#### CLINICAL PRACTICE

Patrick G. O'Malley, M.D., M.P.H., Editor

## Sexual Dysfunction in Women

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This Journal feature begins with a case vignette highlighting a common clinical problem.

Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the author's clinical recommendations.

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CME



A 54-year-old woman presents with low libido, diminished arousal, and anorgasmia. She had undergone a hysterectomy and bilateral salpingo-oophorectomy at 49 years of age owing to menorrhagia and a family history of ovarian cancer. She has been using transdermal estradiol patches and topical vaginal estradiol and has no menopausal symptoms or dyspareunia. She is in a loving relationship with no major life stressors, does not have depression, and takes no other medication. All other clinical characteristics, including her weight and blood pressure, are normal. She has recently become aware that there may be treatment options for low libido and would like to discuss these with you. How would you respond?

### THE CLINICAL PROBLEM

Because there is no universal definition of normal sexual function, what constitutes sexual difficulty is determined by a person's subjective definition of unsatisfactory sexual well-being. The condition is usually described as unsatisfactory interest, arousal, orgasm, or other aspects of sexuality (e.g., sexual self-image), and the symptoms often coexist. The term "sexual dysfunction" is used when at least one of the symptoms is of substantial concern to the affected person.¹ Sexual dysfunction negatively affects mental health, vitality, and social functioning and has an overall effect on quality of life that is of similar magnitude to that associated with chronic back pain or diabetes.²

## CLASSIFICATION OF SEXUAL DYSFUNCTION IN WOMEN

The classification of sexual dysfunction in women continues to evolve, with the *International Classification of Diseases and Related Health Problems*, 11th revision (ICD-11), providing substantive changes to the classification, and hence the diagnosis, of sexual dysfunctions.<sup>3</sup> The ICD-11 recognizes that sexual response is influenced by a complex interplay of biologic, psychological, and social factors (Table 1). Hence, sexual dysfunction is no longer defined as either related to or caused by a disease or medication (organic) or independent of an identifiable cause (nonorganic).<sup>3</sup> This change is clinically important because it allows for associated factors to be recognized and, when possible, managed but does not prevent persons with associated factors from receiving treatment for sexual dysfunction.

Another modification is that the ICD-11 no longer categorizes all sexual dysfunctions according to male or female sex, because most determinants of sexual response are not sex-specific. Only arousal disorder in women and erectile dysfunction in men remain categorized as sex-specific sexual dysfunctions.<sup>3</sup> Unlike the *Diag*-

#### KEY POINTS

#### SEXUAL DYSFUNCTION IN WOMEN

- · Sexual dysfunction in women is common and is associated with impaired well-being and quality of life.
- Many women with sexual dysfunction will not seek care unless prompted by their health care provider.
   However, there are no evidence-based screening recommendations for sexual dysfunction as part of routine care.
- Sexual well-being is determined by a complex interplay of biologic, psychological, and sociocultural
  factors. Therefore, an assessment of sexual dysfunction involves a comprehensive review of the
  patient's general health and psychosocial circumstances and a history of the patient's use of
  prescription and nonprescription medications and other drugs.
- Management pathways for sexual dysfunction include lifestyle modification, counseling and psychosexual therapies, physical therapy, and pharmacologic therapy.

nostic and Statistical Manual of Mental Disorders, fifth edition,<sup>4</sup> the ICD-11 has retained hypoactive sexual desire dysfunction and arousal dysfunction as separate conditions because they have differing etiologic characteristics and risk factors and, in most cases, are associated with different psychological and biologic interventions.<sup>1</sup> Table 1 provides descriptions of sexual dysfunctions.

Although sexual pain disorders may contribute to other sexual dysfunctions,<sup>5</sup> both sexual pain disorders and persistent genital arousal disorder are classified separately in the ICD-11<sup>3</sup> and are not discussed in detail here. However, vaginal symptoms that cause dyspareunia are common, and treatment options are described below.

