Hypoactive sexual desire disorder: How do you identify it and treat it?

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Intended audience: This continuing education (CE) activity has been designed to meet the educational needs of women’s health nurse practitioners (NPs), adult NPs, family NPs, certified nurse midwives (CNMs), and other healthcare providers (HCPs) who see women in their practices.

CE approval period: Now through December 31, 2021

Estimated time to complete this activity: 1 hour

CE approval hours: 1.0 contact hour of CE credit, including 0.25 contact hours of pharmacology content

Goal statement: To acquire specific communication skills involved in sexual history taking and to identify and treat patients in whom HSDD is identified

Needs assessment: Dr. Kellogg-Spadt presents evidence-based practical suggestions for taking a sexual history, particularly with regard to female sexual functioning. Dr. Faught discusses the DSM-V diagnostic criteria for HSDD and the process of diagnosing and treating this disorder based on the literature and her own experience.

Educational objectives: At the conclusion of this educational activity, participants will be able to:
1. Discuss specific communication skills involved in sexual history taking with female patients.
2. Explain the barriers to comprehensive assessment of a female patient with sexual concerns.
3. Identify HSDD and describe available nonpharmacologic and pharmacologic treatments for this disorder.

Accreditation statement: This activity has been evaluated and approved by the Continuing Education Approval Program of the National Association of Nurse Practitioners in Women’s Health (NPWH), and has been approved for 1.0 contact hour of CE credit, including 0.25 contact hours of pharmacology content.

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Susan Kellogg-Spadt, PhD, CRNP, IF, FCST, CSC, discloses that she serves as a consultant, speaker, and/or advisory board member for Materna, Duchesnay, Ipsen, Lupin, MiddlesexMD, AMAG, and Aytu.

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Successful completion of the activity: Successful completion of this activity, J-19-04, requires participants to:
Approximately 1 in 10 women has distressing low sex drive, otherwise known as hypoactive sexual desire disorder (HSDD). How do healthcare providers determine whether a given patient has HSDD? And how should they treat it? The authors address these challenges in this article.

**Key words:** sexual history-taking, female sexual dysfunction, hypoactive sexual desire disorder, HSDD, flibanserin, bremelanotide

Women whose sexual desire and/or arousal has diminished compared with what it used to be, causing them distress, may not make a special appointment to see a healthcare provider (HCP) about this problem. Even if they are seeing an HCP for their annual checkup, they may not mention it. In this article, one expert in the field of sexual medicine reviews the basics and intricacies of taking a sexual history in order to enable women to feel comfortable enough to discuss their sexual problem and the distress they may feel about it. The second expert in this field focuses on one particular type of female sexual dysfunction (FSD)—hypoactive sexual desire disorder, or HSDD—and discusses new and innovative treatments for it.

**Sexual history taking**

Many patients with physical disorders present with pathognomonic symptoms and can be diagnosed based on findings from a history, an examination, and, if needed, laboratory/imaging tests. Mental conditions, including sexual disorders, are more elusive because symptoms usually are not obvious and may not lend themselves to detection via routine screening or diagnostic tests. Because normal sexual function is not necessary for an individual’s survival—although it is certainly necessary for the species’ survival—HCPs might wonder....

**Why assess sexual function in the first place?**

According to the World Health Organization, sexuality is important to quality of life (QOL) and is a basic human right. Sexual problems are common, and an HCP’s inquiry regarding the problem legitimizes and validates it. Because so many patients hesitate to bring up the topic, it is up to HCPs to do so.
tions regarding FSDs described in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition\(^2,3\) in advance of publication of the DSM-IV-Text Revision.\(^4\) Five main categories of FSDs were identified: sexual desire disorders, including HSDD; sexual arousal disorders; orgasmic disorder; dyspareunia; and vaginismus. An essential element of this diagnostic system was the personal distress criterion. In 2013, the DSM-5 merged disorders pertaining to low sexual desire and low sexual arousal into one term, female sexual interest and arousal disorder, and recognized two additional disorders—female orgasmic disorder and genitopelvic pain/penetration disorder, an amalgam of dyspareunia and vaginismus.\(^5\) Although the DSM-5 does not include the term hypoactive sexual desire disorder, this term continues to be used by sexual medicine providers, researchers, and the authors of this article.

How common are FSDs that are severe enough to cause distress?
The PRESIDE (Prevalence of Female Sexual Problems Associated with Distress and Determinants of Treatment Seeking) study, a survey of more than 31,000 U.S. women, revealed that a sexual problem associated with personal distress occurred in 12.0% of respondents and was more common among those aged 45-64 years (14.8%) than among younger women (10.8%) or older women (8.9%).\(^6\) These percentages were considerably lower than the proportion of study respondents who reported sexual problems but no associated distress about them.

