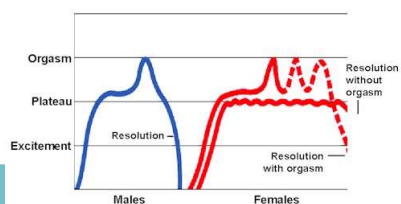


### Normal Female Sexual Response Model Developed by Masters and Johnson



AADE16

### DSM-IV - Definition of Female Sexual Disorder (FSD)

- Disturbances in **sexual desire & the psychophysiological changes** in the sexual response cycle that causes **marked distress and interpersonal difficulty**

The DSM emphasizes the emotional and psychological factors involved in FSD

AADE16

Miron S, Wylie K, Maturitas. 2009; 63:116-8

### Normal Female Sexual Response

First Phase of Female Sexual Response is governed by a combination of:

- Neuromuscular and vaso-congestive events
- Increased clitoral size (diameter and length)
- Vaginal lubrication and wall engorgement

Third Phase of Female Sexual Response

- Orgasm: the culmination of sexual arousal

Diabetes Can Disrupt All Of These Systems

AADE16

Phillips A, Phillips S. Applied Nursing Research. 2015; 28:235-8

### Four Main Classification of FSD

- Hypoactive sexual desire disorder (HSDD); sexual aversion
- Female arousal disorder (FAD)
- Female orgasmic disorder (FOD)
- Sexual pain disorder (SPD)(dyspareunia; vaginismus)

AADE16

### Normal Female Sexual Response

- Integrity of the Sensory & Autonomic Nervous System's response to erotic stimuli
- The smooth muscle relaxation of the female genital erectile tissue
- Increase in blood supply depends on healthy actions of neurotransmitters
- The regulation of blood supply and clitoral erectile function is governed by nitric oxide and cGMP
- Normal levels of hormones for physiologic sexual activity

Diabetes Can Disrupt All Of These Systems

AADE16

Phillips A, Phillips S. Applied Nursing Research. 2015; 28:235-8

### Etiology/Pathophysiology of FSD in Diabetes

- Atherosclerosis: Decreased arterial blood supply
- Metabolic Syndrome: Leads to insulin resistance
- Menopause: Leads to lower estrogen & androgen levels
- FSD: Strongly associated with T1DM and T2DM
- Vascular and neuropathic complications: Decreased nerve stimulation and blood flow

AADE16

Phillips A, Phillips S. Applied Nursing Research. 2015; 28:235-8

### Etiology/Pathophysiology of FSD in Diabetes

- Prolonged hyperglycemia: Reduced lubrication, dyspareunia, & the risk of genitourinary/fungal infections
- Polycystic Ovarian Syndrome: Alterations of Estrogen and Androgen (insulin resistance syndromes)
- Hormonal Imbalances: Thyroid & hypothalamic/pituitary disorders
- Neuropathy: Alter transduction of sexual stimuli and consequent sexual response

**AADE16**

Phillips A, Phillips S. Applied Nursing Research. 2015; 28:235-8

### Some Drugs Associated With FSD

Medication	Desire Disorder	Arousal Disorder	Orgasm Disorder
Antipsychotics	+		+
Barbiturates	+	+	+
Benzodiazepines	+	+	+
Lithium	+	+	+
SSRI's	+	+	+
TCA	+	+	+
Digoxin	+		+
Anti-lipids	+		
Beta Blockers; Spironolactone; Methyldopa	+		
Clonidine	+	+	

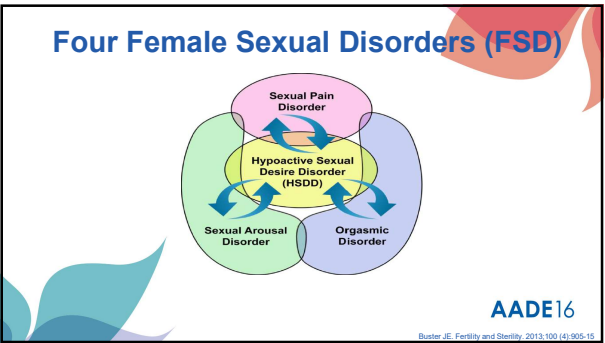
**AADE16**

Buster JE. Fertility and Sterility. 2013;100(4):905-15

### Influences of FSD

Biological Factors	Psychological Factors	Contextual (Social) Factors
Medical (neurological, urogenital diseases); pelvic radiation, surgery	Sexual development	Ethnic/religious norms
Psychiatric (depression)	Personality	Economical/household
Hormonal changes and menopausal status	Sexual Experiences (abuse)	Contraception issues
Pharmacological tx (antidepressants)	Sexual education, body image	Relationship with partner
Substance abuse	Coping strategies	Life stage stressors; family issues; partner's health

