

A collection of orange, round pills. Some are in the upper left corner, slightly out of focus, while one pill is in sharp focus in the lower right quadrant. The background is white.

Public Meeting on Female Sexual Dysfunction Patient-Focused Drug Development

October 27, 2014



Welcome

Sara Eggers, PhD

Office of Strategic Programs

Center for Drug Evaluation and Research

U.S. Food and Drug Administration

October 27, 2014

Agenda

- **Setting the context**
 - Opening Remarks
 - Overview of FDA's Patient-Focused Drug Development Initiative
 - Background on Female Sexual Dysfunction and Therapeutic Options
 - Overview of Discussion Format
- **Discussion Topic 1:** Disease symptoms and daily impacts that matter most to patients
- **Discussion Topic 2:** Patients' perspectives on current approaches to treating female sexual dysfunction
- **Open Public Comment**
- **Closing Remarks**

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Opening Remarks

Audrey Gassman, MD

Deputy Director, Division of Bone, Reproductive and Urologic Products (DBRUP)
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

October 27, 2014

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FDA's Patient-Focused Drug Development Initiative

Theresa Mullin, PhD

Director, Office of Strategic Program
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

October 27, 2014

Patient-Focused Drug Development under PDUFA V

- **FDA is developing a more systematic way of gathering patient perspective on their condition and available treatment options**
 - Patient perspective helps inform our understanding of the context for the assessment of benefit-risk and decision making for new drugs
 - Input can inform FDA's oversight both during drug development and during our review of a marketing application
- **Patient-Focused Drug Development is part of FDA commitments under the fifth reauthorization of the Prescription Drug User Fee Act (PDUFA V)**
 - FDA is convening at least 20 meetings on specific disease areas in 2013 - 2017
 - Meetings will help develop a systematic approach to gathering input

Identifying Disease Areas for the Patient-Focused Meetings

- **In September 2012, FDA announced a preliminary set of diseases as potential meeting candidates**
 - Public input on these nominations was collected. FDA carefully considered these public comments and the perspectives of our drug review divisions at FDA
- **FDA selected a set of 16 diseases selected to be the focus of meetings for fiscal years 2013-2015**
 - Another public process has been initiated to determine the set of diseases for fiscal years 2016-2017
 - Federal Register Notice: <https://federalregister.gov/a/2014-23965>

Disease Areas to be the focus of meetings for FY 2013-2015

FY 2013

- Chronic fatigue syndrome
- HIV
- Lung cancer
- Narcolepsy

FY 2014

- Sickle cell disease
- Fibromyalgia
- Pulmonary arterial hypertension
- Inborn errors of metabolism
- Hemophilia A, Hemophilia B, von Willebrand disease, and other heritable bleeding disorders
- Idiopathic pulmonary fibrosis

FY 2015


- **Female sexual dysfunction**
- Alpha-1 antitrypsin deficiency
- Breast cancer
- Chronic chagas disease
- Irritable bowel syndrome, gastroparesis, and gastroesophageal reflux disease
- Parkinson's disease and Huntington's disease

Tailoring Each Patient-Focused Meeting

- **Each meeting focuses on a set of questions that aim to elicit patients' perspectives on their disease and on treatment approaches**
 - We start with a set of questions that could apply to any disease area; these questions are taken from FDA's benefit-risk framework and represent important considerations in our decision-making
 - We then further tailor the questions to the disease topic of the meeting (e.g., current state of drug development, specific interests of the FDA review division, and the needs of the patient population)
- **Focus on relevant current topics in drug development for the disease at each meeting**
 - E.g., focus on HIV patient perspectives on potential “cure research”
- **We've learned that active patient involvement and participation is key to the success of these meetings.**

“Voice of the Patient” Reports

- Following each meeting, FDA publishes a Voice of the Patient report that summarizes the patient testimony at the meeting, perspectives shared in written docket comments, as well as any unique views provided by those who joined the meeting webcast.
- These reports serve an important function in communicating to both FDA review staff and the regulated industry what improvements patients would most like to see in their daily life.
- FDA believes that the long run impact of this program will be a better, more informed understanding of how we might find ways to develop new treatments for these diseases.

A background image showing several orange, round pills scattered across a white surface. One pill is in sharp focus in the lower right quadrant, while the others are blurred in the background.

Background on Female Sexual Interest/Arousal Disorder

Christina Chang, MD

Clinical Team Leader, DBRUP
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

October 27, 2014

Introduction

- Sexual complaints are common (Laumann 1995)
 - 43% of U.S. women age 18 to 59 reported: lacking interest in sex, lubrication difficulties, inability achieving climax, anxiety about sexual performance, or pain during intercourse
- Adversely affecting quality of life:
 - Emotional well-being
 - Relationship with partner

Laumann et al. Sexual dysfunction in the United States – prevalence and predictors. JAMA. 1995;281:537-44.

