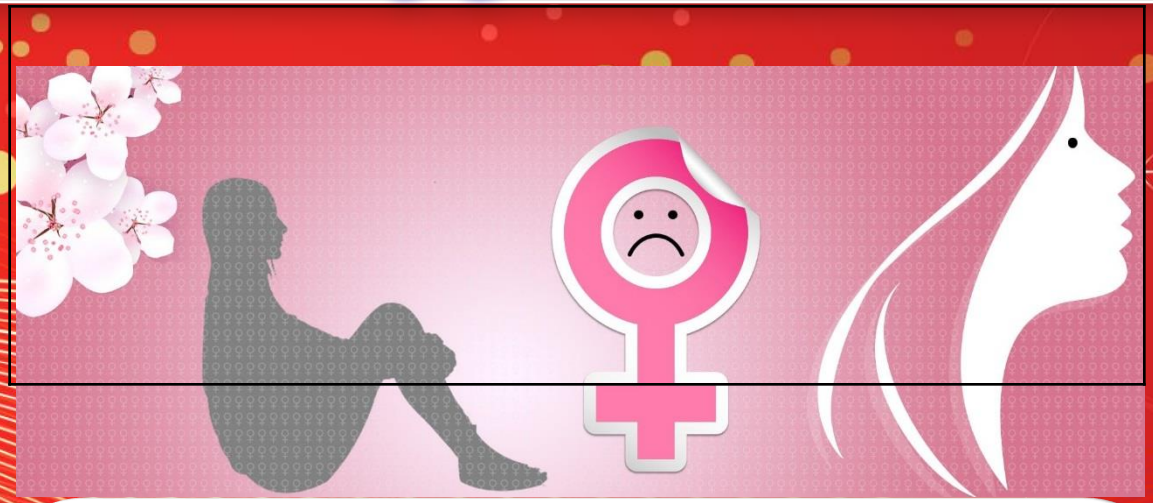
In the name of GOD

Medical treatment of Female Sexual Dysfunction



Fahimeh Ramezani Tehrani
Professor

Reproductive Endocrinology Research Center
Research institute for Endocrine Sciences,
Shahid Beheshti University of Medical Sciences

December 2023

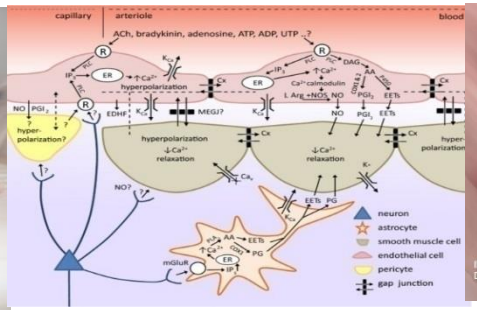
Outlines

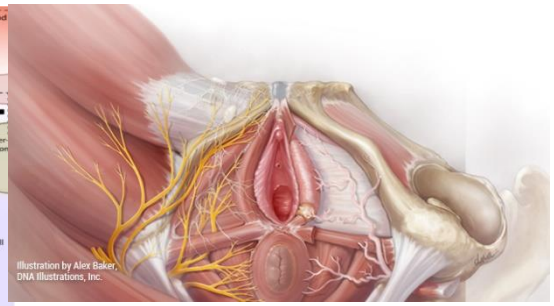
1. Females sexual function &influential factors
2. Sexual Desire/Arousal Dysfunction
3. Orgasm Disorder
4. Genito-Pelvic Pain/ Penetration Disorder

SEXUAL HEALTH &
SEXUAL RIGHTS are
FUNDAMENTAL!
for WELL-BEING

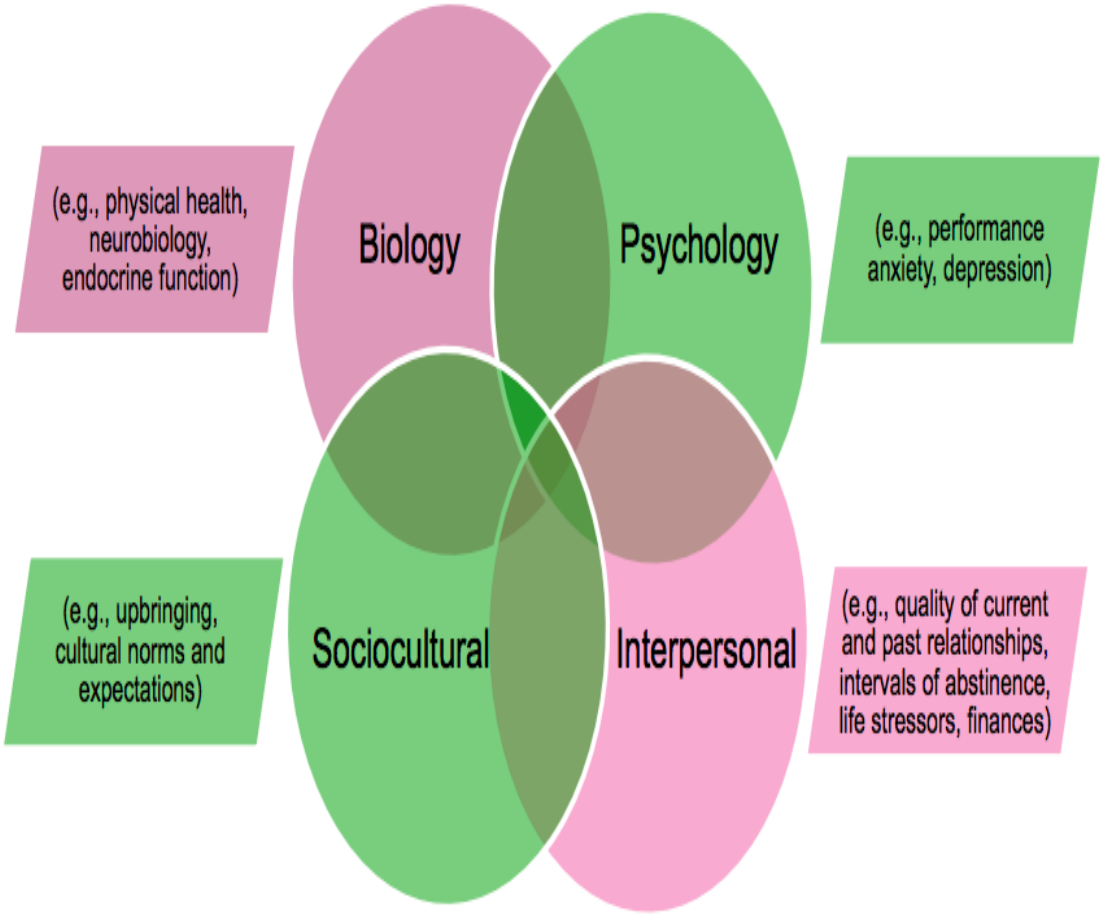
Female Sexual Function Is A Complex

Sexual function results from a complex **neurovascular** process that is controlled by **psychological, social** and **hormonal** inputs.





Biopsychosocial Model of Female Sexual Response



Althof SE, et al. *J Sex Med.* 2005;26:793-800.
Rosen RC, Barsky JL. *Obstet Gynecol Clin North Am.* 2006;334:515-526.

Points need to be considered in approach to Sexuality

- The spectrum of normal sexual response varies from one woman to another
- Sexual response varies throughout a woman's lifetime
- Physicians should be aware of their patients' values, attitude and concerns about their sexuality

FSD IS A CHALLENGING TOPIC

- Sensitive topic
- Inadequate training
- Insufficient clinical time with patients to discuss in depth sexual history
- Limited treatment options

Importance

- Sexual functioning is an important part of the human experience
- Despite marked reductions in sex hormones with menopause and age, there is no universal decline in sexuality.
- More than 75% of the middle-aged women in the study of Women's Health Across the Nation (SWAN) reported that sex was moderately to extremely important.
- FSD can negatively affect health-related quality of life, self-esteem, mood, relationships with sexual partners and general well-being
- More than one half of divorce in Iran is directly **or indirectly related to sexual problems.**

•Quality of Life and Health Burden 2019, J Sex Med 2009, WHO 2011 , Menopause 2020, Fer Stril 2023,

Genetic & sexual dysfunction

Journal of Sex Research
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/hjsr20

Bringing Sex Research into the 21st Century: Genetic and Epigenetic Approaches on Female Sexual Function

Andrea Burri [a] [b]
[a] Department of Twin Research and Genetic Epidemiology, King's College, London
[b] Department of Psychology, University of Zurich
Published online: 12 Mar 2013.

- DRD4-5 locus haplotype (Dopamine receptor) is associated with desire, arousal and FSD score.
- A variant of 5H2 Serotonin gene(GG) is associated with low desire/arousal scores.
- Interleukin receptor gene is associated with vulvudynia
- GWAS approach demonstrated that 5HT1E Serotonin receptor gene is associated with arousal problem and Parvalbumin gene(GABA interneuron) is associated with low FSF.

Fetal programing of sexual function

Molecular and Cellular Endocrinology 382 (2014) 538–549

Contents lists available at ScienceDirect

Molecular and Cellular Endocrinology

journal homepage: www.elsevier.com/locate/mce

Review

Fetal programming of sexual development and reproductive function

Elena Zambrano [a,*], Carolina Guzmán [b], Guadalupe L. Rodríguez-González [a], Marta Durand-Carbajal [a], Peter W. Nathanielsz [c]

Arch Sex Behav (2017) 46:2033–2042
DOI 10.1007/s10508-016-0919-8

ORIGINAL PAPER

A Comparison of Sexual Function in Women with Polycystic Ovary Syndrome (PCOS) Whose Mothers Had PCOS During Their Pregnancy Period with Those Without PCOS

Mahsa Noroozzadeh [1] · Fahimeh Ramezani Tehrani [1] · Mahnaz Bahri Khomami [1] · Fereidoun Azizi [2]

Factors affecting sexual response

- Mental health
  - Depressed women may masturbate more frequently than normal one
    Sexual dysfunction in the partner
- Relationship
- Childhood sexual abuse/rape
- Pregnancy
  - Sexual value system, folklore, religious beliefs
  - Physical changes
  - Body image
  - Medical restrictions
  - Emotional needs
- Postpartum
  - PRL
  - Nursing
  - Low self-esteem
  - Negative body image
- Co-morbidities
  - Cancer
  - Diabetes Mellitus
  - Multiple Sclerosis
  - Endometriosis

Factors with uncertain effect of sexual response

- Aging and menopause
- Androgen deficiency and androgen excess
- Mode of delivery
- Prolapse of genital tract
- Hystrectomy

Hysterectomy

- Decreased sexual pleasure due to lack of uterine contraction?
- Cervix and orgasm?
- There is no definite correlation between sexual activity and method of hysterectomy

Table V. Percentage of patients reporting symptom improvement after the different techı

	TAH	*VH*	*LH*
Urinary symptoms			
Diurnal frequency	26	16.1	10.5
Nocturia	8.2	8.1	7.9
Dysuria	–	–	2.6
Straining to void	4.1	6.5	2.6
Poor stream	6.8	6.5	7.9
Hesitancy	5.5	8.1	7.9
Postmicturition dribble	8.2	16.1	13.2
Sense of incomplete emptying	13.7	16.1	13.2
Stress incontinence	28.8	24.2	18.2
Urge incontinence	13.7	12.9	15.8
Urgency	19.2	22.6	13.2
Leak without warning	13.7	4.8	7.9
Leak during sexual intercourse	13.7	6.5	12.6
Sexual symptoms			
Coital frequency	44.1	44.3	44.7
Deep dyspareunia	18.8	19.7	26.3
Libido	11.6	19.7	2.6[a]
Achievement of orgasm	33.3	32.8	21.1
Overall satisfaction	25.7	28.3	28.9

Urologia. 2007

Mode of delivery

HHS Public Access
Author manuscript
Female Pelvic Med Reconstr Surg. Author manuscript; available in PMC 2015 August 11.

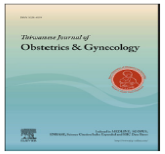
Published in final edited form as:
Female Pelvic Med Reconstr Surg. 2013 ; 19(1): 13–16. doi:10.1097/SPV.0b013e31827bfd7b.

