



Effective Health Care

Diagnosis and treatment of Female Sexual Dysfunction (FSD)

Results of Topic Selection Process & Next Steps

The nominator, American College of Obstetrics and Gynecology (ACOG) is interested in a new evidence review on **Diagnosis and treatment of Female Sexual Dysfunction (FSD)** to inform an update of their clinical practice guideline.

We identified 14 recent reviews and a Canadian Guideline covering the scope of this nomination. Therefore, a new review would be duplicative of an existing product. No further activity on this nomination will be undertaken by the Effective Health Care (EHC) Program.

Topic Brief

Topic Number and Name: #0816, Diagnosis and treatment of Female Sexual Dysfunction (FSD)

Nomination Date: 09/05/2018

Topic Brief Date: 3/8/19

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Conflict of Interest: None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

Background

ACOG is requesting a systematic review to improve the diagnosis and treatment of female sexual dysfunction. The DSM-IV defines female sexual dysfunction (FSD) as any sexual complaint or problem resulting from disorders of desire, arousal, orgasm, or sexual pain that causes marked distress or interpersonal difficulty. FSD is estimated to affect between 5-40% of all women, depending on type. ¹ In premenopausal women, the prevalence of any FSD may be as high as 40% ² The major impacts of FSD are on quality of life and relationships. ³

However, the prevalence is just estimated because making the diagnosis of FSD is not standardized. There is not a single, universally accepted diagnostic tool. There are several scales used to measure sexual dysfunction; most assess the four domains (arousal, desire, orgasm, pain); some include additional domains such as satisfaction and lubrication. Most scales were developed about two decades ago. A 2004 literature review (1957 to 2001) yielded 57 questionnaires which assessed sexual function from the patient perspective; 12 were general questionnaires that included some questions in the sexual domain, and 45 were specific to sexual function. ⁴ In the recent literature, the most commonly used scales are the Female sexual well-being scale (FSWB scale), the Female Sexual Distress Scale (FSDS), the Female Sexual Function Index (FSFI), the Sexual quality of life-female (SQOL-F), Changes in Sexual Functioning Questionnaire-Short-Form (CSFQ-14), and Arizona Sexual Experiences Scale (ASEX).

Additionally, prevalence may be underestimated because there is no accepted guidance for when and how often to screen women for FSD. Some authors recommend using a tool called the Sexual Complaints Screener.⁵ However, the ACOG Practice Bulletin #119 recommends the use of the Brief Sexual Symptom Checklist ⁶ for women who present with symptoms or complaints about sexual function, but does not mention screening asymptomatic women. ¹ This guideline was written in 2011, and confirmed in 2017, but was not based on a systematic review of the evidence.

In addition to identifying if FSD is present, it is necessary to correctly categorize the type of FSD. Treatment options vary depending on the type of disorder (desire, arousal, orgasm, pain), and include psychotherapy, hormonal and pharmacotherapy, as well as devices and procedures (surgery, laser, cryotherapy). A recent review listed 42 different treatment modalities, including 26 different classes of medications. ⁷ In addition, several authors have noted a strong placebo effect. ⁸

The diagnostic dilemma is: when a woman presents to her clinician, what is the best tool to accurately diagnose and classify her sexual dysfunction disorder? Then, once diagnosed, what are the best treatment options for her? Obstacles to diagnosing and treating FSD include a lack of adequate training in the topic, few perceived treatment options, inadequate clinical time to obtain a sexual history, patients' reluctance to initiate the conversation, and the underestimation of the prevalence of sexual dysfunction.

Nominator and Stakeholder Engagement

ACOG provided additional details to focus the scope and develop appropriate contextual questions.

Key Questions and PICOs

The key questions for this nomination are:

1. What is the performance (comparative performance) of instruments/checklists/ tests to diagnose sexual dysfunction in women who present with symptoms or sexual function complaints?

2. What is the effectiveness and comparative effectiveness of interventions (pharmacologic and non-pharmacologic) to treat women with sexual dysfunction?
 - a. In women with desire disorders?
 - b. In women with arousal disorders?
 - c. In women with orgasmic disorders?
 - d. In women with pain/penetration disorders?
3. What are the harms and comparative harms of interventions (pharmacologic and non-pharmacologic) to treat women with sexual dysfunction?

To define the inclusion criteria for the key questions, we specify the population, interventions, comparators, outcomes, and setting (PICOS) of interest (Table 1).

