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Female Sexual Dysfunction

Female sexual dysfunction encompasses various conditions that are characterized by reported personal distress in one or more of the following areas: desire, arousal, orgasm, or pain (1). Although female sexual dysfunction is relatively prevalent, women are unlikely to discuss it with their health care providers unless asked (2), and many health care providers are uncomfortable asking for a variety of reasons, including a lack of adequate knowledge and training in diagnosis and management, inadequate clinical time to address the issue, and an underestimation of the prevalence (2). The purpose of this document is to provide an overview of female sexual dysfunction, to outline updated criteria for diagnosis, and to discuss currently recommended management strategies based on the best available evidence.

Background

Approximately 43% of American women report experiencing sexual problems, with 12% considering this problem to be so bothersome that it leads to personal distress (3). The prevalence of female sexual distress increases through middle age, from approximately 10% among women aged 18–44 years to a peak of 15% among women aged 45–64 years, and then decreases again in older age to about 9% among women aged 65–85 years (3). Some of the more common etiologies of and risk factors for sexual dysfunction are listed in Box 1.

Normal Sexual Response

The original landmark studies regarding a normal sexual response tended to favor linear models (4–6). A more contemporary model of female sexual response is nonlinear and encompasses a variety of sequences of the original four stages of female sexual response as well as other stages (Fig. 1) (7). Central neuroendocrine mechanisms that regulate female sexual response are described today as dynamic, creating a balance between excitatory and inhibitory factors (8–11).

Estrogen plays a critical role in female sexual physiology (including maintenance of genital tissue sensitivity, elasticity, secretions, pH, and microbial flora), urinary continence, pelvic muscle tone, and joint mobility (8, 12). A decrease in circulating estrogen occurs naturally and with surgically or medically induced menopause, but this change has a variable effect on female sexual function (7, 12).

Androgen levels in women peak in the mid-20s, decline steeply in the early reproductive years (until the mid-30s), and level out around age 60, at which point no further decrease is observed (13–15). The role of testosterone in modulating female sexual desire and function is poorly understood. Although there is evidence of benefit for short-term transdermal testosterone therapy in postmenopausal women with low sexual desire, there is not a particular serum level or lower limit of androgens or androgen precursors that is diagnostic of decreased female sexual function (16–18).

Types of Sexual Dysfunction

The American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders*, (Fifth Edition) (DSM-5) identifies four specific types of female sexual dysfunction (1) (Table 1). In addition, the DSM-5 also classifies disorders as "other specified sexual dysfunction" and "unspecified sexual dysfunction."

Box 1. Common Etiologies and Risk Factors for Female Sexual Dysfunction

Anxiety disorder
Diabetes
Depression
Female genital mutilation
Genitourinary syndrome of menopause
History of sexual abuse
Hypertension
Hysterectomy
Intimate partner violence
Medications (psychotropic medications [selective serotonin reuptake inhibitors], antihypertensives, histamine blockers, hormonal medications)
Negative sexual attitudes
Neurologic disease
Personality traits of perfectionism and self-dislike
Postpartum period
- Breastfeeding
- Obstetric trauma

Premature ovarian failure
Psychologic sequelae of gynecologic cancer and breast cancer
Relationship discord
Stress—emotional or environmental
Stress urinary incontinence
Substance use disorder

Female Sexual Interest and Arousal Disorder

Female sexual interest/arousal disorder is a new classification that replaces the DSM-IV terms hypoactive sexual desire disorder and female sexual arousal disorder. (In this document, hypoactive sexual desire disorder is used only when referring to studies that used this specific terminology to describe a condition or outcome measured using DSM-IV-TR criteria.) Fluctuation in sexual interest and arousal can occur across the female life course in relation to modifiable, but commonly overlooked, individual or partner factors, including changes in sleep patterns or chronic poor-quality sleep; stress; changes in body image, shape, or weight; pregnancy; breastfeeding; sedentary lifestyle; alcohol or other substance abuse; and relationship factors (19–26). Many women who say they lack sex drive or libido mean they have lost the physiologic desire for sex. They describe thinking about sex, but their thoughts are about avoidance of sexual activity or about initiation or engagement in sexual activity to preserve the relationship or for their partner's benefit (27). Women also describe a distressing loss of interest but an ability to become aroused in response to a partner's initiation of sexual activity (27).

Although sexual interest and arousal problems can occur in the absence of diagnosed comorbidities (Box 1), new onset could be an indicator of undiagnosed or subclinical conditions, even among younger women (28). Medications, particularly selective serotonin reuptake inhibitors (SSRIs), are commonly associated with arousal impairment (Box 1) (29).

