

Assessment and Treatment of Male Sexual Dysfunction in Primary Care

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Pretest/Posttest

1. Approximately what percentage of men aged 40-70 are likely to experience some degree of erectile dysfunction (ED)?
 - a) 10%
 - b) 30%
 - c) 50%**
 - d) 70%
 - e) 90%
2. Approximately what percentage of men with erectile dysfunction (ED) do not receive treatment for their condition because they either do not seek medical attention or their physician does not discuss it with them?
 - a) 20%
 - b) 40%
 - c) 60%
 - d) 80%**
3. Approximately what percentage of men with heart disease believe that it is important for their physician to speak to them about sexual function?
 - a) 35%
 - b) 55%
 - c) 75%
 - d) 95%**
4. Approximately what percentage of patients taking SSRI antidepressants will experience impairments to their sexual function?
 - a) up to 10%
 - b) up to 30%
 - c) up to 50%**
 - d) up to 70%
 - e) up to 90%

5. What percentage of men aged 70 are likely to have Hypoactive Sexual Desire Disorder (HSDD), also known as low desire?
- a) 0%
 - b) 25%**
 - c) 50%
 - d) 75%
 - e) 100%
6. In what percentage of cases, will sildenafil (Viagra™) improve erectile function in men with psychogenic erectile dysfunction (ED)?
- a) 0%
 - b) 20%
 - c) 40%
 - d) 60%
 - e) 80%**
7. The relative risk of erectile dysfunction among men who smoke is:
- a) 1.5
 - b) 2.2**
 - c) 3.1
 - d) 3.5
 - e) 4.1
8. It is well known that antidepressant medications are associated with decreased sexual desire. What other medications are also associated with low desire?
- A. Antihypertensive
 - B. Antiarrhythmic
 - C. Antineoplastic
 - D. Anticonvulsant
- a) A & D
 - b) A & B
 - c) B & C
 - d) C & D
 - e) All of the above**
9. Which of the following statements regarding Hypoactive Sexual Desire Disorder (HSDD) is true?
- a) Many men who meet the clinical definition of HSDD have testosterone levels in the normal range.**
 - b) A diagnosis of HSDD should not include men who have little interest in sex because they no longer find their partners attractive or are bored with their marriages.
 - c) Both of the above are true.
 - d) Neither of the above are true.

10. Androgen supplementation may help men with low desire associated with below normal testosterone increase their vitality and desire for sex. However, androgen supplementation is not appropriate or safe for men with a variety of medical conditions including which of the following?

- A. Prostate disease
- B. Congestive heart failure
- C. Sleep apnea
- D. Liver disease
- E. Renal disease

- a) A & B & E
- b) A & B & D
- c) A & B & E
- d) C & D & E
- e) **All of the above**

11. According to the American Psychiatric Association, the diagnostic criteria for premature ejaculation includes which of the following?

- A. Ejaculation before, on, or shortly after penetration.
- B. Ejaculation before 20 to 30 penile thrusts.
- C. Ejaculation before 40 to 50 penile thrusts.
- D. Ejaculation before the person wishes it to occur.
- E. Ejaculation less than 4 minutes after penetration.

- b) E
- c) A & E
- d) B & D
- e) **A & D**
- f) C

12. Research suggests that 75% of men ejaculate how many minutes after penetration has begun?

- a) 1 minute
- b) **2 minutes**
- c) 3 minutes
- d) 4 minutes
- e) 5 minutes

13. In cases of severe and persistent premature ejaculation, appropriate treatment can include which of the following?

- A. Learning the “squeeze” technique.
- B. Learning the “stop-start” technique.
- C. SSRI antidepressant.
- D. Sildenafil (Viagra™)

- a) A & B
- b) A & C
- c) B & D
- d) A & B & C
- e) **All of the above**

14. Asking a male patient if he is able to get an erection with self-stimulation (masturbation) can yield useful information for which of the following reasons?

- A. It can help to distinguish between organic and psychogenic erectile dysfunction (ED).
- B. A "no" response by the patient is a possible indication of low desire.
- C. A "no" response by the patient is a possible indication of generalized ED.
- D. A "yes" response by the patient is a clear indication that the patient does not have ED.

- a) A
- b) A & C**
- c) B & D
- d) A & B
- e) D

15. Many men with cardiac conditions take nitrates. Which of the following are appropriate ED treatment options for these men?

- A. Alprostadil
- B. Sildenafil
- C. Vacuum constriction device

- a) A & B
- b) A & C**
- c) B & C
- d) All of the above
- e) None of the above

16. Which of the following questions are likely to yield useful information in brief screening for sexual dysfunction in men?

- A. Do you get fewer erections than when you were younger?
- B. Do you have sexual thoughts or fantasies?
- C. Do you look at sexually explicit videos or magazines?
- D. Do you feel that you ejaculate (come) too quickly?
- E. Do you have pain during or after sex?

- a) A & B & D
- b) A & B & E
- c) A & D & E
- d) B & C & D
- e) B & D & E**

Learning Objectives

1. Become aware of the importance and role of the physician in screening for and treating male sexual dysfunctions.
2. Determine the prevalence and correlates of erectile dysfunction, premature ejaculation, and low desire.
3. Develop the skills to screen male patients for sexual dysfunction.
4. Determine the treatment strategies appropriate for male patients with erectile dysfunction, premature ejaculation and low desire.

Quick Reference

Prevalence: Erectile dysfunction; 52% among men aged 40-70. Premature ejaculation; 30%. Hypoactive sexual desire disorder (low desire); 16% and 26% among men aged 70+.

Implications: There is a strong association between sexual dysfunction and impaired quality of life including significantly reduced individual psychological health and well-being and quality of couple relationships.

Risk factors/predictors: Age, poor physical and/or psychological health are associated with the occurrence of sexual dysfunction. A wide variety of medical conditions including heart disease, diabetes, multiple sclerosis, depression, hypertension, and prostate disease constitute risk factors for the development of sexual dysfunctions among men.

Diagnostic criteria: Erectile dysfunction: Persistent or recurrent inability to attain, or to maintain until completion of the sexual activity, an adequate erection. Premature ejaculation: Persistent or recurrent ejaculation with minimal sexual stimulation before, on, or shortly after penetration and before a person wishes it. Low desire: Persistent or recurrent deficiency or absence of sexual fantasies and desire.

