Female Sexual Interest and Arousal Disorder

How We Can Help When Our Patient's Libido Hits the Brakes

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KEYWORDS

- Female sexual dysfunction • Hypoactive sexual desire disorder
- Female sexual interest and arousal disorder • Low libido
- Comprehensive treatment approach • Sexual pain • Sexual health
- Sexuality counseling

KEY POINTS

- Female sexual interest and arousal disorder is a reality for many women, yet is underdiagnosed and undertreated.
- It has recently been recognized that, although most studies cite more than 40% of women will express concern regarding sexuality, a smaller subset are likely distressed by the issue.
- Research is beginning to look at distress as a necessary factor in diagnosing female sexual interest and arousal disorder. Further research will help in development of treatment options, inclusive of counseling techniques and pharmacotherapy.

INTRODUCTION

Sexuality is a vital aspect of human life, recognized and used in countless different ways. It can wax and wane throughout different time periods and life events, but can be distressing if desire remains low despite a change in circumstances. Low sexual desire is the most common sexual difficulty experienced by women.

When low desire persists and becomes distressful, female sexual interest and arousal disorder (FSIAD) could be the diagnosis. The following is a brief synopsis regarding how to recognize this disorder and how to progress if it is diagnosed.

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FEMALE SEXUAL DYSFUNCTION

Female sexual dysfunction (FSD) is an umbrella term encompassing all aspects of pain, orgasm, desire, and sexual response. Unlike male sexual dysfunction, FSD remains relatively unstudied with few commercially available treatment options. There is complex interplay of psychological, social, cultural, physiologic, and religious undertones to FSD making it difficult for anyone who specializes in any one of those areas to feel competent in treating the disorder.

HYPOACTIVE SEXUAL DESIRE DISORDER AND FEMALE SEXUAL INTEREST AND AROUSAL DISORDER

Hypoactive sexual desire disorder (HSDD) is the subset of FSD that focuses on desire, the most prevalent of the FSDs. It was first defined in the Diagnostic and Statistical Manual of Mental Disorders (DSM) in 1987. The definition has changed several times to date. In 2013, the DSM-V[1,2] was released and has combined HSDD with Female Sexual Arousal Disorder and named it Female Sexual Interest and Arousal Disorder (FSIAD) (see DSM-IV[2] and DSM-V criteria for FSD). It is presently defined by the DSM-V as the absence of or significant reduction in sexual interest/arousal for at least 6 months. Three of the following symptoms must also be present:

- Absent/reduced interest in sexual activity
- Absent/reduced sexual/erotic thoughts/fantasies
- No/reduced initiation of sexual activity; unresponsive to partner's attempt to initiate
- Absent/reduced sexual excitement/pleasure during sexual activity in at least 75% of encounters
- Absent/reduced sexual interest/arousal in response to any internal or external sexual/erotic cues (eg, written, verbal, visual)
- Absent/reduced genital or nongenital sensations during sexual activity in at least 75% of sexual encounters

FSIAD can be classified as generalized or situational, lifelong or acquired, and mild, moderate, or severe in distress. In other words, if a woman has been distressed by her level of sexual interest for greater than 6 months, but goes on vacation with her partner and finds herself in a sea of erotic bliss, she is not likely to have a diagnosis of generalized FSIAD, but rather situational FSIAD.

The problem must also cause clinically significant distress. It must not be better explained by a nonsexual mental disorder, severe relationship distress or other stressors, or effect of a substance/medication or another medical condition.

A critical diagnostic criterion is the element of distress. It is interesting to note that although a certain level of communication or sexual frequency can be distressing to one woman, the same scenario in another woman may feel healthy. No quantitative diagnostic tool exists for FSIAD, only the level of distress caused by the dysfunction.

