Evaluation and management of hypoactive sexual desire disorder in women. Recommendations from the 5th International Consultation on Sexual Medicine (ICSM 2024)

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Invited Review

Evaluation and management of hypoactive sexual desire disorder in women. Recommendations from the 5th International Consultation on Sexual Medicine (ICSM 2024)

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Abstract

Introduction: Hypoactive sexual desire disorder (HSDD) is one of the most common female sexual dysfunctions.
Objectives: To produce a consensus article on the evaluation and management of HSDD.
Methods: An international committee was selected to review available data and present recommendations to the 5th International Consultation on Sexual Medicine. Discussion and revisions were made to highlight state-of-the-art knowledge based on the peer-reviewed medical literature and expertise of experts worldwide.
Results: The consensus article reviews the most up-to-date evidence for definitions of HSDD and its clinical assessment, including psychological, nonhormonal, hormonal, and alternative therapies.
Conclusion: There are many available therapies for HSDD, all of which should be utilized through a biopsychosocial approach to improving this condition.

Keywords: hypoactive sexual desire disorder; low libido; female sexual dysfunction.

Introduction

Hypoactive sexual desire disorder (HSDD) is one of the most common sexual dysfunctions.[1] While its causes are multifactorial, there is increasing attention given to evaluation and management within the sexual medicine community.

Methods

This consensus guideline is part of the International Consultation on Sexual Medicine (ICSM). Experts from across the world were selected to participate in a yearlong process to review the current evidence and produce guidelines and recommendations for evaluation and management of HSDD. An international committee was selected to review available data and present recommendations highlighting state-of-the-art knowledge based on the peer-reviewed medical and psychological literature and the expertise of experts worldwide. All members of the committee were assigned subtopics to review, and the committee jointly presented its findings in person at the 5th ICSM in Madrid, June 28-29, 2024, where members of the International Society for Sexual Medicine (ISSM) gathered to provide in-person feedback and revisions suggestions, which were then incorporated into the final guidelines. A comprehensive review of the literature was undertaken via search keywords within PubMed (HSDD, low libido definitions, and therapeutics), textbooks on female sexual health, and existing ISSM and International Society for the Study of Women's Sexual Health (ISSWSH) publications focusing on women and sexual desire. Each member of the committee undertook a section of focus, with the committee chairs being responsible for all editing, reference checks, and production of the final manuscript.

Results

Definitions of HSDD

Historically, sexual dysfunctions have been considered psychiatric disorders.[2] This is why the diagnostic criteria for sexual

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5th ICSM Recommendation	Level of evidence
1. Hypoactive sexual desire disorder (HSDD) should be considered a distinct entity from the female sexual arousal dysfunction.	Low
2. In this sense, this committee recommends the adoption of the *ICD-11* definition and nomenclature of HSDD in women, which are in line with the ISSWSH consensus.	Moderate
3. Evaluation of HSDD requires a focused history and may require a physical examination.	Moderate
4. A physical examination should be performed only if clinically indicated by physical complaints.	Moderate
5. Several screening tools have shown promise with good validation for HSDD; however, HSDD is a clinical diagnosis and cannot be made by a screening tool but rather by the definitions as outlined in section 2.	Moderate
6. There is evidence for psychological interventions in treating HSDD: sex therapy, cognitive-behavioral therapy, mindfulness-based therapy.	Strong
7. There is evidence for the use of flibanserin in premenopausal women with HSDD.	Strong
8. There is evidence for flibanserin in the treatment of postmenopausal women with HSDD.	Moderate
9. There is evidence for the use of bremelanotide as needed in premenopausal women with HSDD.	Moderate
10. There is evidence for the use of bupropion and buspirone in women with HSDD but poor evidence in the adjunct use of bupropion for SSRI-induced HSDD.	Moderate
11. There is evidence for the use of trazadone and sildenafil in SSRI-induced sexual dysfunction, without clear indications for HSDD specifically.	Moderate
12. In menopausal women with HSDD, testosterone therapy (with or without concurrent estrogen therapy) approximating the physiologic levels of premenopausal women is associated with improvements in HSDD and significantly increases sexual desire.	Moderate
13. Transdermal testosterone therapy administered at physiologic doses does not increase the risk of serious adverse events in low- and moderate-risk patients, including cardiovascular disease and lipid metabolism, but data are not available past 2 months of use.	Moderate
14. There is not evidence that transdermal testosterone increases the risk of breast cancer; however, data from RCTs are insufficient, and women with hormone-sensitive cancer should use caution when considering testosterone therapy.	Moderate
15. There are limited data in late reproductive age women using testosterone therapy for HSDD, and there are insufficient data to recommend use of testosterone therapy in premenopausal women	Low
16. In unselected postmenopausal women, available data do not support a clear effect of systemic estrogens and progestogens on sexual desire. No specific data on women diagnosed with HSDD are available. Therefore, HRT is not recommended with the sole purpose of treating HSDD.	Low
17. In healthy, recently postmenopausal women with natural menopause, transdermal estradiol (plus micronized progesterone) has shown some beneficial effects on sexual desire; however, it has been suggested that this may represent an indirect effect mediated by an improvement in reduced lubrication/sexual pain. No specific data on women diagnosed with HSDD are available.	Low
18. Since oral estrogen therapy increases circulating SHBG, leading to a decrease in free testosterone, transdermal estrogen therapy might be the preferred option when estrogen therapy is chosen, and concerns about sexual function exist (expert opinion).	Low
19. Current evidence does not support a clear effect of HRT (systemic estrogens) on sexual desire in women with surgical menopause and bilateral oophorectomy.	Low
20. In unselected postmenopausal women, SERMs probably slightly improve desire; however, specific data on women diagnosed with HSDD are lacking, and overall quality of the evidence is scarce. Therefore, SERMs are not recommended with the sole purpose of treating HSDD.	Moderate
21. Evidence regarding SERMs combined with estrogens on sexual desire is insufficient to provide recommendations (insufficient data).	Very low
22. In postmenopausal women with HSDD and normal adrenal function, systemic DHEA is not associated with significant improvement in sexual response.	Moderate
23. Safety: data from RCTs do not show a significant effect of DHEA on serious adverse effects, serum lipids, serum glucose, weight, body mass index, or bone mineral density.	Moderate
24. In some small RCTs, tibolone increased measures of sexual desire in natural or surgical postmenopausal women. However, the quality of evidence is low to very low, and the effect was not confirmed in meta-analysis. Overall, the current evidence does not suggest a significant effect of tibolone on sexual desire in postmenopausal women with HSDD.	Moderate
25. Safety: When compared with placebo, tibolone increases recurrent breast cancer rates in women with a history of breast cancer and may increase stroke rates in women >60 years of age. No evidence indicates that tibolone increases the risk of other long-term adverse events or that it differs from HRT with respect to long-term safety.	Strong
26. There is insufficient evidence to recommend the majority of complementary therapies. The strongest evidence appears to be for L-arginine. There is also evidence for aromatherapy, but the trials are small and have not been replicated.	Low