Sexual Response

Sexual response involves complex interactions

- Includes physiology, emotions, relationship with partner, prior experiences, culture/beliefs, etc.
- Changes in any component can affect sexual desire, arousal, or satisfaction
- Sexual dysfunction is characterized by persistent problems **severe enough to cause personal distress**
- Sexually problems and related personal distress reported by 12% of women in one survey (Shifren 2008)

Shifren et al. Sexual problems and distress in United States women – prevalence and correlates. *Obstet Gynecol.* 2008;112:970-8.

Disorders in Female Sexual Function

American Psychiatric Association classifications - Diagnostic and Statistical Manual of Mental Disorders (DSM)

DSM, 4th edition:

- **Hypoactive Sexual Desire Disorder (HSDD)**
- **Female Sexual Arousal Disorder (FSAD)**
- Female Orgasmic Disorder
- Sexual Pain Disorder

DSM, 5th edition:

- **Female Sexual Interest/Arousal Disorder (FSIAD)** combining FSAD and HSDD from DSM-IV
- Female Orgasmic Disorder
- Genito-Pelvic Pain/Penetration Disorder

Diagnostic Criteria for FSIAD

- A. Absence or significantly reduced sexual interest/arousal for at least 6 months (with at least 3 of the following symptoms):
1. Absent/reduced interest in sexual activity
 2. Absent/reduced sexual/erotic thoughts or fantasies
 3. No/reduced initiation of sexual activity; unresponsive to partner's attempt to initiate sexual activity
 4. Absent/reduced sexual excitement/pleasure during sexual activity in at least 75% of encounters
 5. Absent/reduced sexual interest/arousal in response to any internal or external cues (e.g., written, verbal, visual)
 6. Absent/reduced genital or non-genital sensations during sexual activity in at least 75% of sexual encounters

Diagnostic Criteria for FSIAD, Continued

- B. The problem causes clinically significant distress
- C. The sexual dysfunction is not better explained by:
 1. Non-sexual mental disorder
 2. Severe relationship distress (e.g., partner violence) or other stressors
 3. Effects of a substance/medication or another medical condition

Severity of the dysfunction: mild, moderate, or severe

Lifelong vs. acquired

Generalized vs. situational

Treatment

- **Issues with using existing therapies**
 - Sildenafil (used to treat erectile dysfunction) not shown to be effective for the treatment of arousal disorder in women (Basson 2002)*
 - Products containing hormones have potential safety concerns with long-term use
 - Not FDA-approved for sexual dysfunction in women
- **Other therapies:**
 - Individual cognitive behavioral therapy (CBT)
 - Couples sex therapy
- FSIAD is an area of focus for the FDA because the approved therapies (ospemifene and some estrogen products) only address pain during sex associated with menopausal changes in the vulva/vagina

Basson et al. Efficacy and safety of sildenafil citrate in women with sexual dysfunction associated with female sexual arousal disorder. *J Women's Health Gend Based Med.* 2002;11:367-77.

*Note that there are no drugs approved for the treatment of low desire in men (male hypoactive sexual desire disorder, DSM-5)

Challenges in Drug Development for FSIAD

- Diagnosing FSIAD
 - Diagnostic criteria not objectively defined
 - Must exclude relationship difficulties, other medical or psychiatric conditions, or side effects from medications
 - Unknown incidence/prevalence
- Outcomes assessment
 - What should we measure? (What is meaningful to patients?)
 - How should we measure it? (Diaries? Clinical visits? How often?)

Patient-Reported Outcomes

Why your input today is important:

- Patient-reported outcomes (PROs) highlight your unique ability to contribute to the field of drug development
- PROs represent a direct measure of treatment benefit – how someone feels or functions
- FDA encourages the development of well-defined and reliable PRO instruments that capture clinical benefit concepts that are important to patients like you
- Instruments need to be evaluated and then used in adequate, placebo-controlled, double-blinded, randomized clinical trials



Overview of Discussion Format

Sara Eggers, PhD

Office of Strategic Programs

Center for Drug Evaluation and Research

U.S. Food and Drug Administration

October 27, 2014

Discussion Overview

Topic 1: The symptoms that matter most to you

- Which symptoms have the most significant impact on your life?
- How do these symptoms affect your sexual experiences?
- How do your symptoms change over time?

Topic 2: Current approaches to treating FSIAD

- What are you doing to treat your FSIAD and its symptoms?
- How well do your treatments work for you?
- What are their biggest downsides?
- What would you look for in an “ideal” treatment?