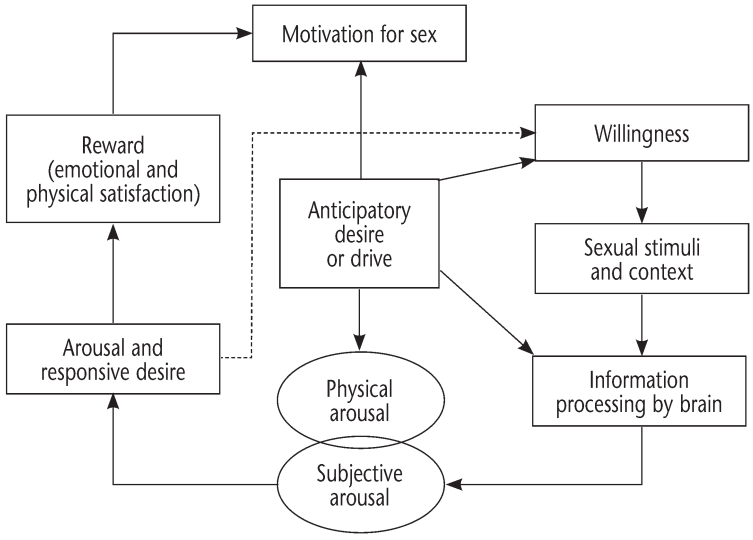

Figure 1. Female sexual response. The circular sexual response cycle shows overlapping phases of variable order. Reasons or motivations for sex are numerous, and sexual desire or drive may or may not be present at the outset but reached after the brain has processed sexual signals as sexual arousal, which conflates with sexual desire. The latter creates an urge for increased arousal, allowing acceptance of increasingly intense sexual stimulation. (Basson R. Sexuality and sexual disorders. Clin Update Womens Health Care 2014;XIII(2);1–108. Available at: https://www.clinicalupdates.org/viewissue.cfm?issue=cuwhc-v13n2. Retrieved February 22, 2019.)

Table 1. *Diagnostic and Statistical Manual of Mental Disorders,* **Fifth Edition, Criteria for Female Sexual Dysfunction**

Disorder	Definition
Female sexual interest/arousal disorder	A lack of, or significant decrease in, at least three of the following: • interest in sexual activity • sexual or erotic thoughts or fantasies • initiation of sexual activity and responsiveness to a partner's initiation • excitement or pleasure during all or almost all sexual activity • interest or arousal in response to internal or external sexual or erotic cues (eg, written, verbal, visual) • genital or nongenital sensations during sexual activity in almost all or all sexual encounters Symptoms have persisted for a minimum of 6 months and cause clinically significant distress in the individual.*
Female orgasmic disorder	Marked delay in, marked infrequency of, or absence of orgasm, or markedly reduced intensity of orgasmic sensations, in almost all or all occasions of sexual activity. Symptoms have persisted for a minimum of 6 months and cause clinically significant distress in the individual.*
Genito–pelvic pain/penetration disorder	The persistent or recurrent presence of one or more of the following symptoms: • difficulty having intercourse • marked vulvovaginal or pelvic pain during intercourse or penetration attempts • marked fear or anxiety about vulvovaginal or pelvic pain anticipating, during, or resulting from vaginal penetration • marked tensing or tightening of the pelvic floor muscles during attempted vaginal penetration Symptoms have persisted for a minimum of 6 months and cause clinically significant distress in the individual.*
Substance/medication-induced sexual dysfunction	A disturbance in sexual function that has a temporal relationship with substance/medication initiation, dose increase, or substance/medication discontinuation and causes clinically significant distress in the individual.†
Other specified sexual dysfunction and other unspecified sexual dysfunction	Distressing symptoms characteristic of a sexual dysfunction that do not meet the criteria of one of the defined categories. The major distinction between other specified sexual dysfunction and other unspecified sexual dysfunction is whether the clinician specifies the reason that the symptoms described do not meet the criteria for one of the other classes.

*A diagnosis of a sexual dysfunction disorder can be made only if the sexual dysfunction is not better explained by a nonsexual mental disorder or as a consequence of severe relationship distress (eg, partner violence) or other significant stressors and is not due to the effects of a substance or medication or another medical condition.

†The disturbance is not better explained by an independent sexual dysfunction disorder. Evidence that suggests a nonsubstance/medication-induced sexual disorder includes a history of an independent sexual dysfunction disorder, symptoms that precede the onset of substance or medication use, or symptoms that persist for at least 1 month after cessation of acute withdrawal or severe intoxication.

Data from American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th ed. Arlington (VA): APA; 2013.

Female Orgasmic Disorder

Female orgasmic disorder is defined as marked delay in, infrequency of, or absence of orgasm or markedly reduced intensity of orgasmic sensations (1). Women with primary orgasmic disorder usually have normal levels of sexual desire (27). Most orgasmic disorders are acquired in relation to a new-onset medical, anatomic, relational, behavioral, or psychologic condition (Box 1) that commonly co-occurs with sexual interest and arousal difficulties or genito–pelvic pain and penetration disorder symptoms (1). In rare instances, acquired orgasmic disorder may be due to underlying neurologic conditions, changes associated with genital or pelvic surgery, and radiation therapy or medication use (1, 7). Although research is very limited, women who have undergone genital cutting procedures may have lifelong or acquired orgasm dysfunction and are known to be at higher risk of sexual dysfunction (30).

Genito–Pelvic Pain and Penetration Disorder

Vaginismus and dyspareunia are now combined into genito–pelvic pain and penetration disorder. This disorder can be lifelong or acquired. Genito–pelvic pain and penetration disorder includes one or more of the following symptoms: tightening of the vaginal muscle with decreased ability or inability to accommodate penetration; tension, pain, or burning felt when penetration is attempted; a decrease in or no desire to have intercourse; avoidance of sexual activity; intense phobia or fear of pain (1). Symptoms of genito–pelvic pain and penetration disorder often co-occur and have overlapping medical, situational, and psychosocial causes and resolve in response to treatment of those conditions (31, 32). Note that individuals whose sexual activity does not include penetration can still have this disorder if they have pain interfering with sexual function.