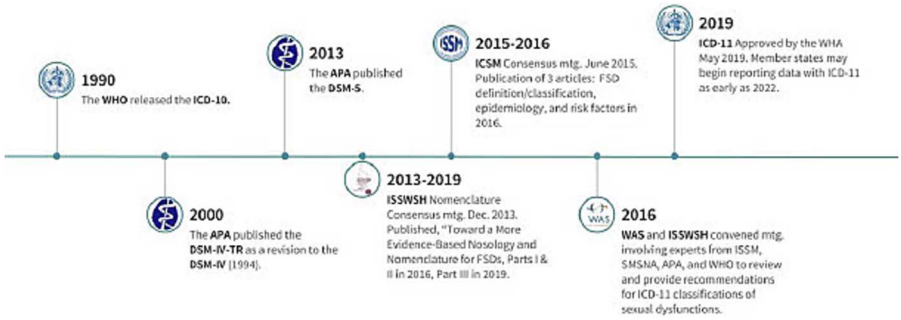

Figure 1. Timeline of female sexual dysfunction definitions, nomenclature, and classifications.[25] APA, American Psychiatric Association; *DSM-IV-TR*, *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision*; *ICD*, *International Classification of Diseases*; ICSM, International Consultation on Sexual Medicine; ISSWSH, International Society for the Study of Women's Sexual Health; WAS, World Association for Sexual Health; WHO, World Health Organization.

dysfunctions in men and women are traditionally based on the multiaxial system of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM*) of the American Psychiatric Association.[3] The timeline of the development of the definitions, nomenclature, and classification of female sexual dysfunction is summarized in Figure 1.

It is important that from the beginning, there were no empirically determined criteria that distinguished normal from abnormal levels of desire. In fact, there is no agreed-on definition of desire from which a desire disorder can be inferred. Instead, a definition of desire must be inferred from the agreed-on definition of its deficiency in HSDD.[2] The incarnation of the *DSM-IV-TR* (fourth edition, text revision) defines HSDD as

> "persistent or recurrent deficiency (or absence) of sexual fantasies/thoughts, and/or desire for or receptivity to sexual activity which causes personal distress."[4]

The definitions were revised when the *DSM-5* (fifth edition) was introduced in 2013.[5] Female HSDD and female sexual arousal disorder have been deleted from the *DSM-5* and replaced by female sexual interest/arousal disorder, which combines elements of subjective sexual desire and arousal into 1 category. Female arousal disorder (defined in the *DSM-IV-TR* as the absence of genital arousal) was not included in the *DSM-5*, because the absence of genital arousal is rarely identified independent of low sexual desire unless related to hypoestrogenism, which by definition is not a psychiatric diagnosis.[6]

In June 2015, members of the Fourth ICSM presented the view that hypoactive sexual desire dysfunction should be kept as a separate entity from female sexual arousal dysfunction.[6] Data on the incidence, prevalence, and risk factors for sexual dysfunction indicate clearly that the separation of these 2 dysfunctions is supported by the current epidemiologic and risk factor literature. This decision is at variance with the *DSM-5*, which combined these 2 dysfunctions into a single disorder.

ICSM vs ISSWSH

The ISSWSH consensus recommendations were reported in 2 simultaneous publications: "Toward a More Evidence-Based Nosology and Nomenclature for Female Sexual Dysfunctions," parts I and II, in *The Journal of Sexual Medicine* in 2016.[7,8] While the ICSM and *International Classification of Diseases* (*ICD*) classify these problems as sexual "dysfunctions," the ISSWSH uses the term "disorders": the convention for conditions associated with phases of the sexual response cycle and consistent with the *DSM* schema.

Similar to the ICSM definitions, the ISSWSH nomenclature retained separate categories for HSDD and female arousal disorders. Although sexual desire and arousal typically occur simultaneously, sexual desire disorder is described in conjunction with arousal that is sufficient for vaginal, clitoral, and labial engorgement that still occurs in response to sexual stimulation but without a concomitant interest in participating in sexual activity.[9] In contrast to the *DSM-5*, the ISSWSH recommended broadening and simplifying the diagnostic criteria and returning to the previous diagnostic label "desire" (instead of "interest") for which there is substantial empirical experimental and clinical evidence.[8]

ICD-11 and HSDD

A new chapter on conditions related to sexual health was proposed for the *ICD-11* (11th revision), focusing on sexual health issues containing a unified classification of sexual dysfunctions to better facilitate the identification and treatment of these conditions. It was suggested that this might also reduce stigmatization of these conditions and encourage their identification and appropriate treatment by non–mental health specialists.[10] Definitions were developed for inclusion in the *ICD-11 for Mortality and Morbidity Statistics*, approved by the World Health Assembly in 2019.[11]

The *ICD-11* defined HSDD as the "absence or marked reduction in desire or motivation to engage in sexual activity as manifested by any of the following: (1) reduced or absent spontaneous desire (sexual thoughts or fantasies); (2) reduced or absent responsive desire to erotic cues and stimulation; (3) inability to sustain desire or interest in sexual activity once initiated."[11]

Clinical assessment of HSDD

Clinical assessment of sexual health includes a comprehensive gynecologic, medical/surgical, and medication history, including relationships and gender identity. Several validated self-administered questionnaires are available for screening of HSDD, such as the Brief Profile of Sexual Function[12] and the 5-question Decreased Sexual Desire Screener,[13] among many others based on patient-reported outcomes and sexual function.[14]

In specific, clinical assessment of HSDD is a challenging task and requires that certain key aspects be addressed in the clinical encounter[15]:

- Description of the low desire if generalized (in every situation with every partner) or situational (often excludes medical factors)
- Onset and duration; identification of symptoms and characteristics, whether lifelong or acquired after months or years of satisfying sexual function and the factors that the patient feels contribute to or precipitate the symptoms
- Assessment of the level of distress and bother and the impact of the dysfunction on one's personal life (mild, moderate, severe)

An effective approach to clinical assessment builds on the PLISSIT model: permission, limited information, specific suggestions, and intensive therapy. Another common approach to communication is "ask, tell, task." Communication is facilitated by "ask," starting with open-ended statements that assure the patient that many women have sexual concerns and then asking the patient if she has had any sexual difficulties. These communication strategies have been extensively covered in the sexual medicine literature.[16]

Adequate time or a separate appointment to address the patient's sexual health concerns may be necessary. A health care provider can start ubiquity statements by asking about medical, social, and life cycle issues, such as "Many women going through menopause [*or* Many women reporting hot flushes] usually report some kind of sexual dysfunction, including low desire." The health care provider can then follow the ubiquity statement with an open-ended invitation, such as "Tell me about it."[17] If a woman reports low desire, it is important to assess the presence of distress related to low desire, which is necessary to diagnose HSDD.[8]

Sexual history

The biopsychosocial model guides the understanding of the multifactorial etiology of female sexual desire and female sexual response.[6]

A proper and focused medical/sexual history is important for diagnosis and treatment. This history taking should be patient centered and biographical, incorporating what patients may have been taught about sex and how their history may play a role in their current concerns. The clinician must be keen to ask about past and present medical, surgical, and obstetric history (when relevant) along with the following, which is not an exhaustive list:

- Chronic medical condition
- An operation, depression, injuries, or other medical condition
- Medication/drug intake or alcohol use
- Pregnancy, recent childbirth
- Menopausal transition symptoms (menstrual, dryness, urinary/genital infections, sleep disorders, mood, vasomotor symptoms, etc)
- Other sexual issues (pain, decreased arousal, or orgasm)
- Sexual partner's health/sexual problems
- Dissatisfaction with relationship or partner
- Stress or fatigue

The clinical assessment of any of the subtypes of female sexual disorders should consider the following information[18]:

- An assessment of past and present sexual desire and other domains (arousal, orgasm, and pain)
- Onset of symptom or symptoms (gradual, rapid)
- Duration (lifelong, acquired), intensity, and level of concern
- Context of problem (generalized, specific)
- Diseases and drugs
- Degree of impact on sexual partner
- Expectations of changes sought
- Assessment of the changes that can be dealt with (personal resources, the health of the individual and her partner, as well as that of their relationship, etc)

During history taking, assessing HSDD can be performed efficiently and effectively. A set of brief questions can be utilized to help the scope of assessment and evaluation.[1] These questions include the following:

- Do you have any sexual concerns?
- How do you feel about your level of sexual desire, arousal, or orgasm?

To facilitate these discussions, ensure a safe, nonjudgmental environment for the patient. This could include educating and training staff to be comfortable with sexual topics, offering patient-friendly materials in the waiting and examination rooms, and including questions about sexual topics on intake forms. Although screening for HSDD is easily performed as part of an office visit, follow-up might be necessary to address sexual concerns and provide counseling or medication management.

When the history elicits distressing low sexual desire, it should proceed toward HSDD, including low motivation for participation in sexual activity, loss of spontaneous sexual desire (eg, sexual thoughts and fantasies), lack of desire in response to erotic cues and stimulation, low initiation and avoidance of situations that could lead to sexual activity, and participation in sexual activity due to obligation or fear of losing her partner.[19]

Low sexual desire is a common symptom of depressive disorders but can also be prevalent in patients with anxiety disorders, somatic symptom disorders, or eating disorders.[20] Thus, when working with patients who have been diagnosed with a mental disorder, clinicians should be careful to assess possible symptoms related to hypoactive sexual desire. This is especially true when patients are using medications such as selective serotonin reuptake inhibitors (SSRIs) with known side effects on sexual functioning. In settings where patients are presenting with low sexual desire as their main concern, clinicians should inquire about a history of mental health problems, particularly depressive symptoms. While short self-report scales such as the Patient Health Questionnaire–9 can be helpful to screen for depressive symptoms, asking patients about whether they experience a lack of interest or motivation in other activities (eg, hobbies) beyond sex can help determine whether low desire symptoms may be part of an ongoing depressive episode.[21]

Physical examination

Generally speaking, physical examinations provide an excellent opportunity for education and reassurance regarding normal genital anatomy and sexual health. Unless clinically indicated by symptoms, a general physical examination with HSDD may contribute to the clinical assessment but not necessarily point to a specific cause of the HSDD. However, physical examinations can help rule out other factors that may be contributing to HSDD, such as concerns of pain with sexual activity or findings consistent with hormone insufficiency states. A focused genital and pelvic examination may be indicated and is recommended when sexual dysfunctions that relate to the genitals are suspected, but it is not required if there is no concern for genital contributions to HSDD. Inspection of the external genitalia and bimanual or

Table 1. Visual examination and corresponding findings in the genital examination.

Examination	Findings
Inspection of external genitalia	Abnormalities, lesions, or signs of infection; dermatoses on the mons pubis, labia majora, and labia minora
Visual examination of vestibule	Redness, swelling, discharge, or lesions at the vaginal opening. Swab test of vestibule
Visual examination of vaginal canal	Changes in color, texture, or abnormal discharge within the vaginal canal; atrophic changes
Evaluation of pelvic floor	Weakness or prolapse of pelvic support structures; pelvic floor muscle assessment for hypertonicity and tenderness
Evaluation of clitoris	Atrophy, phimosis, adhesions, lesions, changes in sensation

speculum examinations can aid in identifying causal signs of certain medical, hormonal insufficiency, or anatomic conditions typical of menopausal transition that relate to sexual dysfunction directly or indirectly, such as pain (narrowness of the vaginal introitus, signs of genital atrophy, etc) or urinary incontinence.[19] The physician should investigate any signs of abuse that are evident on physical examination. Table 1 outlines the physical examination assessment when sexual pain is reported in the history. The findings on this examination may be used to identify referral needs.

Contributing/risk factors

It is strongly recommended that providers look for and identify various factors contributing to sexual complaints across the life span, whether biomedical, sociocultural, psychological, or interpersonal/couple related. Examples of these factors follow:

Biomedical: pregnancy/postpartum, menopausal transition, noncommunicable disease, cancer survivorship, neurotransmitter imbalance, hormonal factors, medications, poor sleep

Pharmacologic: Numerous medications have been associated with sexual dysfunction, which may be a result of direct action (eg, SSRIs, hormones), side effects (eg, anticholinergics), and unanticipated side effects from treatment (eg, weight gain from medication leading to sexual dysfunction).[1]

Psychological: anxiety-related symptoms, chronic stress, depression, and symptoms of posttraumatic stress disorders

Interpersonal: couple/partner/relationship discordance and sexual dysfunction

Cultural: perceptions, stigma, naming/shaming

Therapies for HSDD

Psychological treatments

Psychological factors such as cognitive distraction, rumination, or performance anxiety can disrupt sexual response, including sexual desire.[22] Psychological treatments feature various methods aiming to address these mechanisms and thereby allowing women to experience greater levels of sexual desire and lower their feelings of personal distress.[1] Treatment methods consist of those derived from psychological therapies of mental disorders such as depression (eg, keeping track of symptoms via a diary) as well as methods that target sexual dysfunction symptoms (eg, a lack of sexual desire), such as self-exploration or sensual touch exercises. To date, there is no evidence suggesting that psychological treatments are more or less effective in treating HSDD in pre-, peri-, or postmenopausal women, and most psychological treatment studies include women of all age groups. Thus, findings for psychological treatments for HSDD are presented independent of menopausal status. In 2013, a meta-analysis of randomized controlled trials (RCTs) investigating psychological treatments for HSDD yielded a large effect ($d = 0.91$) for the improvement of low desire symptoms and a medium effect ($d = 0.51$) for sexual satisfaction.[23] Since then, nonrandomized, pilot, and feasibility studies have been published, as well as individual RCTs and meta-analyses of uncontrolled studies, although no meta-analysis of RCTs has been performed to date.[24-33] In the following section, we provide an overview of psychological treatments for HSDD and review relevant intervention studies published within the past 10 years.