### PREVALENCE OF SEXUAL DYSFUNCTION IN WOMEN

Contemporary data regarding the prevalence of sexual dysfunction across the adult female life span are limited, in part because several epidemiologic studies have excluded women who were either sexually inactive or unpartnered or did not include assessments of the degree to which the sexual concern caused distress, which is a necessary criterion for the identification of sexual dysfunction. In addition, findings from some studies are difficult to reconcile owing to the use of different questionnaires for sexual function and sexual distress. For example, in a population-based German study involving 2059 women, 19.4% of the younger participants (18 to 24 years of age) and 31.5% of the older participants (46 to 55 years of age) had low desire; hypoactive sexual desire dysfunction with severe distress in the previous 12 months was reported in 6.2% of participants in the younger age group and 7.3% of participants in the older age group.6 In contrast, a contemporaneous population-based Australian study involving 10,554 women who answered validated questionnaires showed that 27.4% and 58.9% of women 18 to 24 years of age and 45 to 49 years of age, respectively, had low desire, and 12.2% and 31.6%, respectively, had hypoactive sexual desire dysfunction. The discrepancies between the studies reflect different wordings of the questions used, combined with the severity of distress required to classify a participant as having a dysfunction. Nonetheless, both show that low desire progressively increases with age, and sexually-associated distress concurrently declines, so that the peak in hypoactive sexual desire dysfunction in women emerges during midlife (Fig. 1).<sup>7</sup>

The prevalence of arousal dysfunction and orgasm dysfunction is also unclear. The percentages of women with unspecified arousal dysfunction that have been reported in population-based studies are 3 to 9% among women 18 to 44 years of age, 6,8,9 5 to 7.5% among women 45 to 64 years of age, 6,8 and 3 to 6% among women 65 years of age or older.6,8 Anorgasmia with distress has been reported to affect 7 to 8% of women younger than 40 years of age, approximately 5 to 7% of women 40 to 64 years of age, and 3 to 6% of women 65 years of age or older in studies conducted in Europe, the United States, and Australia.6,8,9

The most common sexual difficulty with associated distress in women younger than 40 years of age is poor sexual self-image, a characteristic that was observed in 13.4% of women of this age group in a large Australian study. Risk factors for low sexual self-image dysfunction included breast-feeding, overweight and obesity, and having a partner. A disturbing finding was that 30% of the participants scored above the threshold for sexually related personal distress but did not

Table 1. Summary of ICD-11 Classification	n of Sexual Dysfunction in Women.*
Dysfunction Category	Manifestation or Description
Hypoactive sexual desire dysfunction†	Absence or marked reduction in desire or motivation to engage in sexual activity as manifested by any of the following: reduced or absent spontaneous desire, reduced or absent responsive desire to erotic cues and stimulation, or inability to sustain desire or interest in sexual activity once initiated
Sexual arousal dysfunction†	Despite the desire for sexual activity and adequate sexual stimulation, absence or marked reduction in any of the following: genital response (vulvovaginal lubrication, genital engorgement, or genital sensitivity), nongenital responses (hardening of nipples, flushing of skin, or increased heart rate, blood pressure, or respiration rate), or feelings of sexual arousal (sexual excitement and sexual pleasure)
Orgasmic dysfunction	Absence or marked infrequency of the orgasm experience or markedly diminished intensity of orgasmic sensations, including marked delay in orgasm, despite desire for sexual activity and orgasm and adequate sexual stimulation
Other or unspecified sexual dysfunction	Not specified

<sup>\*</sup> For classification purposes, symptoms should have been episodic or persistent over a period at least several months and associated with clinically significant distress. Etiologic considerations include associations with any of the following: a medical condition, injury, or the effects of surgery or radiation treatment; psychological or behavioral factors, including mental disorders; use of psychoactive substance or medication; lack of knowledge or experience; associated with relationship factors; cultural factors; and other specified etiologic considerations (e.g., gender incongruence, changes in anatomy, pregnancy, postpartum status). ICD-11 denotes the *International Classification of Diseases and Related Health Problems*, 11th revision.

have a specific sexual difficulty. <sup>10</sup> Although several factors were independently associated with nonspecific sexual distress (receiving current treatment for infertility, taking psychotropic medication, smoking, alcohol consumption, and being in paid employment) other potential determinants, such as relationship issues and abuse, were not captured.

