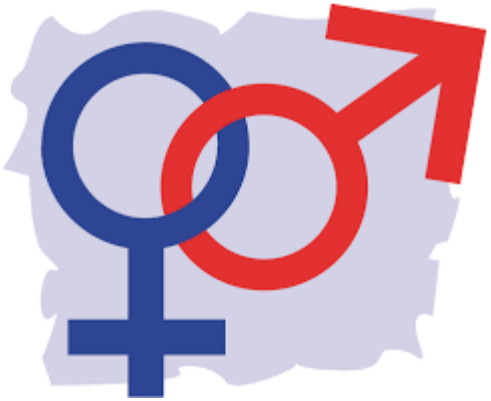

Overview of female sexual dysfunction

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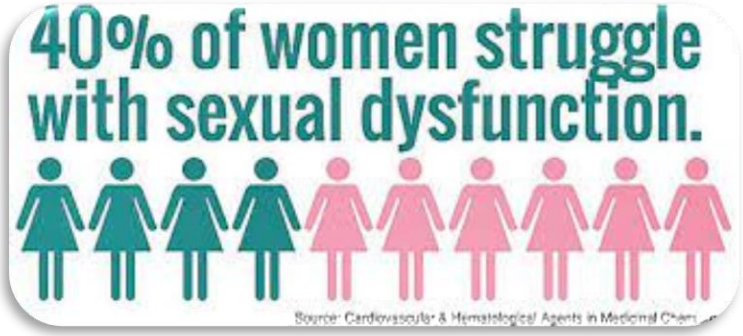
Definition

- Sexual dysfunction is defined as a sexual problem that is **persistent or recurrent** and causes **marked personal distress or interpersonal difficulty**. It must not be better accounted for by a medical or psychiatric condition (ie, anxiety and depression) or due exclusively to the direct physiologic effects of a substance or medication.

- Intervention is warranted when a patient presents with a **distressing sexual concern**, even if it does not strictly meet DSM-5 criteria.

Introduction

- Sexual problems are highly prevalent in females. In the United States, approximately 40 percent of females have sexual concerns, and **12 percent** report distressing sexual problems.
- The prevalence rate of **HSDD*** in Iranian women in the general population was 35% (95% CI: 17.6-52.1%).SAD & SOD represent same value.
- Female sexual dysfunction is **multifactorial.**



***HSDD: Hypoactive sexual desire disorder**
SAD: Sexual Arousal Disorder
SOD: Sexual Orgasm Disorder

I. Shifren JL, Monz BU, Russo PA, et al. Sexual problems and distress in United States women: prevalence and correlates. Obstet Gynecol 2008; 112:970.
II. Ramezani MA, Ahmadi K, Ghaemmaghami A, Marzabadi EA, Pardakhti F. Epidemiology of Sexual Dysfunction in Iran: A Systematic Review and Meta-analysis. Int J Prev Med. 2015 May 20;6:43.

How good are we at talking about sex?

Study 2009:

- GPs ask patients <25% of the time
- Secondary care – asked only 50% of the time

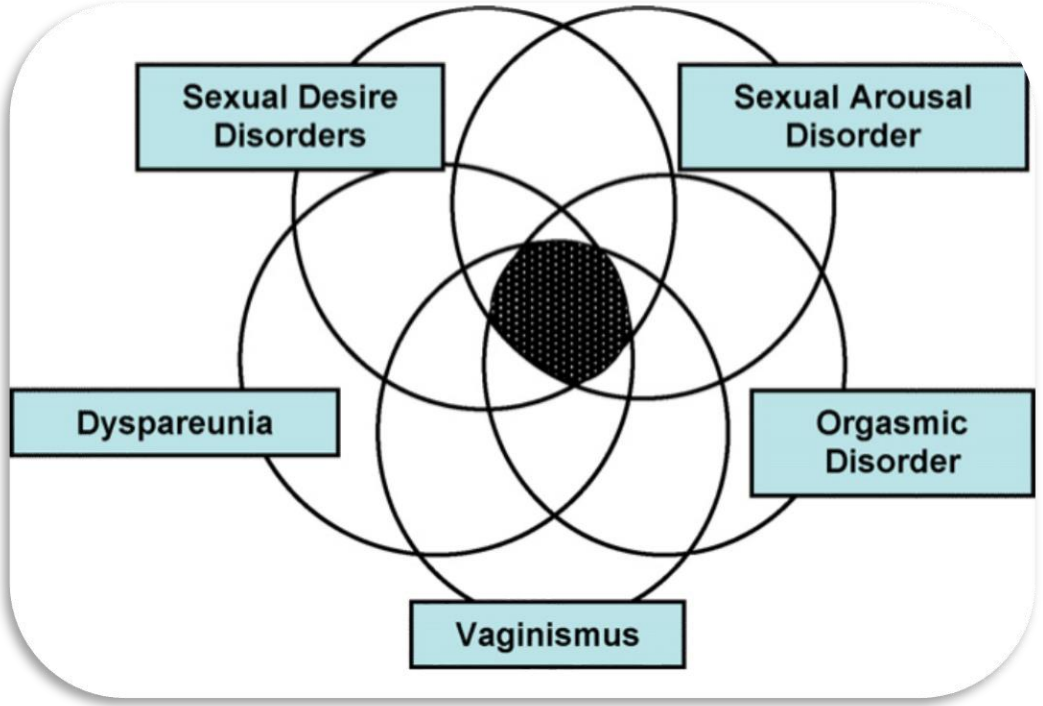
  Due to lack of time and training
- Anybody presenting with period problems, pelvic pain, other gynaecology conditions should be asked about sex routinely. Using a relaxed open question **'how's sex?'**