Evaluation of Pelvic Floor Symptoms and Sexual Function in Primiparous Women Who Underwent Operative Vaginal Delivery Versus Cesarean Delivery for Second-Stage Arrest

Contents lists available at ScienceDirect

Taiwanese Journal of Obstetrics & Gynecology

journal homepage: www.tjog-online.com



Review Article

Pelvic floor dysfunction, and effects of pregnancy and mode of delivery on pelvic floor

There is no definite correlation between sexual activity and method of delivery

Phases of the Sexual Response Cycle

- Phase 1:Excitement
- Phase 2: Plateau
- Phase 3: Orgasm
- Phase 4: Resolution

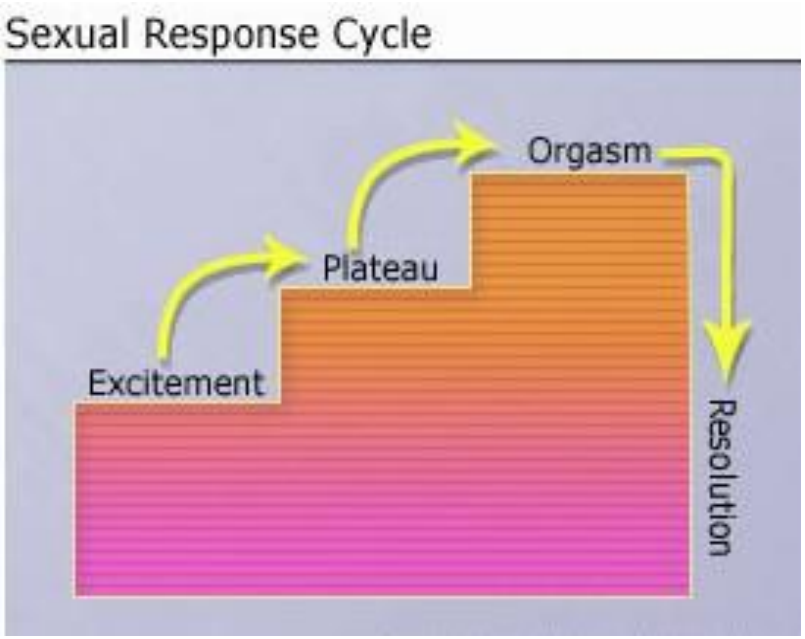
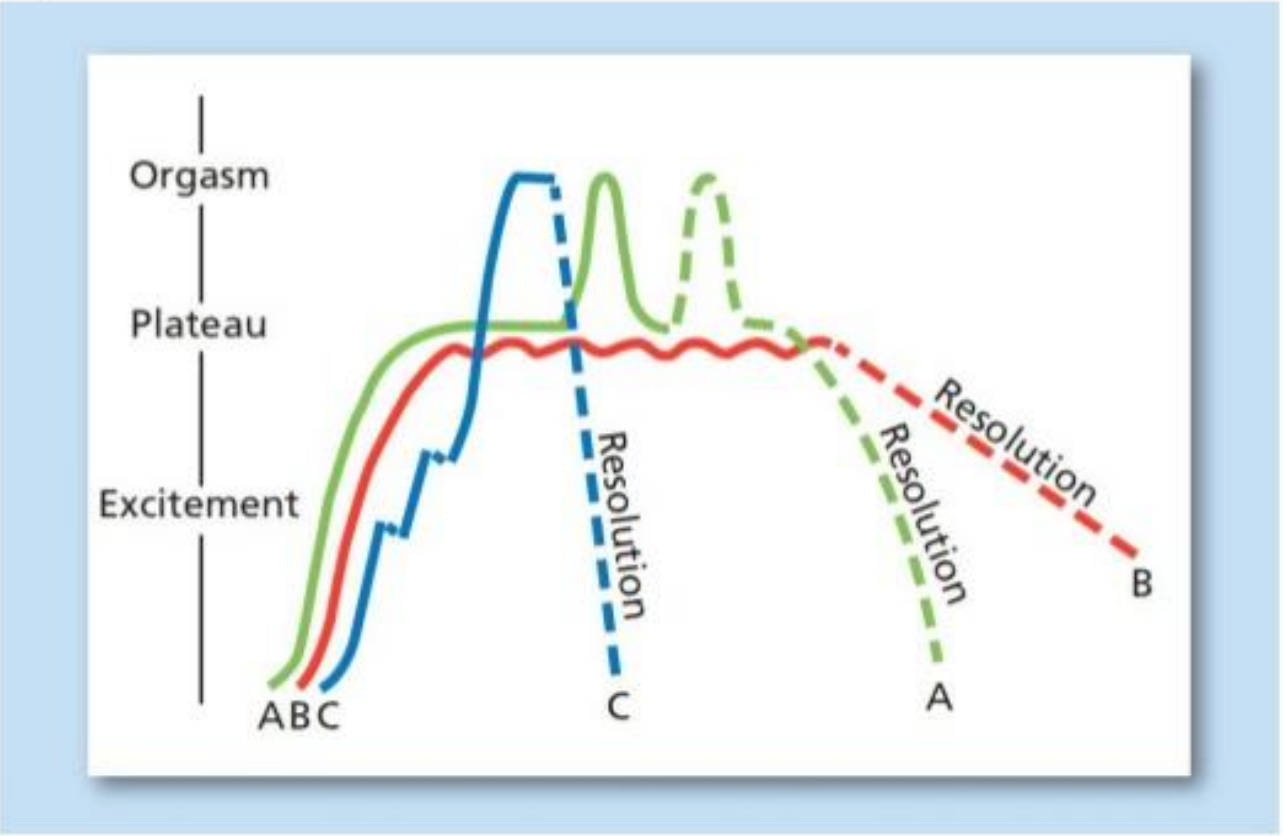


Figure 10.4 The Female Sexual-Response Cycle
Women can experience several different patterns of sexual response. In Pattern A, a woman experiences excitement, a plateau, and orgasm in a manner similar to a man. Unlike a man, the woman does not have a refractory period and can experience several orgasms before entering resolution. In Pattern B, there is a longer plateau period but no orgasm, and in Pattern C, the woman goes from excitement to orgasm to a quick resolution without experiencing a plateau period.

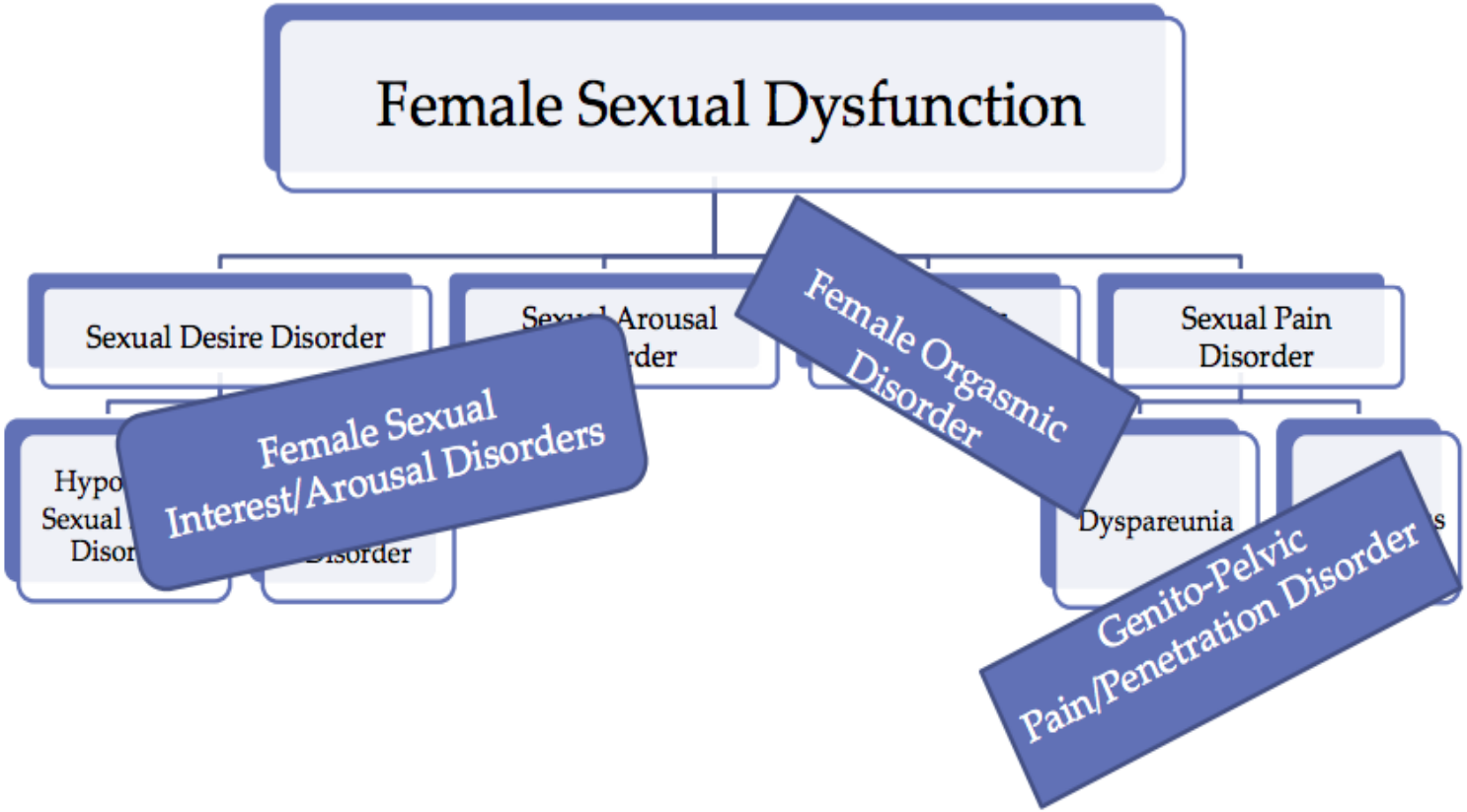


Definitions of Female Sexual Dysfunction

- WHO: the various ways in which an individual is unable to participate in a sexual relationship as he or she would wish.

- DSM-IV*: Disturbances in sexual desire and in the psychophysiological changes that characterize the sexual response cycle and cause marked distress and interpersonal difficulty. (a disturbance in the processes that characterize the sexual response cycle or by pain associated with sexual intercourse.

Classifying FSD/DSM-V

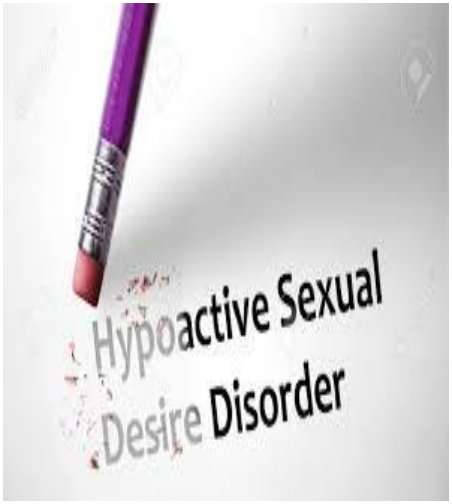


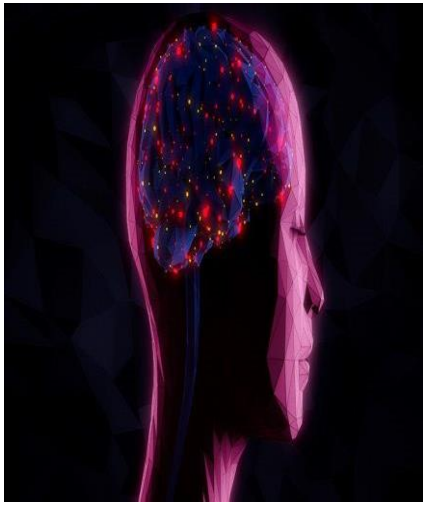
Interest/arousal disorder

A lack of, or significant decrease in, at least three of the following:

- Interest in sexual activity
- Sexual or erotic thoughts or fantasies
- Initiation of sexual activity and responsiveness to a partner's initiation
- Excitement or pleasure during all or almost all sexual activity
- Interest or arousal in response to internal or external sexual orerotic cues (eg, written, verbal, visual)
- Genital or non-genital sensations during sexual activity in almost all or all sexual encounters

Symptoms have persisted for a minimum of 6 months and cause clinically significant distress in the individual.





Clinical Management Guidelines for Obstetrician–GynecologistsVOL. 134, NO. 1, JULY 2019,

Orgasmic disorder

Marked delay in, marked infrequency of, or absence of orgasm, or markedly reduced intensity of orgasmic sensations, in almost all or all occasions of sexual activity.

Symptoms have persisted for a minimum of 6 months and cause clinically significant distress in the individual.