Treatment considerations

Following a stepped care approach as described in the PLISSIT model,[34,35] psychological treatments can vary from low to high intensity depending on the presented symptoms, personal distress, as well as setting variables (eg, time and recourses). The PLISSIT model continues to provide guidance for treatment decisions, often because clinicians have various levels of training in sexual counseling and this model emphasizes the identification of concerns and referrals when appropriate. In a first step, clinicians may ask permission to discuss low desire concerns with the patient (eg, asking about recent changes in desire). Then, limited information can be provided about the prevalence of low desire concerns as well as treatment resources. Normalizing declines of desire in long-term relationships as well as age-related changes in sexual interest can be helpful as well.[22] Offering specific suggestions concerning the use of sexual aids (eg, lubricants) or self-help materials can help patients who are interested in working on the problem on their own. Intensive therapy can include referrals to a clinical psychologist or other expert in providing evidence-based sex therapy. A clinician can deliver care at different steps within this model based on one's comfort and training level and should recognize the need for a referral when necessary.

Psychological treatments for HSDD can be delivered in a group-based, couples, or individual format. In routine care, practical considerations are crucial when selecting a treatment format. While group treatments can be a cost-effective option, their administration requires more resources than what may be available in many clinical settings. As HSDD often manifests in the context of committed relationships and because sexual desire discrepancy between partners is one of the most common reasons for couples seeking therapy (ie, one partner having markedly higher levels of desire than the other), including at least some sessions with both partners into treatment may be beneficial.[36] Mixed results were reported in an effectiveness study investigating a mixed method couples

therapy approach that consisted of sensate focus exercises, self-exploration, as well as a psychodynamic understanding of sexual problems administered in an intensive therapy format over 1 weekend.[37]

There is increasing evidence that psychological treatments for HSDD can be successfully delivered via the internet and are effective in improving sexual functioning in women with mixed sexual dysfunctions, including low desire concerns.[30,32,38] Internet-based treatments for HSDD often feature 6 to 8 modules, accessed on a weekly or biweekly schedule, that include educational information as well as instructions for at-home exercises depending on the treatment rationale (eg, cognitive-behavioral therapy [CBT] or mindfulness-based therapy [MBT]). Internet interventions for HSDD are typically designed as guided interventions, meaning that participants receive feedback to completed modules and can contact study personnel in case of questions.[39] A meta-analysis indicated that internet- or mobile-based interventions are effective for improving women's sexual dysfunctions, and qualitative data on a subsample of women participating in internet-based CBT or MBT suggest high acceptability and feasibility of such treatments.[30,31] Furthermore, in a waitlist-controlled RCT on 57 women with various sexual dysfunctions, in which 96% of participants endorsed low desire concerns, an internet-based intervention including elements of CBT and MBT was shown to be effective in improving sexual desire.[40]

Sex therapy

Sex therapy, a specialized form of counseling or psychotherapy, aims to help individuals and couples with HSDD by employing targeted techniques to tackle problems related to low sexual desire, as well as associated problems in other phases of the sexual response (eg, arousal, orgasm, and pain). Sex therapy can combine sex education, self-exploration, and partnered sensate focus exercises, which involve a series of nondemanding sensual touching exercises.[41] Sensate focus aims to reduce avoidance and anxiety related to sexual activity, improve sexual communication between partners, and gradually reintroduce intimacy through a progression from nongenital to genital touching.[42] A 2013 meta-analysis reported large effects of sexual skills training (including sensate focus) on symptom severity and sexual satisfaction based on 2 comparisons for women with HSDD, suggesting a high level of efficacy (level of evidence, 2).[23] While more recent studies on psychological treatments of HSDD have seldom used sex therapy in isolation, elements of sex therapy are part of the treatment rationales of most published studies and are a key component of psychological treatments for HSDD in clinical practice. While recent studies on psychological treatments of HSDD have seldom used sex therapy in isolation, elements of sex therapy are part of the treatment rationales of most published studies.

Cognitive-behavioral therapy

Contemporary psychological treatments have integrated sex therapy techniques within a broader framework such as CBT. CBT for HSDD includes a variety of methods aiming to register and challenge maladaptive sexuality-related thinking patterns, overcome dysfunctional coping styles (eg, avoidance of sexual activity), and adopt more positive ways of dealing with personal and interpersonal distress related to HSDD. Psychoeducation also is an important component of CBT and can help to foster women's understanding of how biopsychosocial factors are contributing to their sexual desire or lack thereof.[22] A 2013 meta-analysis supported the benefits of CBT for HSDD (level of evidence, 2).[23] Since then, at least 2 RCTs supported the efficacy of this treatment approach (level of evidence, 1). In a sample of 106 women with HSDD (M_{age} = 39.6 years, SD = 8.4) who participated in a waitlist-controlled RCT, 8 sessions of group-based CBT led to a significant increase in different facets of sexual functioning, including sexual desire.[43] In an RCT comparing the efficacy of two 8-session group treatments—MBT vs a supportive sex education program following a CBT rationale—in a sample of 148 women (M_{age} = 39.3 years, SD = 13.2) with sexual interest and arousal disorder per the *DSM-5*, the CBT-related treatment led to large improvements in sexual desire and sexual distress, which were sustained 6 and 12 months after treatment. Furthermore, a positive effect of treatments on relationship satisfaction was observed.[27] In an RCT with 266 participants (M_{age} = 36.4 years, SD = 10.4) comparing a waitlist control with 2 internet-based interventions—consisting of 8 treatment modules and written feedback to completed modules by trained e-coaches—the CBT-based program led to significant increases in sexual desire (d = 1.14) and decreases in sexual distress (d = 1.12), with large effects at 3-month follow-up that persisted at 6-month follow-up (d = 0.75 for sexual desire, d = 1.18 for sexual distress). Additionally examined clinical significance, as assessed with clinical cutoffs and the reliable change index, demonstrated sustained effects at 12-month follow-up (level of evidence, 1).

Mindfulness-based therapy

MBT has emerged as the third wave of CBT and aims to cultivate active awareness of the body in an accepting, nonjudgmental, and compassionate way.[20] MBT for HSDD includes guided mindfulness exercises (eg, breathing or body scan exercises) that are practiced under professional guidance during group or individual sessions and by the participants themselves between sessions, commonly with the help of audio recordings. In addition, sexuality-specific mindfulness exercises (eg, attending to present-moment sensations during sexual activity) and psychoeducational content are part of MBT.

There is meta-analytic evidence for the efficacy of MBT for improvements of low sexual desire in women with different sexual dysfunctions.[44,45] Concerning HSDD, in a waitlist-controlled study, 4 group sessions of MBT significantly improved sexual desire, sexual arousal, lubrication, sexual satisfaction, and overall sexual functioning in women with HSDD and/or female sexual arousal disorder (M_{age} = 41.6 years, SD = 11.9).[24] Thus far, the strongest evidence for the efficacy of MBT for the treatment of low sexual desire in women stems from an RCT comparing 8 sessions of group-based MBT with a supportive sex education program following a cognitive-behavioral rationale in a sample of 148 women (M_{age} = 39.3 years, SD = 13.2) with sexual interest and arousal disorder. MBT led to large improvements in sexual desire and sexual distress, which were retained for a 12-month period.[19] In an waitlist-controlled RCT with 266 participants (M_{age} = 36.4 years, SD = 10.4), an internet-delivered MBT program including 8 treatment modules and written feedback to completed modules by trained e-coaches led to significant increases in sexual desire (d = 1.11) and decreases in sexual distress (d = 0.98), with large effects at 3-month follow-up

that persisted at 6-month follow-up ($d = 0.74$ for sexual desire, $d = 1.00$ for sexual distress). Furthermore, clinical significance testing demonstrated sustained effects at 12-month follow-up (level of evidence, 1). Large pre- to posttest changes in sexual desire ($d = 0.75$ to 1.06) were also reported for 70 women ($M_{age} = 39.2$ years, $SD = 9.8$) participating in an RCT comparing 4 individual sessions of MBT with the same intervention supplemented by encouraging women to schedule sexual activity and to identify their own motives to engage in sex.[33]