Discussion Format

- **We will first hear from a panel of patients**
 - The purpose is to set a good foundation for our discussion
 - They reflect a range of experiences with FSD and FSIAD

- **We will then broaden the dialogue to include patients and patient representatives in the audience**
 - The purpose is to build on the experiences shared by the panel
 - We will ask questions and invite you to raise your hand to respond
 - Please state your first name before answering
 - Please indicate whether you represent an organization or if your travel has been funded

Discussion Format, continued

- **You'll have a chance to answer "polling" questions**
 - Their purpose is to aid our discussion
 - In-person participants, use the "clickers" to respond
 - Web participants, answer the questions through the webcast
 - Patients and patient representatives only, please
- **Web participants can add comments through the webcast**
 - Although they may not all be read or summarized today, your comments will be incorporated into our summary report
 - We'll occasionally go to the phones to give you another opportunity to contribute

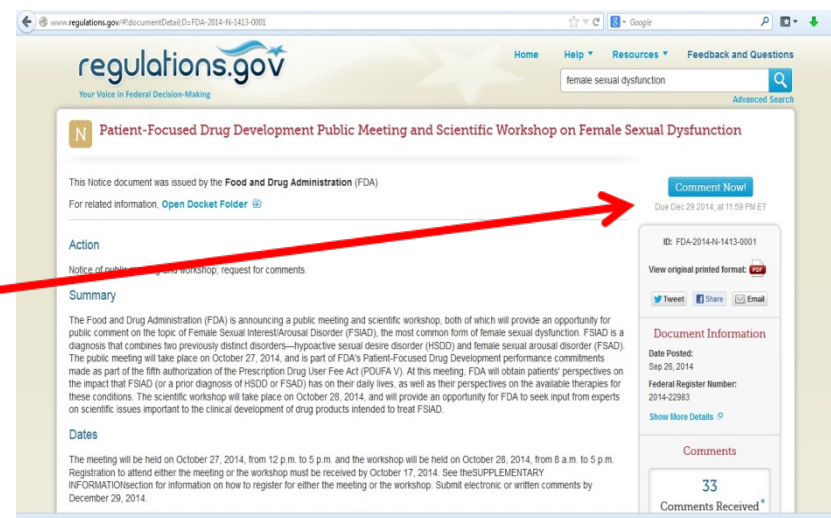
Send us your comments!

- **You can send us comments through the “public docket”.**
 - The docket will be open until December 29, 2014
 - Share your experience, or expand upon something discussed today
 - Comments will be incorporated into our summary report
 - Anyone is welcome to comment

Visit:

<http://www.regulations.gov/#!/documentDetail;D=FDA-2014-N-1413-0001>

Click Comment Now!



Resources at FDA

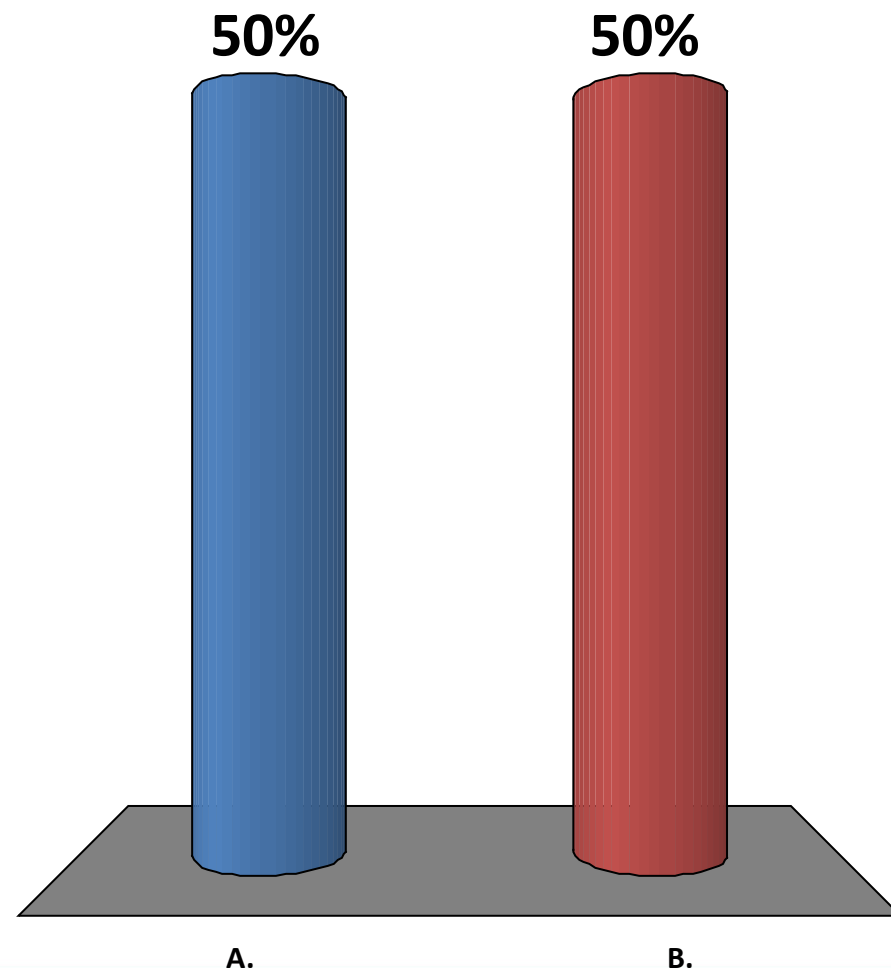
- FDA Office of Health and Constituent Affairs
 - Contact: PatientNetwork@fda.hhs.gov, (301) 796-8460
 - Liaison between FDA and stakeholder organizations
 - Runs the Patient Representative Program
 - Patient Representatives advise FDA at Advisory Committee meetings
- CDER Office of Center Director
 - Professional Affairs and Stakeholder Engagement (PASE)
 - Contact: Rea Blakey, rea.blakey@fda.hhs.gov, (240) 402-6506
 - Facilitates communication and collaboration between CDER and patient and healthcare professional stakeholders and others on issues concerning drug development, drug review and drug safety.