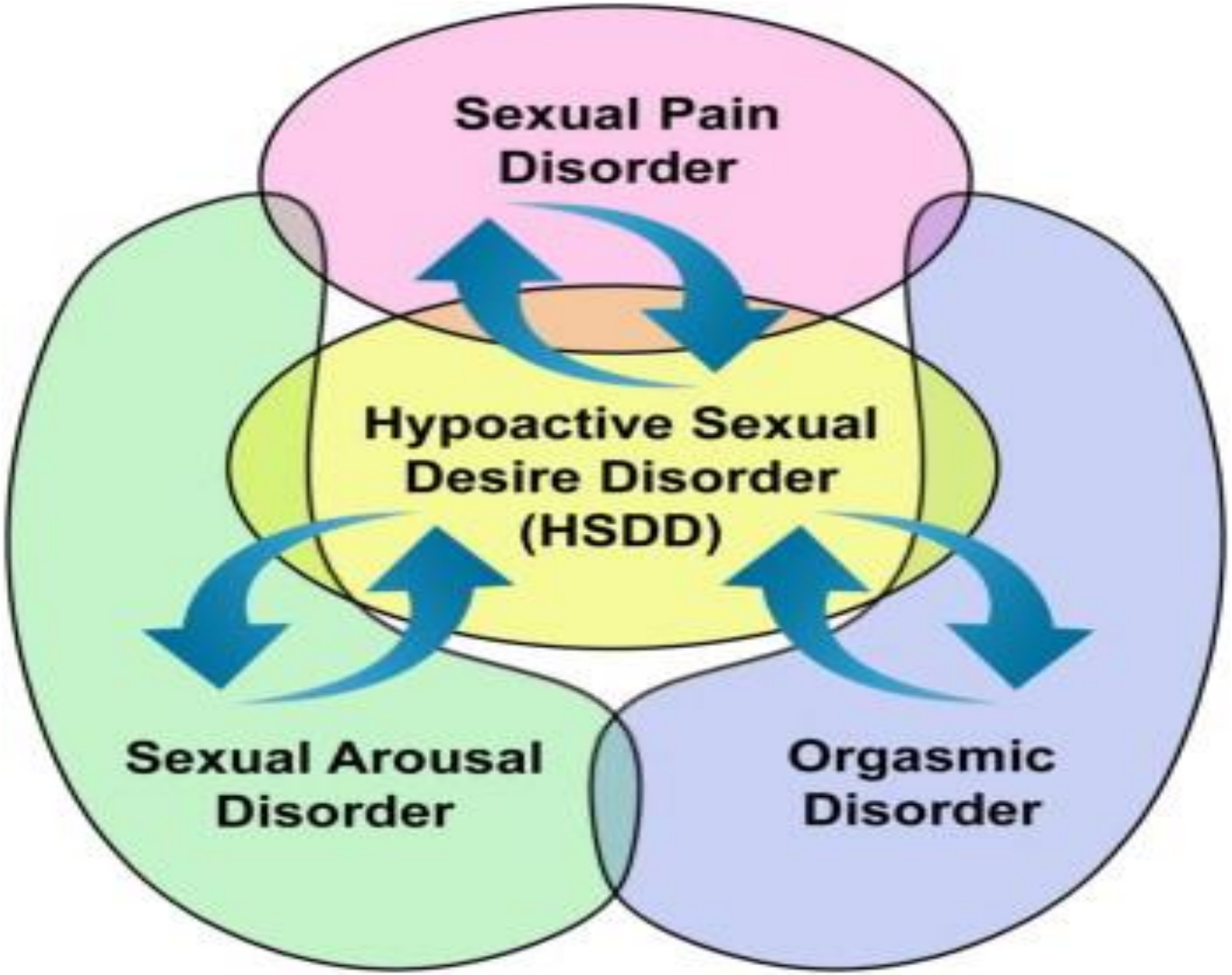
Clinical Management Guidelines for Obstetrician–GynecologistsVOL. 134, NO. 1, JULY 2019,

Genito-pelvic pain/penetration disorder

The persistent or recurrent presence of one or more of the following symptoms:

- difficulty having intercourse
- marked vulvovaginal or pelvic pain during intercourse or penetration attempts
- marked fear or anxiety about vulvovaginal or pelvic pain anticipating, during, or resulting from vaginal penetration
- marked tensing or tightening of the pelvic floor muscles during attempted vaginal penetration
- Symptoms have persisted for a minimum of 6 months and cause clinically significant distress in the individual.

Clinical Management Guidelines for Obstetrician–GynecologistsVOL. 134, NO. 1, JULY 2019,



Buster JE. Sex and the 50 something woman: strategies for restoring satisfaction. Contemp Ob Gyn 2012:32–9.

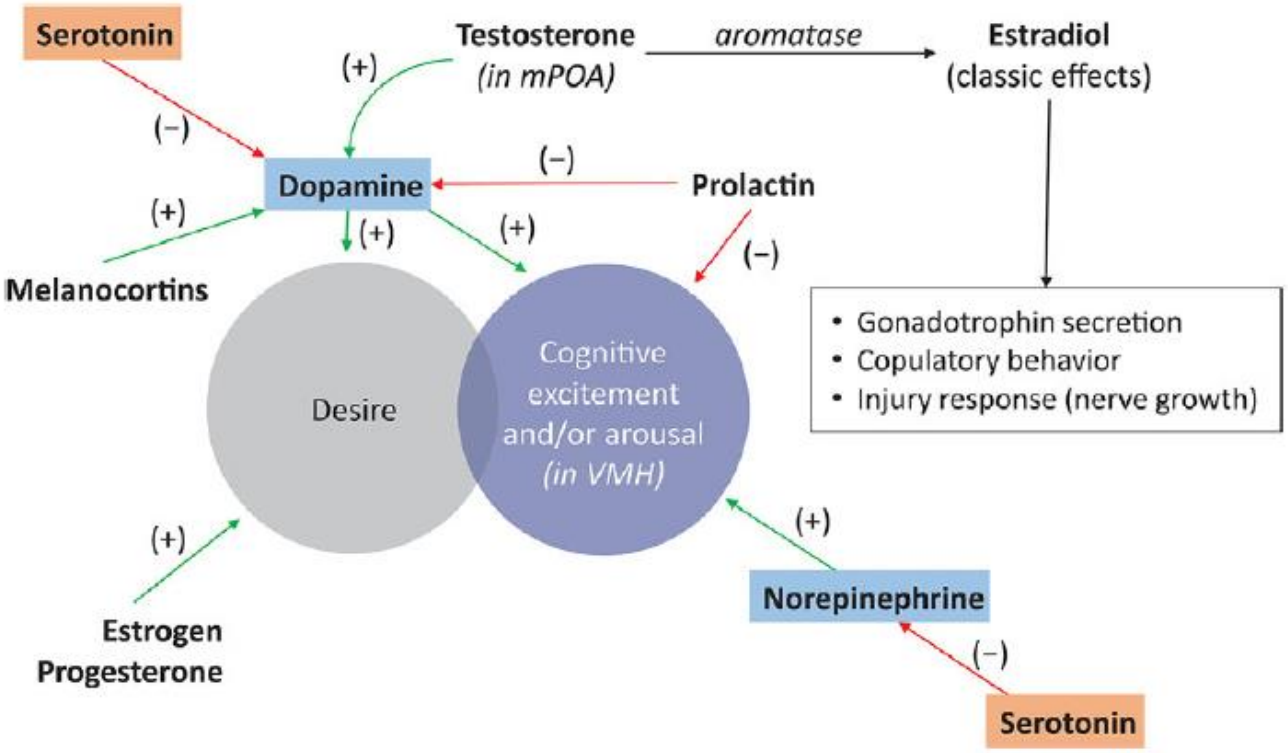
Prevalence

- 38% of women will experience some types of FSD over their lifetime(WHO 2020).

- Meta-analysis on FSD(2016)
  - 28.2% of women lack sexual interest
  - 25% of women do not experience orgasm
  - 20.6% of women report lubrication difficulties
  - 25% of women report sex is not pleasurable

- Iranian sexual health study(Ramezani 2018)
  - Prevalence in reproductive aged women: 37.3%
  - 18% of women had never have experienced orgasm

Central effects of neurotransmitters and hormones on sexual functioning



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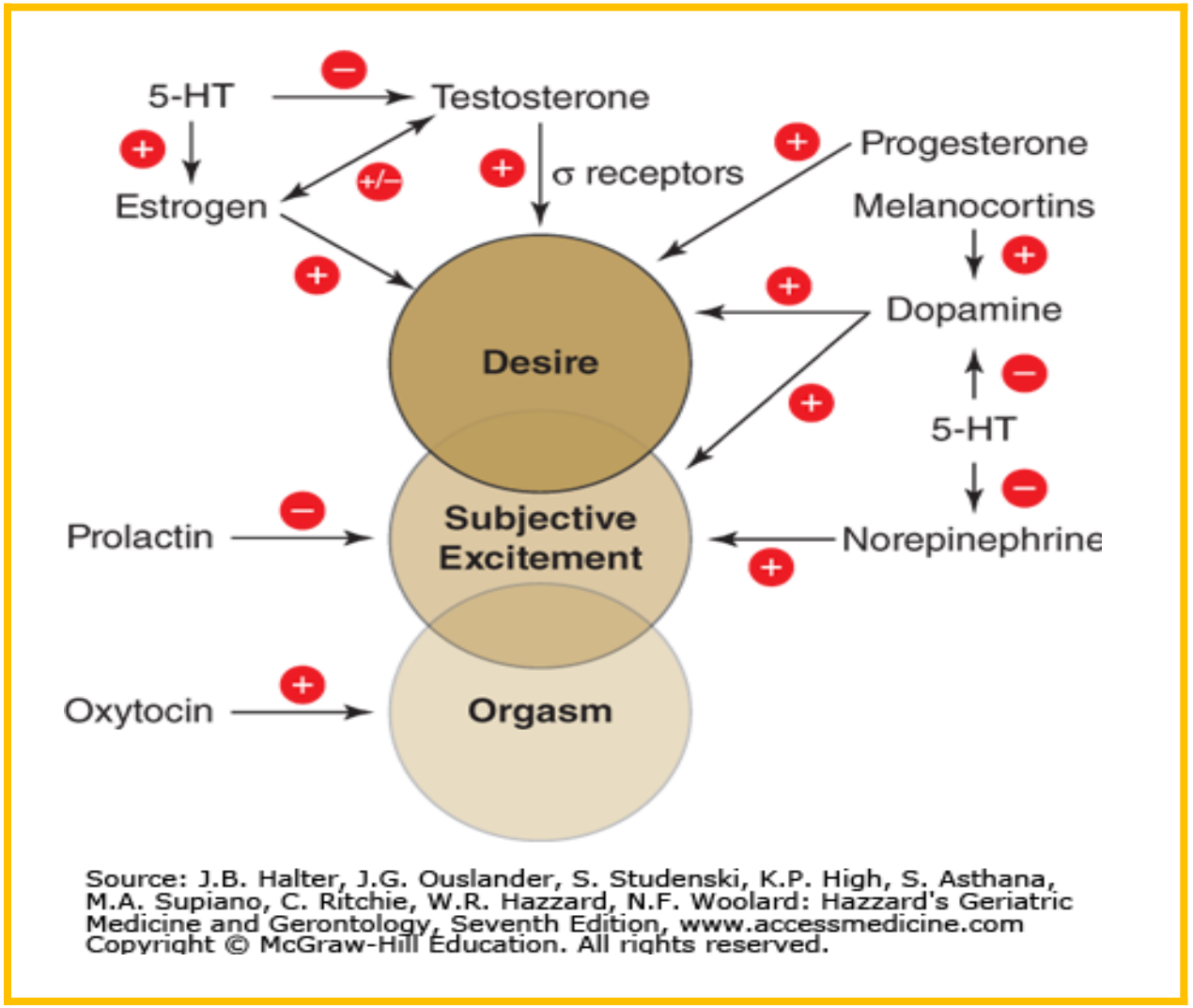
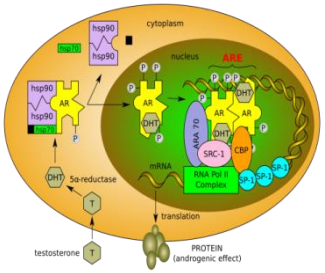
Hormones & Sexual function



Source: J.B. Halter, J.G. Ouslander, S. Studenski, K.P. High, S. Asthana, M.A. Supiano, C. Ritchie, W.R. Hazzard, N.F. Woolard: Hazzard's Geriatric Medicine and Gerontology, Seventh Edition, www.accessmedicine.com

Androgens

- **Androgens** play an important role in healthy female sexual function, especially in sexual interest and desire, arousal, and orgasm



Vulvar epithelium

Vaginal mucosa

Submucosa

Stroma

Smooth muscle

Vascular endothelium

Relaxation vaginal smooth muscle

Nitric oxide synthetize activity

Circulating Androgen Levels and Self-reported Sexual Function in Women

- A community-based, cross-sectional study of 1423 women aged 18 to 75 years,
- who were randomly recruited via the electoral roll in Victoria,
- Main Outcome Measures Domain scores of the Profile of Female Sexual Function (PFSF) and serum levels of total and free testosterone, androstenedione, and dehydroepiandrosterone sulfate
- No clinically significant relationships between having a low score for any PFSF domain and having a low serum total or free testosterone or androstenedione level was demonstrated

JAMA, July 2005, Vol 294

International Journal of Impotence Research
https://doi.org/10.1038/s41443-017-0006-2

ARTICLE

Sexual function in women with polycystic ovary syndrome and their hormonal and clinical correlations

Fatemeh Nasiri Amiri[1] · Fahimeh Ramezani Tehrani[2] · Sedighe Esmailzadeh[1] · Maryam Tohidi[3] · Fereidoun Azizi[4]

Association of PCOS and Its Clinical Signs with Sexual Function among Iranian Women Affected by PCOS

Somayeh Hashemi, MS, Fahimeh Ramezani Tehrani, MD, Maryam Farahmand, MS, and Mahnaz Bahri Khomami, MS

J Sex Med 2014;11:2508–2514

No significant relationships between any FSF domain and total or free testosterone

CAIN PROJECT

DHEAS &Sexual function

Table 4. Relationship Between Low Dehydroepiandrosterone Sulfate Level and Profile of Female Sexual Function Domain Scores*

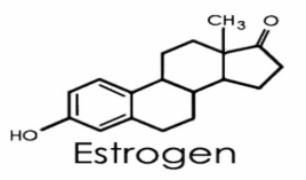
	No. (%) of Women			
	DHEAS <294.8 ng/mL (0.8 μmol/L)	DHEAS ≥294.8 ng/mL (0.8 μmol/L)	OR (95% CI)	*P* Value
Responsiveness				
0 (4.1%)	7 (29.2)	17 (70.8)	3.90 (1.54-9.81)	.004
>0	54 (9.6)	511 (90.4)		
	DHEAS <773.8 ng/mL (2.1 μmol/L)	DHEAS ≥773.8 ng/mL (2.1 μmol/L)		
Desire†				
Lowest 5.1%	5 (29.4)	12 (70.6)	3.86 (1.27-11.67)	.02
Not low	31 (9.7)	287 (90.3)		
Arousal†				
Lowest 5.3%	7 (38.9)	11 (61.1)	6.39 (2.30-17.73)	<.001
Not low	29 (9.1)	291 (90.9)		
Responsiveness†				
Lowest 5.4%	7 (38.3)	11 (61.2)	6.59 (2.37-18.34)	<.001
Not low	28 (8.8)	290 (91.2)		

Abbreviations: CI, confidence interval; DHEAS, dehydroepiandrosterone sulfate; OR, odds ratio.
*The DHEAS cutoff of 294.8 ng/mL applies to women ≥45 years; the cutoff of 773.8 ng/mL applies to women 18 to 44 years.
†For women aged 18 to 44 years, low desire, arousal, and responsiveness were indicated by being in the cutoff closest to the fifth percentile.