PREVALENCE

Studies assessing the impact of low sexual desire have varied widely in endpoints over the years. The difficulty with comparison of data lies in the lack of notation of distress in the previous DSM-IV-TR criteria. A study sampling 741 women across Australia, the Americas, Europe, and Asia reported the prevalence of problems with sexual desire varied from 3.0% to 31.0%. They were evaluated using DSM-IV-TR-IV criteria for HSDD as well as a validated questionnaire.[3] The WISHeS study also used validated

questionnaires and the DSM-IV-TR criteria, thus also not inclusive of distress, and found the range to be between 9% in naturally postmenopausal women and 26% in younger surgically postmenopausal women.[4]

Only recently have studies begun to investigate the prevalence of FSIAD in relation to distress, which is now required for diagnosis. Results from the PRESIDE study, the largest US study to date to survey female sexual problems associated with distress, reveals that of more than 30,000 respondents the prevalence of any sexual problem was 43.1% and sexually related personal distress was reported at a level of 22.2%.[5] The British National Survey of Sexual Attitudes and Lifestyles produced similar findings, noting 34.2% of women reported lacking interest in sex; distress was included in this study as well.[6]

CONTRIBUTING FACTORS

Many medical conditions and numerous medications as well as cigarette smoking can negatively affect sexuality, partially accounting for the varied estimates regarding prevalence (**Table 1**).

In addition to medical conditions, relational patterns of communication affect partner interactions as well as the cultural, spiritual, and religious messages received during adolescence and beyond. The interplay of the physiologic, psychological, and social aspects of a sexual disorder can render previously held communication patterns ineffective.

Physician assistants are uniquely positioned to help their patients by normalizing the stigma around discussions of sexuality. Many patients will not ask, but are hoping that the topic is brought up during their visit.[34] Discussion surrounding many of these myths, not only for healthcare providers (HCP) but also for patients, will help dispel the stigma surrounding healthy sexuality. **Table 2** highlights some of the many reasons sexuality lacks transparency in the medical setting.

HISTORY

A thorough history is integral to making an appropriate diagnosis and developing a specific and beneficial management plan for patients who are afflicted with FSD.

Table 1
Contributing factors to sexual dysfunction

Medical Conditions	Medications
Diabetes[7–10]	Antipsychotics[28]
Coronary artery disease[11]	SSRI[29,30]
Hypertension[12,13]	Tricyclic antidepressants
Hypothyroidism or hyperthyroidism[14]	Chemotherapeutic agents
Congestive heart failure	Aromatase inhibitors
Seizure disorder	Triglyceride-lowering agents
Depression[15–17]	Histamine receptor (H2) blockers
Musculoskeletal/movement disorders[18–20]	Weight loss medications
Chronic pain	Antiepileptics
Genital pain	Immunosuppressants
Substance abuse	Central α-adrenergic agonists
Hormonal disruptions[21,22]	β-Blockers
Endocrine disorders[23]	Diuretics
Arthritis[24]	GnRH agonists
Incontinence: urinary or fecal[25,26]	Oral contraceptives[31–33]
Cancer[27]	

Table 2
Reasons sexuality remains unspoken of in medical clinics

Reasons HCPs Do Not Discuss	Reasons Patients Do Not Discuss
Lack of sufficient training[34]	Fear of judgment
Fear of embarrassment/misunderstood	Fear of embarrassment
Lack of known referral resources	Social norms/expectations ("good" girls shouldn't want more sex)
Time constraints	Insurance won't cover such concerns
Lack of knowledge regarding reimbursement	Lack of awareness of FSIAD
Belief that patient appears happy and healthy so no need to ask	Lack of awareness regarding treatment options
	Told by another HCP that it is normal
	Fear their HCP will try to "fix" their sexuality (expression, interest, identity)
	Fear of job loss/discrimination based on sexual practices

The following are key steps to facilitate obtaining a complete and accurate sexual health history.