Discussion Ground Rules

- We encourage all participants with FSIAD to contribute to the dialogue—partners and advocates are also welcome to contribute
- FDA is here to listen
- Discussion will focus on symptoms and treatment approaches
 - Open Public Comment Period is available to comment on other topics
- The views expressed today are personal opinions
- Respect for one another is paramount
- Let us know how the meeting went today; evaluations at registration desk

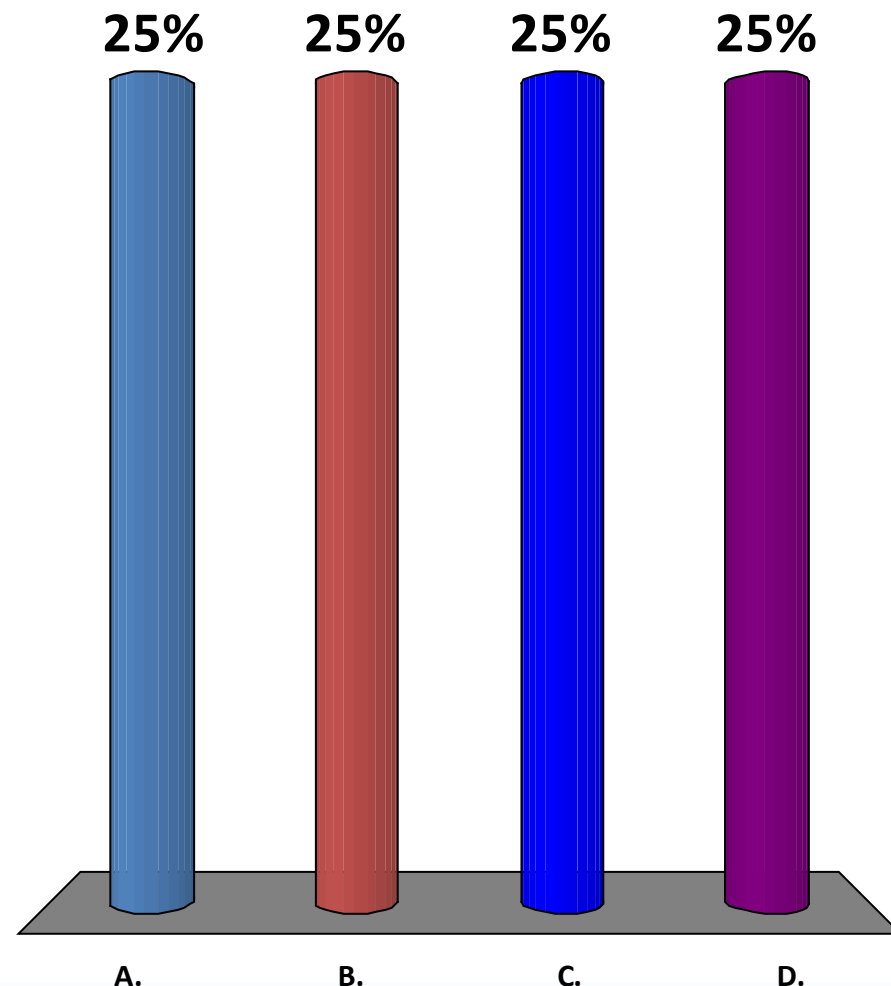
Where do you live?

