Addressing Female Sexual Needs

Essentials of Women’s Health Conference
Big Island, Hawaii

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I have no disclosures to report
Objectives

- Define sexual health, function and dysfunction
- Review the scope of the problem
- Review treatment options within a biopsychosocial framework

Sexual health

WHO definition of sexual health:

- A state of physical, emotional, mental and social well-being in relationship to sexuality
- Not the absence of disease, dysfunction, or infirmary
- Requires positive and respectful approach to sexuality and sexual relationships, including the possibility of having sexual experiences that are
  - pleasurable and safe
  - free of coercion, discrimination and violence

WAS Advisory Council, March 2014
Models of female sexual response

Does not presuppose that desire is the starting point.
Which model is right?

- Masters-Johnson: 35%
- Masters-Johnson-Kaplan: 34%
- Basson: 31%

What about sexual health matters?

Function:
- Desire
- Arousal
- Orgasm
- Frequency

Satisfaction/distress:
- Overall
- Per encounter
- Relationship

What percentage of women reported any of these 3 problems: low arousal, low desire, orgasm difficulties?

- a. 8%
- b. 20%
- c. 43%
- d. 60%

### Measures of sexual function

<table>
<thead>
<tr>
<th>Scale/Instrument</th>
<th>Domains</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female Sexual Distress Scale, Revised (FSDS-R)</td>
<td>Desire, arousal, lubrication, orgasm, satisfaction, pain</td>
</tr>
<tr>
<td>Female Sexual Function Index (FSFI)</td>
<td>Desire, arousal, lubrication, orgasm, satisfaction, pain</td>
</tr>
<tr>
<td>Brief Index of Sexual Functioning – Women (BISF-W)</td>
<td>Interest/desire, sexual activity, satisfaction</td>
</tr>
<tr>
<td>Changes in Sexual Functioning Questionnaire (CSFQ)</td>
<td>Pleasure, desire/frequency, desire/interest, arousal/excitement, orgasm/completion</td>
</tr>
<tr>
<td>Short Form – Personal Experiences Questionnaire (SPEQ)</td>
<td>Sexual responsiveness, sexual frequency, libido</td>
</tr>
<tr>
<td>Sexual Functioning Questionnaire (SFQ)</td>
<td>Desire, physical arousal-sensation, physical arousal-lubrication, enjoyment, orgasm, pain, partner relationship</td>
</tr>
<tr>
<td>Menopause Sexual Interest Questionnaire (MSIQ)</td>
<td>Desire, responsiveness, satisfaction</td>
</tr>
<tr>
<td>Profile of Female Sexual Function (PFSF)</td>
<td>Sexual pleasure, sexual desire, responsiveness, arousal, orgasm, sexual self image, sexual concerns, disinterest</td>
</tr>
<tr>
<td>PROMIS Sexual Function and Satisfaction Scale</td>
<td>Satisfaction with sex life, interest in sexual activity, vaginal lubrication, vaginal discomfort, orgasm-pleasure, orgasm-ability, vulvar discomfort, oral discomfort, oral dryness</td>
</tr>
</tbody>
</table>
Female sexual dysfunction

**DSM 4 definition:**
- Sexual desire disorders (hypoactive desire, sexual aversion)
- Sexual arousal disorders
- Orgasmic disorders
- Pain disorders (dyspareunia, vaginismus)

**DSM 5 definition:**
- Heterogeneous group of disorders
- Clinically significant – sexual response or experience of pleasure


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**DSM 5: sexual dysfunctions**

<table>
<thead>
<tr>
<th>Female orgasmic disorder</th>
<th>Female sexual interest/ arousal disorder</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genito-pelvic pain/ penetration disorder</td>
<td></td>
</tr>
</tbody>
</table>

- Present >6 mos
- Clinically significant distress
- No better explanation (relationship distress, mental health)
Do women care about sex?

- Largest study (13,882 women, 29 countries)
- 65% women sexually active in last year
  - 38% in last week (inverse age relationship)
  - Agrees with US data
- 20-37% reported sex was very/extremely important to life
- 76% women felt satisfactory sex is essential to maintain a relationship
- Sexual well being significantly correlated to self perceived overall health

Laumann et al. 2006
Lindau et al. 2007
Nicolosi et al. 2004

Benefits of positive sexual function

- Improved health-related quality of life
  - physical and emotional satisfaction (with sex and partner)
  - general happiness
  - physical & mental health status
- Effect on health-related QOL similar to women with chronic conditions such as diabetes and back pain

Laumann et al. JAMA 1999
Leiblum et al. Menopause 2006
Biddle et al. Value Health 2009
Ventegodt et al. Arch Sex Behav 1998
How common is problematic sexual function?