Gender and Sexuality

- Women
  - Desire for sex more often linked to relationship status and social norms
  - Tend to be more ashamed of appearance flaws **(May interfere with sexual satisfaction)**

- At all ages, women more likely than men to report sexual dysfunction

Classification



Most patients with sexual concerns have clinical issues that impact more than one aspect of sexual function.

DSM-5 Criteria for Sexual Interest/Arousal Disorder in Women

DSM-5 Criteria for *Sexual Interest*/Arousal Disorder in Women:
• **Diminished, absent, or reduced frequency of at least three of the following for 6 months or more:**
• **Interest in sexual activity**
• **Sexual/erotic thoughts or fantasies**
• **Initiation of sexual activity and responsiveness to partner's attempts to initiate**
• **Sexual excitement/pleasure during 75% sexual encounters**
• **Sexual interest/arousal elicited by any internal or external erotic cues**
• **Genital or nongenital sensations during 75% sexual encounters**
• Causes marked distress or interpersonal problems
• Not due to a medical illness, another psychological disorder (except another sexual dysfunction), or the effects of a drug

Orgasmic Disorders

DSM-5 Criteria for Female Orgasmic Disorder:

On at least 75 percent of sexual occasions:

- **Marked delay, infrequency, or absence of orgasm**
- **Markedly reduced intensity of orgasmic sensation**
- **Causes marked distress or interpersonal problems**
- **Not due to a medical illness, another psychological disorder (except another sexual dysfunction), or the effects of a drug**

DSM-5 Criteria for Genitopelvic Pain/Penetration Disorder

Persistent or recurrent difficulties with at least one of the following:

- **Inability to have vaginal intercourse/penetration**
- **Marked vulvar, vaginal, or pelvic pain during vaginal penetration or intercourse attempts**
- **Marked fear or anxiety about pain or penetration**
- **Marked tensing of the pelvic floor muscles during attempted vaginal penetration**
- **Causes clinically significant distress or interpersonal problems**
- **Not due to another psychological disorder, a medical condition, or the effects of a drug**

Figure: Predictors of Sexual Functioning

	Successful sexual functioning	Poor sexual functioning
Psychological factors	Good emotional health Attraction toward partner Positive attitude toward partner Positive sexual attitude	Depression or anxiety disorders Focus on performance Too much routine Poor self-esteem Uncomfortable environment for sex Rigid, narrow attitude toward sex Negative thoughts about sex
Physical factors	Good physical health Regular appropriate exercise Good nutrition	Smoking Heavy drinking Cardiovascular problems Diabetes Neurological diseases Low physiological arousal SSRI medications Antihypertensive medication Other drugs
Social and sexual history factors	Positive sexual experiences in past Good relationship with partner Sexual knowledge and skills	Rape or sexual abuse Relationship problems, such as anger or poor communication Long periods of abstinence History of hurried sex

Etiology of Sexual Dysfunction: Biological Factors

- The DSM-5 includes separate diagnoses for sexual dysfunctions that are caused by medical illnesses. Somewhat controversial because many sexual dysfunctions have a biological contribution.
- Diseases of vascular system: DM
- Diseases of the nervous system: MS,CP, Spinal cord injury, stroke
- General disease or disability: blindness or deafness
- Low levels of testosterone or estrogen
- Heavy alcohol consumption before sex or history of chronic alcoholism
- Heavy cigarette smoking
- Medications
  - Antihypertensives
  - SSRIs

Hypertension and sexual dysfunction

Sexual dysfunction may be triggered or aggravated by treatment with?