- A. Within the Washington, D.C. metropolitan area (including the Virginia and Maryland suburbs)
- B. Outside of the Washington, D.C. metropolitan area



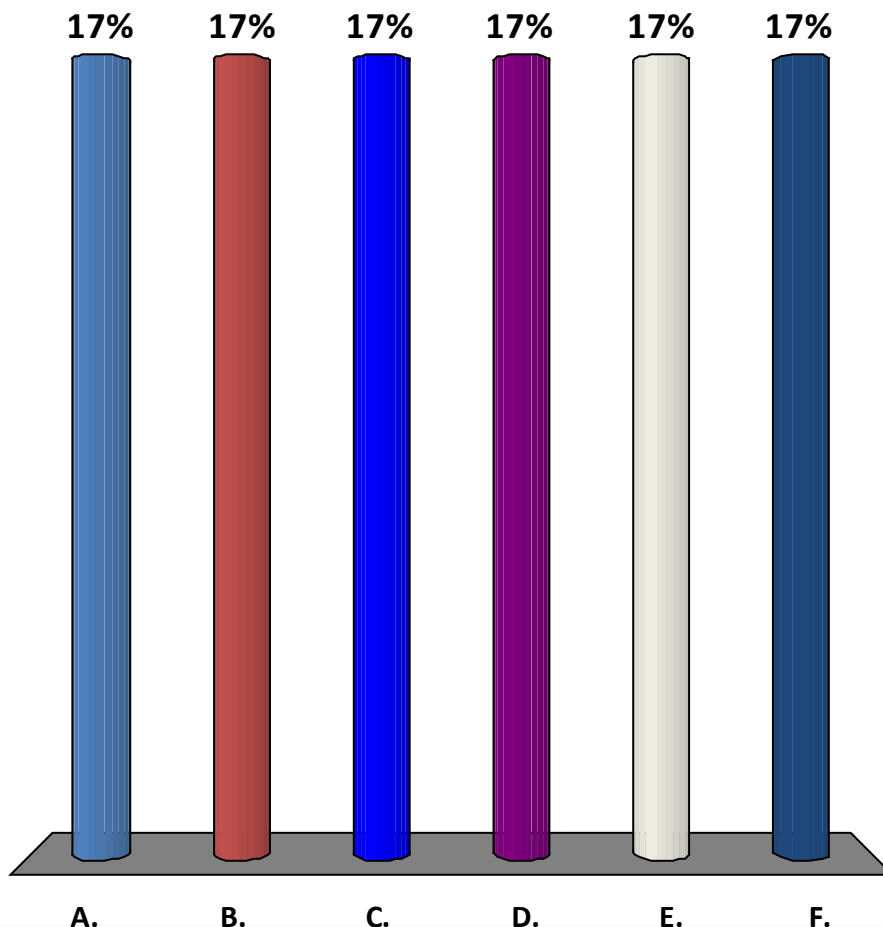
Are you participating today because you, personally, are significantly bothered by:

- A. Absent or reduced desire for/interest in sexual activity or sexual fantasies
- B. Absent or reduced sexual excitement, sexual pleasure or sexual arousal during sexual activity
- C. Both
- D. Neither. I have other symptoms associated with FSD



What is your age?

- A. Younger than 30
- B. 31 – 40
- C. 41 – 50
- D. 51 – 60
- E. 61 – 70
- F. 71 or greater