Substance or Medication-Induced Sexual Dysfunction

Substance or medication-induced sexual dysfunction is defined as a clinically significant disturbance in sexual function that occurred during or soon after taking (or withdrawal from) a substance or medication that is readily known to have the capacity to induce such a change (1). As with the other classes of female sexual dysfunction, this diagnosis requires that the patient experience related distress. Anticholinergic, hormonal, cardiovascular, and psychiatric agents are examples of medications that may be associated with female sexual dysfunction (Box 1) (24). Alcohol, marijuana, and narcotics also may contribute to female sexual dysfunction.

Other Specified and Unspecified Sexual Dysfunction

Other specified sexual dysfunction and other unspecified sexual dysfunction are diagnosed when a patient presents with distressing symptoms characteristic of a sexual dysfunction that do not meet the criteria of one of the defined categories (1). The major distinction between other specified sexual dysfunction and other unspecified sexual dysfunction is whether the clinician specifies the reason that the symptoms described do not meet the criteria for one of the other classes.

Pregnancy-Related Sexual Dysfunction

Any type of sexual dysfunction before pregnancy is a key risk factor for postpartum difficulties. Trauma caused by cesarean delivery, instrumented delivery, episiotomy, and perineal tears also increases the risk of postpartum genito–pelvic pain and penetration disorder and related sexual interest and arousal difficulties (33–36). Breastfeeding also can cause vaginal dryness and thus symptoms of genito–pelvic pain/penetration disorder. Obstetric factors appear to be more significant drivers of postpartum female sexual dysfunction than maternal factors like chronic disrupted sleep, role changes, relational issues, newborn health issues, psychosocial adjustment to parenthood (for the woman and her partner), and body changes (35). Postpartum depression, in addition to being associated with decreased sexual desire and sexual frequency (37), presents a potentially grave health risk that warrants early recognition and intervention (38). Intimate partner violence, which can escalate during pregnancy, is a serious risk to the overall health and well-being of a woman and her newborn and also is associated with postpartum sexual dysfunction (39). Evaluation and management of postpartum female sexual dysfunction are similar to nonpostpartum evaluation, management, and treatment of female sexual dysfunction, with modifications to avoid medical therapies that are contraindicated in a woman who is breastfeeding.

Menopausal-Related Sexual Dysfunction

The term genitourinary syndrome of menopause was introduced in 2014 by the International Society for the Study of Women's Sexual Health and the North American Menopause Society to describe not only vulvovaginal atrophy but the entire constellation of genital, sexual, and urinary symptoms associated with declining levels of circulating estrogen and other steroid hormones that occur during menopause (12). Characteristic symptoms include bothersome vaginal dryness, burning, and irritation; decreased lubrication and pain with intercourse; and

urinary symptoms of urgency, dysuria, and recurrent urinary tract infections (12). It is estimated that up to 50% of menopausal women are affected by symptoms associated with genitourinary syndrome of menopause (40, 41), although genitourinary syndrome of menopause also can present in low-estrogen premenopausal states (eg, postpartum) or during use of antihormonal medications such as aromatase inhibitors (42, 43).

Clinical Considerations and Recommendations

▶ ***How should women be screened for female sexual dysfunction?***

Obstetrician–gynecologists should initiate a clinical discussion of sexual function during routine care visits to identify issues that may require further exploration and to help destigmatize discussion of sexual function for patients (44–46). The use of a brief sexual function self-report checklist, such as the validated single-item version that was developed using the Patient-Reported Outcomes Measurement Information System® research framework (47), during patient intake may help facilitate clinical discussion. Another method of introducing sexual function during a routine health care visit is to use a generalized statement meant to normalize the issue followed by a close-ended question and then an open-ended question (48). For example, "Many women experience concerns about sex. Are you experiencing any issues (yes/no)? What is concerning you?" Another way to broach the topic is to ask broad, open-ended questions during routine history gathering (44). If sexual concerns are identified, a follow-up evaluation is recommended.

▶ ***What is the initial approach to a patient who presents with possible female sexual dysfunction?***

The initial evaluation of a patient with female sexual dysfunction symptoms may require an extended visit and should include a comprehensive history (45, 46, 49–51) and physical examination to evaluate possible gynecologic etiologies. Laboratory testing typically is not necessary in the initial evaluation of female sexual dysfunction unless an undiagnosed medical etiology is suspected.

Comprehensive History

A detailed sexual history should include questions about the patient's sexual and gender identity; the nature, duration, and onset of the symptoms; the presence of personal distress about symptoms; self-care, self-medication, or other efforts to alleviate the symptoms; partner factors, including current number of partners as well as their gender, health problems, and sexual function problems; relationship quality, including communication about the patient's sexual concerns; past and current abuse or violence experienced (44, 52); physical activity, injuries (eg, straddle or coccyx), and behaviors (eg, hygiene and chronic sitting) related to the genito–pelvic area; sleep quality; and body changes or image concerns (eg, mastectomy, ostomy, or pregnancy) (49, 51). Likewise, relationship distress and partner sexual dysfunction also should be identified and addressed. Because dysfunction in one domain can trigger sexual problems in another domain (eg, pain can result in loss of libido), evaluation should identify the temporality of the symptoms and their evolution over time. Information about the use of prescription and over-the-counter medications and substances should be elicited.