Findings suggest that MBT might be effective to alleviate sexual distress in this age group. In a qualitative interview study, 24 women who completed an MBT-based online intervention for HSDD described increases in sexual desire, improved communication, and greater self-acceptance as positive treatment outcomes.[31] MBT enabled women to shift their locus or quality of attention during sex and disengage from negative sexuality-related thoughts.[30] A pilot RCT investigated the acceptability and feasibility of 6 sessions of group-based MBT and psychoeducation delivered via videoconferencing software to improve sexual desire and sexual distress in midlife and older women with HSDD ($M_{age} = 57$ years).[29]

Summary and treatment recommendations

Psychological treatments are effective in improving sexual desire and sexual distress in women with HSDD. Over the last decade, several RCTs have provided additional support for the efficacy of interventions following either a CBT- or MBT-based rationale, showing that both approaches are associated with lasting improvement of HSDD symptoms, which were sustained up to 12 months after treatment. Future directions include well-designed studies showing the types and results of combination therapies, which would be very important to help build standards of care for HSDD.

Nonhormonal treatments for HSDD

Worldwide there are several nonhormonal pharmaceutical drugs that are used to treat HSDD. There is a significant variation in availability, distribution, and regulating body approval for these medications. While hormonal therapies may help women postmenopause, data are lacking for use among premenopausal women. Additionally, much of HSDD treatment is focused on reducing or removing other medications that may cause low desire as a side effect. However, the literature does provide guidance for the following medical treatments.

Central nervous system medications targeting HSDD

Flibanserin is a centrally acting serotonin type 1A agonist and serotonin type 2A receptor antagonist. This means that it is a multifunctional serotonin agonist and antagonist. The exact mechanism of action is unknown, but it is known to enhance 5-HT1A and inhibit 5-HT2A activity, leading to changes in dopamine and norepinephrine in the brain.[46] Increases in dopamine in the prefrontal cortex may facilitate greater attention and focus on sexual stimuli.[2] Clinical trials have demonstrated an increase in sexual desire, a decrease in sexual distress, and an increase in satisfying sexual events as compared with placebo.[47] Over 3000 women were initially studied in 3 original pivotal trials that revealed an increase in sexual desire, a decrease in sexual distress, and an increase in satisfying sexual events as compared with placebo. There is evidence that demonstrates the efficacy and safety of flibanserin in postmenopausal women as well, but flibanserin is not currently approved for postmenopausal women in any country.[48]

Approximately 50% of women with HSDD respond to flibanserin, and it may take up to 8 weeks to notice a response.[17] The most common adverse events are dizziness (9.2%), somnolence (8.3%), nausea (6.5%), and fatigue (3.7%).[49] Discontinuation due to side effects occurred in 13% of premenopausal women.

Flibanserin's original labeling carried a boxed warning in the United States that concomitant alcohol use is contraindicated. Newer data have demonstrated that alcohol use is indeed safe but is associated with more somnolence and sedation, especially if consumed closer to the time of administration.[50,51] The warning has since been removed, and remaining advice is to take flibanserin at bedtime and $\geq$2 hours following the last consumption of alcohol. It is available only in the United States and Canada.

Bremelanotide is a melanocortin 4 receptor agonist. It enhances dopamine and oxytocin release and works directly on peripheral nerves that innervate the clitoris and vagina.[52] Its mechanism of action is also believed to be by downstream stimulation of dopamine receptors in the medial preoptic area following melanocortin 4 receptor binding.[53] The efficacy of bremelanotide was demonstrated in 2 phase 3 randomized placebo-controlled trials showing improvement in sexual desire and a decrease in sexual distress, but notably it did not affect the number of satisfying sexual events.[54,55] In both trials, bremelanotide significantly improved desire and decreased distress as compared with placebo. Approximately 60% of women prescribed bremelanotide had an improvement in desire vs 40% administered placebo.[55]

Bremelanotide comes as an autoinjector to be used 45 minutes prior to sexual activity. The most common adverse effects of bremelanotide are nausea, flushing, and headache, and it should not be used in people with uncontrolled hypertension. All side effects, except for injection site reactions, tended to decrease with additional use beyond the first dose.[56] While not tested in its current formulation, a nasal formulation demonstrated efficacy in postmenopausal women.[57] It is available only in the United States.

Antidepressants

There is strong evidence that traditional SSRIs inhibit sexual function by inhibition of serotonin on central dopamine release.[58] Thus, antidepressants that are not primarily targeting serotonin release and receptors are less likely to have sexual side effects, and some have been studied for primary treatment of HSDD.

Bupropion, an antidepressant that increased dopamine and norepinephrine, has been shown as an effective off-label treatment for HSDD at doses of 150 to 450 mg. Bupropion did show efficacy in a single-blind trial (29% responded) and a double-blind RCT, but the study was underpowered to meet statistical significance.[59,60] The evidence for adding bupropion for people with antidepressant-induced HSDD is mixed, and the best data do not support its efficacy.[61,62]

Buspirone (20-60 mg) is a serotonin 1A partial agonist and is approved as an anxiolytic. It is also used as an off-label treatment for HSDD and did show efficacy in improving desire in patients who were clinically depressed and in those who were prescribed SSRIs. However, there is no study on this medication where HSDD is the primary clinical endpoint.[63]

Trazodone—a phenylpiperazine compound of the serotonin antagonist and reuptake inhibitor class—is commonly prescribed as a sedative, anxiolytic, and antidepressant. Like flibanserin, it binds to several serotonin receptors in the 5HT1 and 5HT2 families. Trazodone has sexual side effects at high doses, such as priapism and persistent genital arousal disorder. Recent research demonstrates efficacy for decreased sexual desire (ie, HSDD) without persistent genital arousal disorder when used at doses as low as 3.5 mg/d as well as for SSRI-induced HSDD.[64,65]

Sildenafil

Sildenafil is well established as a medication for erectile dysfunction by acting on the phosphodiesterase 5 pathways, leading to smooth muscle relaxation. A review of 8 studies demonstrated a possible benefit of sildenafil for the treatment of female sexual dysfunction, while 4 trials did not show any significant differences with treatment.[66] This is likely due to the fact that desire is mediated by dopamine in the central nervous system and sildenafil works on peripheral pathways. Given its mechanism of action, sildenafil might be beneficial for women with dysfunction caused by multiple sclerosis, type 1 diabetes, spinal cord injury, and antidepressant medication use.[66] However, inconsistency for defining HSDD vs female arousal disorder and anorgasmia limits these conclusions, although 1 RCT does support its use in SSRI-induced sexual dysfunctions, including desire.[67]

Hormones and HSDD

In the last decade, preclinical studies have aimed to differentiate between the direct central effects of androgens and those mediated by aromatization into estrogens. In a well-established rodent model, ovariectomized females treated with estradiol, testosterone, and an aromatase inhibitor exhibited significantly more appetitive and receptive behaviors as compared with those treated solely with estradiol.[68] In line with these findings, in the same preclinical model, the nonaromatizable androgen dihydrotestosterone facilitated sexual behavior in ovariectomized rats primed with estradiol, particularly enhancing sequences of appetitive behaviors separate from copulative or reproductive measures.[69] Taken together, these results suggest that aromatization may not be essential for testosterone to augment female sexual desire.