Screening: Brief questions to evaluate the phases of the male sexual response cycle and International Index of Erectile Dysfunction (short form). Laboratory tests include fasting glucose or glycosylated haemoglobin, blood lipid profile, and serum testosterone.

Treatment: Level 1 - All patients: screening for sexual dysfunction and provision of information. Level 2 - Patients with sexual dysfunction: provision of least invasive treatment and brief psychosexual counselling. Level 3 - Patients with poor treatment outcomes: progression to more invasive treatment, referral to medical specialist, referral for sex therapy.

Core Content

Introduction: The Physician's Role in Addressing the Sexual Function of Primary Care Patients

Primary care physicians routinely ask their patients about sexual behaviour with respect to risk behaviours for sexually transmitted infections and for issues related to contraception and fertility. Some physicians, however, are less likely to ask about sexual function. If these issues are not raised by the physician, it is unlikely that these issues will be addressed at all. A survey of adults aged 25 and older found that 85% would like to discuss a sexual problem they might have with a physician but 68% were reluctant to ask a physician about sexual problems and 71% thought that their physicians would dismiss sexual concerns¹. In another study, it was found that 70% of male patients felt it was appropriate for general practitioners to discuss sexual concerns with their patients, and 35% reported sexual concerns but only 2% had a notation on their charts indicating that a consultation about a sexual concern took place². Male patients with a history of cardiac disease likely have concerns about sexual function. A recent study of cardiac patients found that 98% felt that their physician should talk to them about sexual function but only 73% felt that

their physician was comfortable doing so, 60% reported that their physician had ever discussed it with them, and only 15% had ever had a discussion with their physician about specific difficulties they might be having with sexual activity³. Increasing numbers of patients seen in primary medical care are being treated with SSRI antidepressants. Up to 50% of these patients will experience adverse effects on their sexual function⁴. However, physicians consistently underestimate the prevalence of antidepressant-associated sexual dysfunction⁵.

In addition to improving the health and well-being of patients, screening for sexual dysfunction often uncovers previously undiscovered medical conditions. A study conducted at a general medicine outpatient department found that taking a sexual history uncovered new and important medical information in 26% of patients and resulted in changes to medical treatment in 16% of these patients⁶. Research has also suggested that about 60% of otherwise healthy men complaining of erectile dysfunction (ED) have abnormal cholesterol⁷.

Meeting Patient Concerns About Sexual Function With Information and Practical Suggestions

In recent years, important advances have been made in the pharmacological treatment of male sexual dysfunction. As discussed in more detail below, there are now well-established or promising pharmacological agents available for the treatment of erectile dysfunction⁸, neurologically-based premature ejaculation⁹, and low desire¹⁰. However, it should be noted that pharmacological treatments do not address or resolve relationship or psychological problems and that these factors are often the major source of patient distress related to sexuality.¹¹ While the introduction of new pharmacological agents has significantly increased the ability of physicians to effectively treat sexual dysfunctions, it is important to consider that many patient sexual concerns and problems can be effectively addressed by providing basic information, correcting misconceptions and by making practical suggestions for modifying behaviour¹².

Many men enter the physician's office with anxiety or concern about their sexual function that is rooted in a lack of accurate information or unrealistic expectations regarding normal male sexual function. Physicians are in a unique position to provide authoritative information on sexual function that will help to alleviate patient concerns. For example:

1. It is reasonable for middle-aged and elderly men to continue to engage in and enjoy sexual activity. Nevertheless, physicians can help patients to understand that levels of sexual desire, frequency of erections, and rigidity of erections will gradually decline as a natural consequence of the aging process;
2. Men with medical conditions (e.g., diabetes, heart disease, prostate cancer, spinal cord injury, arthritis etc.) often lack information on how their conditions can affect sexual functioning and what steps can be taken to address the sexuality related issues that may result;
3. Many common medications, for example SSRI antidepressants, can impair sexual function. It is important for physicians and their patients to assess how medications a patient is taking may have sexual side effects and how these interactions can be managed;
4. There are many lifestyle modifications that men can take to improve sexual function. For example, improving cardio-vascular conditioning, quitting smoking, and reducing stress will, for many men, enhance their ability for adequate sexual functioning;
5. Many men concerned about their sexual function will also benefit from knowing that initiating sexual activity when well rested (e.g., not late at night), avoiding a heavy meal or more than a moderate amount of alcohol prior to sexual activity can enhance sexual function.

In some cases, the provision of information and practical suggestions for behaviour modification is sufficient to address the patient's concern. Nevertheless, clinically defined sexual dysfunctions are common among men and all men should be systematically screened for sexual dysfunction by their primary care

physicians. As outlined in Table 1, there are three basic levels of intervention for primary care physicians with respect to the assessment and management of male sexual dysfunction.

An Important Consideration in the Pharmacological Management of Sexual Dysfunction

As discussed in detail in this module, there are a number of pharmacological agents that can constitute a key component in the effective treatment of male sexual dysfunctions. However, these medications are contraindicated for use with patients with a range of different medical conditions and they are also contraindicated for use with other specific drugs. It is essential that physicians carefully screen their patients for such contraindications before prescribing pharmacologic agents to enhance sexual function.

Screening and Treating Gay and Bisexual Men for Sexual Dysfunction

In general, gay and bisexual men can be screened and treated for sexual dysfunction in the same manner that heterosexual men are^{13 14}. However, physicians treating gay or bisexual men for sexual dysfunction should be aware of how issues related to sexual identity may, in some cases, be related to problems related to sexual functioning. For example, gay men who have not fully accepted or come to terms with their sexual orientation may, as a consequence, be vulnerable to difficulties in the desire and arousal phases of the sexual response cycle¹⁵. In order to adequately screen for and treat sexual dysfunction among gay and bisexual men, physicians should become, if they are not already, familiar with sexual health issues that are particularly pertinent to gay and bisexual men¹⁶.

Table 1: Levels of Intervention in the Assessment and Management of Male Sexual Dysfunction

Level 1. All Patients

Screening for sexual dysfunction
Provision of information

Level 2. Patients with Sexual Dysfunction

Provision of least invasive treatment
Brief psychosocial counselling

Level 3. Patients with Poor Treatment Outcomes

Progression to more invasive treatment
Referral to medical specialist (e.g. urologist, endocrinologist, psychiatrist)
Referral for sex therapy

Sexual Function and Dysfunction: Basic Definitions and Concepts

A number of definitions for both sexual function and sexual dysfunction are available in the medical-sexological literature. For the purposes of screening for sexual dysfunction by the primary care physician a basic conceptualization of these terms for clinical purposes will suffice. There is general consensus that adequate sexual functioning consists of three basic stages: desire, arousal, and orgasm. Thus, sexual dysfunction can be defined as an impairment or disturbance in one of these stages¹⁷. In addition, sexual function can be affected by coital pain (dyspareunia), peyron's disease, or nongenital pain associated with sexual activity (e.g. coitally exacerbated back pain).