- Laumann 1999: 1,749 US women ages 18-59
  - 43% prevalence based on 7 single item dichotomous questions

- Bancroft 2003: Interview of 987 women ages 20-65
  - 24% prevalence of self-reported “distress”

- Shifren 2008: 31,581 US women >18 years
  - 43% reported sexual problem
  - 22% reported sexual distress
  - 12% reported both sexual problem and distress

Distressing sexual problems: age-stratified

<table>
<thead>
<tr>
<th>Age-stratified prevalence</th>
<th>Desire (all ages) 10%</th>
<th>Arousal (all ages) 5.5%</th>
<th>Orgasm (all ages) 4.7%</th>
<th>Any (all ages) 12.2%</th>
</tr>
</thead>
<tbody>
<tr>
<td>18 - 44 years</td>
<td>8.9</td>
<td>3.3</td>
<td>3.4</td>
<td>10.8</td>
</tr>
<tr>
<td>45 - 64 years</td>
<td>12.3</td>
<td>7.5</td>
<td>5.7</td>
<td>14.8</td>
</tr>
<tr>
<td>65 years or older</td>
<td>7.4</td>
<td>6.0</td>
<td>5.8</td>
<td>8.9</td>
</tr>
</tbody>
</table>

Schifren et al. Obstet Gynecol 2008

Legend:
- Any
- Desire
- Arousal
- Orgasm
Risk factors for sexual dysfunction

Laumann et al. 1999
Laumann et al. 2006
Nicolosi et al. 2004
Lindau et al. 2007
Hayes et al. 2008
Dennerstein et al. 2008

Physical health
Emotional health
Age
Relationship status
Stress
HRT
Education
Fatigue
Endocrine disorders
Mental health
History of abuse
Culture
Operative vag deliv
Med side effects
Surgical menopause
HTN

It’s so complicated!
It’s actually not that complicated

I smile to hide how completely overwhelmed I am.

Step 1. Ask about it in a routine care visit

<table>
<thead>
<tr>
<th>Normalizing statement</th>
<th>Many women experience concerns about sex</th>
</tr>
</thead>
<tbody>
<tr>
<td>Close-ended question</td>
<td>Are you experiencing any issues?</td>
</tr>
<tr>
<td>Open-ended question</td>
<td>What is concerning you?</td>
</tr>
</tbody>
</table>

Follow-up questions:
- Generalized or situational
- Time course
- Specific to certain sex practices
- Longstanding or new
- Function? Distress?

Parish et al. Sex Med Review 2018
ACOG Practice Bulletin No. 213: Female sexual dysfunction
### Single item screen: “checklist screener”

**Table 6**

**Recommended Clinical Screener**

<table>
<thead>
<tr>
<th>Item</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>In the past 12 months, has there ever been a period of 3 months or more when you had any of the following problems or concerns? Check all that apply:</td>
<td></td>
</tr>
<tr>
<td>You wanted to feel more interest in sexual activity</td>
<td></td>
</tr>
<tr>
<td>You had difficulty with erections (penis getting hard or staying hard)</td>
<td>MEN ONLY</td>
</tr>
<tr>
<td>Your vagina felt too dry</td>
<td>WOMEN ONLY</td>
</tr>
<tr>
<td>You had pain during or after sexual activity</td>
<td></td>
</tr>
<tr>
<td>You had difficulty having an orgasm</td>
<td></td>
</tr>
<tr>
<td>You felt anxious about sexual activity</td>
<td></td>
</tr>
<tr>
<td>You did not enjoy sexual activity</td>
<td></td>
</tr>
<tr>
<td>Some other sexual problem or concern</td>
<td></td>
</tr>
<tr>
<td>No sexual problems or concern</td>
<td></td>
</tr>
</tbody>
</table>

Flynn et al. J Gen Intern Med 2015
ACOG Practice Bulletin No. 213: Female sexual dysfunction

You can google it!

Google search result:

**Development and Validation of a Single-Item Screener for Self**
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4579234/
by KE Flynn - 2015 - Cited by 28 - Related articles
Kathryn E. Flynn, PhD, Stacy Tessier-Lindau, MD, [ ... We recommend the checklist screener for its specificity and ability to identify specific problems associated ...]
You've visited this page 2 times. Last visit: 7/7/19

**Development and Validation of a Single-Item Screener for Self**
by KE Flynn - 2015 - Cited by 28 - Related articles
Apr 18, 2015 - Flynn KE(1), Lindau ST(2)(3), Lin L(4), Bense JB(5), Jeffery DS(6), Carter ... and respondents could also be checked against specific problems associated with the checklist screener.