Thiazide or thiazide-like diuretics, conventional beta-blockers, or centrally acting agents (e.g. clonidine)

While

ACE inhibitors, ARBs, CCBs, or vasodilating beta blockers may have neutral or even beneficial effects.

Although α-blockers are inappropriate as monotherapy, they may also be helpful add-on antihypertensives for patients with erectile dysfunction or BPH.

Effects of medications

- **Over 200 prescription and OTC medications** have negative effects on sexuality
- Health care practitioners don't always discuss potential sexual side effects
- **Psychiatric medications**
  - **Antidepressants:** reduced sexual interest, arousal, delayed or absent orgasm in up to 60% of users
  - **Antipsychotics:** frequent loss of arousal, orgasm
  - **Tranquilizers** (valium, xanax, etc.): interfere w/orgasm
- **Antihypertensive medications** (treat high b.p.)Can interfere w/desire, arousal, and orgasm
- **Other medications**
  - **Prescription and OTC gastrointestinal, antihistamine medications** can interfere w/desire, arousal, erection
  - **Methadone** can reduce desire, arousal, orgasm

TABLE 14.4 Sexual Effects of Some Abused and Illicit Drugs

Drug	Effects
Alcohol	Chronic alcohol abuse causes hormonal alterations (reduces size of testes and suppresses hormonal function) and permanently damages the circulatory and nervous systems.
Marijuana	Reduces testosterone levels in men and decreases sexual desire in both sexes.
Tobacco	Adversely affects small blood vessels in the penis and decreases the frequency and duration of erections (Mannino et al., 1994).
Cocaine	Causes erectile disorder and inhibits orgasm in both sexes.
Amphetamines	High doses and chronic use result in inhibition of orgasm and decrease in erection and lubrication.
Barbiturates	Cause decreased desire, erectile disorders, and delayed orgasm.

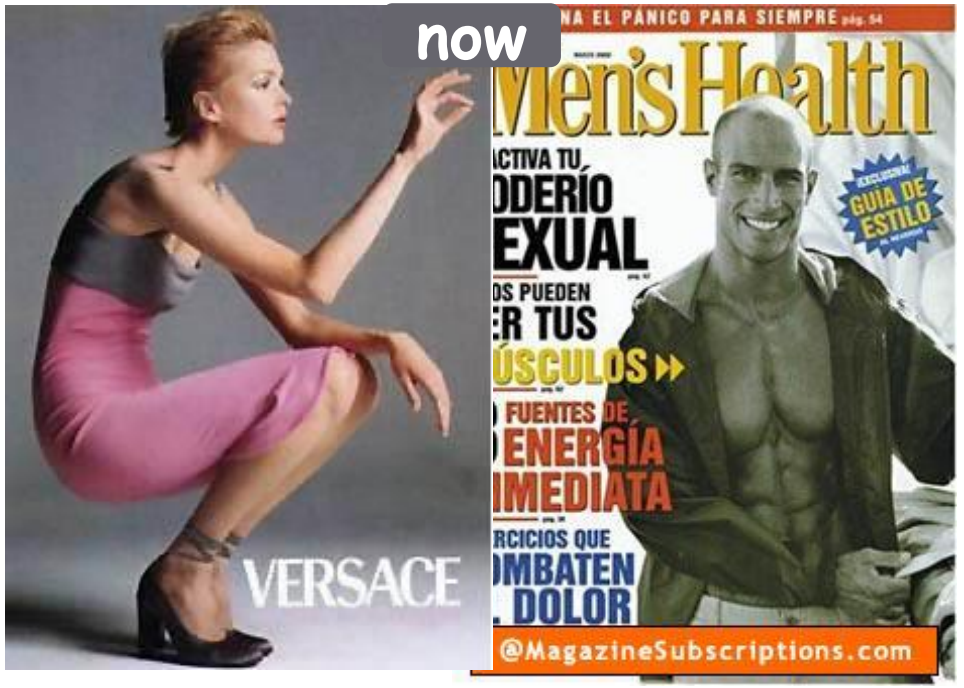
Individual factors (cont.)

- **Self-concept, Self-esteem, self-confidence** correlate w/higher sexual satisfaction in women and men
- **Body image** strongly affects sexuality (women especially)
- **Media images** of women have gotten further and further from the average size of women
- Early 1980s: average model weighed **8% less than the average** American woman; today, it's **23% less.**

Individual factors (cont.)