- *Ask with her clothes on*. Allow her to remain clothed during the history-taking portion of the visit. Answering questions regarding sexual health can be scary, but allowing her to remain clothed will help her feel some level of control and increased comfort.
- *Avoid assumption*. Discuss sexual health with every patient starting at the age of 11 with no ending age. Avoid the assumption that someone is not sexually active based on age, medical status, relationship status, or anything else.
- *Assure confidentiality*. Feeling safe is essential for disclosure of sensitive topics relating to sexual health. Verbalize your commitment to her privacy and to her wellness.
- *Normalize*. Let her know that "as your caregiver, comprehensive health is my primary concern. In that, I ask all of my patients about sexual health."
- *Possible referral point*. If her response feels uncomfortable or unfamiliar to you, now is a good time to make a referral.
- *Match her vocabulary*. If you choose to continue the conversation, meet your patient at her level with vocabulary. Using terms unfamiliar to her will cause a greater divide in the room. If your patient uses a term you are unfamiliar with, ask her what she means. Show her that you are listening and ready to learn from her. This includes her use of pronouns. If unsure, ask every time as identity and sexuality can change.
- *Open with ubiquity-style questions*. This will help normalize potential concerns and will have a higher yield than direct questions. Such statements as "Many women, while breastfeeding, experience vaginal dryness or pain as well as issues with lowered sex drive. How has this been for you?" will allow her to feel more comfortable in disclosing this information as well as less alone in her struggle.
- *Silence*. This is a difficult one! We are accustomed to directing conversations and maximizing our time in the examination room. However, it is important to remember that you may have just asked her a question that no one has ever brought up, and one that may have been weighing on her for some time. She may go through an internal, albeit quick, process of thoughts before answering:
  - No one has asked me that before.
  - How did they know?
  - Did my provider just say the word orgasm?

- Do I out myself?
- Do I trust this provider
- Will my insurance pay for this?
- What can they do anyway?
- I've never told this to anyone.
- Will I be betraying my partner by telling my provider?
- What if they know one of my friends and tell them?

- *Possible referral point*. If her response after the silence is outside your comfort level, now is a good time to reaffirm normality and refer.
- *Follow with specific questions*. Otherwise, once she has responded with a sexual concern, then follow with more specific questions such as, "Are you having difficulty with orgasm?" "Is lubrication a concern for you?" "Are you noticing a decrease in your motivation for sex?" These specific questions will help differentiate between different clinical subtypes of FSIAD.
- *Follow-up positive response with more open-ended questions*. "Tell me more about that."
- *Possible referral point*. Multiple points in this process can serve as referral points, depending on experience and comfort level.
- *Assess patient goals*. By the end of the visit, be sure to ask her to relay her goal to you, remembering it may be different from what you think her goal should be. Verbalizing a goal will set realistic expectations and allow for more accurate assessment of her response to treatment.

Time is essential in medicine, so HCPs can ask and refer immediately, or counsel to their comfort level. It is not the HCP's responsibility to have been taught all the nuances of the human body. It is their responsibility to know what resources are available to enhance care for each of the patients.

EVALUATION

Although many women request hormonal testing to help evaluate potential causes of decreased libido, this is recommended in a select few. A start should be with a comprehensive medical, relationship, and sexual history to help customize the workup for each patient. If a genital examination is indicated, as in cases of FSD related to sexual pain or endocrine changes, the vulva, vagina, pelvic floor, uterus, and adnexa should be fully evaluated. Many screening tools are also available to help the busy clinician assess patients for necessary workup and the need for follow-up (**Table 3**).

Laboratory examination is necessary only when there is reasonable expectation that results will affect the treatment plan. Premature menopause is one example that would require laboratory workup to define.

COUNSELING

Utilization of the PLISSIT model (*P*ermission, *L*imited *I*nformation, *S*pecific *S*uggestions, *I*ntensive *T*herapy) of sex therapy is a helpful tool to bridge the gap with information between permission and intensive therapy. This model was created in 1976 by Jack S. Annon to guide HCPs through the levels of evaluation and treatment.[39] Assessment is broken down into the following 4 core steps:

- *Permission*: First, create an environment where the patient feels comfortable revealing concerns, assuring confidentiality and using either open-ended or ubiquity style questions.