The menopausal transition is very well known as a life stage characterized by a decrease in estradiol levels and has been associated with a decline in sexual function. Women affected by gynecologic cancers, such as breast cancer, frequently undergo antihormonal therapies leading into premature iatrogenic menopause. The reduction in estrogens is particularly pronounced and abrupt following surgical menopause. With regard to sexual function, menopausal status seems to independently affect mostly vaginal lubrication, leading to impaired genital arousal and dyspareunia, which are the direct consequences of the genitourinary syndrome of menopause and related vulvovaginal atrophy.[70] As a consequence, sexual satisfaction is reduced, and in most cases, desire is subsequently damaged.

Androgens physiologically decline with aging, with a significant drop from the mid- to late reproductive years,[71] and some evidence supports the notion that their levels are directly related to sexual function and that androgen deficiency may be correlated with a reduction in sexual desire/arousal, receptivity, and pleasure. For example, Wåhlin-Jacobsen et al demonstrated that sexual desire correlated with free testosterone and androstenedione in a cohort of women; however, in a subgroup aged 25 to 44 years with no use of hormonal contraception, sexual desire correlated with free and total testosterone, androstenedione, and DHEAS (dehydroepiandrosterone sulfate). A recent meta-analysis identified a moderate association between free and total testosterone and sexual desire in pre- and postmenopausal women; in contrast, DHEAS showed a moderate association only with global sexual function.[72] Other conditions causing low androgen levels follow:

- Hypogonadotropic hypogonadism—due to pituitary secreting and nonsecreting adenomas; functional hypothalamic amenorrhea in underweight women, eating disorders, athletes, or chronic stressful conditions
- Primary ovarian insufficiency secondary to surgery, chemotherapy or radiation therapy, autoimmune oophoritis, or genetic defects
- Loss of adrenal production of preandrogens—due to central mechanisms or adrenal insufficiency (Addison's disease, chronic systemic glucocorticoid therapy)
- Hyperprolactinemia—due to medications or alterations of the pituitary
- Reduced bioavailable testosterone secondary to increased sex hormone–binding globulin (SHBG) levels, as in treatment with estroprogestins, antiepileptic medications and thyroxine, chronic liver conditions, and hyperthyroidism[73]

Physiologic states presenting with low androgens levels include pregnancy, puerperium, and lactation.

Testosterone therapy in postmenopausal women

Since 2019, the administration of testosterone therapy to women should adhere to the guidelines outlined in the global consensus position statement, which has received endorsement from leading international bodies dedicated to women's sexual health.[74] Numerous RCTs and a meta-analysis comprising 36 RCTs and 8480 participants have demonstrated the short-term efficacy (24 months) and safety of testosterone in naturally and surgically postmenopausal women.[75] This efficacy is observed whether testosterone is administered alone or in conjunction with estrogen replacement therapy, with dosages approximating physiologic concentrations for premenopausal women.[75] The therapeutic impact of testosterone is deemed moderate. Conversely, there is insufficient evidence to advocate for the use of testosterone in premenopausal women.[74,75] The sole evidence-based indication remains HSDD, although symptoms related to other aspects of sexual function, such as inadequate lubrication or difficulty achieving orgasm—frequently associated with low libido—may also benefit from treatment. Notably, according to meta-analytic findings, testosterone yields significant enhancement in secondary outcomes, such as arousal, responsiveness, self-image, and alleviation of sexual-related concerns and distress, when compared with placebo or alternative treatment.[75] A recent retrospective study involving 81 women with sexual complaints revealed that systemic testosterone administration over 6 months, either alone or in combination with local estrogens, was associated with a positive impact on clitoral blood flow. Specifically, there was an increase noted in clitoral artery peak systolic velocity as assessed by Doppler ultrasound.[76]

The ISSWSH recently gave its endorsement to a clinical practice guideline concerning the utilization of systemic testosterone in addressing HSDD among women.[77] Per this guideline, suitable candidates for such therapy encompass postmenopausal women (whether naturally occurring or through surgery) diagnosed with HSDD, irrespective of whether they are concurrently undergoing estrogen replacement therapy. These symptoms ought to be enduring, widespread, and linked with clinically significant distress and should not be attributable to potentially modifiable factors such as psychiatric conditions, medication usage, or relationship issues. According to the biopsychosocial model of care, consideration may be given to testosterone therapy subsequent to, or simultaneously with, the appropriate management of other psychological, biological, and sociorelational factors that could contribute to low desire.[1,17]

Testosterone remains unapproved for use in women by the majority of regulatory agencies, including the US Food and Drug Administration and the European Medicines Agency. The recommendation is to initiate therapy with a 0.5-mL dose, equivalent to 5 mg of testosterone per day with a bioavailability of approximately 10%. Given the lack of evidence supporting the efficacy and safety of compounded products, it is advisable to prescribe off-label transdermal formulations approved for males at approximately 1/10th of the male dose. This approach aims to emulate the physiologic production rate of 0.3 mg/d (300 mcg/d) in women. Dosage adjustments should be tailored to achieve testosterone concentrations within the physiologic range observed in premenopausal women.[74] On average, the effectiveness of treatment typically becomes noticeable within 6 to 8 weeks and reaches its peak around 12 weeks. If no improvement in sexual desire is perceived by the patient after 6 months, it is recommended to discontinue testosterone therapy. It is important to note that there is a lack of safety data beyond 24 months, and the decision to continue treatment should be carefully discussed with each patient, considering potential risks in the context of her medical history and expectations.[74]

There is no specific target serum testosterone level for treatment. Total testosterone levels should be assessed before initiating therapy to rule out women with midrange to high baseline concentrations. Subsequent measurements should be taken 3 to 6 weeks after starting therapy and after 6 weeks if the dosage is adjusted to ensure proper dosing and prevent overmedication. Once stable levels are achieved, testing should be conducted every 4 to 6 months.[74]

Side effects associated with systemic testosterone treatment include an elevated risk of developing acne and increased hair growth. Patients should be monitored for these effects as well as other indicators of androgen excess and virilization, such as alopecia, clitoromegaly, or voice deepening. However, it is worth noting that these adverse events are typically dose dependent and have not been reported with transdermal formulations or at physiologic levels in premenopausal women.[78]

Transdermal testosterone has not been linked to a deterioration in lipid profile, unlike oral testosterone, which tends to elevate low-density lipoprotein cholesterol levels and is consequently advised against.[75] Additionally, no notable increases in blood pressure, fasting glucose, or insulin levels have been observed in trials spanning up to 24 months, regardless of the route of administration.[75]