J SEX Med 2015

Estrogen

- Estrogen is essential for the maintenance of health
- A decline in serum estrogen levels results in



Thinning of vaginal mucosal epithelium

Atrophy of vaginal wall smooth muscle

Vaginal pH shifts from acidic to alkaline

Vaginal secretion are reduced, contributing to genital symptoms of dryness, irritation/burning, pruritus, and recurrent vaginitis

Vaginal vault becomes pale in appearance

HSSD

Dyspareunia

Estradiol < 35 pg/mL is associated with FSD

Oxytocin and vasopressin

- The hormones oxytocin and vasopressin are implicated in regulating both male and female sexual motivation.
- Oxytocin is released at orgasm and is associated with both sexual pleasure and the formation of emotional bonds.
- Insufficient oxytocin release may subsequently diminish sexual reproduction arousal and motivation in females.
- High levels of vasopressin decreases in sexual motivation for females.

Management of Sexual Desire/Arousal Dysfunction

Decreased Sexual Desire Screener

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 and 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 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. Medication, 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***

When completed, please give this form back to your clinician.

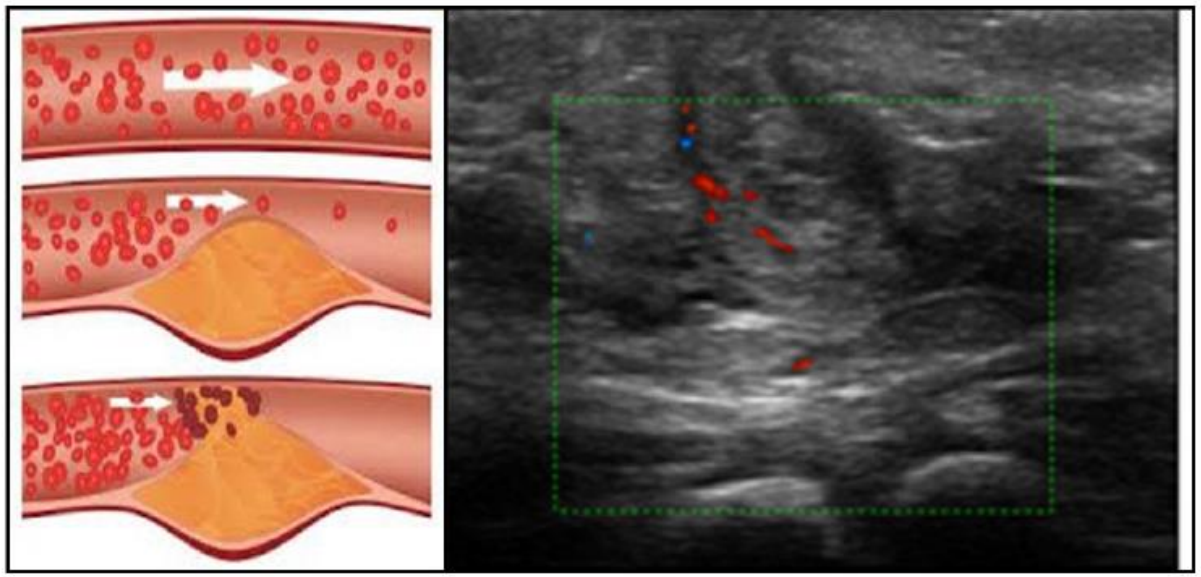
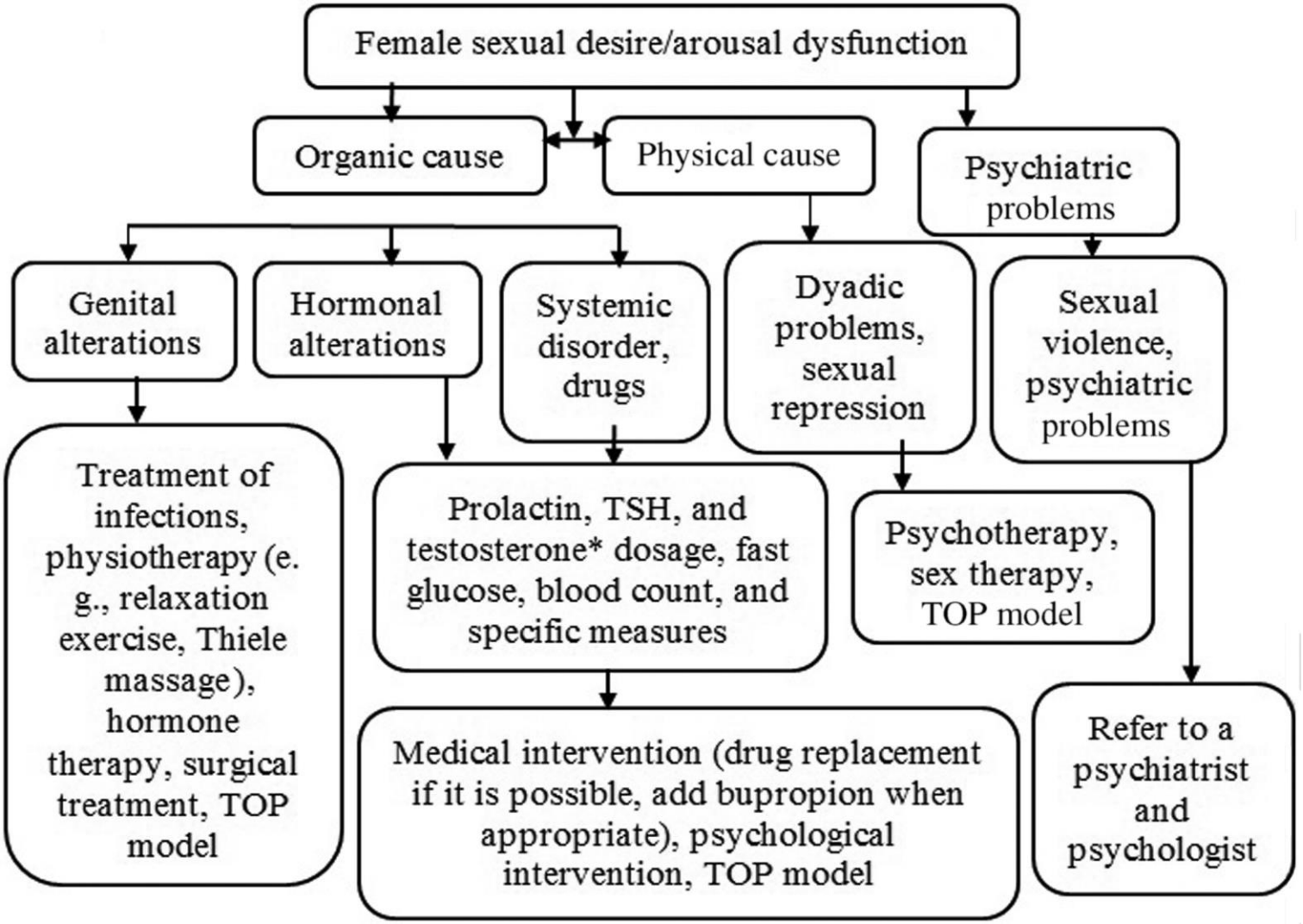


Fig. (1). Clitoral ultrasound as a diagnostic tool for investigating genital vascular alterations in women with sexual dysfunction (*A higher resolution / colour version of this figure is available in the electronic copy of the article*).

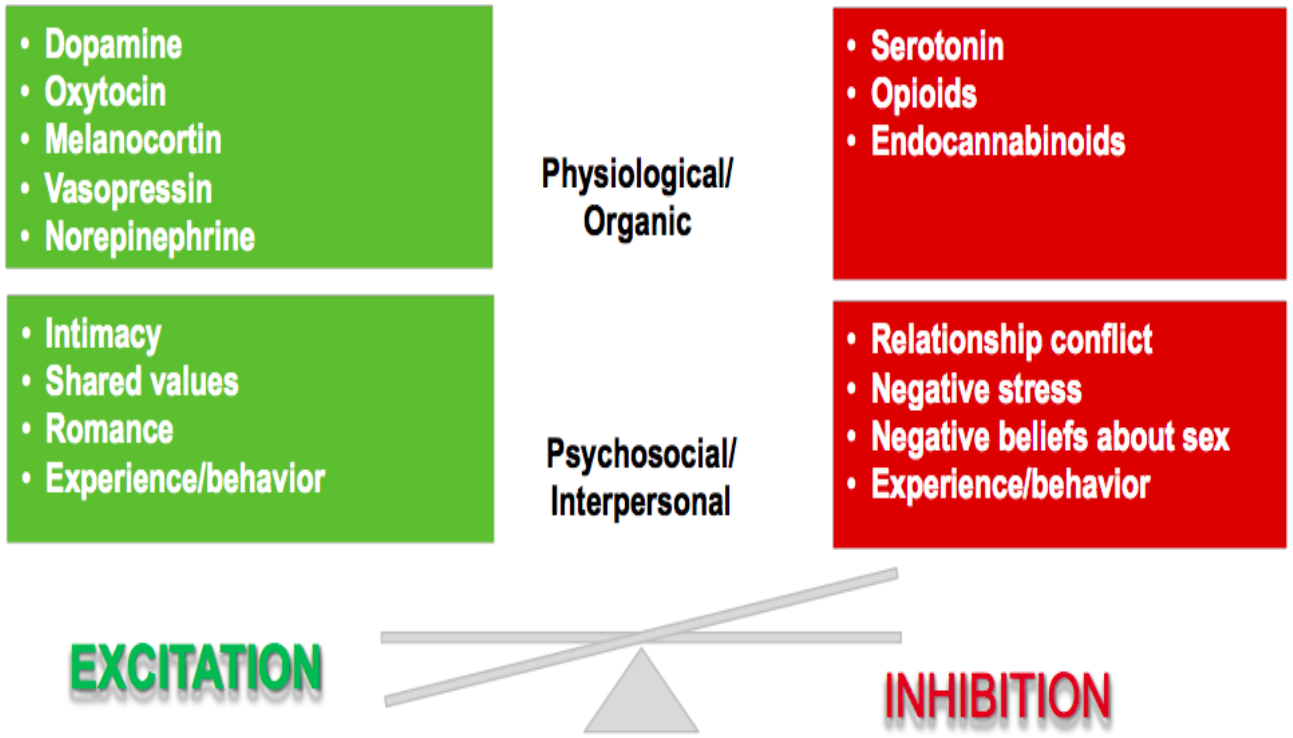
Algorithm for the management of female sexual desire/arousal dysfunction



da Silva Lara, L. A., Scalco, S. C. P., Troncon, J. K. & Lopes, G. P. 2017. A Model for the Management of Female Sexual Dysfunctions. *Revista Brasileira de Ginecologia e Obstetrícia/RBGO Gynecology and Obstetrics,* 39**,** 184-194