**AADE16**



- ### Diseases Associated with Increased Risk of FSD
- Diabetes
  - Cardiovascular Disease
  - HTN
  - Chronic Rheumatic disease
  - Spinal Cord injury
  - Psychiatric disorder
  - Genitourinary disorder
  - Urinary incontinence
  - Pelvic Pain
  - Hysterectomy
  - Malignant gynecological disease
- AADE16**
- Palacios S, Carraro R, Grazzini A, Makutias. 2009;119-123

### HYPOACTIVE SEXUAL DESIRE DISORDER (HSDD)

**AADE16**

### Hypoactive Sexual Desire Disorder (HSDD)

- Persistent or recurrent deficiency or absence of sexual fantasies and desire for sexual activity that causes **marked distress or interpersonal difficulty**



AADE16

Goldfischer ER, Breaux J, et al. J Sex Med. 2011;8:3160-72

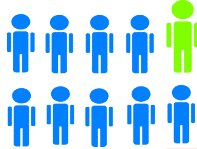
### Why Are We Not Doing Something?



AADE16

### HSDD Prevalence in Premenopausal Women

1 in 10 Premenopausal Women Report Low Sexual Desire With Associated Distress




**HSDD REMAINS UNDERDIAGNOSED & UNDERTREATED**

AADE16

Goldfischer ER, Breaux J, Katz M, et al. J Sex Med. 2011;8:3160-72

### Barriers to Recognition and Diagnosis


- Women's reluctance to discuss sexual problems with a physician
- Physician's lack of training and knowledge of sexual issues
- Concerns over causing patients' embarrassment



AADE16

Goldfischer ER, Breaux J, Katz M, et al. J Sex Med. 2011;8:3160-72

### FSD and Diabetes Control in Women With Diabetes



FSD in 46.7% of Women with Diabetes – Illiterate > Educated

FSD in DM	Increased FSD Risks
Sexual Desire (36.8%)	Age
Orgasm Satisfaction (25.5%)	HbA1c
Orgasm (24.8%)	DM Complications
	Low Literacy

AADE16

Ozcan S, Sahin NK, Bilgin D, Yilmaz SD. Sex Disabil. 2011; 29:251-61

### Major Goal of Successful Therapy

- Goal: Restoration of Sexual Desire

**HSDD is the principal FSD in that, because they flow outward from it, other FSD are frequently resolved when the problems leading to HSDD are resolved**

AADE16

Buster JE. Fertility and Sterility. 2013;100 (4):905-15

### Treatment of HSDD: Manage the Underlying Causes

- Situational, psychiatric and psychosocial dysfunction
  - Re-assurance, marital counseling, formal psychotherapy
- Drugs
  - SSRIs – eliminate or reduce dose
- Chronic Disease
  - Treat HTN, DM, hypothyroidism, hypopituitarism, breast cancer

**AADE16**  
Buster JE. Fertility and Sterility. 2013;100 (4):905-15

### The Blue Pill vs. The Pink Pill

- Sildenafil Citrate (Viagra®) has been studied for Female Sexual Arousal Disorder (FSAD)
  - Not FDA Approved in Women
- Flibanserin (Addyi®) has been studied for Hypoactive Sexual Desire Disorder (HSDD)
  - FDA Approved in Women for HSDD

**AADE16**  
Viagra® 100 mg. Retrieved from www.superpotencialis.com  
Addyi® 100 mg. Retrieved from www.hmg.com

### Treatment of HSDD (Cont'd)

- Depletion of Estrogens
  - Transdermal or intravaginal estrogens
- Depletion of Androgens
  - Transdermal testosterone

**AADE16**  
Buster JE. Fertility and Sterility. 2013;100 (4):905-15

### Blue Pill – Sildenafil (Viagra®)

Evidence	Therapy /Dosage	Population	Effects	Adverse effects
Blinded, prospective, crossover study	Sildenafil 25 or 50 mg, 1 hr. before sex	Premenopausal women with female sexual arousal disorder (FSAD)	Increased arousal, enjoyment, satisfaction, frequency of intercourse, and sexual fantasies	Vision problems, HA
Open-label study - 33 women	Sildenafil 50 mg, 1 hr. before sex	Postmenopausal women self referred for Sexual Dysfunction (SD)	No significant clinical improvement in sexual function	Clitoral discomfort, hypersens. dizziness, HA, dyspepsia