Table 1: Key Questions and PICOS

Key Questions	KQ 1: diagnosis	KQ 2: treatment	K3: Harms
Population	<p>Sexually active women of any age with suspected female sexual dysfunction</p> <p>Exclude postpartum population; exclude partner causes</p>	<p>Women with female sexual dysfunction</p> <ol style="list-style-type: none"> a. Desire disorders b. Arousal disorder c. Orgasmic disorder d. Pain/penetration disorders <p>Exclude postpartum population; exclude partner causes.</p> <p>Examine subgroups (menopausal status, predisposing factors such as sexual trauma, co-morbidities)</p>	<p>Women with female sexual dysfunction (regardless of category of dysfunction)</p> <p>Exclude postpartum, partner causes</p> <p>Examine subgroups (menopausal status, predisposing factors such as sexual trauma, co-morbidities)</p>
Interventions	<ul style="list-style-type: none"> • Brief Sexual Symptom Checklist • Diagnostic instruments • Diagnostic tests 	<ul style="list-style-type: none"> • Medications <ul style="list-style-type: none"> ◦ Androgens ◦ Estrogens ◦ SSRI (Wellbutrin, etc) ◦ others • Behavioral/psychotherapy • Physical interventions (pelvic floor physical therapy, dilation, carbon dioxide fractional laser treatment, lubricants, etc) • Devices 	<ul style="list-style-type: none"> • Medications <ul style="list-style-type: none"> ◦ Androgens ◦ Estrogens ◦ SSRI (Wellbutrin, etc) ◦ others • Behavioral/psychotherapy • Physical interventions (pelvic floor physical therapy, dilation, carbon dioxide fractional laser treatment, lubricants, etc) • Devices
Comparators	Other diagnostic instrument or test	Any other active therapy Placebo	Any other active therapy Placebo

Key Questions	KQ 1: diagnosis	KQ 2: treatment	K3: Harms
Outcomes	Diagnostic accuracy	<u>Benefits:</u> <ul style="list-style-type: none"> Improvement in sexual function: <ul style="list-style-type: none"> desire arousal ability to achieve orgasm painless intercourse Improvement in Quality of Life Resolution of personal distress 	<u>Harms:</u> <ul style="list-style-type: none"> Androgen related (Hirsutism, Acne, virilization) Cardiovascular risk Breast cancer Other
Timing/Setting	Restrict to Very High Index Countries	Restrict to Very High Index Countries	Restrict to Very High Index Countries

Abbreviations: SSRI: selective serotonin receptor inhibitor

Methods

We assessed nomination #0816, Diagnosis and Treatment of Female Sexual Dysfunction (FSD) for priority for a systematic review or other AHRQ EHC report with a hierarchical process using established selection criteria. Assessment of each criterion determined the need to evaluate the next one. See Appendix A for detailed description of the criteria.

1. Determine the *appropriateness* of the nominated topic for inclusion in the EHC program.
2. Establish the overall *importance* of a potential topic as representing a health or healthcare issue in the United States.
3. Determine the *desirability of new evidence review* by examining whether a new systematic review or other AHRQ product would be duplicative.
4. Assess the *potential impact* a new systematic review or other AHRQ product.
5. Assess whether the *current state of the evidence* allows for a systematic review or other AHRQ product (feasibility).
6. Determine the *potential value* of a new systematic review or other AHRQ product.

Appropriateness and Importance

We assessed the nomination for appropriateness and importance.

Desirability of New Review/Duplication

We searched for high-quality, completed or in-process evidence reviews published in the last three years on the key questions of the nomination. See Appendix B for sources searched and Appendix C for details of the Pubmed search.

Results

See Appendix A for detailed assessments of all EPC selection criteria.

Appropriateness and Importance

This is an appropriate and important topic. FSD affects a significant proportion of women in the USA, and there are significant barriers to appropriate diagnosis and treatment. Treatment depends on an accurate diagnosis, and all medical and surgical therapies have associated with benefits and harms. ACOG has a practice bulletin which needs to be updated.

Desirability of New Review/Duplication

A new evidence review would be duplicative of existing evidence reviews. The Pubmed search uncovered 14 systematic reviews that cover parts of the key questions, and thus would be useful to the nominator. See Table 2, Duplication column.