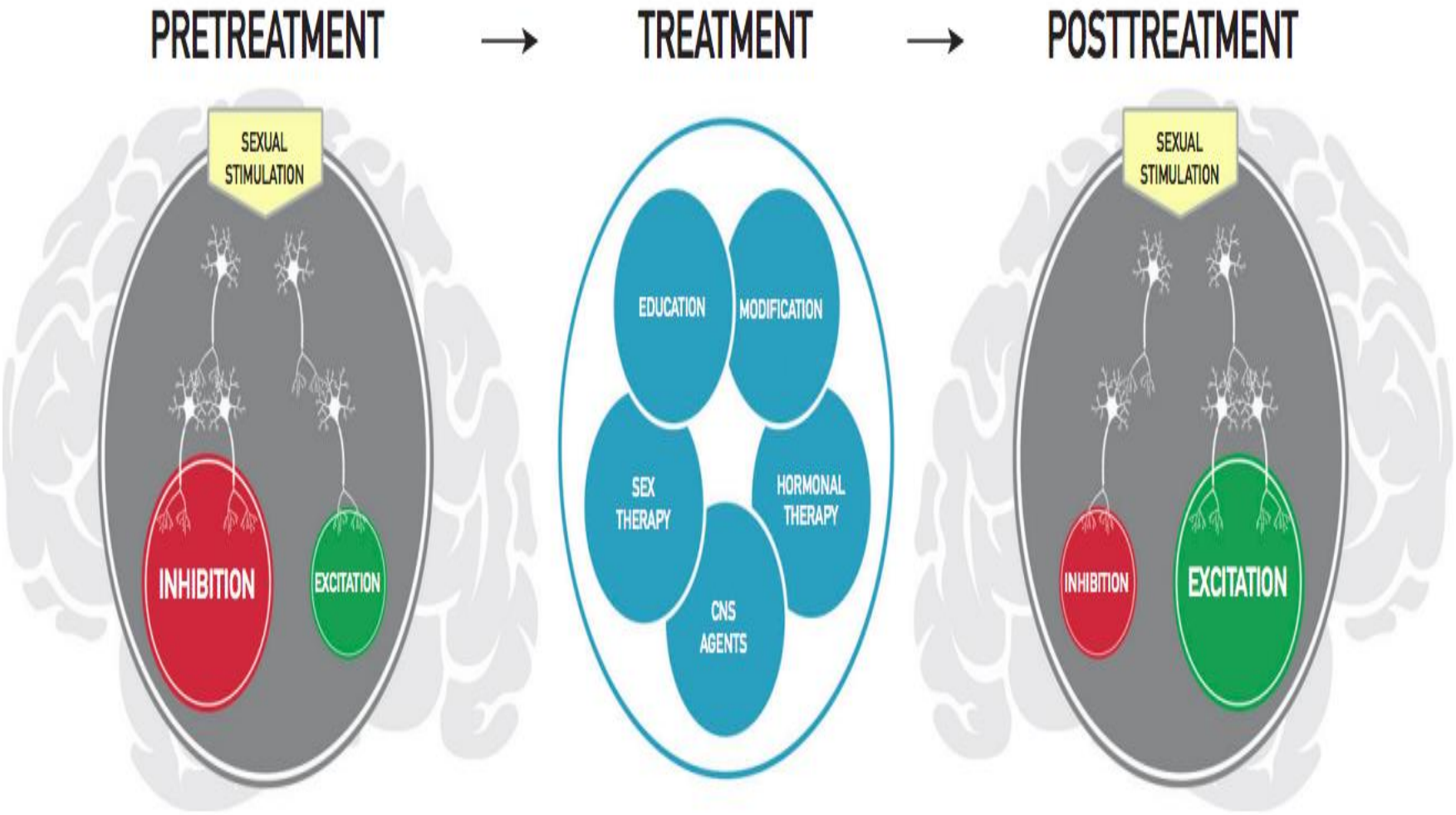
Interest/arousal disorder

Etiology of HSDD: Imbalance Between Excitation/Inhibition



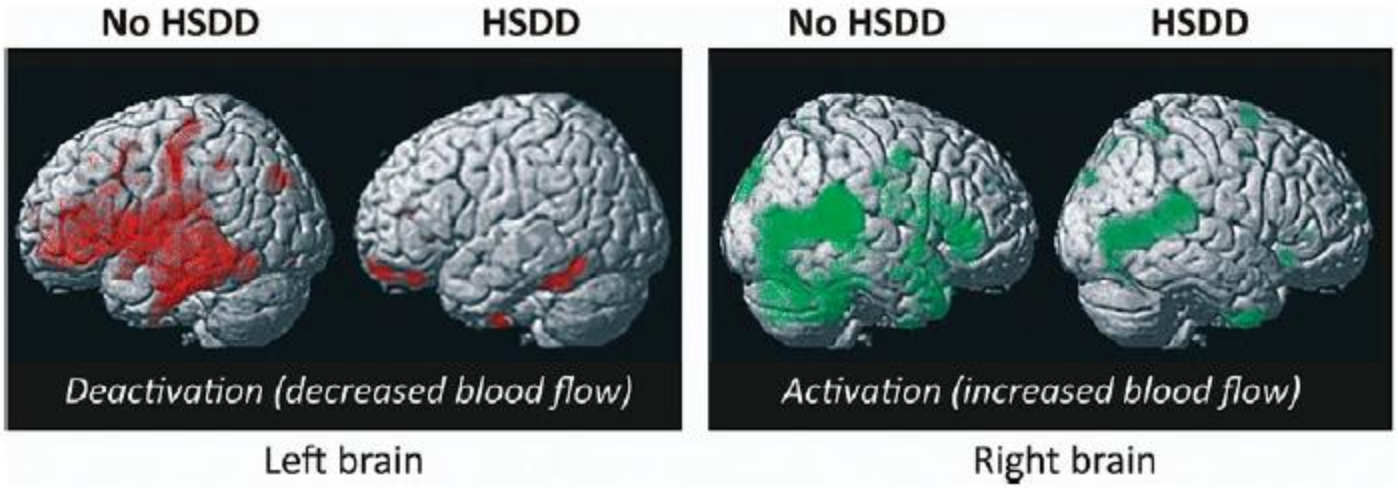
Bancroft J, et al. *J Sex Res*. 2009;46:121-142.
Perelman MA. *J Sex Med*. 2009;6:629-32.

In Women With HSDD
The Effect Of Treatments On Sexual Desire



Imaging of neural activity in women with or without HSDD. Changes in neural activity in response to viewing an erotic video in women with or without HSDD were assessed by PET.

CNS Spectrums 2020



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Flibanserin (tradename Addyi)

NO!

سامانه اطلاعات دارویی کشور
National Formulary OF IRAN

- ***Mechanism action:*** Serotonin A1 receptor agonist; serotonin A2 receptor antagonist. Treat HSDD by increasing levels of dopamine and noradrenaline and lowering levels of serotonin in the brain
- ***First Global Approval (FDA)*** for hypoactive sexual desire disorder (HSDD) in August 2015
- FDA has summarized flibanserin's overall demonstrated efficacy as statistically significant improvements in sexual desire with an estimated increase of ~0.5–1.0 additional sexually satisfying event per month
- ***Administration*:** 100 mg PO once daily at bedtime
- ***Most frequent adverse events:*** Dizziness, somnolence, nausea, fatigue

https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/022526lbl.pdf

Systematic Review and Meta-analysis of Flibanserin's Effects and Adverse Events in Women with Hypoactive Sexual Desire Disorder

- The efficacy of flibanserin in women with HSDD was not found to be significantly different compared with placebo. Additional trials are required to clarify the efficacy of flibanserin for the treatment of HSDD

- The most common causes of heterogeneity were black ethnicity, duration of therapy, age of participants and duration of marital relationship.

- Given the modest efficacy and potential for significant side effects, discussion is ongoing to further define the clinical significance of efficacy results and the broad applicability and use of flibanserin across diverse patient populations

Hassan Saadat S, Panahi Y, Hosseinialhashemi M, Kabir A, Rahmani K, Sahebkar A. Systematic review and meta-analysis of flibanserin's effects and adverse events in women with hypoactive sexual desire disorder. Current drug metabolism. 2017;18(1):78-85.

Bremelanotide (*Vyleesi*™)

- ***Mechanism action***: Melanocortin receptor agonist
- Received its first approval on June 2019 in the USA
- Approved for use in **premenopausal women** with acquired, generalized HSDD, as characterized by low sexual desire that causes marked distress or interpersonal difficulty
- ***Administration***: subcutaneously in the abdomen or thigh, as needed, ≥ 45 min before anticipated sexual activity
- ***The most common side effects***: nausea and vomiting, flushing, injection site reactions and headache.
- ***Pharmacokinetics***: Mean terminal elimination half-life is ≈ 2.7 h and mean clearance is 6.5 L/h / Median time to peak plasma concentration is ≈ 1 h and absolute bioavailability is 100%

https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/210557s000lbl.pdf

Testosterone

- Androgens, including testosterone, are essential hormones for development and maintenance of female sexual anatomy and physiology and modulation of sexual behavior.
- Testosterone has many physiological actions in women,
  - Directly through its cell-specific receptor,
  - None receptor-mediated actions,
  - Conversion to 5a-DHT and Estrogens.
- There is no testosterone level for diagnosis of HSDD or for use as a treatment target.
- Total testosterone and SHBG should be measured before initiating therapy.
- Proper dosing should attain and maintain total testosterone levels in the premenopausal physiological range.
- If an approved female formulation is not available, one-tenth of a standard male dose of 1% transdermal testosterone or about 300 mcg/day can usually achieve the normal premenopausal physiological range.
- Additional testing and alternative strategies may be required to assess failure to respond to typical testosterone treatment, particularly when testosterone or SHBG levels are high.

Testosterone

- ***Mechanism of Action***: ↑sexual activity, libido and pleasure
- ***The most common side effects*** : hirsutism and acne
- Currently, there are **no FDA-approved** testosterone therapies for FSD
- The use of 300 µg/d in **surgical and natural menopause** is an effective plan to manage HSDD in the short- and long-term. In the setting of natural or surgical menopause.
- The use of testosterone has been shown to improve components of FSD including sexual desire, arousal, pleasure, and overall satisfaction.
- There are no compelling data to support that it causes any type of cancers, such as breast cancer or endometrial cancer.
- The transdermal administration route has minimum side effects.
- Administering testosterone orally may increase the risk of blood clots

Safety and efficacy of testosterone for women: a systematic review and meta-analysis of randomised controlled trial data

Rakibul M Islam, Robin J Bell, Sally Green, Matthew J Page, Susan R Davis

Lancet Diabetes Endocrinol 2019

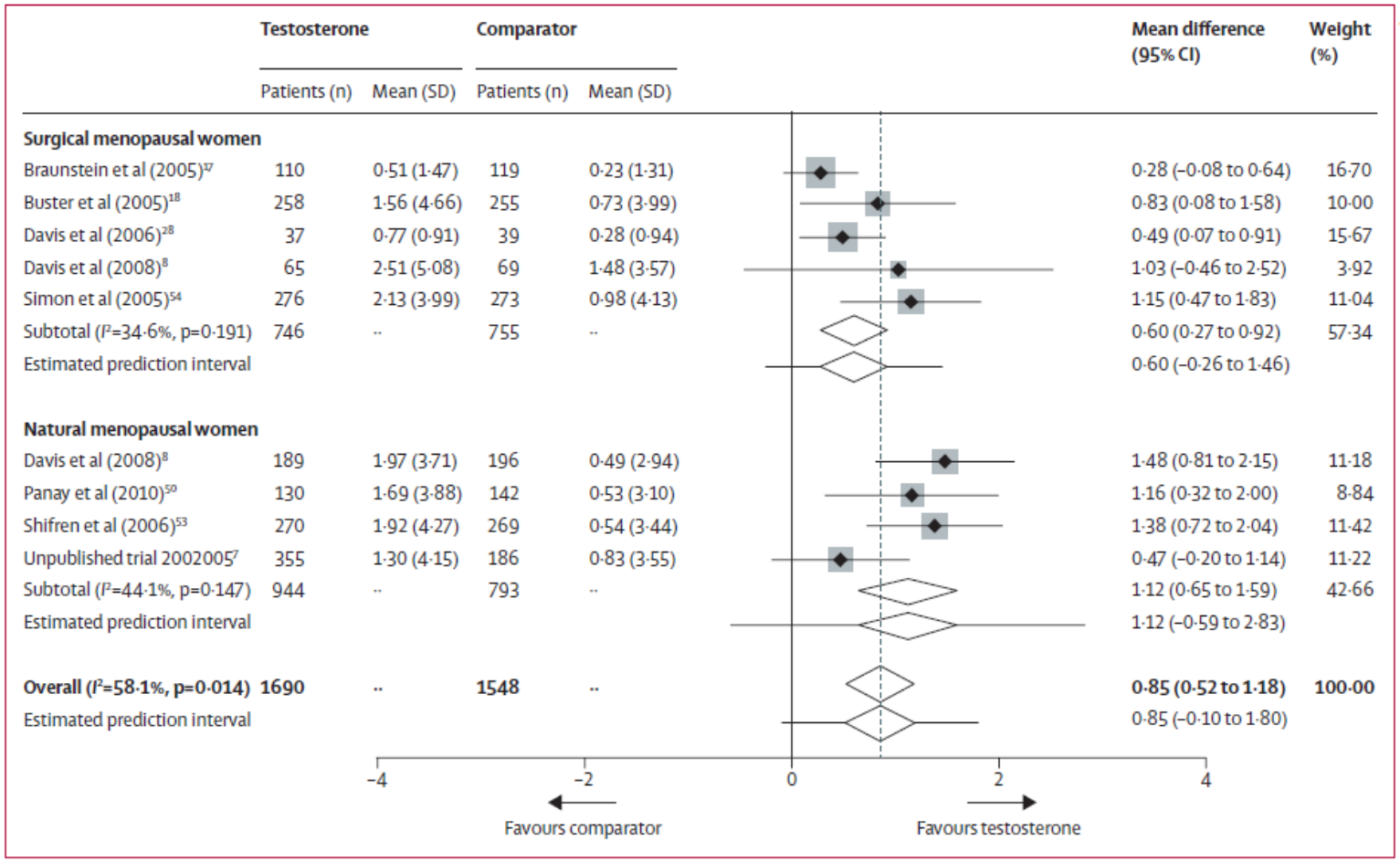


Figure 2: **Effect of testosterone versus comparator on satisfying sexual events, by menopausal status**

CAIN PROJECT

Testosterone therapy and other treatment modalities for female sexual dysfunction

2020

Catherine F. Ingram[a,*], *Kelly S. Payne*[a,*], *Marisa Messore*[b], *and Jason M. Scovell*[a,c]

Evaluation	Treatment	Follow-Up
1. Post-menopausal 2. No cutoff blood T level 3. Diagnosis of HSDD on clinical assessment a) ISSWSH criteria b) ICD criteria (11th edition) 4. Fully evaluate and treat FSD based on biopsychosocial model.	1. Seek to achieve physiological pre-menopausal serum T levels. 2.Use approved male formulation when approved female testosterone unavail-able 3. Avoid compounded T formulations when possible. 4. Avoid formulations that achieve supra-physiologic levels (i.e., pellets and injections) 5. Measure baseline T before initiating T therapy	1. Repeat serum T measurement 3-6 weeks after initiating T therapy 2. Monitor for signs of androgen excess every 6 months 3. Monitor clinical response every 6 months 4. Discontinue after 6 months if no bene-fit is observed

- Testosterone therapy is effective to treat FSD in postmenopausal women.
- More data is required to evaluate the long-term safety data on the effects of TTh on cardiovascular health, breast health, cognitive function, and the musculoskeletal system in women.

