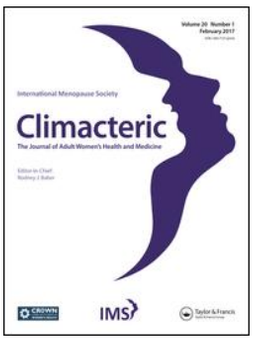

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REVIEW

Sexual well-being after menopause: An International Menopause Society White Paper

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ABSTRACT

Sexual well-being frequently declines following the menopause transition and can be associated with significant personal and relationship distress. This distress is the hallmark of female sexual dysfunction (FSD). FSD is highly prevalent in postmenopausal women. The prevalence of sexual problems increases with age, but conversely this is associated with decreasing distress with advancing age. This pattern has been seen across multiple international populations with varied cultural norms. While the etiology of FSD is multifactorial, the physiological changes of sex hormone insufficiency and postmenopausal symptoms, such as dyspareunia, are primary factors contributing to FSD at midlife. The International Menopause Society is working to increase awareness of FSD and to provide a framework for practitioners to address sexual medicine concerns. This White Paper aims to review the process of care for female sexual well-being following menopause, from initially approaching the discussion of FSD, to identifying clinical signs and symptoms, and ultimately determining the best available biopsychosocial therapies. As with most processes of care, the first step is often the most difficult. Health-care practitioners need to broach the topic of sexuality in the clinical setting. Lack of information on, comfort with, and biases about the topic of sexuality after menopause are significant hurdles that the International Menopause Society addresses in this document. Each member of the Writing Group remains committed to continued advocacy for the validity of FSD as a diagnosis, the need for therapies for women to be both available and included in health insurance coverage, and continued therapeutic research to provide evidence-based solutions.

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Introduction

Sexual well-being following menopause may seem an unattainable goal for many women. Dependent upon the psychosocial circumstances, the biological changes at menopause may be associated with significant personal and relationship distress. Studies across a number of countries have shown that women place high value on sexual intimacy in their relationships[1,2]. Sexual problems at midlife can be divided into chronic sexual symptoms involving sexual desire, arousal, orgasm, and pain. Screening for female sexual concerns is often shortchanged during the clinical encounter because of a multitude of factors including, but not limited to, misinformation, absent or inadequate physician/practitioner training in sexual medicine, the belief that such menopausal changes are a normal and inevitable part of aging, and time constraints. The purpose of this review is to provide clinicians with a framework for:

(1) Approaching the discussion of female sexual well-being following menopause;
(2) Clinically identifying women with sexual dysfunction through patient symptoms, physical signs and validated instruments;
(3) Managing sexual difficulties in postmenopausal women with the available biopsychosocial therapies.

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Table 1. Changes to the classification of female sexual dysfunction (FSD) by the Diagnostic and Statistical Manuals of Mental Disorders.

The Diagnostic and Statistical Manual of Mental Disorder, 5th Edition defined four categories of FSD[3]:
- Female sexual interest and arousal disorder
- Female sexual orgasmic disorder
- Genito-pelvic pain/penetration disorder
- Substance/medication-induced sexual dysfunction

The Diagnostic and Statistical Manual of Mental Disorders, 4th Edition defined seven categories of FSD[7]:
- Hypoactive sexual desire disorder
- Female sexual aversion disorder
- Female sexual arousal disorder
- Female orgasmic disorder
- Vaginismus
- Dyspareunia
- Female sexual disorder due to general medical condition

Types of midlife sexual problems and their epidemiology

Types of midlife sexual problems

Female sexual dysfunctions (FSDs) have distinct classifications, definitions, and diagnostic criteria, as described in the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5)[3], the Fourth International Consultation on Sexual Medicine (ICSM)[4], and the International Classification of Diseases and Related Health Problems (ICD). The latter proposes a new chapter on Conditions Related to Sexual Health for its 11th Revision[5]. Of note, the DSM schema uses the terminology 'sexual disorders', while the ICSM and ICD classification systems characterize these conditions as 'sexual dysfunctions'.

FSDs are characterized as chronic sexual conditions in the domains of desire, arousal, orgasm and pain. FSD is distinguished from normal sexual variability by the presence of sexually related personal distress, which may be associated with interpersonal difficulties (Table 1). It has been proposed that problems should be present for a minimum of 3 months and at least 75% of sexual experiences[6], although this requirement is derived from expert opinion, not research evidence. Sexual dysfunctions may be lifelong or acquired after a period of normal functioning; may be situational (present only in certain situations or with a specific partner) or generalized (present in all situations and all partners); and may be characterized as mild, moderate, or severe. Women may experience difficulty in one or multiple aspects of their sexual response; thus FSDs can overlap and vary over time. The etiology of FSD is often multifactorial and includes biological, psychological, interpersonal, and sociocultural risk factors and contributors[3].

Female sexual interest and arousal disorder was separated into two distinct categories in earlier versions of the DSM[7]. Advocates of merging these categories in DSM-5 cited reasons including the co-occurrence of desire and arousal problems, the complexity of distinguishing desire from other motivations for sexual activity, highlighting the differences between spontaneous versus responsive desire, and emphasizing the relatively low frequency of fantasy in women. However, other experts have recommended restoring separate categories of hypoactive sexual desire disorder/dysfunction (HSDD) and arousal disorder/dysfunction (FSAD) because of the absence of empiric evidence to combine them[4]. The recommendation to maintain the category of HSDD is based on robust observational, clinical sample, and registry data; randomized controlled trials that used the standardized criteria for HSDD to assess responses to pharmacologic interventions; and consistency with the classification in the ICD, 10th Revision[8,9].