Various validated self-report questionnaires to assess sexual function in symptomatic women have been developed for use in the research setting, but they also may be useful adjuncts to the clinical interview and sexual history (53). Examples include the Female Sexual Function Index (54) and the Female Sexual Distress Scale (55).

Physical Examination

In general, a gynecologic examination focused on the areas of concern identified in the history can evaluate the possibility of primary gynecologic pathologies that may be causing or contributing to sexual dysfunction (56). Women undergoing examination for female sexual dysfunction may benefit from the opportunity to view and contribute to the examination with the assistance of a mirror. Brief education about the genital anatomy, including an illustration or figure that identifies the clitoris, labia, urethra, introitus, and vestibule can aid in the patient's ability to communicate the location of pain or other symptoms as well as the health care provider's ability to effectively communicate physical examination findings and treatment recommendations. One method of mapping pain symptoms is to use a cotton swab to lightly touch the vestibule in a systematic manner to localize areas of discomfort (57), although the specificity of this test has been called into question (58).

Diagnosis

A diagnosis of a DSM-5-classified female sexual dysfunction (Table 1) is made when symptoms persist for at least 6 months (except in the case of substance/medication-induced sexual dysfunction) and are sufficient to result in significant personal distress. In addition, diagnosis requires that the symptoms are not better

explained by a nonsexual mental health disorder, a medical condition, severe relationship distress, or other significant life stressors, or the effects of a substance or medication (except in the case of substance/medication-induced sexual dysfunction). It is important to keep in mind that women often experience more than one type of female sexual dysfunction. Even if a woman's sexual function symptoms do not meet DSM-5 criteria, she still may benefit from evaluation and treatment.

▶ *What is the role of psychologic interventions in the treatment of female sexual dysfunction?*

Psychologic interventions, including sexual skills training, cognitive–behavioral therapy (with or without pharmacotherapy), mindfulness-based therapy, and couples therapy, are recommended as part of female sexual dysfunction treatment. Consultation with or referral to mental health specialists with expertise and training in the treatment of female sexual dysfunction (eg, sex therapists, psychologists, psychiatrists, and marriage/relationship counselors) should be considered based on the obstetrician–gynecologist's level of expertise and the patient's individual treatment needs.

Sexual skills training, such as instruction in masturbation, have long been the main treatment option for orgasmic disorders (59). Some patients with orgasmic disorders do experience orgasm with masturbation or other erotic stimulation but do not recognize these experiences as orgasm. In other cases, lack of knowledge about or experience with clitoral stimulation and beliefs that prohibit or associate guilt and shame with masturbation are inciting causes (60). Exercises to improve communication with a partner about sexual needs and preferences, sensate focus exercises, and systematic desensitization (61) as well as education and behavioral techniques to increase a woman's comfort with her body and her sexuality by altering negative attitudes and alleviating anxiety can also help (60). Women with female orgasmic disorder that stems from a history of sexual assault likely will benefit from a trauma-informed psychotherapeutic approach (62).

Group-based or couples-based cognitive–behavioral therapy, which focuses on identifying and changing dysfunctional beliefs, may be useful for improving low sexual interest (61, 63–65). Mindfulness-based therapy, which focuses on stress reduction through attention to the present moment and acceptance of thoughts and feelings without judgment, has been shown to help improve several different types of female sexual dysfunction including sexual interest/arousal disorder and acquired anorgasmia (61, 66).

▶ *What is the role of estrogen therapy or estrogen receptor modulator therapy in the treatment of female sexual dysfunction?*

Low-dose vaginal estrogen therapy is the preferred hormonal treatment for female sexual dysfunction that is due to genitourinary syndrome of menopause. Low-dose systemic hormone therapy, with estrogen alone or in combination with progestin, can be recommended as an alternative to low-dose vaginal estrogen in women experiencing dyspareunia related to genitourinary syndrome of menopause as well as vasomotor symptoms. Ospemifene can be recommended as an alternative to vaginal estrogen for the management of dyspareunia caused by genitourinary syndrome of menopause. A physical examination should be performed to diagnose female sexual dysfunction related to genitourinary syndrome of menopause before starting vaginal or systemic hormone therapy. Estrogen or selective estrogen receptor modulator (SERM) therapy is not recommended for the treatment of female sexual dysfunction that is not due to a hypoestrogenic state.

Clinical assessment is important before presumptively diagnosing genitourinary syndrome of menopause and treating with estrogen therapy or estrogen receptor modulator therapy (67). Evaluation of genitourinary syndrome of menopause includes pelvic examination for changes to the anatomical structures of the vulva and vagina, including but not limited to loss of the labial fat pad, thinning of the labia minora, pale mucosa, and loss of vaginal folds (42).

Vaginal tablets, gels, creams, and rings appear to be equally effective, thus, selection of a formulation should incorporate the patient's preference (68, 69). Minimal systemic absorption occurs with initial use of vaginal estrogen treatments and absorption wanes as the vaginal epithelium matures (70). Low-dose systemic estrogen also is an effective treatment for dyspareunia related to genitourinary syndrome of menopause (71), However, low-dose vaginal estrogen is preferable to low-dose systemic estrogen (alone or with progestin) for the treatment of women with only vaginal symptoms (72) because it has similar effectiveness but lower systemic absorption (73). Low-dose systemic estrogen (alone or with progestin) is the most effective therapy for vasomotor symptoms related to menopause (72) and is an appropriate treatment for women with vasomotor symptoms and dyspareunia related to genitourinary syndrome of menopause.