Table 3
Screeners for hypoactive sexual desire disorder/female sexual interest and arousal disorder

Screening Tool	Assessment
Decreased Sexual Desire Screener	Brief diagnostic tool for HSDD. Sensitivity and specificity 84% and 88%, respectively[35]
Female Sexual Function Index	19-item, self-report scale considered gold-standard measure of female sexual function. Assess domains of desire, arousal, orgasm, pain[36]
Female Sexual Distress Scale-Revised	Distress[37]
Sexual Interest and Desire Inventory-Female	Clinician administered tool to measure severity and change in response to treatment of HSDD[38]

- *Limited Information*: Second, offer limited information based on the history taken and the concern presented. This information could include discussion of the biopsychosocial model of sexual health and the multiple causes for the concern or basic genital anatomy. This type of counseling can educate and empower your patient, thereby dispelling potentially long-held myths and misconceptions regarding sexuality.[40]
- *Specific Suggestions*: Next, specific suggestions may be made, including offering a differential diagnosis. This portion of PLISSIT is whereby HCPs may exercise latitude to determine the extent of counseling performed based on level of comfort or experience with the topic. Recommendations could include the use of specific lubricants or moisturizers for dryness, massage, vibration, dilators, or bibliotherapy. Education on benefits of self-stimulation as well as diet, exercise, stress-reduction, and social norms can positively impact sexual health. Discussions may also include the differences between female and male sexual response cycles, the importance of communication skills, reciprocity and transparency in sexual wants and needs, the use of fantasy, and different ways to achieve orgasms. It may be necessary to normalize self-stimulation and educate regarding techniques, timing, and discussion with partner. Many women are uncomfortable or unfamiliar with the use of a vibrator. Framing the use of vibration in a medical sense, in that it will increase blood flow to an area to assist in tissue health and healing, much like using a vibrating massage wand on a shoulder spasm, can help normalize this process for many women and speed healing.

Insertional pain due to many disorders, such as vulvovaginal atrophy (whether this be due to menopause, breastfeeding, or use of oral contraceptives), lichen sclerosus, vaginismus, and many forms of vulvodynia can benefit from increased touch. Counsel regarding the importance of massage and again liken this to massage of a neck spasm. Increased blood flow to any tissue will speed healing. Massage and vibration are both methods of increasing blood flow to the neck or to the vulva. Specific instructions will help with compliance. If possible, have demonstration vibrators on hand in the clinic to let women see and touch them, thus decreasing fear of the potentially unknown. Using a pelvic floor model, demonstrate specific massage techniques, applying gentle pressure between the thumb and forefinger to massage and stretch the tissue. She may incorporate this massage technique while applying topical medication or moisturizer. Write down instructions regarding technique, pressure, and frequency.

If you feel comfortable, you could introduce techniques such as sensate focus. Sensate focus is a sex therapy technique initially defined by Masters and Johnson, although since refined.[41] This technique works on removing the goal-oriented nature of many sexual encounters and helps remind participants of the joy of being intimate with a partner. It takes penetration off the table for an agreed on amount of time while the couple works on experiencing touch and the many benefits of being mindful of sensations other than strictly genital sensations.

- *Intensive Therapy*: If there is need for referral to other specialists, namely for intensive therapy, this can be made at this point as well.

TREATMENT

Approach to treatment requires acknowledgment of the biopsychosocial aspects of human sexuality.[42] Not to say that HCPs need to be experts in each of these areas, but to say that it is imperative to recognize there are typically multiple contributing factors. The ability to relay this recognition to the patient will also help establish reasonable goals and expectations throughout the course of treatment, thereby increasing compliance and satisfaction. Increased understanding of the process will also aid them in following through with referrals to other specialists who can help address the many factors involved.