### COMMON CONTRIBUTING HEALTH CONDITIONS

Estrogen insufficiency is a hallmark of menopause, hypothalamic amenorrhea, hyperprolactinemia, hypopituitarism, and antiestrogen therapy (aromatase inhibitors or selective estrogen-receptor modulators). Low sexual desire may be related to estrogen-insufficiency symptoms such as hot flashes and night sweats, mood change, sleep disturbance, or vulvovaginal dryness.11 Low testosterone levels have not been consistently associated with low orgasm satisfaction; however, in one analysis, when sociodemographic factors were taken into consideration, low testosterone was independently associated with low orgasm satisfaction in premenopausal women.<sup>10</sup> Serum testosterone levels have not been consistently associated with sexual function in postmenopausal women, 12,13 but representative studies that use a more precise measurement of testosterone are still needed. Other endocrine disorders associated with a greater likelihood of sexual dysfunction include adrenal insufficiency (including adrenal suppression by systemic glucocorticoids),<sup>14</sup> diabetes,<sup>15</sup> and polycystic ovary syndrome.<sup>16</sup>

Chronic disease, particularly conditions that reduce mobility or cause chronic pain, mental health conditions, pelvic-organ prolapse, and cancer therapy may all contribute to sexual dysfunction. An array of psychosocial factors may underlie sexual dysfunction, including relationship difficulties, poor self-image, past or current abuse, stressors, and sociocultural beliefs and expectations. Both depressive symptoms and psychotropic medications are independently and bidirectionally associated with sexual dysfunction.

Findings from a randomized, controlled trial suggest that the use of combined oral contraceptives may cause low sexual desire.<sup>19</sup> However, simply switching contraceptive pills can provide substantial improvement in sexual function, irrespective of the androgenicity of the progestin in the new preparation.<sup>20</sup> Other common medications can cause sexual dysfunction — notably cardiac and antihypertensive medications.<sup>1,17</sup>

<sup>†</sup> Subcategories include lifelong, acquired, generalized, situational, and unspecified.

Figure 1. Prevalence of Sexual Dysfunction in a Representative Sample of 10,554 Women in a Community-Based Australian Study.7

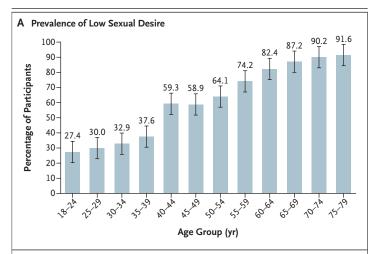
Women 18 to 39 years of age completed the Profile of Female Sexual Function (PFSF), and all others completed the Female Sexual Function Index (FSFI). Responses of "never" or "seldom" to the question "How often in the past 30 days did the following statement apply to you? 'I felt sexual desire'" on the PFSF indicated low desire, and responses of "almost never or never" or "a few times" to the question "How often did you feel sexual desire and interest?" on the FSFI indicated low desire (Panel A). Sexually associated distress was assessed among women in all age groups with the use of the Female Sexual Distress Scale-Revised (Panel B). Hypoactive sexual desire dysfunction was defined as the presence of both low desire and sexually associated distress (Panel C). Percentages shown are absolute percentages, with I bars indicating 95% confidence intervals.

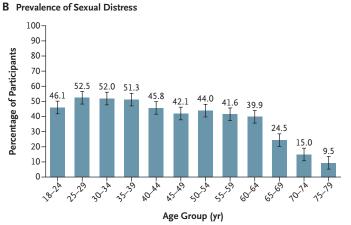
#### STRATEGIES AND EVIDENCE

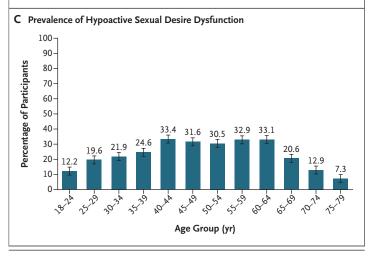
## ASSESSMENT

Available data suggest that less than 50% of persons with sexual difficulties that cause them distress seek help.21 Persons younger than 35 years of age are most likely to seek support from the Internet, whereas older persons are more likely to consult a doctor.21 This difference highlights the potential importance of incorporating screening for sexual difficulties in routine clinical care, although there are no available screening trials evaluating this strategy.