A systematic review and meta-analysis with several placebo-controlled randomized controlled trials (RCTs) as well as an additional RCT have found that ospemifene, a selective estrogen receptor modulator with agonist

(genital tract) and antagonist (breast) tissue selective effects, is effective for treatment of dyspareunia that is due to postmenopausal genitourinary syndrome of menopause (74, 75). The selective estrogen receptor modulator ospemifene was approved for systemic treatment of genitourinary syndrome of menopause by the U.S. Food and Drug Administration (FDA) in 2013. Although it acts as an agonist on the endometrium, ospemifene has not been found to be associated with endometrial cancer or hyperplasia when used continuously for 1 year (76). Some women may experience hot flushes with ospemifene use.

Studies are underway to inform whether and which formulations of estrogen or SERM may be safe for use in menopausal women with estrogen-sensitive cancer. Evidence is insufficient to fully counsel this population about the risks and benefits of vaginal estrogen therapy. Individualized treatment plans should prioritize the patient's preference and prognosis and ideally include the input of the treating oncologist (77, 78). In all cases, the lowest effective dose should be used for the least amount of time to enable function and alleviate symptoms (73, 79).

▶ *What is the role of androgen therapy in the treatment of female sexual interest and arousal disorders?*

Short-term use of transdermal testosterone can be considered as a treatment option for postmenopausal women with sexual interest and arousal disorders who have been appropriately counseled about the potential risks and unknown long-term effects (18, 80). If transdermal testosterone therapy is used in postmenopausal women with sexual interest and arousal disorders, a 3–6-month trial is recommended with assessment of testosterone levels at baseline and after 3–6 weeks of initial use to ensure levels remain within the normal range for reproductive-aged women (18). Transdermal testosterone therapy should be discontinued at 6 months in patients who do not show a response. If ongoing therapy is used, follow-up clinical evaluation and testosterone measurement every 6 months are recommended to assess for androgen excess (18). The long-term safety and efficacy of transdermal testosterone have not been studied.

Evidence is insufficient to recommend for or against testosterone for the treatment of sexual interest and arousal disorders in premenopausal women. Systemic dehydroepiandrosterone (DHEA) is not effective and, therefore, is not recommended for use in the treatment of women with sexual interest/arousal disorders. Other forms of testosterone are available but data are limited, and expert consensus guidance from the Endocrine Society (18) and the North American Menopause Society (81) are not supportive of their use for the treatment of female sexual dysfunction.

Transdermal Testosterone

Evidence is mixed on the safety and efficacy of androgen therapy in the treatment of female sexual interest and arousal disorders, and testosterone is not FDA approved for this indication. For postmenopausal women, short-term transdermal testosterone has been shown to have a beneficial effect on hypoactive sexual desire disorder and arousal (82–86). For premenopausal women, evidence is insufficient regarding the use of testosterone for the treatment of sexual interest and arousal disorders (87, 88). Androgen use is contraindicated in pregnancy and could be harmful to fetal development (89).

Transdermal testosterone delivered by a matrix patch is the most extensively studied of the androgen therapies. The results of a systematic review of seven RCTs (that included more than 3,000 women) that evaluated the use of the 300-microgram testosterone transdermal patch versus placebo for hypoactive sexual desire disorder in the setting of natural or surgical menopause showed significant increases in satisfying sexual episodes, sexual activity, orgasms, and sexual desire (80, 82–86, 90, 91). However, there is little evidence on testosterone's safety, effectiveness, and monitoring for long-term use because most studies have not evaluated use past 6 months (80, 82–86, 90, 92, 93).

The main adverse effects associated with testosterone therapy in women are hirsutism, acne, and virilization (including voice deepening and clitoral enlargement) (82, 83, 90, 93–97). These adverse effects may be irreversible, and long-term safety data are lacking. A 2014 systematic review concluded that there was no evidence that transdermal testosterone therapy increased the risk of cardiovascular disease in women (18), although the effects of long-term testosterone use on cardiovascular disease risk are not known (80). The effects of long-term use of testosterone on breast cancer risk or other cancer risk also are unknown (80), and the limited existing data focus primarily on the risk of estrogen plus testosterone on breast cancer risk, not testosterone alone (98).

Based on randomized controlled data that support efficacy and safety for as long as 6 months (80), and in alignment with the Endocrine Society and the North American Menopause Society guidelines (18, 81), transdermal testosterone therapy can be considered for short-term use in postmenopausal women with female sexual interest and arousal disorder (formerly hypoactive sexual desire disorder) who have been appropriately counseled about the potential risks and unknown long-term effects. Monitoring for androgen excess during treatment is

recommended (18), with the understanding that the long-term safety and efficacy of transdermal testosterone therapy in women have not been studied (80, 82–86, 90, 92, 93). Routine testing of testosterone levels outside of testosterone therapy monitoring has no proven clinical utility and is not recommended (18).