CAIN PROJECT

سامانه اطلاعات دارویی کشور

اشکال تستوسترون در ایران:

- متیل تستوسترون قرص خوراکی mg25
- تستوسترون انانتات تزریقی پرنترال 100 و 250 mg/1mL
- تستوژل ژل، سرنوژل و آندروژل موضعی 1 درصد g5
- آندراستانولون و آندراکتیم ژل موضعی 2.5 % 80 گرم(ژل دی هیدرو تستوسترون)
- سوستانون تزریقی پرنترال، آندرون تزریقی و آندوزیکس-آی اچ پرنترال 250 میلی گرم (تزریقی تستوسترون انانتات)
- آندرون و آندوزیکس-آی اچ تزریقی پرنترال 100 میلی گرم (تزریقی تستوسترون انانتات)
- آندریول تستوکپس کپسول خوراکی 40) mgکپسول تستوسترون اندکانوات

Dehydroepiandrosterone

Cochrane Database of Systematic Reviews :

Dehydroepiandrosterone for women in the peri or postmenopausal

DHEA may slightly improve sexual function compared with placebo

No large differences in treatment effects were found for sexual function when comparing DHEA to HT (mean difference

Side effects: unwanted hair growth (hirsutism)

DHEA may increase estrogen and testosterone levels

DHT

•آندراکتیم ژل موضعی ۲.۵ ٪ ۸۰ g(ژل دی هیدرو تستوسترون)

Scheers CS, Armstrong S, Cantineau AEP, Farquhar C, Jordan V. Dehydroepiandrosterone for women in the peri- or postmenopausal phase. Cochrane Database of Systematic Reviews 2015, Issue 1. Art. No.: CD011066

Bupropion

- For women with antidepressant-induced female sexual dysfunction, supplementation with bupropion may improve symptoms.
- A Cochrane review: Data from three studies in men and women of bupropion 150 mg twice daily indicate a benefit over placebo on rating scale scores (SMD 1.60, 95% CI 1.40 to 1.81), but response rates in two studies of bupropion 150 mg once daily demonstrated no statistically

Taylor MJ, Rudkin L, Bullemor-Day P, Lubin J, Chukwujekwu C, Hawton K. Strategies for managing sexual dysfunction induced by antidepressant medication. Cochrane Database of Systematic Reviews 2013, Issue 5.

Bupropion

- ***Mechanism of Action:*** The neurochemical mechanism

- ***The most common side effects***: agitation, dry mouth, insomnia, headache/migraine, nausea/vomiting, constipation, and tremor. Currently, there are no FDA-approved Bupropion therapies for FSD

- **بوپروپیون قرص خوراکی ۱۰۰ میلیگرم**
- **ولبان قرص پیوسته رهش خوراکی ۱۵۰ میلیگرم (قرص پیوسته رهش بوپروپیون هیدروکلراید)**
- **زیبوترین قرص خوراکی ۷۵ میلیگرم (قرص بوپروپیون هیدروکلراید)**
- **دپوبان قرص پیوسته رهش خوراکی ۱۵۰ میلیگرم (قرص پیوسته رهش بوپروپیون هیدروکلراید)**

Scheers CS, Armstrong S, Cantineau AEP, Farquhar C, Jordan V. Dehydroepiandrosterone for women in the peri- or postmenopausal phase. Cochrane Database of Systematic Reviews 2015, Issue 1. Art. No.: CD011066

Current Neuropharmacology, 2022, *20*, 1941-1955

SYSTEMATIC REVIEW ARTICLE

The Role of Bupropion in the Treatment of Women with Sexual Desire Disorder: A Systematic Review and Meta-Analysis

Bupropionis the only antidepressant without serotonergic activity and has a dual effect on dopamine and norepinephrine neurotransmitter systems.

Table 6. Summary of results of bupropion on sexual desire outcome.

Study	NHMRC Evidence Hierarchy	Quality	Scale	Improvement in Sexual Desire/Interest
Safarinejad 2011 [20]	Level II	100%	FSFI, CGI-SF	↑***
Safarinejad 2010 [21]	Level II	100%	BISFW, GEQ	↑***
Segraves 2004 [17]	Level II	100%	CSFQ	↔
Thase 2006 [22]	Level II	100%	CSFQ	↑*
Clayton 2004 [23]	Level II	94%	CSFQ	↔
Kennedy 2006 [24]	Level II	94%	Sex FX	↔
Hartmann 2012 [25]	Level III-3	100%	FSFI	↔
DeFronzoDobkin 2006 [26]	Level III-3	93%	CSFQ	↑**
Segraves 2001 [27]	Level III-3	87%	CGI-I, investigator rated scale	↑***
Mathias 2006 [28]	Level III-3	64%	ASEX	↑*
Gitlin 2002 [29]	Level IV	79%	ASEX	↑**

Legend: ↑= increase; ↔ = no improvement.

Sildenafil Citrate

- Generalists should pursue a global approach to the patient with sexual difficulties, while non-hormonal treatment such as PDE5 inhibitors (eg, sildenafil citrate) should be kept as the last option.
- Has been evaluated but not FDA approved for the treatment of female sexual interest/arousal difficulties.

•***Mechanism of Action***: ↑cGMP availability; mediates vascular smooth muscle (VSM) relaxation

•***The most common adverse events*** : headache, flushing, dyspepsia, nasal congestion, and transient visual disturbances and transient visual disturbances

MENU nature reviews urology

Review Article | Published: April 2009

Sildenafil citrate for female sexual arousal disorder: a future possibility?

Corina Schoen & Gloria Bachmann

Nature Reviews Urology **6**, 216–222(2009) | Cite this article

33 Accesses | **26** Citations | **0** Altmetric | Metrics

Sildenafil Citrate

Drug Design, Development and Therapy

Dovepress
open access to scientific and medical research

Open Access Full Text Article

COMMENTARY

Women taking the "blue pill" (sildenafil citrate): such a big deal?

This article was published in the following Dove Press journal:
Drug Design, Development and Therapy
7 November 2014
Number of times this article has been viewed

مهار کننده های فسفودی استراز نوع ۵

- سیلدنافیل ژل موضعی ۱ ٪ ۱۵ و ۲۰ گرم (ژل سیلدنافیل سیترات)
- ویاگرا یا سیلدنافیل قرص خوراکی ۵۰ و ۱۰۰ mg قرص سیلدنافیل (بصورت سیترات))
- سیلدنافیل قرص بازشونده در دهان خوراکی ۲۵ و ۵۰ mg (قرص بازشونده در دهان سیلدنافیل (بصورت سیترات))
- یوفوژل (ویژه آقایان) و یوفوژل (ویژه بانوان) ژل موضعی ۱ ٪ ۲۰)gژل سیلدنافیل سیترات)
- یوفوژل (ویژه بانوان) ژل موضعی ۱ ٪ ۲۰gژل سیلدنافیل سیترات)
- ارکژل ژل موضعی ۱ ٪ ۱۵)gژل سیلدنافیل سیترات)
- دیرکتا ژل موضعی ۱ ٪ ۳۰)gژل سیلدنافیل سیترات)
- ویگاژل ژل موضعی ۱ ٪ ۳۰)gژل سیلدنافیل سیترات)
- تادالافیل قرص خوراکی ۲.۵، ۵، ۱۰ و ۲۰) mgقرص تادالافیل)

CAIN PROJECT

Genital vibratory

- Genital vibratory stimulation device use resulted in uniform improvements in sexual function, satisfaction, sexually related distress and genital sensation.
- In 2000,the FDA approved a battery-powered clitoral suction device intended to improve arousal and orgasm by increasing blood flow and engorgement

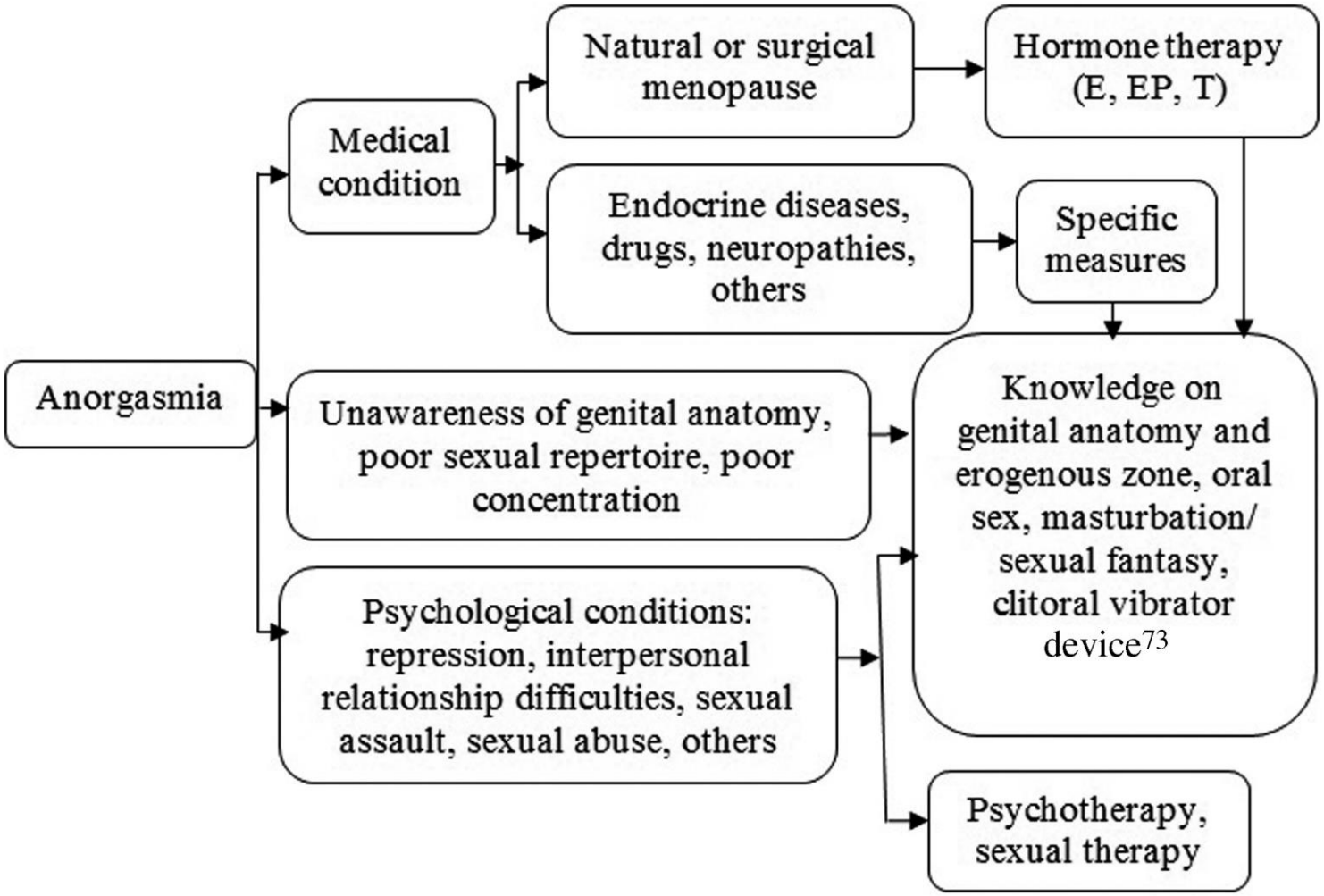
FIGURE 1. Eroscillator GVSD (A) and its variety of attachments (B).

Female Pelvic Medicine & Reconstructive Surgery. 23(4):256–262, JULY/AUGUST 2017
DOI: 10.1097/SPV.0000000000000357

Management of Orgasmic disorder

CAIN PROJECT

Proposed algorithm for the management of female anorgasmia



da Silva Lara, L. A., Scalco, S. C. P., Troncon, J. K. & Lopes, G. P. 2017. A Model for the Management of Female Sexual Dysfunctions. Revista Brasileira de Ginecologia e Obstetrícia/RBGO Gynecology and Obstetrics, 39, 184-194.