**AADE16**  
http://www.ncbi.nlm.nih.gov/pubmed/200801031?url=pubmed/200801031&fromopenview=true

### Evaluation Tools for HSDD

Tool	Description
Satisfying Sexual Encounter (SSE) – eDiary	Diary to enter daily the # of sexual events experienced and their satisfaction
The Female Sexual Function Index (FSFI)	This is a 19-item measure of overall sexual function and includes six domains (desire, arousal, lubrication, orgasm, satisfaction, and pain)
The Female Sexual Distress Scale – Revised (FSDS-R)	Assesses the frequency of sexual distress or bother during the past 7 days

**AADE16**

### Blue Pill – Sildenafil (Viagra®)

Evidence	Therapy/ Dosage	Population	Effects	Adverse effects
DB, RCT	Sildenafil, 10-100 mg, 1 hr. before sexual activity	Pre- and postmenopausal women (some On hormone therapy) with FSAD	No improvement	HA, hot flashes, rhinitis, nausea, vision problems, dyspepsia
DB, PC, crossover study	Sildenafil, 100 mg, 1 hr. before sexual activity	Premenopausal women with T1DM & FSAD	Increased sexual desire, frequency of orgasm, enjoyment, satisfaction, and frequency of sexual fantasies	HA, nausea, vision problems

**AADE16**  
http://www.ncbi.nlm.nih.gov/pubmed/200801031?url=pubmed/200801031&fromopenview=true

### Flibanserin in Premenopausal Women

**Aim**

- To assess the efficacy and safety of flibanserin x 24 weeks of treatment vs. placebo in premenopausal women with HSDD

**Methods**

- Women were treated with open-label, flexible-dose flibanserin (50 mg or 100 mg/day) for 24 weeks. Responders were randomized to flibanserin 100 mg/day vs. placebo x 24 wks.

**Main Outcome Measures**

- Primary Outcome: Change in Satisfying Sexual Encounter (SSE) and desire score

AADE16

Goldfinger ER, Breaux J, Katz M, et al. J Sex Med. 2015;8:3160-72

### Efficacy Endpoints: Change from Baseline to Week 24

	Placebo	Flibanserin 100 mg/day	P value
SSE Count	0.6 (0.1)	1.0	0.004
FSFI-d Score	0.4 (0.1)	0.7 (0.1)	<0.001
FSDS-R Item 13 Score	-0.6 (0.1)	-0.8 (0.1)	0.008
FSDS-R Total Score	-6.3 (0.6)	-8.3 (0.6)	0.006
FSFI Total Score	2.7 (0.4)	4.2 (0.4)	0.003

Key  
 SSE = Satisfying Sexual Event  
 FSFI-d = Female Sexual Function Index Desire  
 FSDS-R = Female Sexual Distress Scale  
 FSFI = Female Sexual Function Index

AADE16

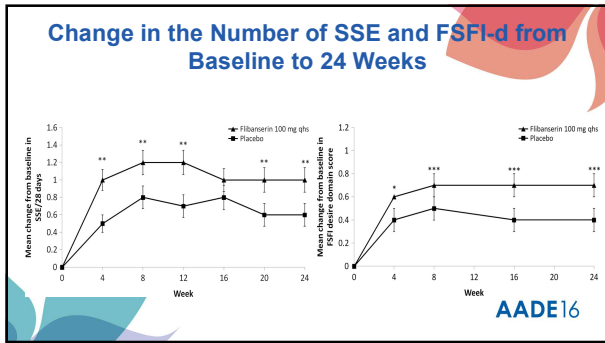
### Flibanserin in Premenopausal Women

**Results**

- Satisfying Sexual Encounter (SSE) Doubled
- Mean Desire Score doubled
- FSFI, FSDS-R total, and Item 13 scores improved
- At the end of the double-blind period, flibanserin was superior to placebo in change from randomization in SSE, desire score, FSFI desire domain and total scores, and FSDS-R total and Item 13 scores ( $P < 0.05$ , for all).
- Flibanserin was well tolerated and withdrawal reactions were not observed.