Sexual dysfunctions can be further classified as lifelong or acquired and generalized or situational. These classifications are important factors in determining the etiology and treatment of sexual dysfunctions.

Table 2: Categories of Male Sexual Dysfunction

Desire	Hypoactive Sexual Desire (Low desire) Sexual Aversion
Arousal	Erectile Dysfunction
Orgasm	Delayed/absent ejaculation Premature ejaculation
Pain	Dyspareunia, peyrone's disease, nongenital pain associated with sexual activity

Table 3: Basic Classifications of Sexual Dysfunction

Lifelong (also know as "primary")	Any sexual dysfunction that has always been present; e.g. a male who has never had an erection.
Acquired (also known as "secondary")	Any sexual dysfunction that follows a period of adequate sexual function.
Generalized	Occurs in all sexual situations and with all partners
Situational	Occurs only in certain situations or with certain partners

Table 4: Etiology of Sexual Dysfunctions: Contextual and Biopsychosocial Factors

Contextual Factors

1. Predisposing	Prior life experiences (e.g., childhood sexual trauma) Inherited characteristics (e.g, diabetes)
2. Precipitating (triggering)	Life events associated with initial onset (e.g., job stress, divorce ect).
3. Maintaining	Ongoing life circumstances or physical conditions that contribute to sexual dysfunction

Biopsychosocial Factors

1. Biological/medical	vascular, hormonal, neurological pharmacological
2. Psychological	cognitive, affective
3. Social/relational	Sociocultural influences (e.g., religious background, sex role) communication, relationship factors

Screening for Sexual Dysfunction

Primary care physicians should have clear procedures for inquiring about sexual function as a routine part of primary health care. This includes:

- A. Developing standard questions to ask patients with respect to sexual function;
- B. Integrating sexual function questions into a general health history.

As indicated in Table 5, there are a number of steps that physicians can take to ensure that physician inquiry about patient's sexuality is effective and comfortable for both the physician and patient.

Table 5: Tips for Inquiring About Sexuality Issues

- Inform patient that you will ask about sexuality
- Assure patient that discussion is confidential
- Inform patient that questions about sexuality are a standard part of assessment
- Use precise, clear and easily understood terminology (not slang)
- Maintain a nonjudgemental attitude and tone
- When asking patients about sexuality respond to their answers with affirmation and information
- Start with general, less sensitive questions and proceed to more detailed, more sensitive questions

To put their patients at ease, some physicians may wish to preface questions about sexual function by noting that such questions are standard and by asking permission to inquire about sexuality. For example,

“I have been asking you questions about different aspects of your health. As part of this, I ask all my patients about their sexual health. So I am going to ask you some questions about sexuality. Is that OK with you?”

General Introductory Questions

An assessment of sexual function can begin with some general questions that will allow the patient an initial opportunity to articulate sexual concerns that they may have in their own terms. For example,

“Many of my patients have questions or concerns related to sexuality. I wonder what your concerns might be?”

or

“Many people have questions or concerns about sex. Are there any questions about sex that you would like to ask?”

Such questions can help to quickly identify patient concerns and areas that need to be focused on. Nevertheless, it is important to specifically and systematically screen the patient for sexual dysfunctions that occur in each phase of the sexual response cycle. This can be done with a few standard questions, as illustrated in Table 6.

Table 6: Evaluating the Phases of the Male Sexual Response Cycle¹⁸

<u>Phase</u>	<u>Question</u>	<u>Possible Indications</u>
Desire	“Do you still feel in the mood, feel desire, have sexual thoughts or fantasies?”	Reduced desire may indicate hormonal or relationship problems, medication side effects, or depression.
Arousal	“Do you have trouble getting or keeping an erection?” “Do you sometimes wake up with an erection?” “Can you get an erection with self-stimulation (masturbation)?”	Waking up with an erection can help distinguish between psychogenic and organic ED. Having erections during masturbation but not during partnered sexual activity may indicate situational, psychogenic ED.
Orgasm	“Do you feel you ejaculate (come) too quickly?” “Do you ever have difficulty reaching orgasm or ejaculating?”	May indicate premature ejaculation. May indicate delayed (retrograde) ejaculation
Resolution	“Do you have pain after sex?”	May indicate Peyronie’s disease

Sexual Dysfunctions Affecting Men

As noted in Table 3, there is a range of sexual dysfunctions that can affect male patients. This module will focus on the three most common male sexual dysfunctions seen in primary medical care: erectile dysfunction, premature ejaculation, and low desire.

Erectle Dysfunction (ED)

Prevalence

Community-based surveys indicate that ED is highly prevalent among men in the general population. The National Health and Social Life Survey in the United States found that 7% of men aged 18-29 and 18% of men aged 50-59 had trouble maintaining or achieving an erection in the previous 12 months¹⁹. Results from the Massachusetts Male Aging Study (MMAS) indicated a combined prevalence of minimal, moderate and complete ED of 52% among men aged 40-70; 35% had moderate to complete ED. The MMAS showed that ED is age-related with a twofold to threefold increase in the prevalence of ED between the ages of 40 and 70. The prevalence of complete ED tripled from 5% to 15% between the ages of 40 and 70²⁰. Rates of ED are considerably higher among men with diabetes, heart disease, renal and liver failure, treated hypertension, depression, untreated ulcer, arthritis, allergy, Alzheimer's disease, Parkinson's disease among other medical conditions^{21 22 23}. It is well established that smoking is implicated in impaired erectile function. For example, a large-scale study involving 32,287 patients found a relative risk of 2.2 among men who smoked²⁴. Despite the increased public awareness of ED resulting from the introduction of sildenafil (Viagra™), it is estimated that more than 80% of men with ED are not treated because they do not seek medical attention or their physicians do not discuss sexual function with them²⁵.