Treatment

- Treatment for female orgasmic disorder consists principally of education and psychosocial interventions; clinical trials of their efficacy are limited.
- *No medications have shown convincing evidence of efficacy for the disorder in clinical trials.*
- Clinical studies have shown the specific effects of oxytocin nasal spray on sexual function and interaction with others (Muin et al., 2017)

Treatment of female orgasmic disorder ,Author:Andrea Bradford, PhDSection Editor:Murray B Stein, MD, MPHDeputy Editor:Richard Hermann, https://www.uptodate.com/contents/treatment-of-female-orgasmic-disorder

Management of genito–pelvic pain and penetration disorders

CAIN PROJECT

Prasterone (INTRAROSA™) Vaginal Insert

- ***Date of Approval***: November 16, 2016
- ***Indication:*** Prasterone is indicated for the treatment of moderate-to-severe dyspareunia due to menopause.
- ***Mechanism of Action***: converted into active androgens and/or estrogens
- ***Administration*** : 6.5 mg, One vaginal insert, once daily at bedtime.
- ***Uniqueness of Drug***: This is the first agent approved to treat women experiencing moderate-to-severe pain during sexual intercourse (dyspareunia), a symptom of vulvar and vaginal atrophy (VVA), due to menopause.
- In addition, Intrarosa is the first FDA-approved product containing the active ingredient prasterone, which is also known as dehydroepiandrosterone (DHEA). Other forms of DHEA are used in dietary supplements that are not approved by the FDA.
- ***Side effects*** : Vaginal Discharge , Abnormal Pap Smear Findings

https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/208470s000lbl.pdf

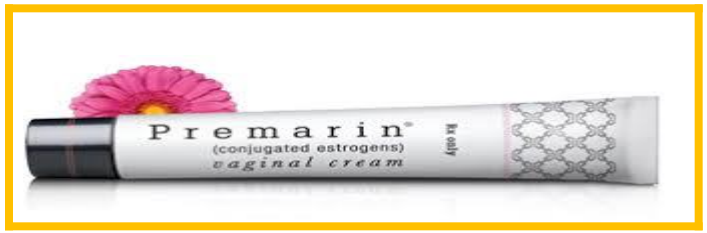
Ospemifene (OSPHENA™)

- ***Date of Approval***: February 26, 2013
- ***Indication:*** treatment of moderate to severe dyspareunia, a symptom of vulvar and vaginal atrophy, due to menopause
- converted into active androgens and/or estrogens
- ***Mechanism of Action:*** an estrogen agonist/antagonist with tissue selective effects
- ***Administration***: 60 mg , One tablet taken orally once daily with food.
- ***Side effects:*** Hot Flashes or Flushes, Vaginal Bleeding

https://www.accessdata.fda.gov/drugsatfda_docs/label/2013/203505s000lbl.pdf

Premarin (conjugated estrogens) Vaginal Cream

- ***Date of Approval***:1946
- ***Mechanism of Action****:* Endogenous estrogen
- ***Indications****:* Treatment of Moderate to Severe Dyspareunia, a Symptom of Vulvar and Vaginal Atrophy, due to Menopause
- ***Administration***: Cyclic administration of 0.5 g intravaginally [daily for 21 days then off for 7 days] for Treatment of Moderate to Severe Dyspareunia, a Symptom of Vulvar and Vaginal Atrophy, due to Menopause. Twice-weekly administration of 0.5 g intravaginally for Treatment of Moderate to Severe Dyspareunia, a Symptom of Vulvar and Vaginal Atrophy, due to Menopause
- Each gram contains 0.625 mg conjugated estrogens
- ***Side effects****:* headache, pelvic pain, vasodilation, breast pain, leucorrhea, metrorrhagia, vaginitis, vulvovaginl disorder



https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/020216s083lbl.pd

Estrace (estradiol tablets)

Mechanism of Action: Exogenous estrogens are metabolized in the same manner as endogenous estrogens

Indications: Treatment of moderate to severe symptoms of vulvar and vaginal atrophy associated with the menopause. When prescribing solely for the treatment of symptoms of vulvar and vaginal atrophy, topical vaginal products should be considered.

Administration: oral administration contains 0.5, 1 or 2 mg of micronized estradiol per tablet

Side effects: Nausea, vomiting, changes in vaginal bleeding pattern

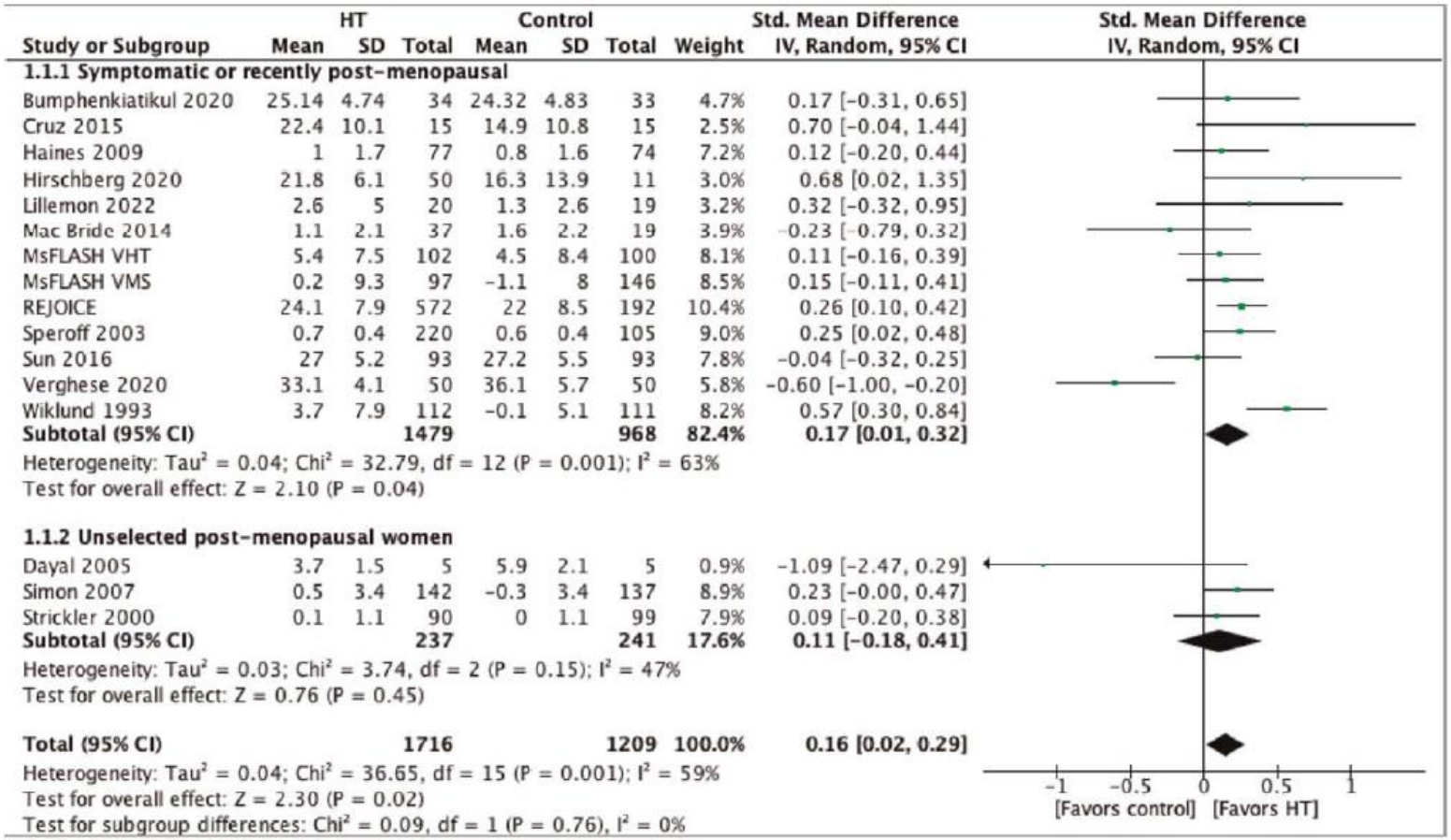
https://www.accessdata.fda.gov/drugsatfda_docs/label/2005/081295s014,084499s042,084500s044lbl.pdf

Vagifem® (estradiol vaginal tablets)

- ***Date of Approval***:1999
- ***Mechanism of Action:*** Endogenous estrogen
- ***Indications:*** Vagifem is an estrogen (estradiol) indicated for the treatment of atrophic vaginitis due to menopause
- ***Administration***: Intravaginally, 1 tablet daily for 2 weeks, followed by 1 tablet twice weekly .
- Vagifem 10 mcg tablet: One vaginal tablet contains 10.3 mcg of estradiol hemihydrate equivalent to 10 mcg of estradiol .
- Vagifem 25 mcg tablet: One vaginal tablet contains 25.8 mcg of estradiol hemihydrate equivalent to 25 mcg of estradiol.
- ***Side effects:*** headache, abdominal pain, back pain

https://www.accessdata.fda.gov/drugsatfda_docs/label/2009/020908s013lbl.pdf

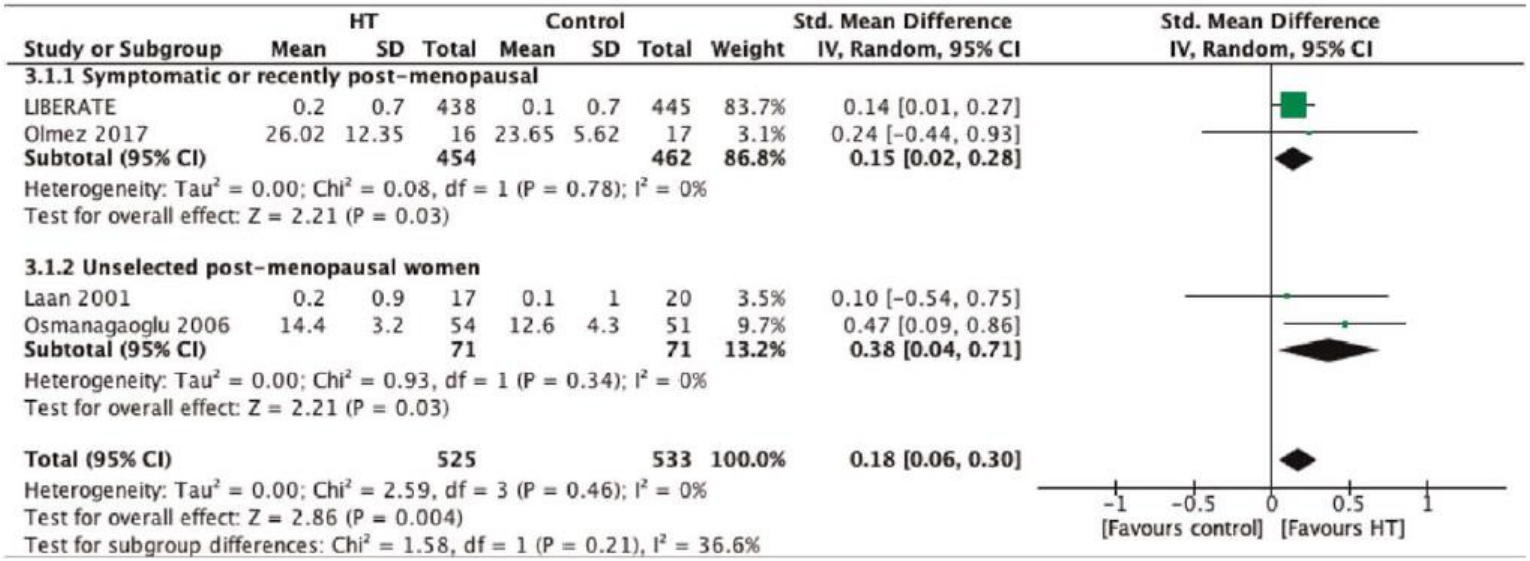
Forest plots showing the comparison of hormone therapy and control for sexual function composite score for estrogen therapy



Menopause, Vol. 30, No. 6, 2023

CAIN PROJECT

Forest plots showing the comparison of hormone therapy and control for sexual function composite score for tibolone

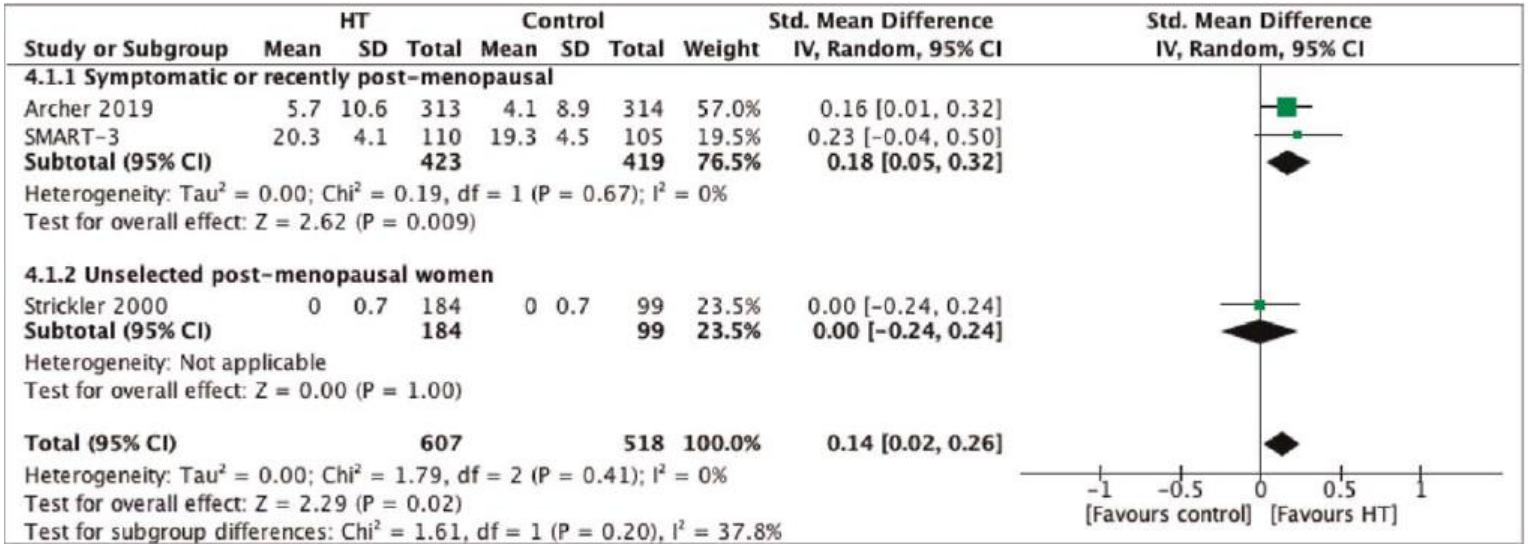


Study or Subgroup	HT Mean	HT SD	HT Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
3.1.1 Symptomatic or recently post-menopausal								
LIBERATE	0.2	0.7	438	0.1	0.7	445	83.7%	0.14 [0.01, 0.27]
Olmez 2017	26.02	12.35	16	23.65	5.62	17	3.1%	0.24 [-0.44, 0.93]
Subtotal (95% CI)			**454**			**462**	**86.8%**	**0.15 [0.02, 0.28]**
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.08$, df = 1 (P = 0.78); $I^2 = 0\%$								
Test for overall effect: Z = 2.21 (P = 0.03)								
3.1.2 Unselected post-menopausal women								
Laan 2001	0.2	0.9	17	0.1	1	20	3.5%	0.10 [-0.54, 0.75]
Osmanagaoglu 2006	14.4	3.2	54	12.6	4.3	51	9.7%	0.47 [0.09, 0.86]
Subtotal (95% CI)			**71**			**71**	**13.2%**	**0.38 [0.04, 0.71]**
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.93$, df = 1 (P = 0.34); $I^2 = 0\%$								
Test for overall effect: Z = 2.21 (P = 0.03)								
Total (95% CI)			**525**			**533**	**100.0%**	**0.18 [0.06, 0.30]**
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.59$, df = 3 (P = 0.46); $I^2 = 0\%$								
Test for overall effect: Z = 2.86 (P = 0.004)								
Test for subgroup differences: $Chi^2 = 1.58$, df = 1 (P = 0.21), $I^2 = 36.6\%$								