AADE16

Goldfinger ER, Breaux J, Katz M, et al. J Sex Med. 2011;8:3160-72



### SNOWDROP TRIAL – Flibanserin

**Objective**

- To assess the efficacy and safety of flibanserin in postmenopausal women with HSDD

**Methods**

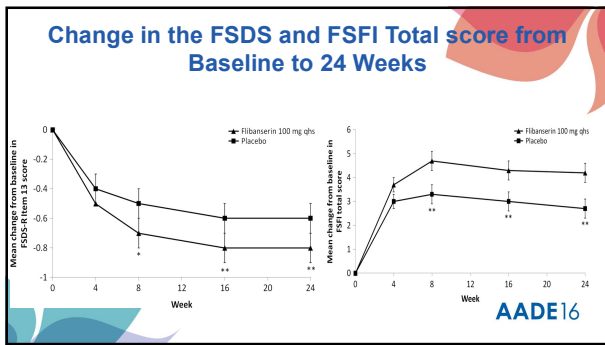
- Naturally postmenopausal women with HSDD received flibanserin 100 mg once daily at bedtime (n = 468) or placebo (n = 481) for 24 weeks

**Co-primary endpoints**

- Changes from baseline to week 24 in the number of satisfying sexual events (SSEs) across 28 days and in the Female Sexual Function Index (FSFI) desire domain score.

AADE16

Simon JA, Kingsberg SA, Shumil B, et al. The Journal of North American Menopause Society 2014; 21(6):633-40



### Flibanserin (Addyi®)

- **Class:** Serotonin 1A receptor agonist and a serotonin 2A receptor antagonist (mechanism unknown)
- **Indication:** Treat acquired, generalized hypoactive sexual desire disorder (HSDD) in premenopausal women. Their low sexual desire is **not** due to:
  - a medical or mental health problem
  - problems in the relationship
  - medicine or other drug use
- Not for the treatment of HSDD in menopausal women, men, children or to improve sexual performance

AADE16

### Question on FDA Approval

- Which of the following therapies is an FDA approved agent for Hypoactive Sexual Desire Disorder?

**PINK**     Sildenafil (Viagra®)  
**BLUE**     Testosterone  
**GREEN**    Flibanserin (Addyi®)  
**YELLOW**   Vagisil® personal lubricating gel

AADE16

### Flibanserin (Addyi®)

**Dosage:** 100 mg at bedtime to reduce adverse effects

**Adverse Effects:** somnolence, insomnia, nausea, HA, dry mouth

**Availability:** Risk Evaluation and Mitigation Strategy (REMS) Program from Certified Providers and Pharmacies

**BOXED WARNING AND CONTRAINDICATION:**  
 Severe hypotension and syncope in patients who drink ETOH, use with moderate/severe CYP3A4 inhibitors or have liver impairment during tx

AADE16

### How many clinicians here present consistently ask patients about FSD?

**A. Never or inconsistently**  
**B. 1-5 times monthly**  
**C. 6-10 times monthly**  
**D. >10 times monthly**

AADE16

### Clinical Pearl

**Sexual Health Is An Important But Neglected Component Of Health Care In Women With Diabetes**

AADE16

### Interview : The Conversation

**Generic:** “Many people have concerns or questions about their sexuality. What questions or problems related to sex would you like to discuss?”

**Health Care Milestone:** “Many women after menopause notice a change in their sexual desire. Have you noticed any changes?”

AADE16

Buster JE. Fertility and Sterility. 2013;100 (4):905-15

### Tips to Facilitate the Dialogue

- Use words and body language that put the patient at ease
- Maintain an open, non-defensive body posture
- Sit and maintain eye contact
- Avoid nervous gestures
- Choose language appropriate to the age, ethnicity, and culture of the patient
- Ask open-ended questions with silences that encourage the patient to speak
- “Tell me about [it]” are probably the four most powerful words in medicine

**AADE16**

Buster JE Fertility and Sterility, 2013;100 (4):905-15

### Mini-Case – Patient Sarah

- HPI: 53-year-old married woman with Type 2 DM and HTN x 10 yrs.; postmenopausal x 1 year
  - Vitals: Weight: 220 lb.; Height 5'4"; BMI 37.8
  - Labs: A1C 8.8% Diet: None
  - FBG 180-220 mg/dL
- Meds: metformin (Glucophage® XR) 1000 mg/d; empagliflozin (Jardiance®) 25 mg/d; liraglutide (Victoza®) 1.8 mg/d; clonidine 0.3mg/d