Epidemiology of midlife sexual problems

Several studies have investigated the prevalence of sexual problems among women. The Prevalence of Female Sexual Problems Associated with Distress and Determinants of Treatment Seeking (PRESIDE) Study[10] investigated the sexual experiences of more than 31 000 women aged 18–102 years across the United States. It reported that the prevalence of any sexual problem in women was 44.2%, with 22.8% of women experiencing distress and 12% of women having a distressing sexual problem. Among the three cohorts, sexual problems, but not associated distress, increased with age: 27.2% (age 18–44 years), 44.6% (age 45–64 years), and 80.1% (age 65 years and older). For these cohorts, decreased sexual desire with distress was reported in 8.9%, 12.3%, and 7.4%, respectively. Arousal problems accompanied by personal distress generally followed the same age-related pattern, but distressing orgasm problems occurred with similar frequency in middle-aged and older women. In contrast, two more recent population-based Australian studies, employing validated questionnaires, reported the prevalence of low sexual desire with associated distress amongst women aged 40–64 years to be 32.2% (95% confidence interval (CI) 30.1–34.2%)[11] and among women aged 65–79 years to be 13.6% (95% CI 11.9–15.4%)[12]. These levels of HSDD are supported by a Malaysian study that reported the prevalence of FSD based on a validated translation of the Female Sexual Function Index to be 29.6%[13] and a Thai study that found that 86% of women reported not experiencing orgasm after menopause[14]. This finding is significant considering 82% of Asian women report that the ability to achieve orgasm is somewhat important, or important[2]. In summary, FSD is highly prevalent globally, and, although the prevalence of HSDD declines with age, many older women experience sexual function problems associated with personal distress.

At midlife and beyond menopause, changes may occur in the intensity and duration of stimulation needed for sexual arousal and orgasm. Inadequate lubrication, vaginal dryness, and dyspareunia become more common, and the orgasmic response may become more muted or take longer to achieve. In survey data regarding symptoms related to vulvovaginal atrophy (VVA), also known as genitourinary syndrome of menopause (GSM), the prevalence of symptomatic VVA is consistently about 50%[15]. The International Vaginal Health: Insights, Views, and Attitudes (VIVA) Study reported the prevalence of specific symptoms including vaginal dryness (83%) and pain during intercourse (42%). Ultimately, 62% of women with discomfort reported the severity of their symptoms to be moderate or severe[16]. The European Vulvovaginal

Epidemiology Survey ($n = 2160$) reported that over 90% of postmenopausal women attending a menopause or gynecology clinic had symptoms and examination findings of VVA[17]. In the largest study assessing VVA amongst Asian women, face-to-face interviews were conducted on 5992 women, aged 45–75 years, in Indonesia, Malaysia, Singapore, Taiwan, and Thailand. Overall, 11% of the interviewed women reported VVA symptoms[18].

Sexual dysfunction in relation to age and menopause

The prevalence of sexual activity declines with age, and women report lower frequency of sexual activity than men at all ages[19]. In an American study, women who expressed self-rated poor general health were less likely to be sexually active[19]. Those respondents with poor general health who remained sexually active were more likely to report sexual problems.

The decrease in circulating estrogen levels during and after the menopause transition, along with the age-associated decline in androgens, independent of menopause, significantly contribute to low desire, poor arousal, dyspareunia, impaired orgasm and consequently reduced sexual satisfaction[20–23]. In addition, menopause may impact emotional and cognitive aspects of sexuality through personal experiences including age at menopause, type of menopause (natural or surgical), physical and mental health, achievement of reproductive goals, education, body image, and self-esteem norms and experiences.

Psychosocial contributions to sexual well-being

Despite the negative impact of aging and reduced hormone production decribed above, some argue that, based on longitudinal findings, relationship issues and other non-biologic factors can strongly impact women's overall sexual experience, other than menopausal changes alone[24]. Psychosocial factors are important in determining sexual function after menopause onset as well[25]. To highlight this, the Massachusetts Women's Health Survey reported that the onset of menopause contributes to reduced sexual desire; nevertheless, anxiety, depression, and other relationship changes including conflict in the family, the condition of the relationship, sexual function, and health of the partner can all contribute significantly to FSD[26].

Quality of life (QoL) is the general well-being of individuals and societies, outlining negative and positive features of life, including life satisfaction, physical health, family, education, employment, wealth, religious beliefs, finance and the environment. It is important not to confuse QoL with health-related QoL (HRQOL). In this sense, FSD and HRQOL are both multidimensional and have a bidirectional relationship across the reproductive life span and beyond. As women age, sexual activity decreases significantly, a fact that has been related to several factors including decreased lubrication, age, marital status, and partner issues[27].

Specifically with respect to QoL, there is a strong association between the QoL of postmenopausal women and their partners. Avis and colleagues[26] found that poor QoL of either partner could result in incompatibilities, failed connections, lack of life satisfaction and impairment of the couple or family relationship, all factors that have an impact on sexuality.

Partner issues strongly correlate with FSD[28] and female QoL[29]. The role of a partner is of equal importance in terms of availability, duration and quality of the relationship, and the general and sexual health of the partner[30]. Feelings and emotions for both partners have each been reported as strong predictors of sexual health[31]. Of note, partnered postmenopausal women are more likely to experience HSDD than non-partnered women[11,12]. Nonetheless, it is important to be aware that unpartnered postmenopausal women may also experience sexual concerns and difficulties that need to be addressed[11,12].

For women at midlife, factors other than partnership status that are independently associated with HSDD include consuming alcohol, vaginal dryness and VVA, moderate to severe depressive symptoms, and the use of psychotropic medication[11,32,33]. Vasomotor symptoms are associated with low desire, sexually related personal distress, and HSDD in women at midlife[11]. Amongst older postmenopausal women (aged 65–79 years), factors independently associated with HSDD include being partnered (four-fold increased risk), vaginal dryness during intercourse, symptomatic pelvic floor dysfunction, and moderate-to-severe depressive symptoms[12].