Menopause, Vol. 30, No. 6, 2023

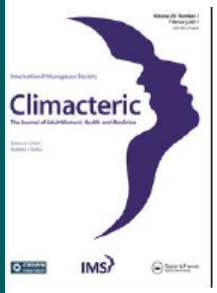
CAIN PROJECT

Forest plots showing the comparison of hormone therapy and control for sexual function composite score for SERM



Menopause, Vol. 30, No. 6, 2023

CAIN PROJECT



Climacteric

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/icmt20

Sustainability of vaginal estrogens for genitourinary syndrome of menopause – a systematic review

Objective GSM signs mostly deteriorated within approximately 4 weeks after vaginal estrogen treatment cessation

- Vaginal estrogens had a more sustainable impact on subjective GSM symptoms up to 3–6months

CAIN PROJECT

Premarin (conjugated estrogens) Vaginal Cream

- استرومارین قرص خوراکی ۱.۲۵ میلیگرم (قرص استروژن کونژوگه)
- اکوئین قرص خوراکی ۰.۶۲۵ میلیگرم (قرص استروژن کونژوگه)
- اکوئین قرص خوراکی ۱.۲۵ mg)قرص استروژن کونژوگه)
- استرین کرم واژینال ۰.۶۲۵ mg/1g(کرم استروژن کونژوگه)
- استرومارین کرم واژینال ۰.۶۲۵ mg/1g(کرم استروژن کونژوگه)

Lubricants

•Lubricants and moisturizers do not cure underlying causes of female sexual dysfunction, but they may help reduce or alleviate dyspareunia that is due to vaginal dryness.

❖ **Aqua Lubeo Natural Personal Lubricant**

- *Date of Approval*:2013
- *Mechanism of Action:* a non-sterile, water based, personal lubricant designed to supplement the body's own natural lubrication fluids. Composed primarily of organic aloe, hydroxyethycelIlu lose, sorbitol. and tocopherols (vitamin E).
- *Indications:* penile and/or vaginal application, intended to moisturize and lubricate, to enhance the ease and comfort of intimate sexual activity and supplement the body's natural lubrication.

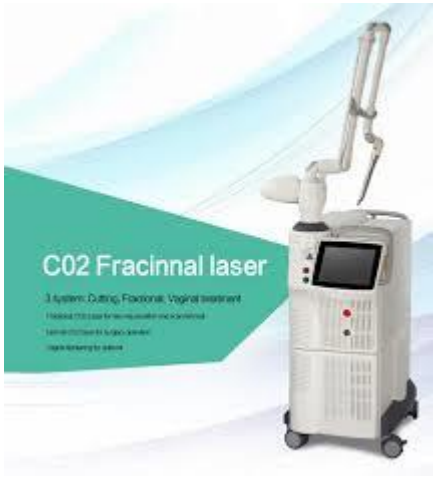
❖ **The Sex Gel**

Date of Approval:2018

https://www.accessdata.fda.gov/drugsatfda_docs/label/2009/020908s013lbl.pdfhttps://www.accessdata.fda.gov/drugsatfda_docs/label/2009/020908s013lbl.pdf/

Vaginal Carbon Dioxide Fractional Laser Treatment

- The safety, efficacy, and cost–benefit of the vaginal carbon dioxide (CO2) fractional laser for treatment of vulvovaginal atrophy are inadequately studied and are not FDA approved.



Female sexual dysfunction. ACOG Practice Bulletin No. 213. American College of Obstetricians and Gynecologists. Obstet Gynecol 2019;134:e1–18.

Can Botox Offer Help Women With Vaginismus? A Systematic Review and Meta-Analysis

- **Results**: Nine cohort studies were included in meta-analysis. Our results indicate that botox can be an option for effective treatment of patients with vaginismus (event rate 1⁄4 0.855, 95% confidence interval 1⁄4 0.764 to 0.915; p-value < 0.001).
- **Side effects**: excessive vaginal Dryness, mild stress incontinence, visual impairment
- 25 to 500 mlanterior vaginal wall muscles, puborectalis muscles in three sites on each sides of vagina, levator ani and pubococcygeus muscles, bulbocavernosus, pubococcygeus, and puborectalis musclesm, Bulpspongiosus muscles
- Mechanism:inhibit the release of acetylcholine from the nerve endings

Velayati A, Jahanian Sadatmahalleh S, Ziaei S, Kazemnejad A. Can Botox Offer Help Women With Vaginismus? A Systematic Review and Meta-Analysis. International Journal of Sexual Health. 2019:1-11

Elagolix (ORILISSA™)

- **Date of Approval**: July 2018
- **Indication:** Management of Moderate to Severe Pain Associated with Endometriosis
- Clinical trial data demonstrated significantly reduced the three most common types of endometriosis pain: daily menstrual pelvic pain, non-menstrual pelvic pain and pain with sex.

https://www.accessdata.fda.gov/drugsatfda_docs/nda/2018/210450Orig1s000TOC.cfm

Female Sexual Dysfunction and the Placebo Effect: A Meta-analysis

The meta-analysis of Level I evidence demonstrates that 67.7% of the treatment effect for female sexual dysfunction is accounted for by placebo. Our findings suggest that the current treatments for female sexual dysfunction are, overall, minimally superior to placebo, which emphasizes the ongoing need for more efficacious treatment for female sexual dysfunction.

Table 2. Mean Difference in Female Sexual Function Index Scores Preintervention vs Postintervention (Placebo vs Treatment)

	Placebo Group		Treatment Group		FSFI Score Difference (95% CI)	
First Author, Year	n	Weighted Effect Size × v^*	n	Weighted Effect Size × v^*	Preplacebo vs Postplacebo	Pretreatment vs Posttreatment
Clayton, 2016[25]	97	4.7094	149	0.2876	1.9 (1.86 to 1.94)	3.6 (3.30–3.90)
Constatine, 2015[26]	456	4.7302	463	0.2884	4.14 (4.136 to 4.14)	6.69 (6.45–6.93)
Derogatis, 2012, 50 mg[27]	295	4.7296	295	0.2885	2.4 (2.395 to 2.40)	3.9 (3.67–4.13)
Derogatis, 2012, 100 mg[†,27]			290	0.2882		5 (4.74–5.26)
Katz, 2013[28]	547	4.7302	543	0.2888	3.5 (3.499 to 3.50)	5.3 (5.11–5.49)
Labrie, 2015[29]	157	4.6853	325	0.2874	6.28 (6.16 to 6.40)	8.85 (8.53–9.17)
Muin, 2015[30]	30	4.0046	30	0.2761	6.045 (6.041 to 6.048)	5.07 (4.26–5.88)
Petersen, 2009[31]	32	4.6254	32	0.2854	5.11 (4.90 to 5.32)	1.64 (1.20–2.08)
Safarinejad, 2011[32]	109	4.2839	109	0.2836	−0.40 (−0.64 to −0.16)	8.1 (7.57–8.63)
Effect summary					3.62 (3.29 to 3.94)	5.35 (4.13–6.57)

FSFI, Female Sexual Function Index.
* Constant (v) calculated for random effects model to adjust for variability in the population of effects.[13]
† Represents distinct treatment cohort in the same Derogatis trial.

Weinberger JM1, Houman J, Caron AT, Patel DN, Baskin AS, Ackerman AL, Eilber KS, Anger JT. Female Sexual Dysfunction and the Placebo Effect: A Meta-analysis. Obstet Gynecol. 2018 Aug;132(2):453-458

Pharmacologic therapeutic options for sexual dysfunction

Table 1. Summary of pharmacologic treatment options for sexual dysfunction in pre and postmenopausal individuals

Therapy	FDA approved vs. off-label	Indications	Dosing	Monitoring
Postmenopausal individuals				
Moisturizers	Over the counter	GSM	Per vagina PRN (usually 2–3×/week; see product labeling)	None
Vaginal estrogen	FDA approved	GSM	0.5–1 g per vagina daily × 2 weeks then twice weekly	None
Vaginal DHEA (prasterone)	FDA approved	GSM	6.5 mg per vagina daily	None
Ospemifene (SERM)	FDA approved	GSM	50 mg oral daily	None
Vaginal testosterone	Investigational	GSM	0.1% per vagina daily	None
Transdermal testosterone	Off-label	HSDD	300 mcg patch or 0.5 ml of 1% gel transdermal daily, titrate to symptoms	Free and total T at 3–6 weeks, level < ULN for premenopausal women
Premenopausal individuals				
Bremelanotide	FDA approved	HSDD	1.75 mg subcutaneous INJ PRN (no more than 1 dose/24 h, 8 doses per month)	None
Flibanserin	FDA approved	HSDD	100 mg oral daily	None

GSM, genitourinary syndrome of menopause; HSDD, hypoactive sexual desire disorder.

CAIN PROJECT

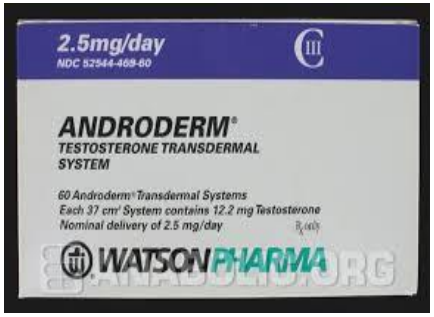
Summary of Recommendations

- **Bremelanotide & Flibanserin** can be considered as a treatment optior hypoactive sexual desire disorder in pre-menopausal women without depression who are appropriately counseled about the risks.
- **Systemic DHEA** is not effective and, therefore, is not recommended for use in the treatment of women with sexual interest/arousal disorders.
- Short-term use of **transdermal testosterone** can be considered as a treatment option for postmenopausal women with sexual interest and arousal disorders who have been appropriately counseled about the potential risks and unknown long-term effects.
- Evidence is insufficient to recommend for or against **testosterone** for the treatment of sexual interest and arousal disorders in **premenopausal** women.
- **Sildenafil** should not be used for the treatment of female interest/arousal disorders outside of clinical trials.
- **Estrogen or SERM** therapy is not recommended for the treatment of female sexual dysfunction that is not due to a hypoestrogenic state.

Female sexual dysfunction. ACOG Practice Bulletin No. 213. American College of Obstetricians and Gynecologists. Obstet Gynecol 2019;134:e1–18.

Summary of Recommendations

- **Low-dose vaginal estrogen therapy** is the preferred hormonal treatment for female sexual dysfunction that is due to genitourinary syndrome of menopause.
- **Low-dose systemic hormone therapy,** with estrogen alone or in combination with progestin, can be recommended as an alternative to low-dose vaginal estrogen in women experiencing dyspareunia related to genitourinary syndrome of menopause as well as vasomotor symptoms.
- **Ospemifene** can be recommended as an alternative to vaginal estrogen for the management of dyspareunia caused by genitourinary syndrome of menopause.
- **Intravaginal prasterone** can be used in postmenopausal women for the treatment of moderate-to-severe dyspareunia that is due to genitourinary syndrome of menopause.
- Vaginal carbon dioxide (CO2) fractional laser for treatment of dyspareunia that is due to genitourinary syndrome of menopause should not be used outside of a research setting.



Female sexual dysfunction. ACOG Practice Bulletin No. 213. American College of Obstetricians and Gynecologists. Obstet Gynecol 2019;134:e1–18.

Non-Pharmacological

Psychotherapy

Counseling

Sex Therapy

Couple Therapy

Yoga

Life Style Changes

Novelty

Privacy

Spare time

Lubricants & Moisturizers

Improve Body Image

Weight loss

Exercise


Thank you
For
Your Attention :)
Any
Questions ?