It is crucial to recognize that women who are unpartnered or sexually inactive may have sexual dysfunction<sup>18</sup> and that sexual dysfunction does not have an age limit. One strategy to ascertain information regarding a patient's sexual function is to pose an open-ended question as to whether the patient has any sexual concerns.<sup>1,22</sup> It is helpful to normalize the conversation by reassuring the patient that sexual concerns are common. If a concern is identified, a simple framework can be applied that comprises eliciting the patient's story; providing a name to or, if more appropriate, reframing the concern in a meaningful way for the patient; acknowledgment of the issues and challenges being met by the patient; and either making time for further assessment or, if preferred by the patient, referring the patient for care. 1,22 This approach informs treatment options that are described below.







and referral pathways (Table 2). Establishing the recency of onset and whether the problem is generalized, situational, or partner-specific is important. For example, life-long sexual dysfunction is addressed by means of psychosocial care, whereas Full assessment will guide the management dysfunction that arises after bilateral oophorec-

# Table 2. Checklist of Factors to Be Considered in the Assessment of Sexual Dysfunction in Women.

### Biologic and hormonal factors

Sex-hormone insufficiency

Depression

Illness

Fatigue

Urinary incontinence

Prescription and nonprescription medication

Alcohol or other drug use

#### Intrapersonal development history

Trauma (sexual, physical, emotional, or medical)

Negative emotions (anxiety, fear, shame, or guilt)

Poor body image

Gender-identity concerns

Level of education

#### **Expectation of negative outcomes**

Past disappointing or painful sex

#### Interpersonal issues

Lack of a partner

Relationship discord

Absence of emotional intimacy

#### **Contextual factors**

Lack of privacy

Safety concerns

Emotional rapport

Cultural norms and religious beliefs

## Lack of appropriate stimuli

Lack of knowledge regarding sexual stimulation

Partner's ill health or sexual dysfunction

tomy may be effectively treated with hormone replacement. A full history will provide information about menstrual irregularity in premenopausal women (possibly due to stress or to hormonal disorders such as hyperprolactinemia or polycystic ovary syndrome), vulvovaginal atrophy symptoms that occur after menopause (e.g., vaginal dryness or irritation [dyspareunia]), pelvic floor disorders (urinary incontinence, fecal incontinence, or prolapse, which may contribute to loss of desire), gynecologic surgery (residual discomfort or concerns about sex), dyspareunia, and vaginismus. Both prescription and nonprescription medications, as well as alcohol consumption and the use of other drugs, may affect

sexual function, so their use should be ascertained.

Physical examination should be guided by the medical history, such as breast examination for galactorrhea if hyperprolactinemia is suspected. Similarly, biochemical assessments and imaging should be performed on the basis of the medical history and examination findings. Hormone measurement and other biochemical testing should be performed only to identify a clinically suspected endocrinopathy or to monitor a known condition. Measurement of testosterone levels offers no diagnostic usefulness because there is no serum testosterone level below which a female patient can be classified as being testosterone-deficient.<sup>23</sup> Serum testosterone should only be measured to provide a baseline value if testosterone therapy is to be initiated.23

#### MANAGEMENT

The management of sexual dysfunction should be guided by the patient's concerns and wishes, as well as by their physical and psychological health and social circumstances, and may involve a partner. Treatment options are summarized in Table 3.