As physical and psychological conditions significantly affect women's QoL during the menopause transition and beyond, QoL is considered an important component of health care. There is, on the other hand, a close relationship between the age of menopause onset and severity of menopausal symptoms and factors such as culture, economic and social circumstances, residency, race, and the woman's attitude about the menopause[34] that can also affect female sexual function. Sexual dissatisfaction negatively impacts both QoL and well-being in women of any age[35]. Both premenopausal and postmenopausal women who experience sexual dissatisfaction have lower overall general and psychological well-being and lower vitality[35]. HSDD is associated with impairment in QoL similar to that experienced by women with diabetes or chronic low back pain[36].

Physical effects of menopause on sexual well-being

VVA symptoms, but not vasomotor symptoms, are associated with HSDD in women at midlife[11]. During the routine office consultation, the 'domino' effect is evident because the clinical relevance of sexual symptoms is higher when physical, psychological and genital symptoms are reported[37]. Moreover, both hormonal and some psychological variables influence sexual function in symptomatic women during the menopause transition and in early menopause[38]. The experiencing of depressive symptoms was shown to be a very important correlate of sexual dysfunction in a community-based United States sample[39], although depressive symptoms

or anxiety did not explain the decline in sexual function in a cohort of 1390 women aged 42–52 years from the Study of Women's Health Across the Nation (SWAN)[40]. On the other hand, weight gain and obesity are considered risk factors for both sexual dysfunction and depressive symptoms, as they have an impact on self-esteem and body image. When urinary incontinence is also documented, sexual problems are more prevalent[41].

Recent data exploring the association between adiposity and sexual function indicate that they change concomitantly, but sexual desire and intercourse frequency diminished in years of greater-than-expected weight gain[42]. In a subset of the SWAN study ($n = 405$, mean age 46.8 years), those with body image dissatisfaction or who perceived themselves as 'unattractive' were at a significantly higher risk to develop clinically significant levels of depressive symptoms[43].

VVA is an important determinant of QoL and sexual well-being at menopause[44]. VVA-associated symptoms relate mainly to estrogen deficiency and include loss of vaginal lubrication, pain during sexual intercourse, itching, burning and overall vaginal discomfort. The term GSM provides a broader description of the genitourinary effects of menopause encompassing VVA, urinary and pelvic manifestations associated with aging, the changed hormonal milieu, and further potential etiologies[45]. VVA may affect about half of all postmenopausal women, contributing to other sexual symptoms (low sex drive, poor arousal and orgasm, reduced sexual satisfaction)[22]. VVA symptoms are frequently associated with vasomotor symptoms, depression and multiple co-existing conditions, such as osteoporosis and urinary incontinence[11–13].

In the CLarifying Vaginal Atrophy's Impact On SEx and Relationships (CLOSER) study, postmenopausal women reporting vaginal discomfort were 'upset their body does not work as it used to', felt 'old and to have lost their youth', and lacked 'self-confidence as a sexual partner'[46]. In this study, one-third of women were concerned that their vaginal discomfort would never go away and 25% feared that the pain would prevent them from having a future sexual life. Moreover, the REVIVE (REal Women's VIews of Treatment Options for Menopausal Vaginal ChangEs) survey in Europe also revealed that VVA symptoms have a significant impact on the ability to be intimate (62%), to enjoy sexual intercourse (72%) and to feel sexual spontaneity (66%)[47]. The same survey in Asia revealed VVA symptoms adversely impacted sexual enjoyment (65%), the ability to be intimate (61%), women's relationship with their partner (55%), and sexual spontaneity (54%)[18]. For postmenopausal women known to have depression or urinary incontinence, a greater impact of vaginal symptoms on multiple domains of functioning and QoL was measured by the multidimensional Day-to-day Impact of Vaginal Aging (DIVA) questionnaire[48]. Given the aforementioned, there is a need to address VVA-associated symptoms proactively during the menopausal consultation to help women manage the potential consequences for their sexual lives.

Menopausal women's sexual dysfunctions: impact on the partner ('it takes two to tango!')

Sexual dysfunctions do not occur in a vacuum; they impact the woman and her partner sexually, emotionally, and interpersonally. In their ground-breaking book, Masters and Johnson wrote, 'There is no such thing as an uninvolved partner in a marriage where sexual dysfunction exists'[49]. Our focus has primarily been on the woman's journey through the menopause transition. Yet this narrow focus neglects the role of the partner as a precipitating factor for her dysfunction or the manner in which the woman's sexual dysfunction(s) may impact the partner.

Here we present an innovative construct, the sexual equilibrium, which characterizes the impact of one partner's sexual function upon the other. In support of this construct, several studies that demonstrate the reciprocal and dynamic nature of a couple's sexual problems are reviewed.

The sexual equilibrium, like Newton's second law of motion, implies that any change in one partner will produce a change in the other[50]. One can readily understand that a menopausal woman's pain with sexual intercourse might affect her partner's sexual function in terms of his desire, erectile function, ejaculation, or satisfaction. Conversely, the man's erectile dysfunction or any other dysfunction, might impact the woman's desire, arousal, orgasm, and satisfaction.

The concept of sexual equilibrium needs to be broadened to include alterations in the interpersonal and emotional realms as well as the sexual. For instance, rather than developing a new and seemingly unexplained sexual problem, the partner may become depressed.

The sexual equilibrium is also relevant when identifying or understanding a woman's, or a couple's, resistance to treatment. Resistance is a term employed to identify roadblocks in ongoing psychotherapies. An interesting phenomenon that may occur in a couple's psychotherapy is that, while one partner appears to be getting better, the other becomes symptomatic, or gets worse. The sexual equilibrium would explain the couple's need for some sexual symptoms.

The vast majority of research regarding a woman's sexual dysfunctions and their impact on her emotional and interpersonal life has been individually focused. Few have examined the role of, or the impact on, the partner. This is really no different from the work in male sexual dysfunction where the primary focus has been on the man rather than the couple. Additionally, if studies did include the partner, they did not necessarily focus on menopausal women. There are few studies that have examined the negative impact of dyspareunia, vulvodynia, or vaginismus on the male partner, but the average age of the subjects in these studies was 26 years[51]. These studies do, however, highlight the principle of sexual equilibrium, where there is a clear effect on both the woman and her partner, interpersonally and sexually[52]. Kaplan and Leiblum independently wrote about the husbands of women with vaginismus developing erectile dysfunction as a reaction to their wife's disorder and urged that these situations be treated with conjoint psychotherapy[53]. Validating their writings is a Turkish study of women with vaginismus, where 66% of male partners reported one or more sexual

dysfunctions (50% had premature ejaculation and 28% had erectile dysfunction and HSDD)[53].