Systemic Dehydroepiandrosterone

Systemic DHEA has been tested but has not shown efficacy in postmenopausal women for treatment of sexual interest and arousal disorders and, therefore, is not recommended for use (99–101). A 2015 Cochrane review did show an improvement in sexual function with DHEA versus placebo (standardized mean difference, 0.31; 95% CI, 0.07–0.55), but the effect was minimal and not all studies were focused on women with female sexual dysfunction (101). No published studies have evaluated the use of DHEA for sexual dysfunction in premenopausal women.

▶ ***What is the role of nonhormonal medications and devices in the treatment of female sexual interest and arousal disorder?***

Flibanserin

Flibanserin can be considered as a treatment option for hypoactive sexual desire disorder in premenopausal women without depression who are appropriately counseled about the risks of alcohol use during treatment. Flibanserin, a serotonin receptor agonist/antagonist, was approved in 2015 by the FDA to treat hypoactive sexual desire disorder in premenopausal women without depression. A systematic review and meta-analysis of the existing studies demonstrated that although the included studies were randomized, their overall quality of evidence for efficacy and safety was very low (102). The results showed minimal or no improvement in hypoactive sexual desire disorder symptoms with flibanserin use, with an average improvement of less than one additional satisfying sexual event per month. In addition, a clinically significant increase in adverse events was reported—the most common being dizziness, somnolence, nausea, and fatigue. Although studies have demonstrated that flibanserin is also associated with a similar slight improvement in hypoactive sexual desire disorder symptoms among postmenopausal women, the drug is not currently FDA approved for use in this population (103).

Flibanserin includes a black box warning about alcohol use during treatment because of an increased risk of syncope and hypotension (104). The prescribing physician and the dispensing pharmacist must complete a risk evaluation and mitigation strategy certification (104). The patient and physician also must complete a patient–provider agreement form regarding the use of alcohol during treatment with flibanserin. These risk-mitigation requirements, along with the high cost of flibanserin, are barriers to patient use of the drug.

Sildenafil Citrate

Sildenafil should not be used for the treatment of female interest/arousal disorders outside of clinical trials. Sildenafil citrate, a phosphodiesterase type 5 inhibitor, has been evaluated but not FDA approved for the treatment of female sexual interest/arousal difficulties. Although it has been hypothesized that sildenafil citrate should increase pelvic blood flow to the clitoris and vagina through a mechanism of action similar to treatments for male erectile dysfunction, the results of randomized clinical trials of women being treated for sexual arousal disorder have been contradictory (105–108). In addition, some of the data that show benefit have been from studies of women who used SSRIs and, thus, may have had medication-induced sexual dysfunction, not female sexual interest and arousal disorder (109). The most common adverse events reported from women taking sildenafil were headache, flushing, dyspepsia, nasal congestion, and transient visual disturbances (106).

Bupropion

For women with antidepressant-induced female sexual dysfunction, supplementation with bupropion (which is a norepinephrine–dopamine reuptake inhibitor) may improve symptoms. A Cochrane review that included studies of women and men found that the addition of bupropion showed benefit, as measured by female sexual dysfunction rating scale scores, compared with placebo (standardized mean difference, 1.60; 95% CI, 1.40–1.81) (110). In one RCT that included only women (N=218) with SSRI-induced sexual dysfunction, participants who received higher doses of bupropion (ie, 150 mg twice daily) reported significantly higher scores on the Female Sexual Function Index than controls (25.9; 95% CI, 22.2–29.4) versus 17.2; 95% CI, 15.8–20.1) (P=.001) at the end of the 12-week trial (111). Additionally, women in the treatment group reported significantly higher desire, arousal, lubrication, orgasm, and satisfaction scores at the end of the trial.

Devices

No device has been found to be effective for the treatment of female interest/arousal disorders. In 2000, the FDA approved a battery-powered clitoral suction device intended to improve arousal and orgasm by increasing blood flow and engorgement (112). However, evidence of its effectiveness is limited to several small pilot studies (113). At this time, its advantages over other

over-the-counter devices, like vibrators, are unclear. A recent prospective study of a genital vibratory stimulation device, although not definitive, did demonstrate improvements in sexual function, satisfaction, sexually related distress, and genital sensation at 3 months; however, there was no control arm (114). Given that most over-the-counter devices are low risk, health care providers may encourage their patients to explore these options.

▶ ***What are the treatment options for genito–pelvic pain and penetration disorders?***

Pelvic floor physical therapy is recommended for the treatment of genito–pelvic pain and penetration disorders to restore muscle function and decrease pain. Intravaginal prasterone, low-dose vaginal estrogen, and ospemifene can be used in postmenopausal women for the treatment of moderate-to-severe dyspareunia that is due to genitourinary syndrome of menopause. Lubricants, topical anesthesia, and moisturizers may help reduce or alleviate dyspareunia. Vaginal carbon dioxide (CO_2) fractional laser for treatment of dyspareunia that is due to genitourinary syndrome of menopause should not be used outside of a research setting.

Genito–pelvic pain and penetration disorder require an individualized, multidisciplinary approach to treat the underlying and exacerbating physical and emotional aspects of the condition. Specialists who may need to be involved include sexual counselors, clinical psychologists, physical therapists, and pain specialists (115). Genito–pelvic pain and penetration disorder may present with a psychologic component such as anxiety (116). Genito–pelvic pain and penetration disorder are commonly comorbid with other sexual dysfunctions including decreased arousal (117) and, in more advanced cases, difficulty with orgasm that may require additional types of intervention. Although it is beyond the scope of this document to review all treatment options in detail, the following is a review of the evidence for the most common types. More information can be found from more comprehensive reviews (74, 118, 119).