What proportion of women seek care for their FSDs? From whom do they seek care?
Among the 3,239 women who participated in the PRESIDE study and who self-reported sexual problems with desire, arousal, and/or orgasm, accompanied by distress, 1,083 (33%) sought formal help.\(^7\) Among this group seeking help, 47% turned first to their gynecologist, 39% to their primary care physician (PCP), 7% to their psychiatrist or psychologist, and 3% to their internist. Of the remaining women with distressful sexual problems, nearly 42% sought help from informal sources (i.e., someone other than an HCP) and 9% did so from an anonymous source such as the Internet, television, radio, or printed material. Nearly 15% of these women did not seek help of any kind.

What are some of the barriers to taking a sexual history?
Patients who have a sexual problem may hesitate to broach the topic with their HCP. But their HCPs may be reluctant too. HCP barriers to taking a sexual history include embarrassment, perception of inadequate knowledge and training in this area, lack of awareness of associated co-morbid conditions that might shed light on or mask an FSD, perception that a QOL-type health problem may be less important than a physical health problem, perception that FSD management is time consuming and reimbursement is poor, and knowledge that few FDA-approved treatments exist.

However, none of these issues need to be barriers to assessing sex-
Box: When screening for female sexual disorders, healthcare providers should...

- Choose words and use body language that put the patient at ease. Maintain an open and non–defensive posture (e.g., do not cross your arms).
- Sit so you are talking with the patient at eye level, and maintain appropriate eye contact while you talk to each other. Do not look only at the chart as you take notes.
- Avoid nervous gestures (e.g., jiggling keys in your pocket, clicking your pen open and closed, tapping your foot).
- Choose language appropriate to the age, ethnicity, and culture of the patient.
- Practice using sexual terminology so that you feel comfortable with it. As much as possible, avoid using slang (especially vulgar terminology) or medicalese.
- Ask open-ended questions rather than those that elicit yes or no.
- Be quiet much of the time! Let the patient continue to speak or elaborate on a statement. Listening is as important a part of communicating as talking.

How should HCPs broach the topic of sexual function with a patient? What type of information should HCPs aim to elicit?

For starters, this discussion should be carried out in private, when the patient is fully clothed. The box lists helpful tips for HCPs to make the patient feel as comfortable as possible. Instead of asking a direct question, HCPs should pose an open-ended ubiquity-style statement/question like this one, filling in the blanks with whatever applies: Many women who are postpartum, approaching 40, going through menopause, getting older or experiencing [a marital problem, a health problem, a life change] develop sexual problems. What changes, if any, have you noticed in this regard? HCPs should then follow an affirmative response with an open-ended statement: Tell me more. And then, HCPs should just be quiet and listen; most patients will tell their story in 60-150 seconds. If necessary, HCPs then can pose specific questions: Are you having problems with desire/interest in sex? Lubrication/dryness? Orgasm or coming?

To assess the magnitude/severity of the sexual problem from the patient’s point of view, HCPs can use a rating scale akin to a pain scale. This scale also can be used to document changes in the patient’s sexual problem over time. HCPs need to determine whether the problem began suddenly or gradually, whether it is lifelong or acquired, and whether it is situational or universal. HCPs should ask about the gender(s) of the patient’s partner(s) in a non-judgmental way (Tell me about your partner or partners); about the use of medications, including OTC/herbal medications; and about health conditions that might be affecting sexual function. If any problems are identified, the HCP may need to schedule a follow-up appointment or refer the patient if the problem exceeds the HCP’s knowledge or comfort level.

Once a sexual problem is revealed, how should HCPs proceed in terms of screening and making a formal diagnosis? Validated tools for assessing sexual function include the Female Sexual Function Index (FSFI) (assesses desire, arousal, orgasm, and pain), the Profile of Female Sexual Function (assesses desire in postmenopausal women), and the Brief Profile of Female Sexual Function (a self-screener for low desire in surgically postmenopausal women). Screening tools focusing on HSDD include the Sexual Interest and Desire Inventory-Female and the Female Sexual Distress Scale-Revised.