Attention should be given to potentially modifiable factors. When possible, medications known to be associated with sexual dysfunction, most commonly antidepressant therapy, should be modified or changed. Lifestyle interventions may reduce sexual difficulties. For example, a post hoc analysis involving women with diabetes and obesity showed that lifestyle intervention might reduce generalized sexual dysfunction, with 28% of persons included in the analysis no longer meeting the diagnostic criteria for sexual dysfunction after lifestyle interventions, as compared with 11% of those who received supportive care. The service of the

Psychosocial interventions are frequently effective in treating sexual dysfunction.<sup>24</sup> These interventions may be in the form of sexual counseling, body awareness counseling, cognitive therapy, couples counseling, or referral to a psychologist (if a mood disorder is identified). Targeted sexual therapy may involve pelvic-floor relaxation training, vaginal dilator therapy (in women with vaginismus),<sup>42</sup> and clitoral devices that may improve clitoral sensation and orgasm in women with an arousal disorder.<sup>43</sup> The efficacy of each of these interventions is difficult to quantitate be-

cause studies have included small, heterogeneous samples across different age ranges and with different outcomes. <sup>24,25,42,43</sup>

#### **PHARMACOTHERAPY**

Although estrogen therapy is not a treatment for generalized sexual dysfunction, hormone therapy should be considered for menopausal symptoms that are troubling to the patient, because symptom relief may reduce sexual symptoms. Dyspareunia due to estrogen insufficiency can be treated with a local topical vaginal estrogen cream, pessary, or ring; prasterone (a form of dehydroepiandrosterone for vaginal use); oral ospemifene; or vaginal moisturizers.44 Vaginal erbium and carbon-dioxide laser therapy have been promoted for relief of dyspareunia. However, in 2018 the Food and Drug Administration warned against the use of these therapies owing to insufficient evidence to support their efficacy and safety for the treatment of dyspareunia.45

Flibanserin and bremelanotide are approved in the United States for treatment in premenopausal women with generalized, acquired hypoactive sexual desire dysfunction. Flibanserin is thought to disinhibit pathways involved in sexual desire. Studies involving both premenopausal and postmenopausal women with hypoactive sexual desire dysfunction showed sufficient efficacy for the approval of flibanserin for premenopausal women in the United States.31 The efficacy of flibanserin is modest.31 In a metaanalysis of eight trials including 5914 participants, flibanserin was shown to have increased the number of satisfying sexual experiences per month by 0.5 but with considerable side effects (e.g., dizziness, somnolence, nausea, and fatigue). Bremelanotide is a melanocortin receptor agonist that is thought to increase dopamine release and thus increase excitation in brain regions that are associated with sexual desire.46 A combined analysis of two trials involving 1267 participants showed a modest improvement in sexual desire and decrease in distress related to low sexual desire with bremelanotide but more nausea, flushing, and headache side effects than with placebo.32

There are no therapies approved in North America for postmenopausal women with hypoactive sexual desire dysfunction, but testosterone has been prescribed off-label for hypoactive sexual desire dysfunction since the 1940s.<sup>47</sup> A trans-

dermal testosterone patch was approved in Europe for surgically postmenopausal women having hypoactive sexual desire dysfunction despite adequate estrogen therapy,<sup>35</sup> but the patch was removed from the market by the manufacturer when the approval was not extended to naturally menopausal women, despite clinical trial data showing efficacy of the patch in those women that was similar to that seen in surgically postmenopausal women.<sup>48</sup> A transdermal 1% testosterone cream<sup>49</sup> has been approved in Australia for the treatment of postmenopausal women with hypoactive sexual desire dysfunction.

An international task force evaluated the available clinical trial data and concluded that transdermal testosterone therapy, which restores serum testosterone levels to approximately those seen in premenopausal women, is moderately effective for the treatment of postmenopausal hypoactive sexual desire dysfunction. Table 3 provides a summary of the trial evidence.23 The task force recommended against the use of oral testosterone therapy owing to potential adverse effects related to lipoprotein levels and inconsistent absorption.23 Clinical trial data have shown that transdermal testosterone, when administered at the recommended doses, may cause a small but significant increase in the likelihood of acne, growth of facial or body hair, and weight gain, and long-term safety data are lacking.34