Table 2. Key Questions and Results for Duplication

Key Question	Duplication (01/2015-11/2018)
KQ 1: Diagnosis of FSD	Total number of identified systematic reviews: 1 <ul style="list-style-type: none">• One SR limited to sexual desire ⁹• One protocol ¹⁰
KQ 2: Treatment of FSD	Total number of identified systematic reviews: 17 <ul style="list-style-type: none">• Cochrane: 1 ¹¹• Others ^{7,8,12-24}
KQ 3: Harms	Total number of identified systematic reviews: 4 <ul style="list-style-type: none">• Cochrane: 1 ¹¹• Others: ²¹⁻²³

Key Question 1: What is the performance (comparative performance) of instruments/checklists/ tests to diagnose sexual dysfunction in women?

We identified one systematic review and five narrative reviews on diagnosis of sexual dysfunction. A recent good quality review searched for instruments to measure *sexual desire* (one of the 4 domains of sexual functioning). The methodological quality of the instruments was evaluated by the COnsensus-based Standards for the selection of health status Measurement Instruments (COSMIN) checklist. Authors found 15 articles on 10 instruments, search date ended November 2017.⁹ We found no recent SRs on diagnosis of the other sexual function domains, or measures of overall sexual functioning.

We found 5 recent general reviews that highlight the difficulty of making an accurate diagnosis of FSD.^{5,25-28} However, none of these are systematic reviews. An exhaustive search for sexual health questionnaires was published in 2004, encompassing literature from 1957 to 2001.⁴ In PROSPERO, we found one in-progress 2016 protocol “Measurement properties of instruments for women's sexual health.” We have contacted the primary author (who is based in Iran), but received no response.¹⁰

The Society of Obstetricians and Gynecologists of Canada published their 2018 Female Sexual Health Consensus Clinical Guidelines, which included recommendations for diagnosis.²⁹ The authors state that they performed a literature search through 2010, however, many references list the source as Uptodate.com (not publically available). Evaluation of the quality of evidence and grading of their recommendations was based on the Canadian task force on preventive services.

Key question 2: What is the effectiveness and comparative effectiveness of interventions (pharmacologic and non-pharmacologic) to treat women with sexual dysfunction?

We identified 17 systematic reviews on treatment of sexual dysfunction. See Table 3.

- One (the 2018 Female Sexual Health Clinical Consensus Guidelines) reported that their assessment of quality and strength of evidence was based on a systematic review; however, the systematic review details were not provided.²⁹
- Five systematic reviews focused on women generally
 - Of these, two recent reviews by Weinberg address effectiveness, but not comparative effectiveness.^{7,8} The first highlights the strong placebo effect, and may not be useful to practitioners and patients.⁸ The second is of undetermined quality, and the search will be more than three years old by February 2019.⁷
 - Three other fair quality reviews address the effectiveness of single interventions (DHEA, mindfulness and phosphodiesterase type 5 inhibitors).

- Four have searches more than three years old (search ended prior to January 2016).^{15,21,22,24}
- Seven reviews focused on menopausal women, and five specifically addressed vaginal atrophy (which is a specific subset of pain disorders)^{11-13,15,19} Two good quality reviews address the effectiveness and comparative effectiveness of hormonal treatment. One is from the Cochrane group¹¹, and the second includes a metanalysis.¹³
- For KQ 2d (sexual pain disorders), we found three reviews.^{14,24,30} The broadest of these (any sexual pain disorder) is likely outdated. The most recent is a good quality SR is limited to therapies for women with vaginismus, and the single outcome is completed vaginal intercourse.¹⁴
- For KQ 2a (desire disorders), we found only one recent good quality review. However, the only intervention studied was topical testosterone.¹⁷

We identified two ongoing systematic reviews that may be relevant:

1. Interventions to treat male and female sexual dysfunctions: an overview of systematic reviews. (from the National Health Service of England, posted in 2017)³¹ Authors indicate that the review will be published in the near future.
2. Absolute/comparative efficacy and tolerability of hormonal and non-hormonal approaches of sexual dysfunctions in postmenopausal women. (from authors in Brazil, posted in 2018)³² Authors indicate that the review will be publicly available in the near future.