PHARMACOTHERAPY

Flibanserin

Flibanserin (Addyi) is the only US Food and Drug Administration (FDA) -approved pharmacotherapeutic agent available for HSDD and is indicated for acquired, generalized HSDD or FSIAD of any severity in premenopausal women. Flibanserin is a 5-HT_{1A} agonist/5-HT_{2A} antagonist that also exhibits weak to moderate antagonism of 5-HT_{2B}, 5-HT_{2C}, and dopamine D4 receptors. Approved in August 2015, it fell short of hype and expectations. It was widely referred to in the media as the female Viagra, leading people to expect an immediate, visible response to this medication. However, this is a centrally acting central nervous system agent taken nightly before change is noted within approximately 8 weeks. Cost, lack of awareness, and the FDA-mandated Risk Evaluation and Mitigation Strategy (REMS) program make this medication difficult to access for most patients. The dual control model of sexual response involves a teeter totter of inhibitory mechanisms and excitatory mechanisms.[43] The excitatory hormones dopamine and norepinephrine, and the inhibitory neurotransmitter serotonin, are proposed to balance with the use of Flibanserin.

The REMS program does pose another barrier to obtaining this medication. Prescribers are required to take a short, 10-minute, 4-question test before being certified to prescribe Flibanserin. Pharmacies also need to take the test before dispensing. Because this was implemented due to findings on the study of Flibanserin with alcohol, it requires the prescriber to evaluate the alcohol study. It is important to note that typical alcohol use was allowed during the studies to approve Flibanserin, and approximately 60% of women admitted to social alcohol use during the study period.[44]

The initial alcohol study was performed in 25 participants; 23 of these participants were men. After a 10-hour fast, participants were fed a light breakfast and instructed to take Addyi (this is intentionally dosed at bedtime) with either 2 or 4 of the following: 12-oz cans of beer with 5% alcohol content, 5-oz glasses of wine with 12% alcohol

content, or 1.5-oz shots of 80-proof spirit. Hypotension or syncope requiring therapeutic intervention of ammonia salts and/or placement in supine or Trendelenburg position occurred in 4 of the 23 subjects coadministered Flibanserin 100 mg and 2 of each of the alcoholic beverages. Six of the subjects coadministered Flibanserin and 4 of the alcoholic beverages experienced orthostatic hypotension when standing from a seated position, and 1 of the 6 required therapeutic intervention.[45] This study design creates debate regarding the REMS program, applicable clinical evidence, and gender bias in sexual research.

A separate, larger alcohol study including women was completed October 2016 but is not yet published. Two further alcohol studies are also currently underway.

The difficulty in predicting the efficacy of Flibanserin in each patient lies within the complexities of the biopsychosocial model of FSD. Each aspect is weighted differently in every patient. Some patients will require more psychosocial work; others will require more biological work. Most, however, will require some combination of both.

Those patients who are not good candidates for, or do not respond to, Flibanserin are left with off-label medications or hormone supplementation if warranted. Because of the relative lack of on-label options, many medications have been studied and used off label for the treatment of HSDD/FSIAD.

Testosterone

Testosterone is produced in both the ovaries and the adrenal glands. Beginning just before the age of 30, testosterone levels begin a slow, steady decline and decrease dramatically after either surgical or natural menopause. Just as the menopausal symptoms of hot flashes and night sweats do not manifest in every woman after the decline of estrogen, decreased libido may not manifest in every woman with a decrease in testosterone. This fact is one of many factors rendering the success of testosterone therapy in women a difficult endpoint to assess. However, there are multiple studies showing efficacy of testosterone supplementation in both premenopausal and postmenopausal women for the treatment of HSDD. In fact, testosterone use in women has been studied with increasing frequency in recent years. Although still not FDA approved, off-label testosterone use has shown efficacy in clinical trials in women who are surgically menopausal and treated with estrogen and progesterone, surgically and naturally menopausal not treated with estrogen and progesterone, and premenopausal.[46–50]

Many providers are apprehensive to use testosterone in premenopausal women because of concerns regarding virilization as well as potential androgenic effects on the fetus in the case of pregnancy. Thirty-four premenopausal women with low libido and low testosterone levels were evaluated in a 12-week study using 1% testosterone cream, 10 mg applied daily to the thigh, and showed improvement in well-being, mood, and sexual function.[51]

Testosterone can be administered in many different forms: oral, transdermal, injections, or implants. However, the use of testosterone in women with HSDD remains quite controversial, with some studies showing efficacy, and others highlighting potential side effects. Nonetheless, testosterone has been used in women with symptoms of androgen deficiency since 1930. Despite the lack of conclusive evidence regarding the long-term effects of testosterone use in women, there is little doubt in the literature that it does help improve the female sexual response.