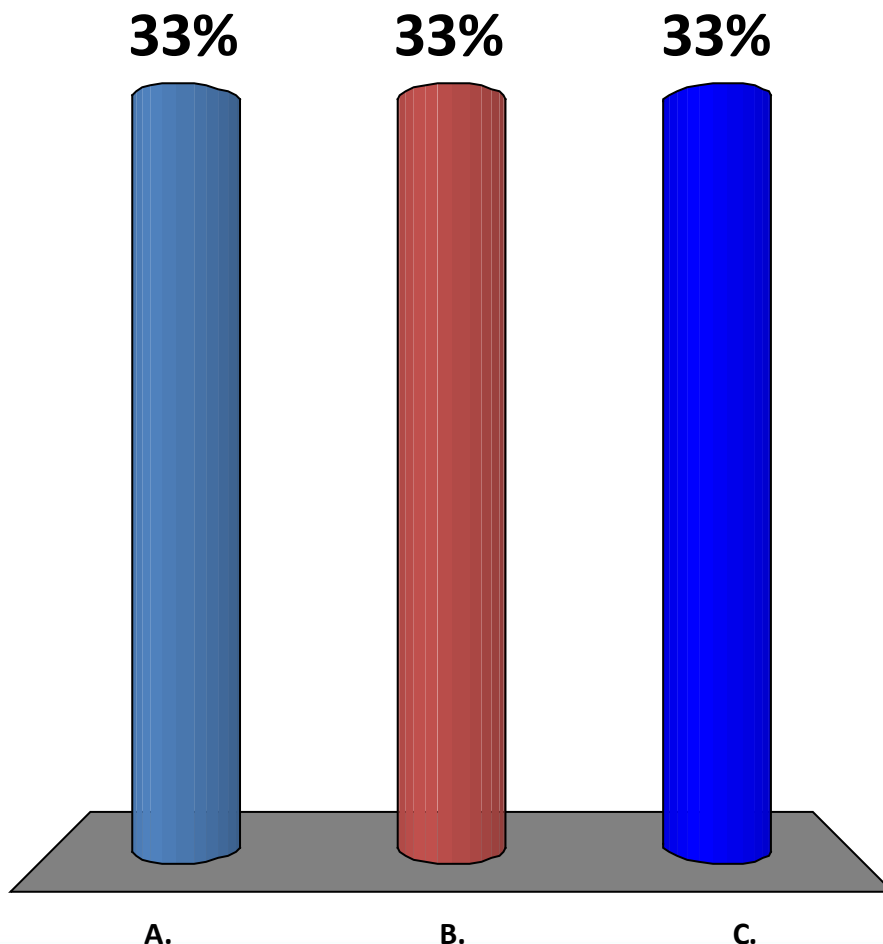


Have you received a diagnosis of female sexual interest/arousal disorder (FSIAD), hypoactive sexual desire disorder (HSDD), or female sexual arousal disorder (FSAD) from a healthcare provider?

A. Yes

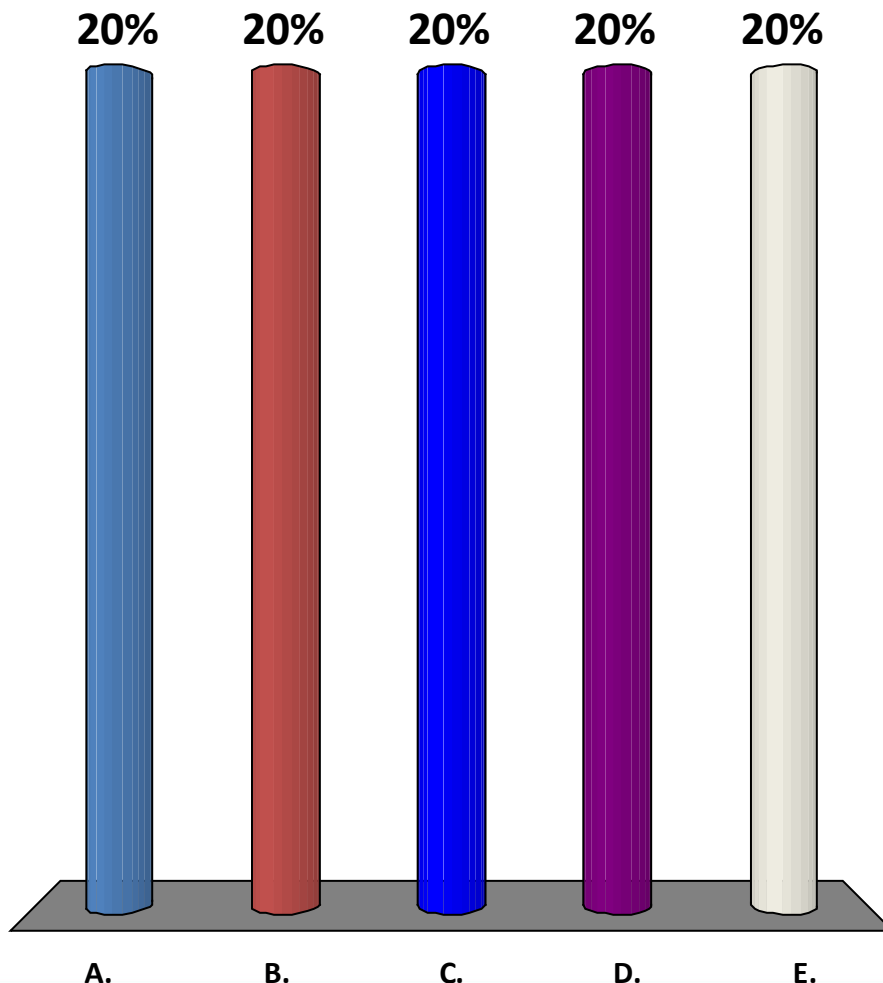
B. No

C. I'm not sure



How long have you had symptoms of FSIAD (or HSDD, FSAD)?

- A. Less than 5 years
- B. 5 – 10 years
- C. 10 – 20 years
- D. More than 20 years
- E. I'm not sure