Nonetheless, it has been estimated that more than 2 million prescriptions of testosterone are written each year for women in the United States, many of which are probably for compounded preparations.<sup>50</sup> Compounded formulations are not subject to requirements for pharmacokinetic profiling, and their uncertain absorption may cause overdose and harm.23 The international task force recommendation that if an approved female-specific testosterone formulation is unavailable and testosterone therapy is considered indicated for treatment of postmenopausal hypoactive sexual desire dysfunction, the preferred option is a fractionated dose of a regulator-approved male formulation.<sup>23</sup> When transdermal testosterone is prescribed, regular monitoring of serum testosterone concentrations and clinical assessment for signs of androgen excess are recommended.23

Systemic dehydroepiandrosterone therapy has not been shown to improve sexual dysfunction in randomized, double-blind clinical trials involving women with intact adrenals<sup>51</sup> or with adrenal

Table 3. Recognized Treatment Options.**		
Category and Treatment	Strength of Evidence	Potential Adverse Events
Nonpharmacotherapy		
Psychosocial therapy — sexual education and counseling, body awareness, cognitive therapy, couples therapy, social interventions	Varies; primarily from small trials in differing populations <sup>24,25</sup>	Not applicable
Physical therapy — pelvic floor physiotherapy; FDA-approved clitoral vacuum device may improve sensation, lubrication, orgasm with or without arousal disorder	Varies according to patient population <sup>26</sup>	Not applicable
Pharmacotherapy†		
Vaginal dryness causing dyspareunia		Constituents vary; some may cause irritation, impair sperm motility, or contain parabens <sup>27</sup>
Lubricants for vaginal dryness associated with sexual activity <sup>27,28</sup>	Moderate evidence for reduced dyspareunia <sup>27,28</sup>	
Vaginal moisturizers for dryness, itch, and soreness <sup>27</sup>	Strong evidence for reduced dyspareunia <sup>27,28</sup>	
Vaginal dryness in postmenopausal women		
Estradiol vaginal tablet (FDA-approved at a dose of 0.01 mg nightly for 2 wk, then 2 or 3 times per wk); estriol ovule (0.5 mg nightly for 2 wk, then 2 or 3 times per wk); estriol cream (0.5 mg nightly for 3 wk, then 2 times per wk); estriol gel (0.05 g nightly for 3 wk, then 2 times per wk); estriol gel (0.05 g nightly for 3 wk, then 2 times per wk); estradiol 0.01% cream (FDA-approved at a dose of 2 to 4 g daily for 1 to 2 wk, then 1 g applied 1 or 2 times per wk); estradiol 2-mg ring (FDA-approved at a dose of 0.0075 mg per day, replaced every 90 days; and conjugated estrogen cream 0.625 mg per gram (FDA-approved for cyclic use of 0.5 to 2 g intravaginally once daily for 21 days, then off for 7 days)	Moderate efficacy shown for vaginal dryness and dyspareunia, with similar efficacy in all formulations <sup>29</sup>	Vaginal discharge, vulvovaginal candidiasis, vaginal bleeding, and breast pain; dose and formulation dependent <sup>30</sup>
Prasterone insert (6.5 mg nightly)‡	Strong evidence of reducing dyspareunia <sup>28</sup>	Vaginal discharge <sup>30</sup>
Ospemifene tablet (60 mg taken orally once daily)‡	Moderate evidence of improvement in sexual function <sup>28</sup>	Vasomotor symptoms, vaginal discharge and candidiasis, may increase endometrial thickness?
Hypoactive sexual desire dysfunction in premenopausal women		
Flibanserin (100 mg taken orally once daily at bedtime) ‡∬	Evidence of modest effect (approximately 0.5 to 0.65 additional satisfactory sexual events per month) <sup>31</sup>	Somnolence, sedation, or fatigue (28%) <sup>31</sup> ; owing to potential hypotension and syncope, caution regarding alcohol consumed within 2 hr before or after taking filbanserin; contraindicated with concurrent strong CYP3A4 inhibitor medication or liver impairment <sup>31</sup>
Bremelanotide (1.75 mg administered subcutaneously 45 min before sexual activity)‡	Evidence of modest effect on sexual desire vs. placebo (0.35-point difference out of a possible total score of \$); no evidence for increased satisfactory sexual events <sup>32</sup>	Nausea (40% of patients; may resolve with use), facial flushing (in 20%), headache (in 11%)³²