**(PDF) Development and Validation of a Single-Item Screener for Self**
https://www.researchgate.net/.../779217360.Development...and...Validation...of...a...Single...Kathryn E Flynn at Medical College of Wisconsin ... We recommend the checklist screener for its specificity and ability to identify specific problems associated ...
Step 2. Use the categories

- Female orgasmic disorder
- Female sexual interest/arousal disorder
- Genito-pelvic pain/penetration disorder
- Substance- or medication-induced sexual dysfunction

Step 3. Use a multidisciplinary approach

- Biopsychosocial model of sexual function
  - Biological
  - Sociological
  - Psychological
  - Integrated approach
Female orgasmic disorder

- Presence of either of the following on all or almost all (75-100%) occasions of sexual activity
  - Marked delay in, marked infrequency of, or absence of orgasm
  - Markedly reduced intensity of orgasmic sensations
- Prevalence = 3 – 6%
- Primary or secondary – often co-occurs with other disorders
- Usually normal levels of sexual desire

Basson et al. J Sex Med 2004
Dunn et al. Bio Lett 2005
Binik et al. Arch Sex Behav 2002

Female orgasmic disorder

Primary – often associated with
- abuse/ trauma, genetic
- typically normal arousal/ desire
- typically doesn’t resolve on its own

Secondary – often associated with another type of dysfunction
- Psychosocial issues
- Age
- Personality
- Religious / cultural beliefs
- Hx of surgery or radiation
- Meds side effects

Dunn et al. Bio Lett 2005
Binik et al. Arch Sex Behav 2002
Treatment of female orgasmic disorder

Treat the underlying disorder!

- psychotherapy (CBT, systematic desensitization if anxiety)
- couples counseling
- masturbation, +/- mechanical devices
- sensate focus

Monetjo Gonzalez et al. / Sex Marital Ther 1997
Meston et al. / Annu Rev Sex Res 2004
Buster et al. / Fertil Steril 2013

McMullen et al. / J Consult Clin Psychol 1979
Billups et al. / World J Urol 2002
LoPiccolo et al. / Arch Sex Behav 1972

Step 2. Use the categories

Female orgasmic disorder
Female sexual interest/ arousal disorder
Genito-pelvic pain/ penetration disorder
Substance- or medication-induced

DSM 5
Sexual dysfunction
Sexual interest/ arousal disorder

Lack of, or significantly reduced, sexual interest/arousal, as manifested by at least three of the following:

1. Absent OR reduced interest in sexual activity
2. Absent OR reduced sexual/erotic thoughts or fantasies
3. No OR reduced initiation of sexual activity, and typically un receptive to a partner’s attempt to initiate
4. Absent OR reduced sexual excitement/pleasure during sexual activity in almost all or (approximately 75-100%) sexual encounters (in identified situational contexts or generalized, in all contexts).
5. Absent OR reduced sexual interest/arousal in response to any internal or external sexual/erotic cues (e.g. written, verbal, visual).
6. Absent OR reduced genital or nongenital sensations during sexual activity in almost all or all (approximately 75-100%) sexual encounters (in identified situational contexts or, if generalized, in all contexts).

Sexual interest/ arousal disorder

- Decreased libido = most common sexual complaint (70%)
- Address non-hormonal variables (trauma, relationship, other)
- Useful questions:
  - When did you notice your decrease in sexual interest?
  - Is it lifelong problem or a new onset?
  - Did this occur gradually or all of a sudden?
  - How often do you self-stimulate in a day, week or year?
  - How often are you sexually active in a day, week or year?
  - Are you attracted to other individuals?
  - Does a sexual book or movie affect you?

Kingberg et al. Menopause 2013
Biomedical factors

- **Hormones**
  - Estrogen: ↓ lubrication, labial retraction, pain, vaginitis
  - Testosterone: ↓ with age
    - Free T lower in women w/ FSIAD (premenopausal women)
  - Atherosclerosis and endothelial dysfunction
    - Vaginal engorgement insufficiency
    - Clitoral erectile dysfunction

- **Medication side effects**

Krychman et al. J Sex Med 2011
Pluchino et al. Arch Gynecol Obstet 2013
Simon et al. Climacteric 2013

Androgens and age

<table>
<thead>
<tr>
<th>TT (ng/dl)</th>
<th>FT (pmol/L)</th>
<th>DHEA-S (µmol/L)</th>
<th>Androstenedione (nmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-24 (n=22)</td>
<td>35-34 (n=97)</td>
<td>35-44 (n=153)</td>
<td>45-54 (n=140)</td>
</tr>
</tbody>
</table>
Testosterone as treatment