Table 3: Summary of 17 recent systematic reviews on treatment (KQ2), sorted by subpopulation. (* denotes outdated search)

Author, Year	Search end date	Population (women)	Intervention	Outcome	Details
Weinberger, 2018 ⁸	Sep 2016	All	Placebo vs. any pharmacotherapy	FSFI total score	MA
Weinberger, 2018 ⁷	Feb 2016	All	42 Treatment modalities vs. any other	Any sexual function	Study quality not assessed, SOE not graded
Stephenson, 2017 ¹⁸	March 2016	All	Mindfulness-based therapy (MBT)	Any sexual function	Study quality not assessed, MA
Gao, 2016 ²³	Jan 2016	All	phosphodiesterase type 5 inhibitors (PDE5is) vs. placebo	Any sexual function	Study quality not assessed, MA
Peixoto, 2017 ²⁰	Aug 2016	Men and women	DHEA	Any sexual function	SOE not graded
Sauer, 2018 ¹²	May 2017	Meno/ peri-menopausal with vaginal atrophy	DHEA (intravaginal) vs. other	Dyspareunia, Sexual function	Single database, SOE not graded
Pitsouni, 2018 ¹³	May 2017	Menopausal with vaginal atrophy	Vaginal estrogens vs. non-hormonal or hormonal	Dyspareunia, dryness, orgasm, sexual function	MA
Lethaby, 2016 ¹¹	April 2016	Menopausal with vaginal atrophy	Topical estrogen vs. other	Dyspareunia	Cochrane update
Lee, 2018 ¹⁵	Mar 2015*	Menopausal with vaginal atrophy	Any medication therapy	Dyspareunia	Study quality not assessed, Network MA
Pitsouni, 2017 ¹⁹	October 2016	Menopausal women with dyspareunia	Laser therapy vs other	Dyspareunia, sexual satisfaction	MA
Khadivzadeh, 2018 ¹⁶	"2017"	Menopausal	Fennel (with or without other therapy) vs. other	Sexual activity, dyspareunia	
Achilli, 2017 ²¹	Oct 2014*	Menopausal + HSDD	Transdermal testosterone vs. placebo	SSE, sexual activity, orgasms, desire	MA
Maseroli, 2018 ¹⁴	Apr 2018	Women with vaginismus	Medical or psychosocial interventions	Completed penetrative intercourse	MA
Morin, 2017 ³⁰	Oct 2016	Women with provoked vulvodynia	physical therapy modalities vs. other	Dyspareunia, sexual function	SOE not graded
Al-Abbadey, 2016 ²⁴	Nov 2014*	Sexual pain disorders	Any therapy	Any sexual function	SOE not graded
Ganesan 2018 ¹⁷	"2018"	HSDD	Transdermal testosterone vs. other	Sexual activity or function, personal Distress	Rapid review
Jaspers, 2016 ²²	June 2015*	HSDD	Flibanserin vs. other	SSE, desire	MA

Abbreviations: FSFI= Female Sexual Function Index; HSDD= Hypoactive sexual desire disorder; MA= meta-analysis performed; SOE= Strength of Evidence, SSE=Satisfying sexual events,

Key question 3: What are the harms and comparative harms of interventions (pharmacologic and non-pharmacologic) to treat women with sexual dysfunction?

We found four SRs that specifically evaluated harms or adverse events associated with therapy for FSD.^{11,21-23} Each addressed a single intervention. Achilles (testosterone for desire disorder), Jaspers (flibanserin for desire disorder) and Gao (phosphodiesterase type 5 inhibitors for any FSD) may have outdated searches. The Cochrane review by Lethaby is limited to vaginal estrogens for dyspareunia related to atrophy.

Summary of Findings

- Appropriateness and importance: The topic is both appropriate and important.
- Duplication: A new review would be duplicative of existing products.

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Appendix A. Selection Criteria Assessment

Selection Criteria	Assessment
1. Appropriateness	
1a. Does the nomination represent a health care drug, intervention, device, technology, or health care system/setting available (or soon to be available) in the U.S.?	Yes
1b. Is the nomination a request for a systematic review?	Yes
1c. Is the focus on effectiveness or comparative effectiveness?	Yes
1d. Is the nomination focus supported by a logic model or biologic plausibility? Is it consistent or coherent with what is known about the topic?	Yes
2. Importance	
2a. Represents a significant disease burden; large proportion of the population	FSD affects 5-40% of women in the US
2b. Is of high public interest; affects health care decision making, outcomes, or costs for a large proportion of the US population or for a vulnerable population	Yes. There are significant barriers to appropriate diagnosis and treatment.
2c. Represents important uncertainty for decision makers	Yes. Clinicians need guidance to assess patients for symptoms. Treatment depends on an accurate diagnosis.
2d. Incorporates issues around both clinical benefits and potential clinical harms	Yes. Medical and surgical therapies are all associated with benefits and harms
2e. Represents high costs due to common use, high unit costs, or high associated costs to consumers, to patients, to health care systems, or to payers	Yes.
3. Desirability of a New Evidence Review/Duplication	
3. Would not be redundant (i.e., the proposed topic is not already covered by available or soon-to-be available high-quality systematic review by AHRQ or others)	Several recent reviews cover parts of the topic

