urethral bleeding and hypotension. Patients should have the first dose given with medical or nursing supervision. The dosage is contraindicated when the patient's partner is pregnant or is likely to conceive. There is some evidence that effectiveness may be improved by using MUSE in combination

with sildenafil or a constriction ring.<sup>39</sup>

Intracavernosal injection (ICI) therapy, which injects alprostadil into the intracavernosal penile body, is extremely effective. The technique of injection must be taught using video and direct observation by a nursing or medical technician. The dose should be cautiously increased in non-responders, as priapism may occur. In patients with needle phobia or dexterity problems, auto-injecting devices are available. Alprostadil is the most widely used agent and is effective in >80% of patients. Penile pain may occur. Penile fibrosis and priapism are rare side effects. Although many cases of fibrosis will resolve spontaneously, clinicians should inform patients that this is a recognized side effect. The use of ICI is generally contraindicated in patients with penile plaques, including Peyronie's disease. Other injectable agents include smooth-muscle relaxants papaverine, moxislyte, and phentolamine. Combinations of papaverine, alprostadil, and "tri-mix" (alprostadil, papaverine, and phentolamine) are useful in more resistant cases, which are typically patients with marked arterial disease. As some of these agents are unlicensed, patients must give informed consent and be made aware in advance of potential complications such as priapism and fibrosis. Vasointestinal polypeptide is combined with phentolamine, which is also available on a named-patient basis. The most common side effects are facial flushing and tachycardia, but there is a lower incidence of pain when compared with intraurethral alprostadil.

Vacuum devices are noninvasive and effective in most men with erectile dysfunction, including those with vascular problems. A cylindrical tube is placed over the penis and a vacuum created by using either a hand-held or electrical pump draws air out of the cylinder. The negative pressure around the shaft of the penis draws blood into the erectile tissue, thereby creating an artificial erection. A constriction ring is placed around the base of the shaft of the penis before the tube is removed, which maintains the erection. The ring should not be used for >30 minutes at a time. The process is fairly immediate and the device may be used during foreplay by both partners if willing. Side effects include a gradual discoloration and feeling of coldness to the penis while the ring is attached as well as the possibility of bruising and difficulties with ejaculation. If the glans does not become firm, one option is to augment this treatment with MUSE. This is a passive treatment and can be effective in non-responders to most other treatments. When effective, vacuum devices remain the treatment of choice and paired with sildenafil.<sup>39,40</sup>

When surgical disease has been identified using color Doppler ultrasound and typically following trauma (eg, pelvic injury, penile fracture, fistulae between the corpora cavernosa, and spongiosum, etc) in men <40 years of age, arterial reconstruction may be considered. The inferior epigastric artery is rerouted and anastomosed to the dorsal penile artery or vein. The success rate is approximately 65%. Patients with proven veno-occlusive disorder are rarely suitable for surgical intervention. In patients with severe arterial disease and/or Peyronie's disease, when erections are not possible or there is a considerable bend in the penis, the use of penile prostheses (implants) may be beneficial. The patient and partner should be fully counseled with regard to the limited benefit that can be obtained. Malleable semi-rigid implants and inflatable hydraulic implants are available, although there are cost implications. The implant does not restore normal erectile processes but makes the penis rigid enough for sexual intercourse. The glans may remain flaccid. Long-term results are satisfactory in up to 90% of patients.

Patients with veno-occlusive disorder may find value in using penile rings, which act in an occlusive way once the original erection is attained.<sup>41</sup> Many men use these rings to strengthen the firmness and size of their erection regardless of any sexual dysfunction; thus, their use may be normalized for patients. Patients should be advised not to wear them for >30 minutes at a time. Pelvic-floor training has also been reported as a useful treatment for mild veno-occlusive disorder and erectile dysfunction in general.<sup>42</sup>

Dopamine, serotonin, and nitric oxide have an important role in sexual function, and antidepressants (including SSRIs) and antipsychotics that interfere with their transmission are likely to bring about sexual problems, including erectile dysfunction. A review of sexual dysfunction in depression and schizophrenia is provided by Baldwin and Mayers.<sup>43</sup>

## Conclusion

A careful assessment that establishes the etiologic factors of erectile dysfunction, shares a decision pathway on the appropriateness for further investigation, and describes therapy choices from which the patient may select, will lead to a successful outcome. In more complicated or treatment-resistant cases, there is a need for integrated assessment and intervention services that offer patients the best and most appropriate treatment, whether it be physical, couples counseling, conjoint sex therapy, individual psychotherapy, psychiatric intervention, or a combination of the above. **PP**

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