**AADE16**

### Sexual Dysfunction in Diabetes

Diabetes Specific Questions	Rationale
What medications are you taking?	Possible influences to be addressed
Are you experiencing stress or depressive symptoms?	Review if depression is present or therapy needs to be addressed
Have you recently had a baby?	Determine if there was a difficult delivery, birth injuries, sleep, or support
Do you feel tired all the time?	Anxiety, stress, depression, hypoglycemia causing fatigue
Do you experience vaginal dryness?	Related to DM control, neuropathy, medication, hormones, menopause

**AADE16**

Phillips A, Phillips S. Applied Nursing Research. 2016; 28:235-4

### Engaging Sarah

We need to engage Sarah in a conversation regarding sexual problems now that she has reached a new life milestone?

A. “Many people have concerns or questions about their sexuality. What questions or problems related to sex would you like to discuss?”

B. “Many women after menopause notice a change in their sexual desire. Have you noticed any changes?”

**AADE16**

### Sexual Dysfunction in Diabetes

Diabetes Specific Questions	Rationale
Do you feel uncomfortable or experience pain during sex?	Determine if this is causing sexual anxiety
Do you experience recurrent thrush or urine infections?	Is this suboptimal DM control; fungal infections are easily treated
Do you feel there is a problem with your relationship with your partner?	Explore marital tensions, guilt about relationships
Do you feel embarrassed by having sex?	Discover past negative experiences/abuse
Do you feel you have a poor self image?	Woman can discuss feelings of depression or low self esteem (obesity)
Have you ever experienced sexual or physical abuse?	Discover past negative experience

**AADE16**

Phillips A, Phillips S. Applied Nursing Research. 2015; 28:235-4

### Case Discussion: Sarah

- Sarah describes tiredness, irritability, has a loss of interest in sex and is unhappy with her weight problems
- She states that it was >2 years since she last made love. She knows that she does not have any interest but does not know why.

**AADE16**

Clegg M, Toomer Alison, Wylie K, Maturitas. 2012;72:160-4



### Case Discussion: Sarah

- She states that 2 years ago the interest was there, but there were no pleasurable feelings, no physical response; and feelings of dryness and soreness persisted after sexual activity.
- She thinks that this loss of feeling may have led to the interest going but is not sure. She feels it may be part of the menopause but other friends she knows do not feel like this, although a lot of the women at the diabetes clinic seem to understand

AADE16

### Which of the following therapy(ies)/ changes will Sarah receive today?

- A. Initiate Sildenafil (Viagra®) 100 mg/day
- B. Initiate Flibanserin (Addyi®) 100 mg/day
- C. Initiate Personal Lubricating Gel
- D. Initiate Basal insulin
- E. Discontinue Clonidine and switch to an ACE Inhibitor

AADE16

### What are some of the areas for consideration based on Sarah's conversation?

AADE16

### Conclusion

- Sexual health matters
- Clinicians must ask about FSD and HSDD
- Effective treatments are available
- A sex therapist may be consulted in more difficult cases

AADE16

### Areas for Consideration

- Diabetes causes sexual dysfunction (46.7%)
- Vaginal Dryness
- Medication
- Evaluate: blood glucose/lipids/estrogen/testosterone/thyroid
- Review for depression
- Examine patient for vulval/vaginal infection and/or atrophy
- Refer to psychosexual counselling if required
- Follow up patient using multimodal/multidisciplinary approach

AADE16

### Question for Audience

- In evaluating this presentation,

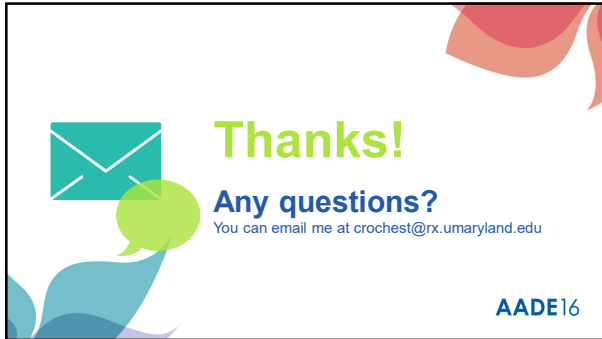
RED I learned at least one important fact today

BLUE I am still "muddy" about one point

GREEN I need one area clarified today

YELLOW I slept through, so I have no questions

AADE16



**Thanks!**

**Any questions?**  
You can email me at [crochest@rx.umaryland.edu](mailto:crochest@rx.umaryland.edu)

AADE16