Abbreviations: AHRQ=Agency for Healthcare Research and Quality; FSD=female sexual dysfunction; KQ=Key Question

Appendix B. Search for Evidence Reviews (Duplication)

Listed below are the sources searched, hierarchically

Primary Search	Search results
AHRQ: Evidence reports and technology assessments https://effectivehealthcare.ahrq.gov/ ; https://www.ahrq.gov/research/findings/ta/index.html ; https://www.ahrq.gov/research/findings/evidence-based-reports/search.html	Strategy: sexual 0
VA Products: PBM, and HSR&D (ESP) publications, and VA/DoD EBCPG Program https://www.hsrd.research.va.gov/publications/esp/	Strategy: sexual 0
Cochrane Systematic Reviews http://www.cochranelibrary.com/	Strategy: sexual One: estrogen for vaginal atrophy
HTA (CRD database): Health Technology Assessments http://www.crd.york.ac.uk/crdweb/	0
PubMed Health http://www.ncbi.nlm.nih.gov/pubmedhealth/	
Secondary Search	
PROSPERO Database (international prospective register of systematic reviews and protocols) http://www.crd.york.ac.uk/prospero/	>10 protocols found, most focused on a single disease Two may overlap: <ol style="list-style-type: none"> 1. Measurement properties of instruments for women's sexual health (Iran, 2016) 2. Interventions to treat male and female sexual dysfunctions: an overview of systematic reviews (NHS, 2017)
Tertiary Search	search
PubMed https://www.ncbi.nlm.nih.gov/pubmed/	Search string for SR Search (((((((sexual[Title/Abstract]) AND function[Title/Abstract])) OR ((sexual[Title/Abstract]) AND dysfunction[Title/Abstract]))) AND ((female[Title/Abstract]) OR women[Title/Abstract])) AND Review[ptyp] AND "last 5 years"[PDat] AND Humans[Mesh] AND English[lang])) NOT cancer[Title/Abstract] Filters: Review; Publication date from 2015/01/01 to 2018/12/31; Humans; English

Appendix C. Search Strategy & Results (Duplication)

Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to November 26, 2018

Date searched: November 27, 2018

Searched by: Robin Paynter, MLIS

#	Searches	Results
1	sexual dysfunctions, psychological/ or dyspareunia/	7602
2	(dyspareunia or (hypoactive* adj2 desire*) or "pain penetration disorder*" or "painful intercourse" or ((arousal or desire or orgasm* or sexual) adj2 (disorder* or dysfunction*))).ti,ab,kf.	16250
3	or/1-2	19729
4	female/ and humans/	7082798
5	(female or females or women or woman).ti,ab,kf.	1794346
6	or/4-5	7555122
7	and/3,6	13642
8	Diagnosis/ or di.fs.	2413381
9	(diagnos* or "brief sexual symptom" or checklist* or instrument* or questionnaire*).ti,ab,kf.	2875571
10	or/8-9	4339192
11	and/7,10	6255
12	limit 11 to (adaptive clinical trial or clinical trial, all or controlled clinical trial or equivalence trial or pragmatic clinical trial or randomized controlled trial)	692
13	limit 12 to yr="2013 -Current"	Diagnosis Trials 299
14	limit 13 to english language	290
15	limit 11 to (meta analysis or randomized controlled trial)	341
16	limit 15 to yr="2015 -Current"	95
17	limit 16 to english language	Diagnosis and SRs MAs 95
18	Treatment Outcome/ or (dt or px or rh or th).fs.	4959751
19	(androgen* or behavior* or behaviour* or device* or dilat* or drug or drugs or estrogen* or intervention* or laser* or lubricant* or lubricat* or medicat* or nonpharmacolog* or non-pharmacolog* or pharmacolog* or psychotherap* or psycho-therap* or SSRI or therap* or treat* or welbutrin).ti,ab,kf.	8948403
20	or/18-19	10772776

#	Searches	Results
21	and/7,20	11000
22	limit 21 to (adaptive clinical trial or clinical trial, all or controlled clinical trial or equivalence trial or pragmatic clinical trial or randomized controlled trial)	1223
23	limit 22 to yr="2013 -Current"	Treatment Trials 438
24	limit 23 to english language	425
25	limit 21 to (meta analysis or systematic reviews)	652
26	limit 25 to yr="2015 -Current"	245
27	limit 26 to english language	Treatment SRs and MAs 230