The CLOSER survey evaluated the impact of VVA on the sexual relationship between postmenopausal women and their male partners[46]. It included 4100 females and 4100 males representing nine different countries. Both women and men reported intimacy avoidance because sex would be painful (55% of women vs. 61% of men), or because both partners had diminished sexual desire (46% of women vs. 43% of men). Twenty percent of women and their male partners ceased sexual activity when VVA symptoms were present. Almost 60% of women used local vaginal moisturizers and lubricants but, interestingly, only 15% of the male partners were cognizant of this practice. Forty-one percent of the sample was prescribed some form of local estrogen therapy (LET). The use of LET for vaginal discomfort had a positive impact on the self-esteem of postmenopausal women, especially in feeling happy that their body was functioning properly (45%) and experiencing an overall improvement in their sex life (38%). There was general agreement between male and female respondents regarding improvements in their sex life following LET use.

The sexual equilibrium is also apparent in male studies of erectile dysfunction and premature ejaculation. Pre-sildenafil reports of men using either intracavernosal injection or vacuum pump therapy for erectile dysfunction demonstrated that, after 12 months, the female partners reported statistically significant changes in sexual satisfaction, arousal, frequency of intercourse and frequency of coital orgasm[54]. Subsequently, use of phosphodiesterase-5 inhibitors (i.e. sildenafil, vardenafil, tadalafil and avanafil) by men for erectile dysfunction was shown to significantly improve the female partner's sexual function[55]. Hobbs and colleagues also documented that 77.7% of premature ejaculation partners had at least one sexual dysfunction, compared to 42.7% of the control group[56]. The most common dysfunctions in the premature ejaculation partners were problems with arousal-sensation (55.2%) and orgasm (51.9%).

The sexual equilibrium is an important and powerful concept for clinicians to bear in mind when treating menopausal women for sexual symptoms. Keeping this notion, front and center, allows clinicians of all backgrounds to better understand and properly consider the partner's responses to the woman's sexual problem and help the couple work through the sexual, psychological and interpersonal issues related to the sexual dysfunction.

Clinical assessment: the history

In epidemiological studies, the most common sexual dysfunction reported in the United States is HSDD[10] which, in postmenopausal women, is frequently co-morbid with other sexual dysfunctions[10,57]– arousal and orgasmic dysfunctions and sexual pain disorders, often related to VVA/GSM. Among older women with HSDD, that overlap is about 50%[58] to 65%[59] for arousal dysfunction and over 70% with orgasmic dysfunction[4]. Thus, in assessing sexual function in postmenopausal women, all phases of the sexual response cycle and sexual pain must be evaluated. A new HSDD Process of Care algorithm has been developed by the International Society for The Study of Women's Sexual Health (ISSWSH)[60] to facilitate assessment by a health-care provider (Figure 1); if the woman does not spontaneously report a sexual problem in the first 5 minutes of a routine office visit (12% of postmenopausal women do begin the discussion), the provider should introduce the topic, as 36% of women then report sexual dysfunction[61]. The dialog may be started with a ubiquity assertion such as, 'Many postmenopausal women experience problems with their sexual functioning or pain with sex,' followed by questions regarding sexual activity/history, concerns, and associated distress or through the use of a brief screening tool such as the Decreased Sexual Desire Screener[62] (Figure 2).

Sexual function should be assessed considering either partnered or unpartnered sexual activity; if the former, any desire discrepancy must be associated with distress, often referred to as 'bother' in the woman to warrant intervention. Distress may be manifested by frustration, grief, guilt, incompetence, loss, sadness, sorrow or worry[8]. Questioning should lead to identification of sexual dysfunctions (e.g. sexual complaint plus distress), distinguishing subtypes of HSDD (e.g. generalized vs. situational and acquired vs. life-long), duration of symptoms and the temporal relationship of each type of sexual dysfunction to the other (e.g. which came first), and identifying associated modifiable factors, as these should be addressed prior to specific interventions for the sexual dysfunction(s) (i.e. treat dyspareunia due to menopause before addressing low sexual desire)[60].

A biopsychosocial assessment is vital in ascertaining potentially reversible factors and is especially important with aging in postmenopausal women. These factors include medical and psychiatric conditions, such as endocrine disorders, menopausal status, genitourinary conditions, neurologic diseases, cancer diagnoses, and depression; the effect of medications/substances; relationship difficulties; partner sexual dysfunction; as well as any history of sexual trauma. Depression is the most common co-morbidity associated with distressing low sexual desire, occurring in about 40% of women with HSDD[63], and is bi-directionally related to sexual dysfunction, with its presence associated with a 50–70% increased risk of sexual dysfunction, while the occurrence of sexual dysfunction increases the risk of depression by 130–210%[64]. Antidepressant medications are common contributors to sexual dysfunction, as are other psychotropic medications, narcotics, hormonal preparations, cardiovascular drugs, antihistamines and histamine-2 blockers, chemotherapeutic and adjunctive cancer agents, and drugs of abuse[60]. When indicated by the woman's history, a focused physical/genital examination to identify vulvovaginal conditions such as atrophy, neurologic processes, dermatologic and traumatic/infectious illnesses, and to evaluate genital pain, and laboratory studies (e.g. sex steroid levels to assess reproductive status; sex hormone binding globulin (SHBG) and testosterone levels if considering supplementation; thyroid function tests; metabolic status; and prolactin levels) may direct care[60].