Diagnostic Criteria

According to the American Psychiatric Association's diagnostic criteria, erectile dysfunction (or disorder) is defined as the "Persistent or recurrent inability to attain, or to maintain until completion of the sexual activity, an adequate erection"²⁶. It is important to note the terms "persistent" and "recurrent" in this definition as nearly all adult men will experience isolated and infrequent instances where they will be unable to attain or maintain a satisfactory erection. For men who do experience persistent or recurrent ED, it is important to distinguish between "generalized ED" and "situational ED". "Generalized ED means that a full erection does not occur under any circumstances; situational ED means that full erection occurs in some circumstances but not others"²⁷.

Generalized ED

With generalized ED, full erection does not occur under any circumstances including:

- sleep (erections during sleep are common among men without generalized ED)
- masturbation
- use of erotica (e.g., sexually explicit magazines, videos ect.)
- sexual non-intercourse play with a partner
- attempted intercourse

Situational ED

With situational ED, a erection occurs in some circumstances but not others. For example, a man can attain and maintain a erection;

- when asleep but not when awake
- during masturbation when alone but not when with a partner
- when engaged in non-coital sex play with a partner but not during intercourse
- when well rested and relaxed but not when tired and stressed.

Table 7: Conditions Associated with ED²⁸

Aging	Hyperprolactinemia	Peyronie's disease
Chronic disease	Hypothyroidism/	Priapism
Diabetes mellitus	Hyperthyroidism	Anatomic abnormalities
Heart disease	Life style	Medications
Hypertension	Smoking	Psychological issues
Lipid disorders	Chronic alcohol abuse	Depression
Renal failure	Neurogenic factors	Anxiety
Liver disease	Spinal cord injury	Social stressors
Vascular disease	Multiple sclerosis	Trauma/ injury
Endocrine abnormalities	Herniated disk	Pelvic trauma/ surgery
Hypogonadism	Penile injury/disease	Pelvic radiation

Drugs Associated with ED

A wide range of medications have been associated with sexual dysfunction, including ED^{29 30}. However, it the common antidepressant medications that are most frequently associated with ED. Research suggests that bupropion IR and SR and nefazodone are associated with the lowest risk of sexual dysfunction, whereas SSRIs are associated with higher rates³¹. Research suggests that sildenafil (ViagraTM) improves erectile function in men with antidepressant-associated ED³². There have been conflicting reports on the impact of antihypertensive medications on erectile function³³.

A Written Evaluation Tool for ED

If an initial sexual function screening (see above) has suggested ED, the physician may wish to more precisely explore the nature and severity of the ED by having the patient fill-out a short questionnaire such as the five-item International Index of Erectile Function.³⁴

Table 8: International Index of Erectile Dysfunction (IIEF-5)

1. How do you rate your confidence that you could get and keep an erection?

Very low	Low	Moderate	High	Very high
1	2	3	4	5

2. When you had erections with sexual stimulation, how often were your erections hard enough for penetration?

Almost never/ Never	A few times (much less than half the time)	Sometimes (about half the time)	Most times (much more than half the time)	Almost always/always
1	2	3	4	5

3. During sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner?

Almost never/ Never	A few times (much less than Half the time)	Sometimes (about half the time)	Most times (much more than half the time)	Almost always/always
1	2	3	4	5

4. During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?

Extremely Difficult	Very difficult	difficult	Slightly difficult	Not difficult
1	2	3	4	5

5. When you attempted sexual intercourse, how often was it satisfactory for you?

Almost never Never	A few times (much less than Half the time)	Sometimes (about half the time)	Most times (much more than half the time)	Almost always/always
1	2	3	4	5

Each question provides a range of responses on a scale of 1 to 5 where 1 is the least functional and 5 is the most functional. Total scores range from 5 to 25 with a score of 5 to 7 indicating severe ED and a score of 22 to 25 indicating no ED. Having patients with suspected ED fill-out the IIEF-5 can provide important information about erectile difficulties and provide a basis for physician patient discussion. When discussing the patient's questionnaire responses, the physician should also inquire about levels of sexual desire and opportunities for sexual activity to ensure that low scores are actually indicative of ED³⁵. Physician's who want a more detailed ED assessment tool, can use the 15-item IIEF from which the IIEF-5 was adapted³⁶.

Management and Treatment of ED

Management of patients with ED should consist of three basic elements: medical/psychosexual history; physical exam/laboratory tests; treatment (Table 9). Treatment of ED should proceed from the most appropriate, least invasive therapy and proceed to more invasive therapies if the patient fails to respond (Table 10).

Table 9: Management of Patients with ED³⁷

1. Medical and psychosexual history
2. Laboratory tests
 - Fasting glucose or glycosylated haemoglobin
 - Blood lipid profile
 - Serum testosterone
3. Treatment

Table 10: First Line (least invasive) to Third Line (most invasive) Treatments for ED³⁸

First Line	Oral therapy (e.g., sildenafil) Psychosexual counselling Vacum constriction device
Second Line	Intraurethral agents (e.g., MUSE™) Intracavernosal injection
Third Line	Penile prosthesis implant Arterial and venous surgery

Oral Sildenafil for the Treatment of Erectile Dysfunction

Sildenafil is an effective First Line therapy for ED with organic, psychogenic, and mixed causes. Sildenafil inhibits cyclic guanosine monophosphate hydrolysis in the corpus cavernosum and as a result increases penile response to sexual arousal^{39 40}. Although not all men with ED will respond to sildenafil, it has been shown to be highly effective in improving erectile function (attaining and maintaining an erection) for most men with ED⁴¹. Dosage ranges from 25mg to 50mg to 100mg. Typically, dosage begins at 25mg or 50mg and if there is little or no response after 2 attempts at sexual activity the dosage is increased to 100mg⁴². Side effects (headache, flushing, dyspepsia) occur in less than 20% of men taking sildenafil⁴³. As discussed in more detail below, treatment with sildenafil is contraindicated in men with unbalanced cardiac conditions and/or taking nitrates. Research suggests that sildenafil can be effective in treating ED resulting from serious medical conditions including:

- Radiation-induced erectile dysfunction in patients with prostate cancer;
- Diabetes mellitus;
- Spinal cord injuries and neurologic disorders⁴⁴.