Transdermal testosterone 1% cream (0.5 to 1 ml applied topically once daily); Longf-label in most countries; female-specific 1% transdermal testosterone cream approved in Australia and South Africa	Low-quality clinical trial evidence for this formulation <sup>33</sup> ; strong evidence for transdermal testosterone overall <sup>34</sup> ; increase in 1–1.4 satisfactory sexual events per month <sup>35,36</sup>	Acne, increased hair growth, and weight gain.34
Genital arousal dysfunction in premenopausal and postmenopausal women		Headache, flushing, and dyspepsia.37
Sildenafil for spinal cord injury–associated arousal dysfunction (50 mg taken lr before sexual encounter) <sup>38</sup>	Improved subjective arousal in small double- blind trial <sup>38</sup>	
Sildenafil for antidepressant-associated arousal dysfunction (50 mg taken before sexual encounter) <sup>37</sup>	Low-quality evidence from small open-label trial <sup>37</sup>	
Tadalafil for type 1 diabetes-associated arousal dysfunction (5 mg daily) 39	Low-quality evidence from small open-label trial39	

Specialized interventions for sexual pain disorders or hyperactive sexual desire dysfunction are not included. FDA denotes Food and Drug Administration The availability of hormonal and nonhormonal treatments and indications for use from regulatory bodies vary among countries. This use is approved in Canada for persons up to 60 years of age. This use is FDA-approved.

insufficiency.<sup>52</sup> Bupropion and buspirone are psychotropic medications that have been used off-label in patients with sexual dysfunction, but efficacy and safety data are insufficient, and currently neither therapy can be recommended.<sup>17</sup>

Effective pharmacotherapies for arousal and orgasm dysfunction are lacking. Small studies suggest potential benefits of phosphodiesterase-5 (PDE5) inhibitors for arousal difficulties in women with spinal cord injury<sup>38</sup> and antidepressant-associated arousal dysfunction.<sup>37</sup> PDF5 inhibitors have also shown promise for the treatment of genital arousal dysfunction in women with type 1 diabetes.<sup>39</sup> There is no evidence of benefit of PDF5 inhibitor therapy in healthy women with arousal dysfunction.<sup>53</sup>

#### GUIDELINES

The International Society for the Study of Women's Sexual Health has published processes of care for the identification of sexual concerns and problems in women¹ and for the assessment of hypoactive sexual desire dysfunction.¹7 The processes of care are valuable resources for enhancing the skills and capabilities of both primary health care providers and medical specialists. The Global Consensus Position Statement on Testosterone for Women, developed and endorsed by leading women's health groups worldwide and available in 14 languages, provides comprehensive guidance regarding the use of testosterone therapy in women.²³ The recommendations in this article align with these guidelines.

### AREAS OF UNCERTAINTY

Clarification of the prevalence of sexual dysfunction relies on an investment in quality epidemiologic studies that are inclusive of all women, irrespective of gender identity, sexual preference, and partner status. Furthermore, the understanding of the physiology of female sexuality has been constrained by the necessary reliance on animal models, anatomical and functional studies involving humans, and imaging. The uncertainty of the biologic features of the brain in sexual function in women hinders the understanding of dysfunction and in turn the development of pharmacotherapies. Clinical trials to further evaluate available psychosocial interventions and pharmacotherapies are still needed. Consequently, treat-

ment algorithms, particularly regarding arousal and orgasm dysfunction, remain inadequate because they are limited to modification of contributing factors, counseling, and physical therapies.

# CONCLUSIONS AND RECOMMENDATIONS

With regard to the patient described in the vignette, I would seek to identify relationship issues, major psychosocial contributors, or modifiable factors and to determine whether the loss of libido was of meaningful concern to the patient. If the

diagnosis of hypoactive sexual desire dysfunction was established, I would address any psychosocial issues as appropriate, and I would discuss treatment options. In most countries, the approach would involve off-label pharmacotherapy, with the most evidence-based option currently being the administration of transdermal testosterone at a dose appropriate for a female patient. Unfortunately, this case highlights the ongoing inadequacy of treatment options for women with sexual dysfunction.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

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