According to the DSM-5, a diagnosis of female sexual interest/arousal disorder, which embraces HSDD, is made when a person displays a lack of, or significantly reduced, sexual interest/arousal, as manifested by at least three of the following: (1) absent/reduced interest in sexual activity; (2) absent/reduced sexual/erotic thoughts or fantasies; (3) no/reduced initiation of sexual activity and unresponsive to partner’s attempts to initiate; (4) absent/reduced sexual excitement/pleasure during sexual activity in almost all or all (75%-100%) sexual encounters; (5) absent/reduced sexual interest/arousal in response to any internal or external sexual/erotic cues (written, verbal, visual); and/or (6) absent/reduced genital or nongenital sensations during sexual activity.

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activity in almost all or all sexual encounters. Of note, frequency of sexual activity is not a component of the HSDD diagnosis. Symptoms must have persisted for at least 6 months and must not be better explained by a nonsexual mental disorder or be a consequence of severe relationship distress or other major stressors or be due to the effects of substances/medications or other health condition. Also, the patient must find the symptoms distressful.

If a patient meets DSM-5 criteria for HSDD, what is the next step?
If an HCP is not comfortable managing HSDD, then the HCP can validate the patient’s concerns and offer referral(s) to a qualified practitioner. To minimize any chance that a patient might feel rejected or dismissed by her HCP, the referral can be described as a collaborative consult. If an HCP does feel able to treat a patient with HSDD, the HCP should start by educating the patient about her disorder and addressing any identified modifiable biopsychosocial factors such as underlying health conditions, medications, and/or relationship discord that may be causing or exacerbating the HSDD. Depending on the patient’s needs and wishes, the next step may be to initiate counseling or psychotherapy to modify thoughts, beliefs, behaviors, emotions, and/or relationship communication/behaviors that may be interfering with sexual desire. In many cases, another nonpharmacologic approach and/or a pharmacologic approach may be advisable.

Which nonpharmacologic interventions are available for HSDD?
Clitoral stimulators, vibrating pumps, and similar devices marketed as sexual aids or toys can enhance sexual arousal in women who feel comfortable using them. According to the Basson model of female sexual response, sexual arousal often precedes desire. Hence, women who use these products may find that they enhance their sex drive as well. Not all women are receptive to the idea of using devices to enhance their sex drive, however. HCPs must use their judgment to select appropriate candidates. At the same time, some women who seem reticent at first may be more interested in trying a product if their HCP normalizes the use of sexual aids and toys by describing them as physical therapy for the vagina.

What types of pharmacologic treatment are available for HSDD?
Two FDA-approved prescription medications and one OTC medication are available.

Flibanserin
Four years ago, flibanserin (Addyi®) was the first drug to be approved by the FDA for HSDD in premenopausal women. FDA approval was contingent on HCPs and patients heeding the Risk Evaluation and Mitigation Strategies (REMS) program warning that flibanserin users are at increased risk for hypotension and syncope if they ingest alcoholic beverages. This information was conveyed in a boxed warning on the product’s package insert. Flibanserin’s mechanism of action is attributed to its high affinity for 5-HTA1 and 5-HTA2 receptors, displaying agonist activity on 5-HTA1 and antagonist activity on 5-HTA2, resulting in lowering of serotonin in the brain. Just as important, flibanserin increases brain levels of norepinephrine and dopamine, the latter of which facilitates sexual functioning in both women and men. Efficacy and safety of flibanserin (100 mg orally at bedtime) were established in three 24-week, randomized, double-blind, placebo-controlled trials that were named after flowers: DAISY, VIOLET, and BEGONIA. All study participants were premenopausal (mean age, 36 years) and had HSDD for a mean duration of 5 years. Most were Caucasian and in a monogamous relationship (mean duration, 11 years). These relationships were all heterosexual because the FSFI, used as a screening tool in this study, is not validated for lesbian relationships. The studies demonstrated that flibanserin recipients, compared with placebo recipients, reported increased sexual desire, decreased sexual distress, and an increased number of sexually satisfying events (SSEs). In the BEGONIA trial, for example, flibanserin use was associated with a 53% improvement in desire, a 29% reduction in distress, and 6-8 more SSEs per month (1 more than with placebo). The most common adverse events (AEs) in flibanserin recipients were somnolence, dizziness, and nausea. AEs led to drug cessation in 9.6% of flibanserin users and 3.7% of placebo users. In the experience of one of the authors of the present article (BF), flibanserin works well in about half of the women who try it (and not at all in the other half), and the benefits are usually apparent within 8 weeks. If a woman is deriving no benefit after 8 weeks, she can stop the drug abruptly.