Alprostadil for the Treatment of Erectile Dysfunction

Intraurethral alprostadil (MUSE™) administered transurethraly, can be an effective treatment for ED^{45 46} which may be particularly appropriate for men who are contraindicated for sildenafil (e.g., patients taking nitrates) or for whom sildenafil is not effective. MUSE is a small, medicated pellet that is inserted into the urethra with erection occurring five to ten minutes after insertion and lasting 30 to 60 minutes. Alprostadil can also be administered intracavernously and this approach may be more effective and preferable for some patients^{47 48}. Alprostadil is contraindicated for men with a number of conditions including hypersensitivity to alprostadil, urethral stricture, balanitis (inflammation/infection of the glans of the penis), severe hypospadias and curvature, acute or chronic urethritis, sickle cell anemia or trait, thrombocytopenia, polycythemia, or multiple myeloma. Alprostadil is also contraindicated for patients prone to venous thrombosis or who have hyperviscosity syndrome and are therefore at increased risk for priapism. Alprostadil should not be used for intercourse with a partner who is pregnant unless a condom is used. Physicians considering treating patients with alprostadil should carefully screen each patient for all possible contraindications and carefully monitor the dosage.

New Oral Therapies for ED

In addition to sildenafil (Viagra™), two new oral therapies for ED may soon be available in North America. Tadalafil (Cialis™) and vardenafil (Levitra™) have been approved for use in Europe. Both of these drugs are, like sildenafil, phosphodiesterase 5 (PDE5) inhibitors. Among the differences between these drugs and sildenafil are that they take effect sooner and one impacts on erectile function for more than a day. Clinical trials of both tadalafil⁴⁹ and vardenafil⁵⁰ indicate that they are effective treatments for ED. Apomorphine, also an oral therapy for ED, has shown promise in clinical trials and may become available in North America⁵¹.

The Importance of Integrating Biomedical Treatments and Psychosexual Counselling in the Management of ED

Because of its effectiveness, relative non-invasiveness, and ease of administration, sildenafil (Viagra™) has become a standard therapy in the treatment of ED. As various authors have cautioned, however, the success of new pharmacological agents in treating sexual dysfunction has led to an increased emphasis on the biological causes for sexual dysfunction and, perhaps, a simplistic tendency to seek simple medical solutions to problems which have multiple dimensions that are both biological and psychosocial^{52 53}. For example, it is important to recognize that while sildenafil may produce an erection it may not necessarily improve a man's sexual relationship with his partner and it may in some cases give rise to other sexual and relationship problems. Therefore, it should be standard practice for physicians writing prescriptions for sildenafil (and other pharmacologic agents to treat sexual dysfunctions) to provide brief psychosexual counselling. Table 11 outlines some of the issues that may need to be addressed by men taking oral therapy for ED.

Table 11: Psychosexual Issues for Men Using Oral Therapy for ED

- Satisfying sexual relationships depend on much more than the existence of a firm erection.
- Recognize the need to address the role of sex in the context of the man's relationship(s).
- How will the man's partner respond to his restored erectile function? (In some cases the partner will have adapted well to the man's lack of erection and is satisfied with the ways, sexual and otherwise that they have compensated for it.)
- Recognize that restored erectile function can bring to light other sexual dysfunctions (i.e., premature ejaculation, low desire).

Treatment of Psychogenic Erectile Dysfunction

ED is considered to be psychogenic when it is due primarily or exclusively to psychological or interpersonal factors. It may co-exist with low desire and is often associated with depression and anxiety disorders. Sexual performance anxiety, relationship conflicts, or couple sexual compatibility issues may be involved. Biological factors (e.g., heart disease, diabetes, hypogonadism) should be ruled out before a diagnosis of psychogenic ED is made. Note that many cases of ED will be of a mixed etiology (i.e., both biological and psychogenic factors are involved). There are four basic treatment modalities for psychogenic ED⁵⁴:

1. **Anxiety reduction and desensitization.** This approach is aimed at reducing performance anxiety and enhancing relaxation. Initial avoidance of intercourse and use of nondemanding, nongenital pleasuring (sensate focus) exercises and then gradually proceeding to progressively more genitally focused activities are techniques used in this approach;
2. **Cognitive behavioural interventions.** This approach focuses on correcting the information deficits, misconceptions, and unrealistic expectations that many men and their partners hold with respect to sexual function and adequate sexual performance.
3. **Sexual stimulation techniques.** This approach focuses on helping the man and his partner expand their sexual repertoire beyond penile-vaginal or penile-anal intercourse. For example, a man and his partner can be encouraged focus on manual and oral forms of sexual stimulation thereby reducing the need for a firm erection.
4. **Interpersonal and Systemic interventions.** Relationship conflicts can lead to or exacerbate ED. This approach focuses on status and dominance issues, intimacy and trust, and loss of sexual attraction.

Given the efficacy and safety of sildenafil (ViagraTM), it can be appropriately used as an adjunctive intervention in the management of psychogenic ED⁵⁵. Research suggests that treatment with sildenafil improves erectile function in about 80% of men with psychogenic ED⁵⁶.

ED and the Cardiac Patient

As previously noted, patients with known or suspected cardiac disease will have sexual concerns. Many of these concerns will be related to their ability to function sexually and the safety of doing so. In general, most men will be able to gradually resume normal sexual activity several weeks or months after myocardial infarction. Careful evaluation of functional capacity and thorough discussion with the patient about the risks of physical and sexual activity are essential. Higher-risk patients, including those with unstable angina, myocardial infarction in the previous two weeks, stroke, and uncontrolled hypertension, should be stabilized with appropriate and specific treatment (cardiac or vascular) before resuming sexual activity or receiving treatment for sexual dysfunction⁵⁷. Many cardiac patients take nitrates. It has been well established that treatment with sildenafil (ViagraTM) is contraindicated for patients taking nitrates in any form^{58 59}. There has been concern and published reports of myocardial infarction associated with the use of sildenafil⁶⁰. A recent study found that in men with stable coronary artery disease and ED, sildenafil had no effect on symptoms, exercise duration, or presence or extent of exercise-induced ischemia assessed by echocardiography. Thus, in this study, patients with stable coronary artery disease and who were not taking nitrates, sildenafil did not induce myocardial infarction⁶¹. Physicians considering treating their patients with

known or suspected heart disease need to carefully evaluate the potential risks, discuss them with the patient, check for contraindications, and consult the relevant literature^{62 63 64}. For cardiac patients with ED for whom sildenafil is not appropriate, other treatment options (e.g., alprostadil) should be explored.