Regarding the safety profile concerning androgen- and estrogen-sensitive tumors, well-powered RCTs designed to assess the primary outcomes of breast cancer, endometrial cancer, and ovarian cancer incidence are necessary to provide comprehensive safety data in these areas. Currently, testosterone should not be prescribed to women who have a history of, or are at high risk for, these types of malignancies. In several small-scale trials, no changes in mammographic breast density have been observed, and there has been no indication of an increased risk of breast cancer or endometrial hyperplasia or cancer among previous testosterone users for up to 24 months, with a possible lower-than-expected incidence for up to 10 years following use of a testosterone implant.[79,80] It is important to note that testosterone therapy in postmenopausal women has not been associated with a significant rise in estradiol levels, as evidenced by a meta-analysis suggesting that aromatization may not be clinically significant, at least at the systemic level.[81] Regular clinical surveillance, such as pelvic examination and mammography, is recommended for women undergoing testosterone therapy, in accordance with age and the specific guidelines of the country.[77]

Testosterone therapy in pre- and perimenopausal women

Data regarding the benefit of testosterone in premenopausal women are limited to women in the late reproductive years. In a meta-analysis by Islam et al,[75] the 3 small studies that included premenopausal women showed no benefit over placebo or a comparator for the frequency of satisfying sexual events, total sexual function score, or any sexual function domain for which data were available, including desire (level of evidence, 1). These 3 trials were characterized by several methodological flaws: small sample size, testosterone measurement via immunoassay, inclusion of women using combined hormonal contraceptives, use of different testosterone dosages, heterogeneous conditions at enrollment (ie, SSRI/SNRI [serotonin-norepinephrine reuptake inhibitor]–emergent loss of libido), a relatively short follow-up, and a strong placebo effect. Furthermore, it is worth mentioning that the influence of low testosterone levels on desire in premenopausal women may be even more complex to disentangle than in postmenopausal women given the influence of the menstrual cycle phase, which represents an additional obstacle in establishing normal values and treatment targets. In addition, due to the possible virilizing effect of testosterone on the developing fetus, premenopausal women prescribed testosterone should be advised to use a "medically acceptable" form of contraception, considering the possible adverse effects of hormonal contraceptives on desire.

Estrogen-based therapy in postmenopausal women

In 2016, the panel of experts from the ISSM noted that only a limited number of clinical trials had investigated estrogen therapy with sexual function as a primary outcome. They concluded that the majority of current evidence did not support a significant impact of estrogen on sexual interest, arousal, and orgasmic response, independent of its role in managing menopausal symptoms. Consequently, they advised against the use of systemic estrogen therapy solely for treating female sexual dysfunction.[82] Furthermore, the panel highlighted that oral estrogen therapy leads to increased

levels of circulating SHBG, resulting in reduced free testosterone. Thus, it suggested that transdermal estrogen combined with testosterone might be preferable when addressing sexual function concerns in women experiencing menopausal symptoms. In 2022, a systematic literature review focusing on patients with surgical menopause and bilateral salpingo-oophorectomy identified only 1 study investigating the effects of estrogen on sexual functioning, which found no beneficial effects. However, a statistically significant improvement in psychological well-being was observed with estradiol as compared with control in a meta-analysis comprising only 2 randomized clinical trials (RCTs).[83] Therefore, current evidence does not support a clear effect of systemic estrogens on sexual desire in women with surgical menopause (level of evidence, 2).

Since then, a Cochrane database systematic review has been conducted, including 3 studies.[84] The main findings highlighted that for women within 5 years of their last period, treatment with estrogen alone probably slightly improves overall sexual function based on the sexual function composite score as compared with placebo. In women whose last period was >5 years earlier, estrogen alone probably makes little or no difference to sexual function based on sexual function scores as compared with a placebo. Concerning the subanalysis on sexual desire scores, which could be conducted only in unselected postmenopausal women, the authors concluded for uncertainty of the effect of estrogen alone vs placebo or no intervention, with a low quality of evidence. No specific data on an HSDD population are available. In this study, no conclusive information could be drawn on the efficacy of combined estrogen and progesterone replacement therapy. However, trials comparing estrogen replacement therapy alone with combined estrogen and progestin have suggested that progestin may have an inhibitory effect on sexuality, although conclusive data on this matter are lacking.[85] This phenomenon has been attributed to the mood-dampening effect of progestin and/or its antiandrogenic activity.

Noteworthy, a large prospective trial based on a randomized, double-blinded, placebo-controlled design was conducted in 2017 to investigate menopausal hormone therapy among 670 healthy, recently menopausal women. It revealed several aspects of sexual function after randomization to 0.45-mg/d oral conjugated equine estrogens (o-CEE), 50-μg/d transdermal 17β-estradiol (t-E2), or placebo with micronized progesterone.[86] When compared with placebo, the t-E2 group showed significant improvements in desire, arousal, orgasm, and satisfaction scores at 18 months and significant improvements in scores for lubrication and pain at all 3 time points. The t-E2 group also showed improved scores relative to the o-CEE group in the domains of desire and arousal but only at 18 months; conversely, treatment with o-CEE demonstrated fewer significant improvements relative to placebo. It is crucial to highlight that the overall improvement in Female Sexual Function Index (FSFI) in the o-CEE–treated group at 36 months appears to be predominantly due to significant improvements in the physical aspects of sexual function (lubrication and pain), although not in libido-related aspects. Potential reduction in the bioavailability of testosterone (high SHBG) may explain the lower efficacy of o-CEE relative to t-E2 in libido-associated domains.[86] For these reasons, it has been suggested that the positive effect of transdermal estradiol on desire represents an indirect effect mediated by an improvement in reduced lubrication/sexual pain (level of evidence, 2).

Other hormonal therapies in postmenopausal women

SERMs (selective estrogen receptor modulators).

Ospemifene, an oral medication taken at a dose of 60 mg daily, was the first compound to receive approval from the US Food and Drug Administration in 2013 and the European Medicines Agency in 2014 for treating moderate to severe dyspareunia caused by the genitourinary syndrome of menopause in menopausal women.[87] The efficacy and safety of this compound were evaluated in double-blind phase 3 trials, where it was found to effectively reduce vaginal dryness and dyspareunia. These effects were assessed through changes in vaginal pH, maturation index, and severity of the "most bothersome symptom."[88] The effect of ospemifene on sexual desire has been evaluated in 2 RCTs,[88,89] with the second showing significant improvement in FSFI desire score at 4 and 12 weeks of treatment. In a review article, Lara et al meta-analyzed the results of these 2 studies and found ospemifene (vs placebo or no intervention) to probably slightly improve desire; the effect was small with analysis based on low-quality trials. The positive effect of ospemifene on desire is likely mediated by the reduction in genitourinary syndrome symptoms and has not been tested in women with primary HSDD, not secondary to dyspareunia.[84]

Data are scant regarding the effect of other SERMs (bazedoxifene, raloxifene, lasofoxifene) or SERMs combined with estrogens on sexual desire.

Systemic DHEA (dehydroepiandrosterone).