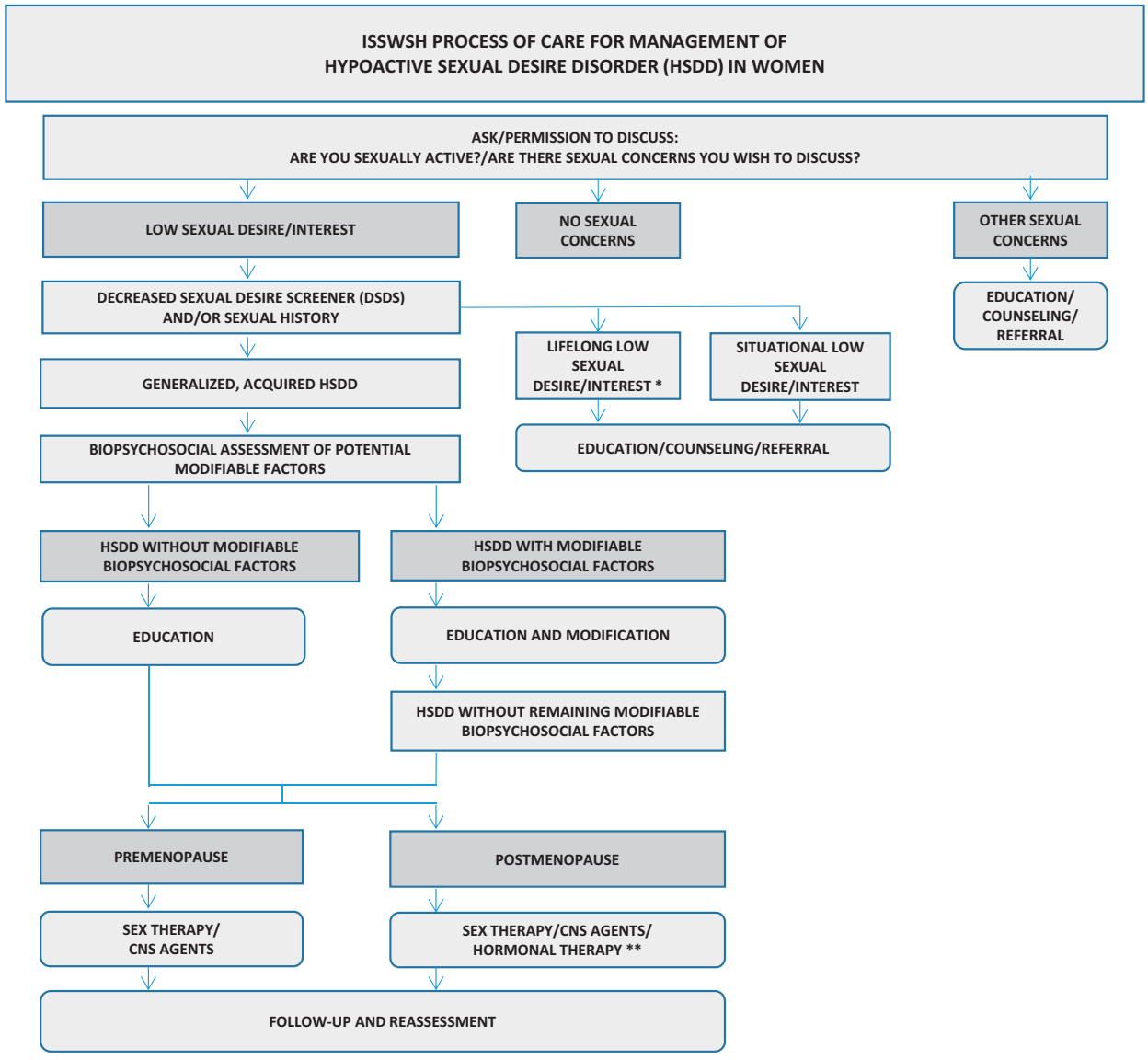

Figure 1. Process of care for assessment and management of hypoactive sexual desire disorder (HSDD) developed by the International Society for the Study of Women's Sexual Health[60] (ISSWSH). The algorithm begins with asking or having permission to discuss sexual concerns and focuses specifically on women who have concerns with their low sexual desire/interest. Initiation of diagnosis starts with the Decreased Sexual Desire Screener or a sexual history. Women with other sexual dysfunctions or those with lifelong or situational low sexual desire/interest are not specifically addressed in this algorithm. Women with generalized acquired HSDD then undergo a focused medical assessment to identify potentially modifiable biopsychosocial factors. Therapeutic intervention begins with education/modification of recognized modifiable factors. Women whose HSDD persists are categorized by menopausal status, and appropriate therapeutic interventions are then followed/reassessed. CNS, central nervous system. *Women with lifelong low sexual desire/interest without distress/bother may characterize themselves as asexual and should not be considered for treatment. **Women in the late reproductive years. Reproduced with permission from Elsevier.

Clinical assessment: the physical examination and laboratory evaluation

The physical examination is an important component in the initial assessment of sexual well-being or dysfunction for midlife women. For example, the confirmation by a healthcare practitioner of normal genitourinary anatomy is an integral part of the therapeutic relationship. It provides relief for the patient that there is nothing wrong anatomically that is causing sexual dysfunction. Similarly, the finding of VVA, a treatable condition, can direct effective therapies in reducing dyspareunia that often starts the cascade of sexual avoidance in midlife women.

The patient and clinician work in a partnership during this emotionally and physically sensitive examination. Patient permission as well as feedback about specific areas of discomfort are useful for tailoring the examination and minimizing pain.