Premature Ejaculation (PE)

The loss or absence of ejaculatory control can, for many men, represent a significant detriment to their quality of life. This is especially true when it prevents a couple from meaningful enjoyment of sexual activity or significantly reduces the likelihood of desired conception. Premature ejaculation (also known as rapid ejaculation) has generally been thought of as a psychogenic problem related to sexual performance anxiety. Although there is some disagreement in the field regarding the relative roles of neurobiology and psychology in the etiology of PE⁶⁵, an integrated approach accounting for both psychological and neurobiological factors is recommended⁶⁶.

Defining Premature Ejaculation

Clinical definitions of PE have been inconsistent⁶⁷. Initial attempts to develop definitions of PE often focused on simple objective criteria such as number of penile thrusts or time to ejaculation. More recently, subjective criteria such as ejaculation prior to the desired time, lack of control over the ejaculatory response, and partner dissatisfaction with the timing of ejaculation have been used. The American Psychiatric Association diagnostic criteria for PE de-emphasizes objective criteria and focuses on the judgement of the clinician in making a determination⁶⁸.

Prevalence

In general about 30% of men between the ages of 18 and 59 believe that they “climax” too early⁶⁹. It is worth noting that in his landmark studies of human sexual behaviour, Kinsey found that 75% of men ejaculated within 2 minutes of penetration⁷⁰. Because definitions of premature ejaculation are often subjective and have varied across research studies, it is difficult to get a clear picture of the true prevalence of PE. Estimates of PE in primary care settings range from 4% to 31%⁷¹.

Diagnostic Criteria for PE⁷²

- A. Persistent or recurrent ejaculation with minimal sexual stimulation before, on, or shortly after penetration and before a person wishes it. The clinician must take into account factors that affect duration of the excitement phase, such as age, novelty of the sexual partner or situation, and recent frequency of sexual activity.
- B. The disturbance causes marked distress or interpersonal difficulty.
- C. The premature ejaculation is not due exclusively to the direct effects of a substance (e.g., withdrawal from opioids) or a general medical condition.

Etiology of PE

As noted above, the etiology of PE can be seen in terms of psychogenic and organic/neurobiological factors. In assessing the psychogenic aspects of PE it is important to consider that in most cases a specific case of PE involves an interplay between a couple and their individual patterns of sexual response with one or both partners being dissatisfied with the duration of intercourse⁷³. With respect to organic/neurobiological factors, low testosterone, low seminal plasma magnesium levels, hyperthyroxinemia, short frenum of prepuce, penile hypersensitivity, reflex hyperexcitability, prostatic inflammation/infections, chronic prostatitis, as well as neurologic disorders (multiple sclerosis, spina bifida, tumour of the spinal cord) have been associated with PE⁷⁴.

Treating PE

The degree to which a primary care physician will want to become involved in the treatment of PE will vary considerably from physician to physician. The primary responsibility of the primary care physician is to rule out, particularly among men who complain of the sudden onset of PE or who ejaculate very rapidly, underlying medical conditions. In addition, providing effective education and counselling for PE can often require that the physician treat both the male patient and his partner together, something that may be beyond the scope of the physician's practice. In such a case, the physician should be prepared to provide a referral to a qualified sex therapist. However, beginning with a noninvasive education-based approach a physician can provide practical information suggestions that may be helpful to a patient with PE. For example, the information and advice provided in Table 12 may help to alleviate anxiety and concern about PE.

Table 12: Information for Men Concerned About PE⁷⁵

- 1 PE is a very common concern for men. About a third of men think that they ejaculate (come) too early.
5. It can be helpful to refocus on enjoyment and pleasure for both partners rather than on "am I going to last?" which tends to turn sex into a performance.
6. Talking to your partner about your PE concerns and learning about their concerns and wishes often reduces the pressure that you feel about the desire to last longer.
7. If you don't speak to your partner about your concerns, the pressure you feel will only grow, making sex less enjoyable and more difficult.
8. Try to find out as much as you can about your partner's sexual interests and needs. For example, many men believe that in order to sexually satisfy a woman, a man must be able to be inside a woman, thrusting vigorously and continuously for long periods of time. Most women disagree. In fact, many, if not most women find non-genital caresses, mutual masturbation, and oral sex just as pleasurable as intercourse.
9. Men who have not ejaculated in a long time will ejaculate more quickly. Masturbating several hours before partnered sexual activity may prolong the time to ejaculation.
10. Men can talk to their partners about experimenting with the "squeeze" and "stop-start" techniques as well as doing Kegel exercises. Using these techniques should be looked upon by the couple as a fun and pleasurable activity. Information on these techniques is widely available in book stores.

Cognitive-behavioural techniques such as the squeeze and stop-start methods are most likely to be successful with couples where both partners are highly motivated and in an otherwise good relationship. Men with occasional sexual partners or couples with underlying relationship issues are less likely to be successful with the use these techniques.

Primary care physicians can effectively provide brief psychosexual counselling and information on PE. However, it should be remembered that the etiology of PE can be complex and that in cases where it causes or is related to profound personal or interpersonal issues, the primary care physician may wish to refer the patients to a specialist with expertise in treating PE.

Recent advances in the understanding of the organic and non-organic factors involved in PE has lead to the development of new treatments that involve pharmacological agents. For example, recent reports have demonstrated the effectiveness of a treatment approach combining psychological/behavioural counselling, SSRI (paroxetine), and sildenafil (ViagraTM)^{76 77}. Increasingly, combining drug and nondrug options is seen as a viable first-line approach to the treatment of PE in the primary care setting⁷⁸.

Low Desire (Hypoactive Sexual Desire Disorder [HSDD])

Prevalence

Among men aged 18-59 in the general population, 14%-17% report a lack of interest in sex.⁷⁹ Low sexual desire has been found to be strongly correlated with age. One community-based study found that 26% of men aged 70 and over had HSDD⁸⁰.

Gradual decreases in sexual desire are considered a natural consequence of the aging process. Although men's interest in sex declines gradually beyond the fifth decade of life, at least a quarter of men are interested in having regular sexual activity (i.e., more often than monthly) into their eighties⁸¹. Decreased desire is more likely to cause distress to a patient if there are relatively sudden declines in desire rather than a gradual drop-off. Many older couples will adjust to a decline in sexual desire and genital sexual activity. However, for some individuals and couples, sexual activity remains an important aspect of individual and relationship well-being. Many men, however, are too embarrassed to bring up this topic with their physician even if it is of concern to them.