- Transdermal testosterone
  - RCTs (total n=3000 postmenopausal women) – increase in sexual desire (in combo w/ estrogen)
  - Dose-related
  - 300mcg/day or more
  - Minimal side effects

- Testosterone cream/spray
  - RCTs – increase in sexual function and satisfying events

- Risks: hirsutism, decr HDL, CV complications, ? breast cancer

- Endocrine society recommends 3-6 month trial of T

Wierman et al. J Clin Endocrinol Metab 2014

Testosterone recommendations

- Not FDA approved
- Evidence for short-term benefit in postmenopausal women
- Insufficient evidence in premenopausal women
- Use transdermal – insufficient evidence for other forms
- Can consider as 3-6 month trial (d/c at 6mos if no response)
  - Testosterone: baseline, 3-6 wks, Q6 months (level = repro-age woman)
- Long term safety and efficacy unclear

ACOG Practice Bulletin No. 213: Female sexual dysfunction 2019
Flibanserin

- FDA approved (Aug 2015) in premenopausal women for decreased sexual desire
- Full agonist of the 5-HT1A receptor
- Originally developed as an antidepressant
  - re-purposed for low sexual desire

DHEA (dihydroepiandrosteronedione)

- Studies in postmenopausal women → no efficacy
- No studies in premenopausal women
- Cochrane review: Improvement in sexual function
  - Effect was small, may not be clinically significant
  - Not all populations were women w/ sexual dysfunction
Flibanserin

- 4 phase 3 trials
- Increases # of satisfying sexual events (SSEs) per month by 0.5
  - Placebo group reported incr of 2.7–3.7 times/month
  - Flibanserin group reported incr of 2.8–4.5 times/month
- Side effects: dizziness, sleepiness, nausea
- + alcohol = hypotension
  - Symptomatic hypotension in 17% after 2 glasses of wine

Simon et al. Menopause 2013

Flibanserin recommendations

- Consider for **premenopausal** women without depression
- Counsel about alcohol use
- Although studies showing benefit were randomized, quality was low
- Meta-analysis ➔ minimal or no improvement in symptoms
  - < 1 additional satisfying sexual event per month

Drug development

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Composition</th>
<th>Mechanism</th>
<th>Phase Completion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lybrido</td>
<td>sildenafil + testosterone</td>
<td>Emotional Brain</td>
<td>Phase II completed for HSDD</td>
</tr>
<tr>
<td>Lyntos</td>
<td>buspirone + testosterone</td>
<td>Emotional Brain</td>
<td>Phase II in progress for HSDD</td>
</tr>
<tr>
<td>OHEA Vaginal Ointes (Prazosin)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bremelanotide (PT-141) subq injection (PL6663)</td>
<td>melatonin receptor modulator</td>
<td>Melatonin Technologies</td>
<td>Phase III completed for FVA in postmenopausal women; Phase III new dosing underway</td>
</tr>
<tr>
<td>Apresiasi clitoral topical cream (Flomox®)</td>
<td>Prostaglandin E1 (PGE1)</td>
<td>Apoioos Bio</td>
<td>Phase III completed for FSAD</td>
</tr>
<tr>
<td>Topical testosterone gel (Lutador)</td>
<td>testosterone</td>
<td>BioSante Pharmaceuticals</td>
<td>Phase III efficacy (failed) Phase III safety (stopped early)</td>
</tr>
<tr>
<td>Intranasal testosterone gel (TetraMax™)</td>
<td>testosterone</td>
<td>Trimel Pharmaceuticals</td>
<td>Phase II in progress for anorgasmia</td>
</tr>
<tr>
<td>Extended release daily oral buspirone and bupropion (Lorevys™)</td>
<td>buspirone and trazodone</td>
<td>SP-1 Biopharma</td>
<td>Phase III set to begin</td>
</tr>
<tr>
<td>Transdermal sildenafil delivery system</td>
<td>sildenafil</td>
<td>Strategic Science &amp; Technologies, LLC</td>
<td>Phase II</td>
</tr>
</tbody>
</table>

### Bremelanotide

- FDA approved June 2019 for premenopausal women
- Acts on melanocortin receptors
- Subcutaneous injection, 45min before sexual activity
- Max 1 dose in 24 hours, 8 doses per month
- RCTs in > 1200 premeno women
  - Increase in sexual desire score (25% brem vs 17% placebo)
  - Decrease in distress score (35% brem vs 31% placebo)
  - No difference in # of satisfying sexual events
Bremelanotide side effects