- Self-image

then



Management

- Improvement of one sexual problem may result in improvement in another.
- Nonpharmacologic options should be the initial treatment for most patients.
- All currently available pharmacologic therapies for female sexual dysfunction (except approved treatments for vulvovaginal atrophy) are of limited efficacy and associated with side effects and risks.

Treatments of Sexual Dysfunction

- Evaluation (Female Sexual Distress Scale)
- Assess patient goals (set realistic goals)
- Address partner issues
- Treat associated conditions
- Anxiety reduction
- Lifestyle changes
- Improving body image
- Medications and physical treatments

Medication therapy

Androgen

Use and limitations

- Levels of endogenous androgens do not predict sexual function for females.
- Testosterone levels should not be used in determining the etiology of a sexual problem or in assessing efficacy of treatment, as no clear association between androgen levels and sexual function has been found in several large, well-designed studies.
- However, androgen therapy that increases serum concentrations to the upper limit of normal has been shown to improve female sexual function in **selected populations of postmenopausal women**.

- **But** are not advised due to potential risks and side effects.

I. Shifren JL, Davis SR. Androgens in postmenopausal women: a review. Menopause 2017; 24:970.
II. Wierman ME, Arlt W, Basson R, et al. Androgen therapy in women: a reappraisal: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2014; 99:3489.
III. Huang G, Basaria S, Travison TG, et al. Testosterone dose-response relationships in hysterectomized women with or without oophorectomy: effects on sexual function, body composition, muscle performance and physical function in a randomized trial. Menopause 2014; 21:612.

Use of androgen

- Discussion of androgen therapy with a patient must include a full explanation of the potential benefits and risks.
- In addition, they must be informed that none of the commonly used androgen therapies are approved by the US FDA for treating female sexual dysfunction because of limited clinical trial data, **limited efficacy** compared with placebo, or concerns about **long-term safety**.

Place in treatment

- **Other safer interventions prior to the testosterone prescription**, including low-dose vaginal estrogen, relationship interventions (eg, sex therapy, date nights, use of sexual aids such as vibrators, books), and adjustment of antidepressant medication (when indicated).

Testosterone alone

- For postmenopausal women who are not using concurrent estrogen therapy, one large, controlled trial reported similar results as discussed. In this trial, **814 naturally or surgically postmenopausal women with HSDD** were randomly assigned to receive transdermal testosterone **(daily dose of 150 or 300 mcg)** or a placebo patch.
- The testosterone **300 mcg group** reported significantly more **SSEs*** than the placebo group (an increase of 2.1 versus 0.7 episodes per four weeks); this was not true for the 150 mcg dose (increase of 1.2 episodes). However, both testosterone doses were associated with significant improvements in desire and reduction in distress about sexual dysfunction.

***SSE: sexually satisfying events**

Davis SR, Moreau M, Kroll R, et al. Testosterone for low libido in postmenopausal women not taking estrogen. **N Engl J Med 2008; 359:2005**.

Use of androgen in Premenopausal patients

- Data regarding androgen treatment of premenopausal women are few and inconclusive.

- There were **no significant improvements** in any other measure of sexuality, including desire, pleasure, or orgasm.

I. Davis S, Papalia MA, Norman RJ, et al. Safety and efficacy of a testosterone metered-dose transdermal spray for treating decreased sexual satisfaction in premenopausal women: a randomized trial. Ann Intern Med 2008; 148:569.
II. Goldstat R, Briganti E, Tran J, et al. Transdermal testosterone therapy improves well-being, mood, and sexual function in premenopausal women. Menopause 2003; 10:390.

Selected formulation

- Formulations (testosterone, methyltestosterone) and delivery methods (oral, transdermal patch, topical gel) vary across studies.
- Regarding dosing, in general, trials indicate that a transdermal testosterone dose of 300 mcg/day for six months is safe and effective in women who are receiving concomitant estrogen therapy.
- Benefits were reported for many aspects of sexuality, including **desire, responsiveness, orgasm, and satisfaction.**

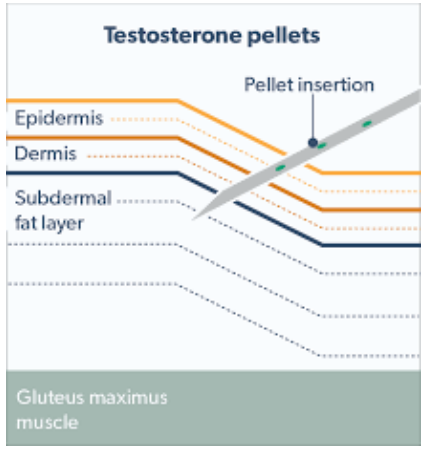
Female testosterone patch

- These patches would be the preferred product for females electing testosterone therapy **but are no longer available, even in Europe**.