Etiology of Low Desire

In most instances, a case of low desire in a man can be traced to one of, or a combination of four possible factors;

1. Reduced androgen levels (i.e., testosterone)
2. Medication side-effects (particularly SSRI's)
3. Chronic illness
4. Psychosexual issues (e.g., diminished partner attractiveness, marital boredom).

Diagnostic Criteria for Low Desire (Hypoactive Sexual Desire Disorder)⁸²

- A. persistent or recurrent deficiency or absence of sexual fantasies and desire. The clinician should take into account the variety of factors that can affect sexual functioning including age and life circumstances.
- B. The presence of low desire causes marked distress or interpersonal difficulties.
- C. The presence of low desire is not due exclusively to the physiological impact of drug abuse, a medication or a general medical condition.

The etiology of low desire can be complex and low testosterone may not, in many cases, explain low desire in male patients. For example, many men with low desire have mean total and free testosterone levels that are in the normal range.⁸³

For the male patient who reports little or no interest in sexual activity, it is important for the clinician to clarify if the problem relates to desire or arousal. For example, a man who says that he has no interest in sex may be referring to the fact that he is having difficulty getting an erection not that he is not interested in being sexual. There are several questions that the clinician can ask the patient to obtain a clearer picture.

Patient Questions to Distinguish Between Low Desire and Erectile Dysfunction⁸⁴

- "Despite your lack of interest, can you still get an erection?"
- "Compared to your past, how would you rate your interest in sex?"
- "If you can get an erection, do you think that you would be interested in having sex?"

Table 13: Common Medications Associated with Low Desire⁸⁵

- Antihypertensive
- Antiarrhythmic
- Antineoplastic
- Anticonvulsant
- Antidepressant

Treating Low Desire

The effective treatment of low desire among men is dependent on accurately identifying the etiology of the problem and proceeding with the appropriate course of treatment. For example, providing androgen supplementation to a man with low desire but normal range testosterone will do little to increase his sexual desire. It should also be noted that although a primary factor may be identified, low sexual desire will in many cases be multidimensional. For example, a man's gradually or suddenly declining androgen levels may have initially prompted his flagging desire but the problem was exacerbated by his decreased sense of masculinity, increased tension with his partner caused by his apparent lack of sexual interest, and the emotional stress (e.g., depression) that he subsequently felt. As a result, even if, for example, androgen supplementation was indicated for a man with low desire and below normal testosterone, it is more than likely that he will also require, at a minimum, brief psychosexual counselling. This may involve helping him to:

- understand the various factors involved in his low desire;
- set realistic expectations for his future sexual life;
- communicate clearly and openly with his partner about their sexual relationship.

Addressing Low Desire Associated with Reduced Androgen

Low sexual desire associated with low testosterone levels will often be accompanied by other symptoms including erectile dysfunction, fatigue, lethargy, mood swings, loss of motivation, and reduced physical vitality⁸⁶. It should also be noted that these symptoms can be associated not only with decreased testosterone but also with decreases in other hormones such as growth hormone, melatonin, and dehydroepiandrosterone⁸⁷. Laboratory tests to determine testosterone levels should measure bioavailable testosterone, including free and albumin-bound fractions. To reduce expenses, some physicians may wish to measure free testosterone first and then proceed to a test for bioavailable testosterone if the results are not clear. To account for circadian rhythm, assessment should be done between 8 and 11 am. If the testosterone level is below or at the lower limit, the results should be confirmed with a second test of LH and follicle-stimulating hormone⁸⁸.

Preliminary studies indicate that androgen supplementation can increase sexual desire among men with low serum testosterone levels⁸⁹. Both physicians and patients must be aware of and consider the potential risks of androgen therapy, especially among older men who are more likely to have coexisting medical conditions. Patients should be carefully screened for any contraindications before androgen therapy is considered. For example, patients with liver or renal disease may be particularly predisposed to the development of gynecomastia. The risks of androgen therapy include:

- Water retention (Can lead to hypertension, peripheral edema, exacerbation of congestive heart failure)
- development of polycythemia
- development of hepatotoxicity
- development of detrimental effects on the cardiovascular system
- exacerbation of sleep apnea
- exacerbation of benign or malignant prostate disease⁹⁰.

Physicians should comprehensively consult the relevant medical literature concerning all possible risks and contraindications of androgen therapy⁹¹.

Addressing Low Desire Associated with Medication Side Effects

As noted above, lowered sexual desire is associated with a number of medications. In some cases it may be possible to substitute a different but equivalent medication that has less of an impact on a patient's level of desire. This is particularly the case with antidepressants which are well known to negatively impact on sexual desire and erectile function⁹². Among men taking antidepressants, 38% to 50% report impairments in sexual desire depending on the antidepressant being used⁹³. Research suggests that bupropion and nefazodone have fewer sexual side effects than SSRIs⁹⁴. It is important to note that many patients with antidepressant-associated low desire will also have ED and that sildenafil (Viagra™) improves erectile function in many of these patients⁹⁵.

Addressing Low Desire Associated with Chronic Illness

Low desire and other sexual dysfunctions emanating from chronic illness are often associated with both the physiological impact of the illness and psycho-social issues such as poor body image and depression⁹⁶. It is important, therefore, for the physician during the course of assessment to, as much as possible, differentiate between the physiological and psychological factors at play. For example, the illness itself, and medical treatments for it will in many cases have a direct impact on sexual function. Thus, in some cases, medical intervention can help to alleviate the negative impact on desire. Just as importantly, physicians can provide practical advice and brief psycho-sexual counselling. For example, a patient with musculoskeletal disease could be educated about positional changes for sexual intercourse or less demanding pleasuring that will make sexual activity more appealing and feasible or a patient with cancer who's low desire results from chemotherapy and negative body image can benefit from physician initiated discussion of strategies to maintain, restore and adjust sexuality⁹⁷. The range of different chronic illnesses is vast and each can have a specific impact on sexuality and physicians should consult resources appropriate to each illness⁹⁸.

Addressing Low Desire Associated with Psychosexual Issues

Low desire associated with psychosexual issues can have a complex etiology. Persons who have experienced sexual trauma, abuse, or assault in childhood, adolescence or adulthood can be prone to low desire. Often, low desire is associated with problems in a couple relationship. In both cases, the physician, after an initial assessment, may wish to provide a referral for psychological counselling or sex therapy. With respect to low desire resulting from relationship concerns, it may be helpful for the physician to be aware of the common issues related to low sexual desire that couples may face and to provide brief psychosexual counselling. These issues are listed in Table 14. Such counselling can be brief and solution focused, emphasizing current couple behaviours and practical suggestions, many of which can revolve around enhanced couple communication.