- Side effects: nausea, vomiting, flushing, headaches (40%)
- Darkening of gums and skin (1%) – didn’t go away in half
- Higher blood pressure
- Lowers levels of naltrexone (med for alcohol or opioid dependence)

Step 2. Use the categories

Female orgasmic disorder  Female sexual interest/ arousal disorder

DSM 5
Sexual dysfunction

Genito-pelvic pain/ penetration disorder

Substance- or medication-induced
Genito-pelvic pain/penetration disorder

Persistent or recurrent difficulties towards vaginal penetration manifested as at least one of the following:

- Vaginal penetration during intercourse
- Marked vulvovaginal or pelvic pain during intercourse or penetration attempts
- Marked fear or anxiety about vulvovaginal or pelvic pain in anticipation of, during, or as a result of vaginal penetration
- Marked tensing or tightening of the pelvic floor muscles during attempted vaginal penetration.

Genito-pelvic pain/penetration disorder

Take a good history

- When did the pain start?
- When do you feel the pain?
- Does it get better after penetration?
- Can you describe it? Is it burning, aching, stabbing, etc…
- Do you stop sexual activity because of the pain?
- Does anything make it better or worse?
Vestibulodynia

**Provoked pain with touching**

**Etiologies...**

- Neuropathic pain
- Pelvic floor muscle dysfunction
- Vaginal infections / disorders
  - Candidiasis
  - Lichen sclerosus/ planus
  - Atrophy

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Treatment for vestibulodynia

<table>
<thead>
<tr>
<th>Topical treatment</th>
<th>Oral treatment</th>
</tr>
</thead>
</table>
| • Physical therapy
  • Pelvic floor muscle therapy
  • Biofeedback | • Psychotherapy
  • Sexual therapy |

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Steege et al. Obstet Gynecol 2009
Latthe et al. BMJ 2006
De Andres et al. Pain Pract 2016

Masheb et al. Pain 2009
Topical treatments

- Many studies, poor quality (no controls)
- **Lidocaine gel 5%**
  - No difference vs placebo in an RCT
- **Gabapentin 2%, 6%**
  - 80% of patients improved, full improvement in 29%, uncontrolled
- **Nitroglycerin 0.2%**
  - 91% reported improvement (pilot study)

Boardman et al. Obstet Gynecol 2008
Zolnoun Obstet Gynecol 2003

Prasterone – intravaginal DHEA

- FDA approved in 2016 for **postmenopausal** women with dyspareunia
- Decrease in pain with sexual activity

Labrie et al. Menopause 2016
Oral treatments for vestibulodynia

- **Ospemifene**, a SERM effective for dyspareunia secondary to genitourinary syndrome of menopause
- **TCAs** and other antidepressants
  - insufficient evidence to recommend their use
  - Most useful for unprovoked vulvodynia (may be less useful in provoked, and in vestibulodynia)
- **Gabapentin** and other anticonvulsants
  - Some evidence to support its use
  - 50 – 80% w/ improvement in symptoms across several studies
  
  Leo et al. J Sex Med 2013
  Foster et al. Obstet Gynecol 2010
  Harris et al. J Reprod Med 2007

Physical therapy for vestibulodynia

*Patients w/ vestibulodynia tend to have increased pelvic muscle resting tone and decreased contraction tone*

- Physical therapy
  - 51% = significant improvement
  - 20% = mod improvement
- Ultrasound
- Electrical stimulation
- Biofeedback

Bergeron et al. J Sex Marital Ther 2002
Glazer J Reprod Med 1995
McKay J Reprod Med 2001
When considering medication treatment

- Placebo effect is big
- 67% of treatment effect is accounted for by placebo
- Current treatments are minimally superior to placebo

Weinberger et al. Obstet Gynecol 2018

Final thoughts

- Level A evidence:
  - Dyspareunia related to menopause → vaginal estrofen, ospemiphene, HRT

- Level B evidence:
  - Psychological interventions are recommended as part of treatment
  - PhyIntravaginal prasterone for dyspareunia in postmeno women
  - Can consider flibanserin and bremelanotide

- Level C evidence:
  - Screen in routine care visits
  - Monitor for androgen excess in setting of T use
  - Pelvic floor PT for genito pelvic pain and penetration disorder

ACOG Practice Bulletin 2013. Female sexual dysfunction 2019
Resources!

BOOKS
- Becoming Orgasmic (Heiman)
- Getting the Sex You Want (Leiblum)
- Naked at Our Age (Price)
- Come as You Are (Nagoski)
- She Comes First (Kerner) – for male partners.

WEBSITES
- North American Menopause Society (menopause.org)
- MiddlesexMD (middlesexmd.com) - useful, evidence-based information for patients regarding menopause and sex.