- In the United States, no androgen therapies for female sexual dysfunction are approved by the FDA, which declined approval of a testosterone patch for females pending additional long-term safety data.

Injectable or implantable preparations

- Use of injectable or implantable preparations ("pellets") of testosterone are available but not advised for females.
- Administration is uncomfortable and inconvenient, and dosing is almost always supraphysiologic.
- In addition, if side effects occur, removal of the implanted or injected testosterone is not possible. Testosterone levels remain elevated for a minimum of one month and often longer.



I. Invasive
II. Leaves scar tissue
III. Unable to modify dosage between implant

Davis SR, Baber R, Panay N, et al. Global Consensus Position Statement on the Use of Testosterone Therapy for Women. Climacteric 2019; 22:429.

Oral formulations

- Use of oral formulations is limited by the potential for adverse changes in lipids and liver function tests following first-pass hepatic metabolism.
- Methyltestosterone is available by prescription in the United States in a fixed-dose combination with a high dose of oral estrogen.
- Oral DHEA is available **without a prescription**; doses of **25 to 50 mg/day** raise circulating androgen levels into the **physiologic range**.
- As this product is subject to minimal regulatory oversight, hormone content is highly variable.

I. Davis SR, Baber R, Panay N, et al. Global Consensus Position Statement on the Use of Testosterone Therapy for Women. Climacteric 2019; 22:429.
II. Morales AJ, Nolan JJ, Nelson JC, Yen SS. Effects of replacement dose of dehydroepiandrosterone in men and women of advancing age. J Clin Endocrinol Metab 1994; 78:1360.
III. Parasrampuria J, Schwartz K, Petesch R. Quality control of dehydroepiandrosterone dietary supplement products. JAMA 1998; 280:1565.

Major issues regarding side effects

- Cosmetic, androgenic side effects, such as hirsutism and acne, are usually mild; **irreversible**, virilizing changes (eg, voice deepening, clitoromegaly).
- Serum HDL cholesterol concentrations.

✓**Most androgens are aromatized to estrogens**; thus, risks of estrogen therapy are also possible with androgen treatment. A possible association between testosterone administration and breast cancer risk has been reported.

Davis SR, Moreau M, Kroll R, et al. Testosterone for low libido in postmenopausal women not taking estrogen. N Engl J Med 2008; 359:2005.

Contraindications

- These medications should not be used in patients with **cardiovascular disease**, **hepatic disease, endometrial hyperplasia or cancer, or breast cancer** and should be used with caution in patients at high risk for these disorders.

Shifren JL, Davis SR. Androgens in postmenopausal women: a review. Menopause 2017; 24:970.

Estrogens

- The Women's Health Initiative, a set of randomized trials in over 27,000 postmenopausal women, found that **systemic estrogen** with or without progestin therapy did not improve sexual satisfaction and may be harmful.

Hays J, Ockene JK, Brunner RL, et al. Effects of estrogen plus progestin on health-related quality of life. N Engl J Med 2003; 348:1839.

Tibolone

- Tibolone is a synthetic steroid whose metabolites have estrogenic, progestogenic, and androgenic properties.
- **Labeled indication:** Vasomotor symptoms associated with menopause

- It was not approved by the FDA due to concerns about risk of **breast cancer, endometrial cancer, and stroke** but is used by postmenopausal patients in Europe and other countries.

- **Not available in USA.**

Basson R. Women's sexual function and dysfunction: current uncertainties, future directions. Int J Impot Res 2008; 20:466.

Flibanserin

- Flibanserin is a **centrally acting serotonin receptor agonist/antagonist** that results in transient decreases in serotonin and increases in dopamine and norepinephrine in certain regions of the brain.
- Flibanserin was rejected twice for approval by the FDA due to concerns regarding both efficacy and safety.
- **It was approved by the FDA in August 2015** for **premenopausal patients** with HSDD after review of additional safety information and efforts by consumer groups.
- Flibanserin is the **first drug approved by the FDA for female sexual dysfunction** in premenopausal patients.