Patient Education

Education about the vulvovaginal anatomy and pelvic floor can help women understand the mechanisms and etiology of genito–pelvic pain and penetration disorder symptoms (119, 120). Self-care counseling should include elimination of common vulvovaginal contact irritants, including soaps, douches, wipes, scented products, and undergarment pads (115). Pointing out inflammatory skin changes to the patient around the vulva and anus may help motivate elimination of wipes or other irritants.

Psychologic Interventions

A 2013 Cochrane review included five RCTs that compared control with systematic desensitization with and without therapy for treatment of vaginismus (119). All of the RCTs were considered at moderate or high risk of bias and found no significant improvement in symptoms. A 2013 study not included in the Cochrane review that used self-dilation in combination with psychotherapy was shown in an RCT to increase the ability of women to have intercourse (121).

Dilation

Several products, prescription and over-the-counter, that enable vaginal self-dilation to alleviate vaginismus, release pelvic floor muscle trigger points, or correct vaginal stenosis after radiation therapy or other injury are available. Although the literature is scant on optimal strategies for dilator use (timing, duration, technique), self-dilation in the presence of a partner and therapist combined with psychotherapy was shown in an RCT of women with vaginismus to increase the ability of women to have intercourse (121). Because patients will use the technique at home, having the patient try the technique in the office may be helpful.

Physical Therapy

Women with dyspareunia due to vaginismus or more general pelvic floor dysfunction, including high-tone dysfunction and laxity associated with hypoestrogenism, may benefit from pelvic floor physical therapy (64). Physical therapy treatment techniques include internal (vaginal and rectal) and external soft-tissue mobilization and myofascial release; trigger-point pressure; visceral, urogenital, and joint manipulation; electrical stimulation; therapeutic exercises; active pelvic floor retraining; biofeedback; bladder and bowel retraining; instruction in dietary revisions; therapeutic ultrasonography; and home vaginal dilation (115, 122, 123). Ideally, the clinician that provides gynecologic assessment works in collaboration with a pelvic physical therapist trained in transvaginal, transanal (if necessary), and dyspareunia treatment. Women may subconsciously recruit and chronically contract the levator ani and introital muscles, and physical therapy may result in better ability to relax these muscles.

Medications

Intravaginal prasterone (a DHEA preparation) gained FDA approval in November 2016 for treatment of postmenopausal women who are experiencing moderate-to-severe dyspareunia. Its efficacy was evaluated in a 12-week prospective, randomized placebo-controlled trial of 482 postmenopausal women who had identified

dyspareunia as their most bothersome symptom of vulvovaginal atrophy (124). An intent-to-treat analysis found a decrease in pain at sexual activity by 1.42 severity score units from baseline or 0.36 unit over placebo. No drug-related significant adverse events were reported.

Most other medications that have been studied for genito–pelvic pain and penetration disorder have limited or noncompelling evidence of benefit. Many of these agents are used for generalized anxiety but do not demonstrate benefit for the localized symptoms associated with genito–pelvic pain and penetration disorder (118, 125–128). Localized treatment with botulinum toxin type A is still under investigation, and its use is not recommended outside of a research setting. Small nonrandomized studies that have examined the injection of botulinum toxin type A into the puborectalis and pubococcygeus muscles as treatment for dyspareunia have shown a decrease in self-reported painful intercourse, but adverse events included postinjection cold-like symptoms (35% of women) and vulvar irritation (one report) (129). In many cases, genito–pelvic pain and penetration disorder is treatable without these more experimental therapies, which should be pursued in the context of well-designed clinical trials.

For menopausal women with dyspareunia related to genitourinary syndrome of menopause, low-dose vaginal estrogen therapy has been shown to be as effective as systemic therapy (71, 130, 131) with minimal systemic absorption (70). The SERM ospemifene also is effective for treatment of dyspareunia that is due to postmenopausal genitourinary syndrome of menopause (74, 75). However, insufficient evidence is available to recommend the use of systemic estrogen or SERM therapies for nonatrophic causes of female sexual dysfunction (132).

Lubricants

Lubricants and moisturizers do not cure underlying causes of female sexual dysfunction, but they may help reduce or alleviate dyspareunia that is due to vaginal dryness. These products are classified by the FDA as cosmetics, as such they are not subject to the type of testing required for drugs and may contain skin irritants that can exacerbate dyspareunia like parabens and propylene glycol (43).

Commonly used moisturizers include hyaluronic-based and polycarbophil products recommended for regular use two to three times per week (133, 134). Food-grade oils, such as coconut, olive, and vegetable oils are less expensive than synthetic moisturizers and, thus, may be a reasonable alternative (134). However, oils are not compatible with condoms. Water-based lubricants may dry out more quickly causing friction, which may cause discomfort. Silicone-based lubricants do not cause dryness and are compatible with condoms. Insufficient evidence exists to recommend use of one product type over the other, thus it is important to take into account compatibility with condoms and patient sensitivities and preferences.