Because testosterone is not FDA approved for use in women, there remains little guidance regarding dosing, counseling, and monitoring. Although it is

generally recommended that providers regularly observe women for signs of virilization, the American Association of Clinical Endocrinologists has offered monitoring guidelines for women using testosterone supplementation. Recommendations include semiannual clinical breast examinations along with annual mammography, lipid panel, complete blood count, and endometrial sonography. Some experts also recommend baseline and regular testing of calculated free testosterone.[52]

Androgenic side effects may be seen, such as acne, hirsutism, deepening of the voice, enlarging of musculature, or enlarging of clitoris. These effects, however, are typically only seen at supraphysiologic doses.[53] Although there is a lack of data regarding long-term cardiovascular effects, no significant effects have been demonstrated on the lipid panel, fasting glucose, insulin, liver function, or blood counts in women.[47]

Bupropion

Bupropion can also be used off-label in selective serotonin reuptake inhibitors (SSRI) -induced sexual dysfunction. A double-blinded sham-controlled study demonstrated an increase in sexual frequency and desire as compared with placebo after administration of Bupropion (150 mg twice a day). The women in this study were diagnosed with SSRI-induced sexual dysfunction using a validated questionnaire.[54] These findings have been repeated in multiple studies finding success with either the addition of Bupropion to the SSRI or the substitution of Bupropion for the SSRI.

Buspirone

Buspirone is another centrally acting medication that modulates the excitatory and inhibitory pathways involved in sexual response. It may be used as an off-label adjunct for HSDD as well, despite limited safety and efficacy data.[55]

Sildenafil

In postmenopausal women, sildenafil has shown improvements in vaginal lubrication and clitoral sensitivity, but has not proven to be effective at increasing overall sexual function.[56] Female sildenafil users with FSD secondary to multiple sclerosis, diabetes, or antidepressant use, however, note a small, but significant improvement in sexual function.[57]

Combination Therapy

A recent study shows promising effects with the use of combination therapy with testosterone and buspirone or testosterone and sildenafil. This study showed an increase in satisfying sexual events (SSE), although it did not measure distress.[58]

What's on the Horizon?

Society is beginning to recognize the importance of female sexual health as a subset of overall health. As such, further studies are being conducted to help increase understanding regarding cause as well as treatment options for HSDD/FSIAD. As these studies are completed, medications are being studied and developed that may have positive effects on female sexuality. **Table 4** lists upcoming medications currently under review with the FDA for the treatment of FSD.

Table 4
What's on the horizon in sexual medicine

Drug Name	Drug Component(s)	Pharma Sponsor	Approval Status
Lybrido (on demand oral tablet)	Sildenafil + Testosterone	Emotional Brain	Phase III for HSDD
Lybridos (on demand oral tablet)	Buspirone + Testosterone	Emotional Brain	Phase III for HSDD
Tefina (intranasal testosterone gel)	Testosterone	Trimel Pharmaceuticals	Phase II complete for anorgasmia
Lorexys (daily oral combination)	Trazadone + Bupropion	S1 Biopharma	Phase IIa complete for HSDD
Rekynda (Bremelanotide) (on demand subQ injection)	Melanocortin agonist	AMAG Pharmaceuticals and Palatin Technologies	2 Phase III trials completed for HSDD/FSIAD, coprimary endpoints met

SUMMARY

Sexuality has long been a culturally taboo topic of discussion and to this day remains misunderstood and often misrepresented. As physician assistants, we have made a commitment to improve the overall health of our patients. This commitment is not possible while excluding sexual health. Our best avenue to this end is to further our own knowledge regarding the possibilities surrounding human sexuality and to be aware of our own preconceived notions, experiences, and biases. Once we understand the vast complexities of human relationships, our judgments begin to pale and our minds begin to open. This space is where we can best offer comprehensive, nonjudgmental, empathic, and informed health care to each patient we have the honor to treat.

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