Separate studies that prompted the FDA REMS program warning about concomitant use of flibanserin and alcohol were weak/flawed in their design or interpretation. Results of a 2017 study of 96 healthy premenopausal women showed that concomitant administration of mild (0.2 g/kg) or moderate (0.4 g/kg) amounts of alcohol did not affect
the AE profile of flibanserin with respect to dizziness, hypotension, somnolence, or drowsiness. The incidence of dizziness associated with use of flibanserin alone was, by comparison, greater with flibanserin plus ethanol 0.6 g/kg but similar to that with flibanserin plus ethanol 0.2 g/kg or 0.4 g/kg. The incidence of orthostatic hypotension was similar across all treatments, regardless of ethanol dose. No instances of syncope occurred. As a result, the boxed warning on the Addyi package insert was updated to reflect that women who consume one to two standard alcoholic drinks should wait at least 2 hours before taking Addyi at bedtime, and skip the dose altogether if the woman consumes three or more alcoholic beverages that evening.

Bremelanotide
Bremelanotide (BMT; Vyleesi™), a melanocortin receptor (MCR) agonist, is the first and only as-needed treatment that is FDA approved for premenopausal women with acquired, generalized HSDD that causes marked distress or interpersonal difficulty. FDA approval for Vyleesi was granted on June 21, 2019. This MCR agonist non-selectively activates several receptor subtypes with the following order of potency: MC1R, MC4R, MC3R, MC5R, MC2R. BMT 1.75 mg, contained in a pre-filled autoinjector, is self-administered subcutaneously (SC) into the abdomen or thigh at least 45 minutes before anticipated sexual activity. Duration of efficacy after each dose is unknown; the optimal window for BMT dosing has not been fully characterized.

Efficacy and safety of BMT for HSDD were established by the RECONNECT trial. The core phase of the trial consisted of a no-treatment screening month to confirm the diagnosis of HSDD, an at-home placebo self-dosing month, and two identical phase 3 trials. More than 1,200 premenopausal women were randomized in double-blind fashion to receive BMT or placebo for 24 weeks. Most participants were white (85.6%) and from U.S. sites (96.6%); mean age of the group was 39 years. Of note, unlike the studies of flibanserin, BMT studies included women who were not heterosexual. From baseline to end-of-study, BMT users, relative to placebo users, experienced significant increases in sexual desire and significant reductions in distress related to low sexual desire. In both trials, BMT was associated with significant improvements in other components of sexual functioning: arousal, lubrication, and orgasm. Bremelanotide users experienced more nausea, flushing, and headache than did placebo users, but these AEs were generally mild or moderate in intensity and subsided with the second or third injection.

Women who completed the core phase of the RECONNECT trial could enroll in a 52-week open-label extension if they had not experienced serious AEs during the core phase. Of 856 eligible patients, 684 participated in the open-label extension—self-dosing at home with BMT 1.75 mg as needed—and 272 completed it. Overall, participants experienced sustained improvement in their HSDD symptoms. Again, the most common treatment-emergent AEs were nausea, flushing, and headache; the only severe AE experienced by more than one participant in both studies was nausea.

Ristela
Ristela™ is intended for use in women of any age and choice-of-partner status who want to increase their level of arousal and orgasm, as well as to improve their overall desire.
sexual desire and satisfaction. This plant-based, nonhormonal OTC product became available in the United States this year, although the ingredients in it have been studied in European women for more than 7 years. The main ingredients are pine bark extract, arginine, citrulline, and rose hips extract (PACR). In a double-blind, placebo-controlled study, 80 women aged 40-50 years received PACR (n = 40) or placebo (n = 40), 2 tablets in the morning and 2 tablets in the evening, for 8 weeks. The total FSFI score improved by 60% after 1 month and by 73% after 2 months of treatment with PACR compared with baseline values; respective increases were 40% and 46% in the placebo group, a significant difference. No unwanted effects were reported. According to the manufacturer, the daily dose of Ristela is 2 tablets taken once a day, either at morning or at night, with or without food.

Conclusion
Healthcare providers who see women in their practice should screen for sexual problems on a regular basis because many women hesitate to reveal such problems on their own. Women who are diagnosed with HSDD and who want to address this problem have several options. Nonpharmacologic approaches include counseling and the use of devices marketed as sex aids or toys. Pharmacologic approaches, currently limited to premenopausal women, include a medication taken orally at bedtime on a daily basis and a medication taken by self-administered SC injection on an as-needed basis. Women of any age with low sexual desire/arousal can try a new plant-based OTC oral medication. HCPs can only wonder what the 2020s will bring in terms of new HSDD treatments for women of all ages.

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