Vaginal Carbon Dioxide Fractional Laser Treatment

The safety, efficacy, and cost–benefit of the vaginal carbon dioxide (CO_2) fractional laser for treatment of vulvovaginal atrophy are inadequately studied and are not FDA approved. Although preliminary data show some potential benefit for vulvovaginal atrophy, these studies have not been placebo controlled (135), and long-term outcomes have not been described (135, 136). In addition, the cost of treatment is high relative to other options. Additional data are needed to further assess the efficacy and safety of this procedure in treating vulvovaginal atrophy, particularly for long-term benefit (137).

Summary of Recommendations

The following recommendations are based on good and consistent scientific evidence (Level A):

- Low-dose vaginal estrogen therapy is the preferred hormonal treatment for female sexual dysfunction that is due to genitourinary syndrome of menopause.
- Low-dose systemic hormone therapy, with estrogen alone or in combination with progestin, can be recommended as an alternative to low-dose vaginal estrogen in women experiencing dyspareunia related to genitourinary syndrome of menopause as well as vasomotor symptoms.
- Ospemifene can be recommended as an alternative to vaginal estrogen for the management of dyspareunia caused by genitourinary syndrome of menopause.
- Systemic DHEA is not effective and, therefore, is not recommended for use in the treatment of women with sexual interest/arousal disorders.

The following recommendations are based on limited or inconsistent scientific evidence (Level B):

- Psychologic interventions, including sexual skills training, cognitive–behavioral therapy (with or without pharmacotherapy), mindfulness-based therapy, and couples therapy, are recommended as part of female sexual dysfunction treatment.
- A physical examination should be performed to diagnose female sexual dysfunction related to

genitourinary syndrome of menopause before starting vaginal or systemic hormone therapy.

- Short-term use of transdermal testosterone can be considered as a treatment option for postmenopausal women with sexual interest and arousal disorders who have been appropriately counseled about the potential risks and unknown long-term effects.
- Evidence is insufficient to recommend for or against testosterone for the treatment of sexual interest and arousal disorders in premenopausal women.
- Sildenafil should not be used for the treatment of female interest/arousal disorders outside of clinical trials.
- Intravaginal prasterone, low-dose vaginal estrogen, and ospemifene can be used in postmenopausal women for the treatment of moderate-to-severe dyspareunia that is due to genitourinary syndrome of menopause.
- Estrogen or SERM therapy is not recommended for the treatment of female sexual dysfunction that is not due to a hypoestrogenic state.
- Vaginal carbon dioxide (CO_2) fractional laser for treatment of dyspareunia that is due to genitourinary syndrome of menopause should not be used outside of a research setting.
- Flibanserin can be considered as a treatment option for hypoactive sexual desire disorder in premenopausal women without depression who are appropriately counseled about the risks of alcohol use during treatment.

The following recommendations are based primarily on consensus and expert opinion (Level C):

- Obstetrician–gynecologists should initiate a clinical discussion of sexual function during routine care visits to identify issues that may require further exploration and to help destigmatize discussion of sexual function for patients.
- The initial evaluation of a patient with female sexual dysfunction symptoms may require an extended visit and should include a comprehensive history and physical examination to evaluate possible gynecologic etiologies.
- Laboratory testing typically is not necessary in the initial evaluation of female sexual dysfunction unless an undiagnosed medical etiology is suspected.
- If transdermal testosterone therapy is used in postmenopausal women with sexual interest and arousal disorders, a 3–6-month trial is recommended with assessment of testosterone levels at baseline and after 3–6 weeks of initial use to ensure levels remain within the normal range for reproductive-aged women. Transdermal testosterone therapy should be discontinued at 6 months in patients who do not show a response. If ongoing therapy is used, follow-up clinical evaluation and testosterone measurement every 6 months are recommended to assess for androgen excess. The long-term safety and efficacy of transdermal testosterone have not been studied.
- Pelvic floor physical therapy is recommended for the treatment of genito–pelvic pain and penetration disorders to restore muscle function and decrease pain.
- Lubricants, topical anesthesia, and moisturizers may help reduce or alleviate dyspareunia.

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The MEDLINE database, the Cochrane Library, and the American College of Obstetricians and Gynecologists' own internal resources and documents were used to conduct a literature search to locate relevant articles published between January 2000–December 2018. The search was restricted to articles published in the English language. Priority was given to articles reporting results of original research, although review articles and commentaries also were consulted. Abstracts of research presented at symposia and scientific conferences were not considered adequate for inclusion in this document. Guidelines published by organizations or institutions such as the National Institutes of Health and the American College of Obstetricians and Gynecologists were reviewed, and additional studies were located by reviewing bibliographies of identified articles. When reliable research was not available, expert opinions from obstetrician–gynecologists were used.

Studies were reviewed and evaluated for quality according to the method outlined by the U.S. Preventive Services Task Force:

- I Evidence obtained from at least one properly designed randomized controlled trial.
- II-1 Evidence obtained from well-designed controlled trials without randomization.
- II-2 Evidence obtained from well-designed cohort or case–control analytic studies, preferably from more than one center or research group.
- II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.
- III Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Based on the highest level of evidence found in the data, recommendations are provided and graded according to the following categories:

Level A—Recommendations are based on good and consistent scientific evidence.

Level B—Recommendations are based on limited or inconsistent scientific evidence.

Level C—Recommendations are based primarily on consensus and expert opinion.

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