Table 14: Issues Related to Low Desire in Couple Relationships⁹⁹

- Partner differences in the desired frequency of sexual contact.
- Attitudes towards sexual behaviour and arousal.
- Power and control issues related to initiation and type of sexual contact.
- Ineffective communication related to sexuality.
- Conflict in view of sexual contact as a "right to pleasure".
- Sexual interaction bogged down in ritual and routine.
- Issues of parental privacy.
- Discovery of extramarital relationships.
- Issues related to jealousy and/or possessiveness.
- Issues related to infertility and pregnancy.
- Sexual problems related to life cycle changes and the ageing process.
- Sexual problems related to illness and disability of one or both partners.

Case Studies

Case # 1

A 49 year-old male patient complains that he is unable to get erections with the same frequency or stiffness as in the past. On occasion (about 25% of the time) he is unable to get an erection hard enough to have intercourse with his partner. While this happened “once in a blue moon” when he was in his twenties, he is upset that it happens more often now. His wife has asked him if he is still attracted to her. The patient would like a prescription for Viagra™.

Which of the following best categorizes this man’s condition?

- a) This man does not have ED.
- b) Generalized ED.
- c) Acquired, generalized ED.
- d) Acquired, situational ED.**
- e) Situational ED.

Upon administering the IIEF-5, the patient scores 17, indicating that he has moderate ED. Laboratory tests come back normal, he is generally in good health and he leads a healthy lifestyle. Which of the following may be helpful to this man?

- A) Sildenafil (Viagra™)
 - B) Androgen supplementation
 - C) Sensate focus exercises
 - D) Information on normal sexual functioning at middle-age
-
- a) All of the above
 - b) C & D
 - c) A & C & D**
 - d) B & C & D
 - e) A & B & D

Case Study #2

Prior to specific screening for sexual dysfunction, when asked if he has any sexual concerns, A 63 year-old man who has been widowed for the past 3 years informs you that he has begun dating again and has started a relationship with a woman of a similar age. They have not had sex but she has not so subtly signalled that she would like to engage in sexual activity with him. Although in his mind the idea of becoming sexually active again appeals to him and he certainly does feel attracted to this woman, he says “I just don’t seem to want it like I used to. Maybe I’m too old for this.”

After providing this man with basic information on age-related declines in sexual function, the next step would be to:

- A. Order laboratory tests to measure bioavailable testosterone.
- B. Check his chart and up-to-date medical history for factors associated with low desire.
- C. Advise him to talk to his new partner about reducing expectations regarding sex.
- D. Proceed with standard screening for sexual dysfunction.
- E. If not contraindicated, ask him if he would be interested in trying Viagra™.

- a) A & D
- b) B & C
- c) C & D
- d) B & D**
- e) B & E

During the initial screening for sexual dysfunction, the patient reveals that he occasionally has a sexual dream but does not think about sex as much as he used to. He used to masturbate now and then but has not done so since his wife died. He sometimes wakes up with an erection but it is probably not firm enough for intercourse. Administering the IIEF-5 does not seem appropriate since he is not currently sexually active. He recalls that he and his wife enjoyed a vigorous and pleasurable sex life. He does not feel guilty about his new partner as he feels his wife would want him to move on and be happy but he doesn't feel "in the mood for sex". His chart reveals that at his last visit (12 months ago) his testosterone levels were in the normal range. His chart also reveals that soon after the death of his wife he was given a prescription for antidepressants which he continues to use. Which of the following constitute an appropriate course of action?

- A. Advise him to talk to his new partner about reducing expectations regarding sex.
- B. Laboratory tests to up-date assessment of hormone levels.
- C. If not contraindicated, ask him if he would be interested in trying Viagra™.
- D. Look into switching to an antidepressant medication with less of an impact on sexual function.

- a) All except A are appropriate at this point.**
- b) All except B are appropriate at this point.
- c) All except C are appropriate at this point.
- d) All except D are appropriate at this point.

Case Study #3

Upon being asked during routine screening for sexual dysfunction "Do you feel you ejaculate (come) too quickly?" a 27 year-old man, after some hesitation, responds that "Well I didn't think so but my marriage is in trouble and I think how fast I come has got a lot to do with it." With further questioning about the history of his problems, the man reveals that about 2 years after his marriage 5 years ago, he and his wife had sex less and less often to the point where now its about once a month at the most. Over the same period, they seemed to grow more distant and experienced conflicts in other areas of their marriage. The man described their sex life during their dating years and first year or so of marriage as "really great." He described their sexual encounters as brief but passionate. His description of their sexual encounters suggested that little foreplay occurred, that they proceeded to directly to intercourse which lasted from 1 to 4 minutes. His wife was clearly became less interested in sex as time went on. When asked if his wife experienced orgasm during their sexual encounters, the patient responded "I don't know, I guess so."

At this point, the physician can best respond to this patient's concern by providing which of the following?

- A) The name of a qualified couples counsellor.
- B) A prescription for paroxetine.
- C) A prescription for sildenafil.
- D) Information on male/female sexual response and the importance of sexual communication.
- E) Recommendation to try the "stop-start" and "squeeze" techniques.

- a) A only
- b) A & D**
- c) A & D & E
- d) B & C & D
- e) All of the above.

A year later, the patient returns to your office for his annual check-up. He reports that he and his wife have been seeing a couples counsellor and their relationship has gradually been improving. He reports that they are working together on a number of levels to build their life together. Their counsellor does not focus much on sexual issues but did suggest that they buy a copy of *The Joy of Sex*. The couple did buy the book and have expanded their sexual repertoire to include non-genital foreplay and oral sex. Although their sex life has improved, the patient is still concerned about his lack of ejaculatory control. In fact it has become worse, to the point that he often ejaculates before penetration. This is a concern not only because the couple would like to enjoy intercourse but also because they are planning to conceive a child.

At this point, the physician can best help the patient by taking which of the following courses of action?

- a) Screen for organic/neurobiological factors.
- b) Suggest that the couple may want to try the "stop-start" and "squeeze" techniques.
- c) Consider treatment with paroxetine and/or other appropriate medications.
- d) A & C.
- e) **All of the above**

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