Joffe HV, Chang C, Sewell C, et al. FDA Approval of Flibanserin--Treating Hypoactive Sexual Desire Disorder. N Engl J Med 2016; 374:101.

Flibanserin

- The FDA approved flibanserin for **premenopausal** patients with low sexual desire with associated distress at a daily dose of 100 mg at bedtime.

- Flibanserin is not indicated for the treatment of sexual dysfunction in postmenopausal patients.

Flibanserin. US Food and Drug Administration (FDA) approved product information. Revised August 2019. US National Library of Medicine. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=3819daf3-e935-2c53-c527-e1d57922f394#ID_9936ccb4-268d-e60b-efbc-c5f21c5f6d3e (Accessed on October 14, 2019).

Flibanserin

Warning Box

- Flibanserin can cause hypotension and syncope. These risks are increased when combined with alcohol or cytochrome P450 3A4 (CYP3A4) inhibitors (eg, fluconazole).

- Flibanserin ingestion should be delayed by **at least two hours after alcohol ingestion**; patients who consume three or more alcoholic beverages are advised to skip their evening flibanserin dose.
- Use of either alcohol or moderate to strong CYP3A4 inhibitors in combination with flibanserin is contraindicated.
- Start 2 weeks after the last dose of the CYP3A4 inhibitor.

Limitation

- The clinical role of flibanserin may be limited by the need for daily dosing, common adverse effects (eg, somnolence, dizziness), and safety concerns regarding combining flibanserin with alcohol or certain medications (eg, fluconazole, antidepressants); hypersensitivity reactions (eg, anaphylaxis, angioedema) have also been reported.

I. Flibanserin [package insert]. Raleigh, NC: Sprout Pharmaceuticals; 2019. http://https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/022526s009lbl.pdf (Accessed on October 14, 2019).
II. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/022526s010lbl.pdf (Accessed on October 05, 2021).

Bupropion

- If a patient with a distressing sexual problem greatly desires a pharmacologic intervention, **after nonpharmacologic treatments have been tried, bupropion is often the first choice in our practice.**

- Bupropion is FDA approved to treat depression and assist with smoking cessation; use for sexual dysfunction, including that induced by SSRIs, is an off-label indication.

Bupropion vs flibanserin

- As a centrally acting agent, the mechanism of action is likely similar to that of flibanserin.
- **Bupropion is preferred** to flibanserin in our practice, as long-term safety data are available, and risks and side effects are well characterized.
- Generic formulations are available, so cost is low.
- Bupropion should be dosed in the morning, and patients should be observed for increased anxiety, insomnia, and hypertension.
- **Patients must be informed** of potential risks and side effects and off-label nature of use.

Buspirone & Apomorphine

- Some data suggest that buspirone (typically used as an antianxiety medication) is **helpful for decreased libido**.
- **Apomorphine is a dopamine agonist** that has been used for the treatment of male erectile dysfunction, although it is not FDA approved for this indication.
- One small study of limited quality reported improved sexual function in **premenopausal women**.
- Use of this drug is not advised due to limited data on efficacy and significant side effects, including nausea, vomiting, dizziness, and hypotension

Bremelanotide

- Bremelanotide, a melanocortin receptor agonist, was **approved by the FDA in June 2019** for treatment of HSDD in **premenopausal patients**.
- The medication is administered as a subcutaneous injection (1.75 mg) **at least 45 minutes before anticipated sexual activity.**

Bremelanotide

- ✓An **advantage of bremelanotide** compared with flibanserin is that it is taken prior to anticipated sexual activity rather than every day, potentially reducing risks and side effects and avoiding the need to take a daily medication.

Adverse reactions

- Serious adverse reactions occurred in 1.1 percent of women treated with bremelanotide (compared with 0.5 percent with placebo).
- Common adverse reactions included nausea (40 percent; mostly with first injection; 13 percent of women required anti-emetic medications), vomiting (5 percent), flushing (20 percent), headache (11 percent), and hyperpigmentation (1 percent; possibly permanent).
- Some women had a transient increase in blood pressure, and bremelanotide should not be used in women with **uncontrolled hypertension** or known **cardiovascular disease**.
- Bremelanotide is associated with fetal harm in animal studies, so patients must use **effective contraception**.

Phosphodiesterase inhibitors

- Positive effects of sildenafil **on sexual arousal and orgasm** have been demonstrated in **premenopausal women with SSRI-associated sexual dysfunction**.
- Randomized trial data also suggest that PDE-5 inhibitors may be helpful in treating sexual dysfunction in women with **diabetes, multiple sclerosis, or spinal cord injuries**.
- Further study is needed in these populations.