In 2013, a systematic review and meta-analysis aimed at investigating the benefit of DHEA in postmenopausal women with normal adrenal function.[90] The meta-analysis on sexual function comprised 5 RCTs and concluded that DHEA treatment was not associated with significant improvements in libido or overall sexual function (level of evidence, 1). No relevant studies on the topic have been published since.

Tibolone.

Tibolone is a synthetic steroid with a peculiar profile, since its metabolites possess estrogenic, progestogenic, and androgenic properties in various tissues. While tibolone is available in Europe, it is not marketed in the United States. It is primarily used for managing climacteric symptoms and preventing osteoporosis in postmenopausal women. Additionally, it has been investigated as a potential treatment for sexual symptoms in this population due to its perceived added value in enhancing sexual function. However, evidence regarding the clinical efficacy of tibolone specifically for female sexual dysfunction as the primary outcome is limited. The androgenic effects of tibolone are believed to occur through direct stimulation of the androgen receptor and by increasing circulating testosterone levels through a reduction in SHBG concentrations.[91] A study comparing tibolone vs conventional hormone replacement therapy found that it effectively improves scores on the desire, arousal, and orgasm domains of the FSFI and increases free androgen and estrogen indexes.[91] Additionally, 6-month treatment with tibolone, when compared with hormone replacement therapy, significantly enhanced clitoral peak systolic velocity and improved measures of sexual function as assessed by the McCoy Female Sexuality Questionnaire.[92] In 2016, a prospective controlled cohort

study enrolled 30 women with premature ovarian failure who were treated with 2.5 mg of oral tibolone daily for at least 1 year, and it showed that administration of tibolone was associated with significant improvement in libido, with an increase in frequency of coitus and general satisfaction.[93] Positive results on global sexual function had been reported in other randomized trials.[94-96] (levels of evidence, 2 and 3). In a 2023 Cochrane database meta-analysis, authors were able to conduct 2 separate analyses—one on symptomatic or early postmenopausal women, the other on unselected postmenopausal women—from only 1 RCT, with uncertain results.[84]

Combined therapy.

There were 2 small RCTs showing that sublingual testosterone (0.5 mg) in combination with sildenafil (50 mg) or buspirone (10 mg) increased desire in pre- and postmenopausal women. There were no serious events reported. Given the small nature of these studies, there are insufficient data to make a recommendation for this therapy, but there will likely be new studies to determine its efficacy in the future.

Prasterone.

Prasterone has been approved as a once-daily, vaginally administered ovule indicated to treat postmenopausal women experiencing moderate to severe dyspareunia as a symptom of vulvar and vaginal atrophy. Studies on the efficacy of prasterone on sexual desire are lacking. In a prospective, placebo-controlled, phase 3 RCT with desire, arousal, and orgasm as the main outcome measures in 56 postmenopausal women treated with 6.5 mg of prasterone daily for 12 weeks, the change in the desire domain of the Abbreviated Sexual Function Questionnaire did not reach statistical significance, independent of the presence of dyspareunia at baseline (level of evidence, 2).[97] There are insufficient data to make any recommendation on the use of intravaginal prasterone for HSDD.

Oxytocin is a pituitary hormone best known for its affects on uterine contractility and breastfeeding but has been established as an important hormone in mood, pair bonding, and sexuality.[98] As such, there has been significant interest in pharmacotherapy with oxytocin, which has a very short half-life and has been challenging to administer. Intranasal oxytocin (24-32 IU) may increase desire and intensity of orgasm, although evidence is quite mixed and appears to have more support for use in men than women.[99-101] There is insufficient evidence to make any recommendations regarding the use of oxytocin.

Complementary and alternative therapies

Nutraceuticals

There are limited data to assist with making recommendations of common nutraceuticals (plant-based therapies not requiring a prescription). There is some evidence related to increased blood flow with specific nutraceuticals, although this is more likely to affect arousal rather than desire. Numerous products have been studied in men related to erectile dysfunction as well as sexual desire.[102] Herbs that have been touted as being effective for the treatment of sexual dysfunction are listed in a detailed table from Bolour and Braunstein.[103] A popular medication is a combination of pine bark extract, L-arginine, L-citrulline, and rose hip extract, which was shown in 1 trial to improve sexual health in perimenopausal women.[104] L-arginine is a known vasodilator and has been shown to improve symptoms of HSDD in multiple studies, although the quality of data is mixed.[105]

Acupuncture

There are limited data to support the use of acupuncture, although 1 pilot study did show significant improvement in sexual desire scores on the FSFI in a small cohort of women.[106] At this time, the data are insufficient to make a recommendation.

Aromatherapy

Aromatherapy is the practice of using extracted aromatic plant oils and materials through inhalation or oral and topical administration by bathing, compressing, and massaging. The therapeutic properties of this approach are believed to be through psychological and physiologic systems (eg, amygdala and hippocampus).[107] For premenopausal, postmenopausal, and breastfeeding women, several small studies have shown benefits in sexual function, including desire, from various preparations of oils, nearly all with lavender.[107-109] Data are weak to moderate (grade B, level 3).

Yoga

Yoga is a popular form of complementary and alternative therapy. It is practiced in developing and developed countries. Many patients and yoga protagonists claim that it is useful in improving sexual functions and treating sexual disorders.[110] One randomized trial did show improvement in all domains of the FSFI after a 12-week yoga program.[111] Other populations have been studied, such as women who are breastfeeding and those with metabolic syndrome, with mixed results and no clear benefit to desire specifically.[112,113] Yoga therefore has insufficient evidence to recommend at this time.

Physical therapy and hypnosis

Physical therapy is well established as a treatment for sexual pain, which could help with desire, although there is no evidence to support its use where HSDD is the primary outcome.

Hypnosis is also a method that has been reported to improve desire, but there is no research examining the effects of hypnosis on HSDD.

Lifestyle modification

Last, there is no substitute for the importance of a healthy lifestyle in terms of sexual health. It is well established that lifestyle modifications may improve sexual function.[114] However, contrary to what many providers may assume, obesity and weight loss treatments do not seem to affect sexual desire in women.[115,116] Thus, for providers, the most important counseling can be on the value of maintaining a healthy lifestyle in terms of diet, exercise, sleep, and substance use rather than simply a desired weight (level 5, expert opinion).

Discussion and conclusion

The ICSM organized this consensus article to assist providers with evaluation and management of HSDD and highlight the many treatment options now available to women. The management steps require taking a biopsychosocial approach to evaluation and a clear understanding of the definition of HSDD. Treatment options include education, addressing comorbid conditions or medications, psychological therapy,

central nervous system agents, hormone therapy, and alternative therapies. Recommendations for any of these treatments need to take the patient's goals into account and balance the risks and benefits to each proposed treatment. As the science evolves, we anticipate future treatment options for this common condition.

Abbreviations

DHEA, dehydroepiandrosterone; HRT, hormone replacement therapy; *ICD-11*, *International Classification of Diseases, 11th Revision*; ICSM, International Consultation on Sexual Medicine; ISSWSH, International Society for the Study of Women's Sexual Health; RCT, randomized controlled trial; SERM, selective estrogen receptor modulator; SHBG, sex hormone–binding globulin; SSRI, selective serotonin reuptake inhibitor.

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