The physical examination starts with a general inspection of the patient and her vital signs, palpation of the thyroid, breasts and abdomen, and presence and distribution of pubic hair. The most anxious patient is reassured by inspection of the vulva without a speculum as the initial part of the examination. The characteristics of the clitoris including any adhesions or abnormalities under the clitoral hood, labia minora, majora and anus are evaluated. Vulvar skin conditions that produce adhesions, erythema, ulcers, leukoplakia or pustules, papules and nodules may be confirmed. Gentle separation of the labia minora is performed to evaluate the urethra, hymenal area, vestibule, and posterior fourchette. If

THE DECREASED SEXUAL DESIRE SCREENER IS INTENDED TO ASSIST YOUR CLINICIAN IN THE ASSESSMENT OF YOUR DECREASED SEXUAL DESIRE. PLEASE ANSWER EACH OF THE FOLLOWING QUESTIONS BY CIRCLING EITHER YES OR NO.	
1. In the past, was your level of sexual desire or interest good & satisfying to you?	Yes / No
2. Has there been a decrease in your level of sexual desire or interest?	Yes / No
3. Are you bothered by your decreased level of sexual desire or interest?	Yes / No
4. Would you like your level of sexual desire or interest to increase?	Yes / No
5. Please circle all of the factors that you feel may be contributing to your current decrease in sexual desire or interest:	
a. An operation, depression, injuries, or other medical condition	Yes / No
b. Medications, drugs, or alcohol you are currently taking	Yes / No
c. Pregnancy, recent childbirth, menopausal symptoms	Yes / No
d. Other sexual issues you may be having (pain, decreased arousal or orgasm)	Yes / No
e. Your partner's sexual problems	Yes / No
f. Dissatisfaction with your relationship or partner	Yes / No
g. Stress or fatigue	Yes / No

Figure 2. The Decreased Sexual Desire Screener[62]. Brief diagnostic assessment for generalized, acquired hypoactive sexual desire disorder (HSDD). A 'no' response to any one of the first four questions excludes a diagnosis of acquired HSDD. The woman may have situational or longstanding low sexual desire/interest. A 'yes' response to all questions 1–4 and 'no' to all items in question 5 suggest generalized acquired HSDD. 'Yes' to any items in question 5 necessitates evaluation of differential diagnoses and determination if low interest is situational/generalized and acquired. Reproduced with permission from Elsevier.

the patient has vulvar pain or painful intercourse, the Q-tip test is then useful in mapping out tender areas, especially of the vestibule[65].

Digital palpation to assess vaginal caliber and the pelvic floor musculature is necessary to confirm hypertonicity, vaginismus, trigger points, and rarely vaginal adhesions or stenosis. With the history of previous pelvic surgery, palpation of the vaginal vault for tenderness or extrusion of vaginal mesh has become increasingly important. Throughout the examination, the finding of pallor of the tissues, shrinkage or absence of the labia minora, flattening of the labial majora fat pads, shrinkage of the introitus, lack of lubrication, decreased elasticity and rugae within the vagina as well as vaginal shortening[45] can substantiate the diagnosis of VVA. The presence of abnormal discharge may be noted. Determination of the vaginal pH using litmus paper is useful, but not mandatory for diagnosis of GSM. This can confirm the alkaline pH (>5.5) within the vagina seen in VVA.

The gentle introduction of the speculum with the patient's permission confirms the normalcy of the cervix, presence of inflammation, or lesions. The physical findings and history will direct cervical smear tests or cultures for yeast, bacterial vaginosis or sexually transmitted infections. Rotation of the speculum by 90° and separation of the blades to view the anterior and posterior vaginal walls are indicated if pelvic floor relaxation is suspected. Bimanual examination to rule out tenderness of the bladder, vaginal walls, cervix, uterus or adnexa or any additional uterine or adnexal enlargement usually completes the examination[6]. In the presence of deep pelvic pain, rectovaginal examination may be useful for rectovaginal nodules found in endometriosis or cul-de-sac pathology.

Recommended laboratory tests for sexual health are minimal unless a specific history points to clinical concerns. These might include thyroid stimulating hormone to ensure the patient is euthyroid, fasting blood glucose or hemoglobin A1C to diagnose pre-diabetes/diabetes, iron stores for the perimenopausal woman with heavy bleeding, and prolactin if suspicious in the clinical context. Levels of testosterone have been correlated with sexual desire[21,66] but not with a diagnosis of sexual dysfunction[20,67]. Baseline levels of testosterone and SHBG should be obtained with subsequent monitoring if testosterone is prescribed[60,68].

Treatment: psychosocial/sexual counseling

Female sexual function is best conceptualized from a biopsychosocial model, reflecting a woman's fluctuations in health status, neurochemical balance, psychological issues, interpersonal concerns and sociocultural beliefs and values[69]. Menopause clinicians should be familiar with the most common psychotherapeutic techniques to treat their patients' sexual concerns. Some can be used within office-based counseling, and some will be used by sexual medicine experts

when health-care providers refer patients to specialists for sex therapy. Depending on the etiology of a sexual problem, psychotherapy may be used alone or in conjunction with medical treatments (multimodal therapy), which may include psychotherapy with hormonal and non-hormonal pharmacologic therapies and/or pelvic floor physical therapy or medical devices. Even when the etiology of a sexual problem is primarily biologic, cognitive behavioral therapy can help to improve symptoms[60].

Psychological factors that impact sexual function include psychiatric conditions such as anxiety or depression, personality variables, poor self-image, as well as trauma from a history of sexual, alcohol, or substance abuse, perceived stress and cognitive distractibility[70].

Sociocultural factors such as limited sexual health education, religious or cultural mores or values, and societal factors such as age discrimination can also negatively impact sexual functioning. Therefore, an understanding of the context in which a woman presents with sexual concerns is important in determining the optimal treatment approach[70]. Furthermore, the presence or absence of a partner, the quality of a woman's relationship, and the sexual health of her partner are factors that also need to be considered when evaluating sexual dysfunction in women and should inform treatment decisions[11,70]. For example, dyspareunia resulting from VVA/GSM may cause a woman to avoid sexual activity and subsequently lead to relationship conflict. In this case, treating the GSM would be the primary focus. However, psychotherapy may be an essential treatment in order to address the associated anxiety and avoidance behaviors as well as negative cognitive associations that may have developed after pairing sexual activity with pain. In contrast, when sexual problems are the result of relationship conflict (such as lack of sexual desire resulting from discontent with a partner), the primary treatment would be counseling/psychotherapy to address the underlying interpersonal conflict rather than focusing on the sexual consequence. In general, sex therapy is a short-term (approximately 3 months) treatment, which can be conducted in an individual, couple, or group setting[69].