I. Caruso S, Rugolo S, Agnello C, et al. Sildenafil improves sexual functioning in premenopausal women with type 1 diabetes who are affected by sexual arousal disorder: a double-blind, crossover, placebo-controlled pilot study. Fertil Steril 2006; 85:1496.
II. Dasgupta R, Wiseman OJ, Kanabar G, et al. Efficacy of sildenafil in the treatment of female sexual dysfunction due to multiple sclerosis. J Urol 2004; 171:1189.
III. Sipski ML, Rosen RC, Alexander CJ, Hamer RM. Sildenafil effects on sexual and cardiovascular responses in women with spinal cord injury. Urology 2000; 55:812.

Orgasmic disorder

- Treatment for female orgasmic disorder consists principally of **education, psychosocial interventions, and the use of devices**, including vibrators.
- **Vibrators** may improve the ability to achieve orgasm by increasing clitoral blood flow.

Sexual enhancement/Sex therapy

- Self-awareness
- Communication
- Sensate focus
- Takes the pressure off of “performance” and achieving orgasm

Sexual pain

- Sexual pain (also referred to as dyspareunia or genitopelvic pain/penetration disorder) is managed based on the etiology.
- Three common causes of sexual pain in females are **GSM***, which includes hypoestrogenic vulvovaginal atrophy; **provoked pelvic floor hypertonus** (including vaginismus); and **vulvodynia**.

*Genitourinary syndrome of menopause

Pain related to specific conditions

Imperial College Healthcare NHS Trust

Superficial/ vulvar

- Infectious – candida, herpes simplex virus
- Inflammatory/dermatologic – lichens planus, lichens sclerosus, vulvar dermatitis
- Hormonal – vulvo-vaginal atrophy
- Trauma - post operative delivery, perineal trauma, radiotherapy,
- Structural – septum, congenital
- Neurological - neuropathic pain, neurological disease
- Malignancy (vaginal or vulval neoplasia)

Deep

- Non-gynaecological (IBS, inflammatory bowel disease, UTI)
- Pelvic congestion syndrome
- Endometriosis
- Adnexal or pelvic pathology (cysts, fibroids, pelvic malignancies)
- Infectious - PID
- Iatrogenic - vaginal shortening or narrowing, post radiotherapy changes
- Chronic pelvic pain
- Pelvic floor dysfunction (mechanical, anatomical factors, retroversion, prolapse

Genitourinary syndrome of menopause

- Hypoestrogenism due to menopause is the main cause of GSM.
- Management options for sexual pain associated with GSM include nonhormonal vaginal lubricants and moisturizers, low-dose vaginal estrogen, vaginal DHEA, and oral ospemifene (an estrogen agonist/antagonist).
- Vaginal laser or radiofrequency devices have been developed, but their safety/efficacy is not established.
- Given high cost, potential risk, and experimental nature of use, **we do not advise laser treatment for GSM except in research studies.**

low-dose vaginal estrogen

It can remain for 90 days

Provoked pelvic floor hypertonus

- Vaginismus may be effectively treated with **physical therapy** by a therapist with expertise in managing disorders of the pelvic floor.
- Specific techniques may include the use of **vaginal dilators and myofascial release** of muscle tension in muscles of the pelvic floor, thighs, and abdomen, with or without **biofeedback.**
- **Desensitization techniques** are then applied to give the patient control over muscle tonicity/relaxation.

- Other therapeutic approaches include **sex therapy**, **progressive relaxation**, **sensate focus**, **electromyography**, use of **benzodiazepines**, **hypnotherapy**, and **botulinum toxin** type A injections.

MDT - biopsychosocial approach

Imperial College Healthcare NHS Trust

- **Antidepressants (amitriptyline)**
- **Anticonvulsants (gabapentin, pregablin)**
- Topical (lidocaine) – one study demonstrated only 20% improvement to pain
- Topical oestrogen – lack of evidence
- Botox – several small studies demonstrate efficacy, no RCT's to confirm
- Surgery – **vulvar vestibulectomy**

Useful patient resources

- Websites:

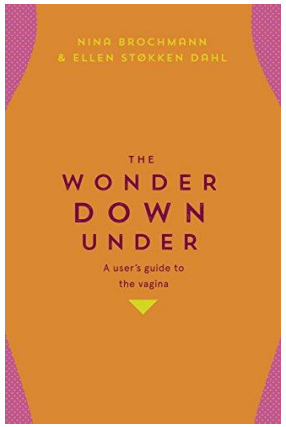
www.bssvd.org

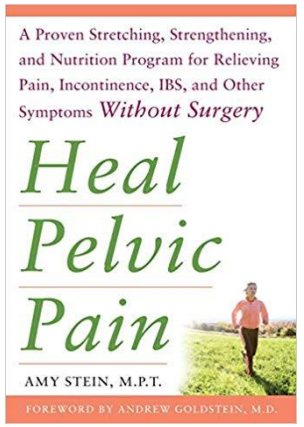
www.vulvalpainsociety.org

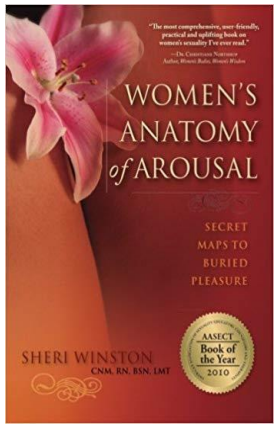
www.omgyes.com

www.vaginismus.org

4. Dilators/wands/sex toys







The clitoris vacuum device (Eros) is the only FDA approved treatment for women's sexual arousal and orgasmic disorders.

Vulvar pain syndromes

- Vulvar pain syndromes are a common cause of dyspareunia. **Contact dermatitis** from products applied to the vulva, incontinence, and daily pad use contribute to vulvar pain. Identifying and avoiding the irritant and effective management of incontinence improves pain from these causes.
- Contraceptive foam/jelly, latex condoms/diaphragms can irritate vaginas of some women.
- Management of general or local vulvodynia without a clear etiology includes pelvic physical therapy, psychotherapy, and topical or systemic medications.

Treatments that are not recommended

Herbal supplements

- Many patients are interested in trying over-the-counter herbal supplements, which are advertised widely and claim to increase sexual desire and pleasure. Patients should be informed that the **safety and efficacy of these products are unproven**, there is minimal regulatory oversight, and they are often costly.
- Nonetheless, given a **30 percent predicted placebo response** and few reported side effects, patients may elect a trial of these alternatives after being fully informed of the above limitations.

Herbal supplement

One such product is a proprietary blend of herbal supplements (Avlimil). Many of the components of Avlimil are estrogenic, and **animal study data suggest** that the product may stimulate growth of **estrogen-dependent breast tumors** .

Ju YH, Doerge DR, Helferich WG. A dietary supplement for female sexual dysfunction, Avlimil, stimulates the growth of estrogen-dependent breast tumors (MCF-7) implanted in ovariectomized athymic nude mice. Food Chem Toxicol 2008; 46:310.

Herbal supplement

Another product, a botanical feminine massage oil **(Zestra),** is applied to the clitoris, labia, and vagina. A randomized, double-blind crossover trial in 20 women reported **increased sexual arousal, orgasm, and pleasure** compared with a placebo oil; the only adverse effect reported was **mild genital burning**.

Ferguson DM, Steidle CP, Singh GS, et al. Randomized, placebo-controlled, double blind, crossover design trial of the efficacy and safety of Zestra for Women in women with and without female sexual arousal disorder. J Sex Marital Ther 2003; 29 Suppl 1:33.

آفرودیت

ED

HSDD

- Tribulus terrestris (خارخاسک)
- Zingiber officinale (زنجبیل)
- Cinnamomum verum (دارچین)
- Crocus sativus (زعفران)

I. Maleki-Saghooni N, Mirzaeii K, Hosseinzadeh H, Sadeghi R, Irani M. A systematic review and meta-analysis of clinical trials on saffron (Crocus sativus) effectiveness and safety on erectile dysfunction and semenparameters. Avicenna J Phytomed. 2018;8(3):198-209.

II. Vale FBC, Zanolla Dias de Souza K, Rezende CR, Geber S. Efficacy of Tribulus Terrestris for the treatment of premenopausal women with hypoactive sexual desire disorder: a randomized double-blinded, placebo-controlled trial. Gynecol Endocrinol. 2018;34(5):442-5.

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Take home message

Androgen: post-menopausal women HSDD, responsiveness, orgasm

FDA approved

Flibanserin (oral; 100 mg tab): premenopausal women HSDD 100 mg bedtime

Bremlanotide (Injection): premenopausal women HSDD before anticipated sexual activity

Treatment for female orgasmic disorder consists principally of **non pharmacologic** treatment (education, psychosocial interventions, and the **use of devices**)

Thank you
Any question?