Discussion Topic 1

Disease symptoms and daily impacts that matter most to patients

Sara Eggers

Facilitator

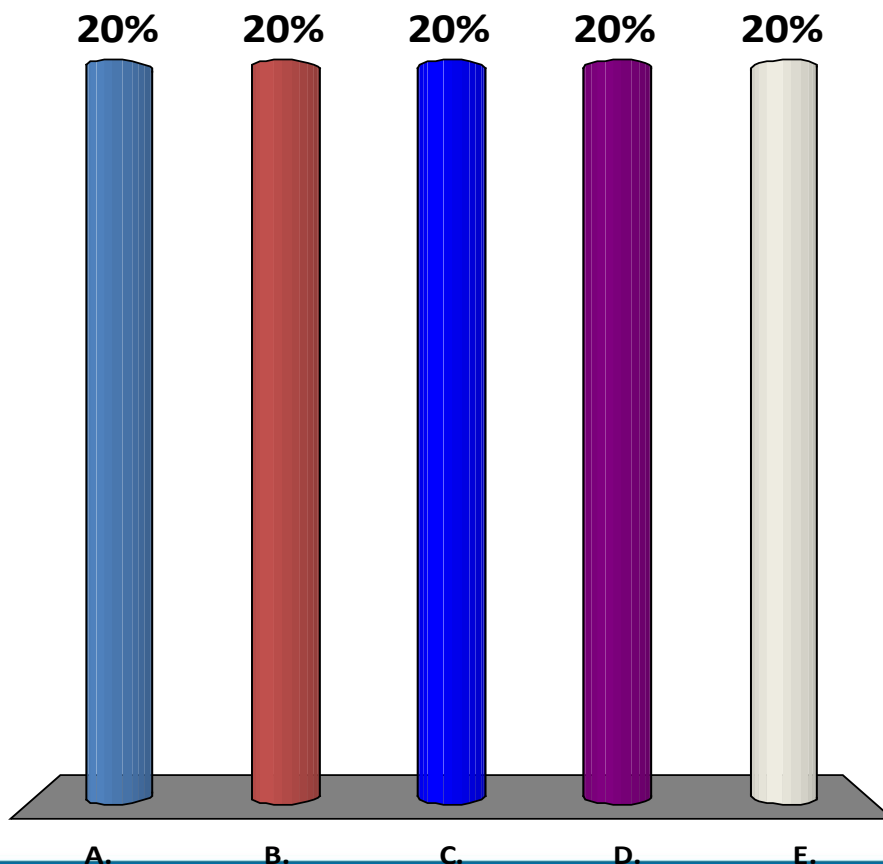


Topic 1 Discussion: Disease symptoms and daily impacts that matter most to patients

- Of all the symptoms that you experience because of your condition, which 1-3 symptoms have the most significant impact on your life?
- Do your symptoms wax and wane over time?
 - Which symptoms vary most?
 - Is there anything that makes your symptoms better? Worse?
- If you were asked to rate your symptoms over time, how often would you need to record to ensure that you accurately remember your symptoms?
- Overall, have you experienced your condition and its symptoms getting progressively worse, improving, or remaining stable over the past few years?
- What worries you most about your condition?

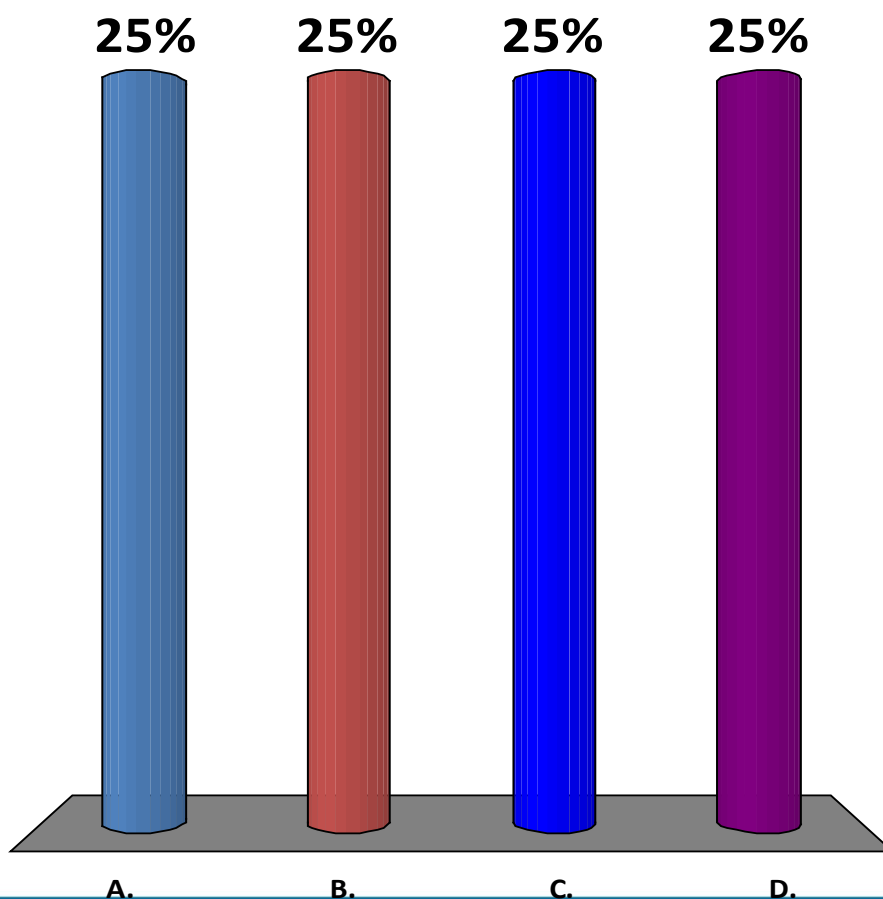
For those of you who experience absent or reduced sexual interest, which of the following effects do you consider to have the most significant impact on your daily life? Please choose up to 2 effects.