Combining medical and psychotherapeutic interventions when treating a sexual problem is often the logical extension of the biopsychosocial model, since more than one factor may be contributing to sexual dysfunction. Psychotherapy should be individualized and focused on the primary factors(s) affecting sexual function and on those most distressing to the woman[67].

Sex therapy is a specialized form of counseling or psychotherapy using specific techniques to address problems of sexual desire, arousal, orgasm, and pain. It focuses on the psychological and sociocultural factors contributing to sexual problems or is used to improve coping skills or cognitive and behavioral changes to minimize the sexual 'fall-out' from physiologic/medical problems. Interventions generally consist of psycho-education, couple's exercises including sensate focus (a graded series of 'non-demand' sensual touching exercises), and individual and group psychotherapeutic approaches including cognitive behavioral therapy (CBT) and mindfulness cognitive behavioral therapy[71].

The goals of psychotherapy interventions are to modify thoughts, behaviors, expectations, beliefs, and emotions as well as improving relationship communication and reducing cognitive distraction[67,72]. Almost every sexual dysfunction (HSDD, arousal dysfunction, orgasmic dysfunction, dyspareunia) can be addressed, at least in part, with some psychological interventions (individual, couple, CBT, sensate focus, mindfulness, etc.). Psychotherapy may be sufficient for some sexual problems, but may not be sufficient for others. Mindfulness-based cognitive behavioral sex therapy (MBCST) has demonstrated efficacy for improving desire. MBCST includes psycho-education about sexual response and cognitive therapy as well as mindfulness. It also involves skills practice of mindfulness techniques, body scans, and non-masturbatory genital self-stimulation[73,74].

Some common goals and strategies of other sex therapy/psychotherapy interventions include assigning homework referred to as sensate focus exercises, with the goal of desensitizing an individual or couple to sexual activity that causes anxiety or avoidance and increases pleasure and self and partner awareness[49]. Other interventions include helping to expand a stale or problematic sexual repertoire or altering negative or rigid beliefs about sexuality.

The PLISSIT (Permission, Limited Information, Specific Suggestions, and Intensive Therapy) model[75] describes a stepped approach to office-based sexual counseling. Although first described more than 40 years ago, it remains a relevant guide to providing sexual counseling because it meets clinicians at whatever level they are comfortable with in addressing sexual problems and emphasizes identification of concerns and referrals when necessary. *Permission* refers to giving women permission to ask about/discuss sexual concerns. *Limited information* refers to the clinician providing basic information about a sexual problem, anatomy or some resources. *Specific suggestions* would include directed advice regarding sexual techniques or aids, self-help materials, and the use of products like lubricants. *Intensive therapy* requires a referral to a licensed sexual medicine expert or couples therapist and is beyond the scope of most gynecologic and associated menopause practitioners.

Clinical treatments

Local vaginal therapy

The treatment of VVA/GSM has been described extensively elsewhere for both well women[76] and women after breast cancer[77]. In summary, traditional options include vaginal estrogen therapy, vaginal moisturizers, and lubricants for sexual intercourse. More recently, an intravaginal preparation of dehydroepiandrosterone (DHEA) has been found to be efficacious, when used daily, and approved in the United States and Europe for the treatment of moderate to severe dyspareunia, a symptom of VVA. Unfortunately, less frequent use (twice weekly) has not been shown to be clinically effective[78]. There is significant interest in the potential use of low-dose vaginal testosterone as a treatment for VVA, but efficacy and safety are yet to be confirmed[79]. Preliminary data suggest that microablative fractional CO_2 laser or the non-

ablative vaginal Erbium YAG laser treatment has the potential to ameliorate distressing VVA symptoms after a diagnosis of breast cancer[80,81]. Large placebo-controlled randomized trials, with long-term safety follow-up, and additional economic analyses are needed before laser can be considered an established effective and safe therapy for VVA.

Systemic hormonal therapy

The hormones most studied as potential treatments for female sexual dysfunction are estrogens and androgens, with some studies also having examined the effects of DHEA, oxytocin and progesterone. Dyspareunia, secondary to postmenopausal VVA, is common amongst both younger and older postmenopausal women[82–84]. Vaginal estrogen therapy alleviates VVA symptoms, is inexpensive and safe. Nonetheless, this highly effective therapy remains under-prescribed, with less than 10% of postmenopausal women being treated[82–84]. When systemic estrogen therapy is taken for menopausal symptoms (i.e. vasomotor instability), the improvement in well-being with symptom alleviation may result in improved libido as well as relief of VVA[85]. Some women also require vaginal estrogen as well as systemic estrogen effectively to alleviate VVA symptoms.

Testosterone, administered transdermally as a cream, patch or gel, or as an implanted pellet, improves sexual well-being in postmenopausal women with low sexual desire associated with distress[68,86]. Transdermal testosterone has been shown to significantly improve low libido in naturally or surgically postmenopausal women using systemic estrogen, with or without progestogen, as well as women not using menopausal hormone therapy. Testosterone therapy should not be considered until a full clinical assessment is undertaken and potentially modifiable factors are addressed[68]. There is no diagnostic cut-off level of testosterone or any other androgen that will identify women most likely to respond to transdermal testosterone[20]. However, treatment with testosterone is less likely to be effective in women with a SHBG level above the normal range[87]. Despite established efficacy of testosterone therapy for loss of libido, long-term safety data are limited, although the available safety data are reassuring with no evidence of increased likelihood of cardio-metabolic disease or cancer[88]. The main limitation pertaining to testosterone therapy is the lack of approved formulations for women, other than in Australia, leaving clinicians with no option but to prescribe compounded testosterone formulations or modified regimens of approved male formulations. Formulations approved for men are not recommended for use in women because of the high risk of overdosing and consequent virilization. Some dosage forms are more easily adapted to use in women when alternatives are not available, but these still have potential for delivery of excessive doses[68]. When testosterone is prescribed, the blood level of calculated free testosterone should not exceed the normal premenopausal range. This requires frequent monitoring of blood levels, with the recommendation that a level is checked after 3 weeks of initiating therapy and then routinely every 6 months, with dose titration if the upper limit of normal is exceeded[68]. Women should be advised that treatment should be considered a trial, benefit is not usually experienced until 4–6 weeks of treatment and that treatment should be ceased if there is no improvement after 6 months[68].

Systematic reviews of the clinical trials of systemic DHEA in women with adrenal insufficiency (primary and/or secondary) and otherwise normal women have shown no significant effect of DHEA on sexual function[89,90]. Therefore, systemic DHEA should not be used to treat sexual interest and arousal dysfunctions. Oxytocin appears to improve emotional responsiveness and social behavior, but has not been shown to be effective for the treatment of sexual dysfunction in women[91]. There are no studies to support the use of progesterone as a treatment for sexual dysfunction in women[91].

In summary, approved formulations of local vaginal estrogen and vaginal DHEA are effective treatments for dyspareunia secondary to VVA. Transdermal testosterone is effective for the treatment of low desire with associated distress. Approved testosterone products for women are urgently needed.

Systemic non-hormonal therapy

Ospemifene, a selective estrogen receptor modulator or SERM, is a systemic non-hormonal therapy approved in the US and EU for the treatment of dyspareunia due to VVA. Albeit a systemic non-hormonal therapy, it acts locally as an estrogen. Preliminary data from randomized, placebo-controlled trials suggest that ospemifene can improve sexual function (desire, arousal, lubrication, orgasm, sexual satisfaction, and provide pain reduction) measured by the Female Sexual Function Index (FSFI) in postmenopausal women with VVA[92].

Flibanserin is currently the only United States Food and Drug Administration (FDA)-approved medication for generalized, acquired HSDD in premenopausal women. It was recently approved for this same indication in Canada. It is not currently approved for use in postmenopausal women, as the sponsor (Boehringer Ingelheim) did not apply to the FDA for this indication, and stopped the generally required second clinical trial demonstrating safety and efficacy before its completion. Flibanserin (100 mg dosed at bedtime) is a non-hormonal, centrally acting, daily, oral, multifunctional serotonin agonist and antagonist (MSAA). Efficacy was established in three pivotal trials in over 3500 premenopausal women, demonstrating a statistically significant and clinically meaningful improvement in the level of sexual desire and the number of satisfying sexual events, and a decrease in distress compared to placebo[93–95]. Clinical trials of flibanserin in postmenopausal women have demonstrated similar efficacy and safety, in this population[96] as in premenopausal women[93–95]. Approximately 50–60% of women with HSDD respond to flibanserin, and it may take up to 8 weeks for efficacy to emerge. The most common adverse events in both premenopausal and postmenopausal women are dizziness (9.2%), somnolence (8.3%), nausea (6.5%), and fatigue (3.7%); placebo-corrected

rates are similar to other central nervous system (CNS) active agents. Most adverse events are mild, transient, and mitigated with bedtime dosing. In the trials, subject discontinuation due to adverse events was approximately 13% in premenopausal women treated with flibanserin compared to 6% with placebo. Flibanserin labeling in the United States, but not in Canada, has a boxed warning with alcohol contraindicated, based on the results of an alcohol challenge study showing an increase in sedation, syncope and hypotension in the treatment group, although alcohol use was not restricted in the larger group of clinical trials, and did not significantly increase such adverse events over placebo in the three major pivotal trials[93–95]. A post-approval risk evaluation and mitigation program in the United States, but not in Canada, requires certification of prescribers and pharmacies in consenting patients to avoid alcohol.

Other CNS-active agents, approved for other indications, have been used off-label for the treatment of HSDD despite limited efficacy and safety data. Bupropion, which acts to enhance dopamine and norepinephrine, has been shown to improve arousal and orgasm in a randomized, double-blind, placebo-controlled trial. The use of doses of 300–400 mg/day also improved HSDD, but the difference for the desire endpoint was not statistically significant[97]. Side-effects of bupropion used for treatment of major depression or smoking cessation include tremor (13.5%), agitation (9.7%), dry mouth (9.2%), constipation (8.2%), dizziness (6.1%) and nausea/vomiting (4%)[98]. In women with antidepressant-induced sexual dysfunction, the addition of bupropion SR (300 mg/day) improved sexual desire vs. placebo[99].

Buspirone, which reduces serotonin inhibition, is another off-label treatment that has been used for antidepressant-associated sexual dysfunction. One trial demonstrated improvement in sexual function in depressed women with selective serotonin reuptake inhibitor-induced sexual dysfunction with buspirone (30–60 mg/day) compared to placebo (58% vs. 30%)[100]. The most common side-effects of buspirone in studies of generalized anxiety disorder (approved indication) are dizziness (9%), nervousness (4%), nausea (3%), and headache (3%). Drug development research for HSDD has been directed at finding CNS agents that specifically activate stimulatory pathways or reduce inhibitory pathways regulating sexual desire[101]. Potential future therapies include bremelanotide[102] and combination therapies: testosterone/sildenafil, testosterone/buspirone[103] and bupropion/trazodone[104].

Conclusion

Positive sexual function at midlife can enhance personal and relationship quality, improve longevity and enhance quality of life. Yet many women suffer from low desire, arousal and orgasmic dysfunction with or without sexual pain due to VVA/GSM following menopause. Both women and their practitioners are reluctant to bring sexual problems to light, and so they often go untreated, resulting in detrimental effects in the relationship despite safe and effective available treatments. It is hoped that this short 'how to' manuscript can help those practitioners caring for menopausal women to open the dialog and provide or facilitate appropriate treatment.

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