- A. No or reduced interest in sexual activity
- B. No or reduced sexual/erotic thoughts or fantasies
- C. No or reduced initiation of sexual activity
- D. Not being responsive to my partner's attempt to initiate sexual activity
- E. Other



For those of you who experience absent or reduced sexual arousal, which of the following effects do you consider to have the most significant impact on your daily life? Please choose up to 2 effects.

- A. No or reduced sexual excitement/pleasure during sexual activity
- B. No or reduced sexual arousal in response to written, verbal or visual cues
- C. No or reduced genital or non-genital sensation during sexual activity
- D. Other





BREAK



Discussion Topic 2

Patients' perspectives on current approaches to treating Female Sexual Dysfunction

Sara Eggers

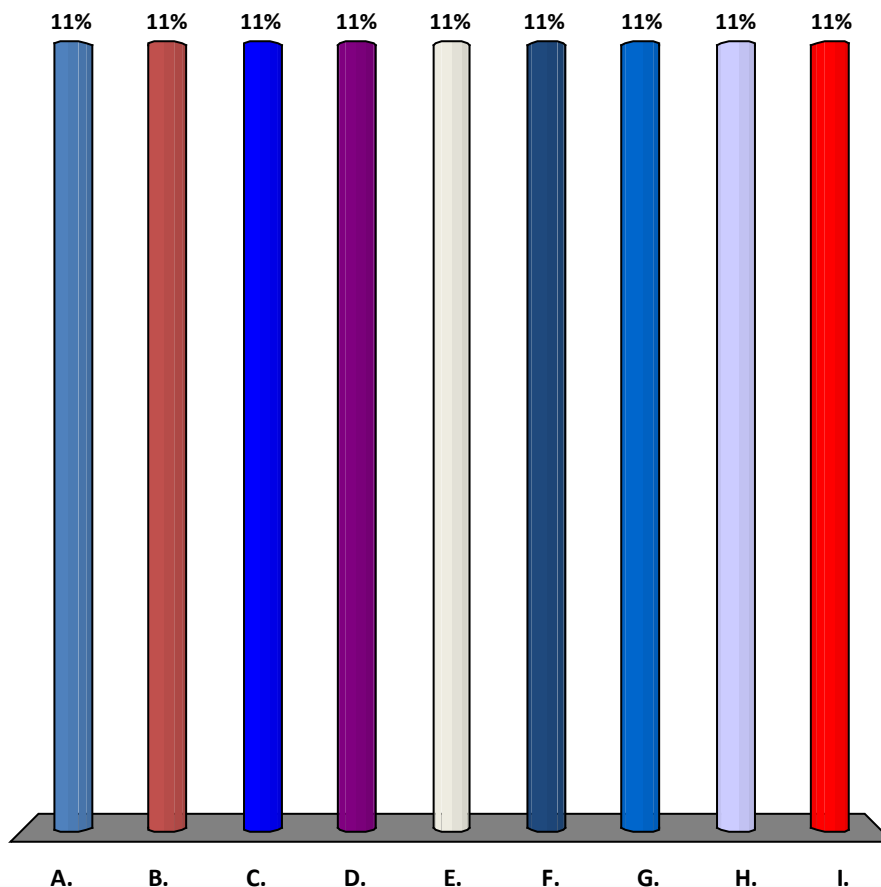
Facilitator

Topic 2 Discussion: Patients' perspectives on current approaches to treating Female Sexual Dysfunction

1. What are you currently doing to help treat your condition or its symptoms?
2. How well do your current treatments specifically treat the most significant symptoms of your condition?
3. How well have your treatments improved your sexual experience?
4. How has your treatment regimen changed over time, and why?
5. Are there any downsides to the treatments you have used?
6. What specific things would you look for in an ideal treatment for your condition?
 - What symptom would you most like a treatment to target?
 - What would you consider to be a meaningful improvement in this symptom?

What are you currently doing to treat your condition or its symptoms? Please select all that apply.

- A. Prescription medicines
- B. Over-the-counter products (for example, a lubricant)
- C. Physical therapy, massage, or acupuncture
- D. Dietary supplements or diet changes
- E. Lifestyle changes, such as exercise or avoiding stressful situations
- F. Behavioral therapies or couples sex therapy
- G. Support group
- H. Other
- I. I am not doing or taking any therapies





Open Public Comment Period



Closing Remarks

Sandra Kweder, MD

Deputy Director, Office of New Drugs
Center for Drug Evaluation and Research
U.S. Food and Drug Administration