What Sexual Behaviors Relate to Decreased Sexual Desire in Women? A Review and Proposal for End Points in Treatment Trials for Hypoactive Sexual Desire Disorder

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ABSTRACT

Introduction: Counts of satisfying sexual events (SSEs) per month have been criticized as an end point in treatment trials of women with hypoactive sexual desire disorder (HSDD) but grounding improvement in sexual desire by assessing changes in sexual behavior remains of some importance.

Methods: We conducted a literature review to find validated measurements that are specific sexual behavioral correlates of low sexual desire. We compared expert-proposed criteria for dysfunctional desire, expert-developed sets of scale items, and self-rated scales developed before issuance of, or in accordance with, the Food and Drug Administration's guidance on developing patient-reported outcomes. Behavioral measurements of HSDD were isolated from these sets of criteria or scales.

Main Outcome Measures: We outline a plan to evaluate such behavioral measurements of HSDD with reference to SSEs.

Results: Eleven rating scales, four expert-originated and seven self-rated scales mainly derived from patient input were identified as well validated and relevant to HSDD. Three recent sets of diagnostic criteria for conditions such as HSDD were compared with the scales. Twenty-four different symptoms were found in the scales. Content found relevant to HSDD during development of the rating scales varied highly among measurements, including the self-rated scales developed in conformity with current recommendations for patient-reported outcome measurements. The only item on all sets was desire for sexual activity. Four other items were in approximately at least half the sets: sexual thoughts or fantasies, frequency of sexual activity, receptivity, and initiations. Sexual thoughts or fantasies were in every expert-derived set but in only three of the seven patient-derived sets. Receptivity was in five of the seven expert-derived sets vs two of the seven patient-derived sets. Frequency of sexual activity was in one of the seven expert-derived sets but in five of the patient-derived sets. Initiation was in approximately half the two sets. All other items were on one to three sets each. We identified three sexual behaviors of validated specificity for female HSDD: frequency of sexual activity, receptivity, and initiations. Six or seven items are relevant and informative. The item on frequency of sexual activity in the Changes in Sexual Functioning—Female scale is the only item that covers frequency of dyadic and solitary sexual activity. An item in the Female Sexual Desire Questionnaire (FSDQ) covers the intuitively relevant topic of frequency of sexual activity motivated by the woman's desire. Three FSDQ items on initiations and two items on receptivity reflect expert opinion on the sexual behaviors of most relevance to HSDD, but the FSDQ has not been validated in women with HSDD.

Conclusions: SSEs have been discredited as the primary measurement in clinical trials of women with HSDD, but it would be meaningful to include at least one sexual behavioral symptom specific to HSDD as an end point. Expert-recommended sexual behaviors specifically related to HSDD are irregularly represented in self-rating scales whether developed as in the Food and Drug Administration guidance on patient-reported outcomes or not. Six or seven items on sexual behavior in self-rated scales can be recommended for relevance to women with HSDD in clinical trials. Items on female sexual behavior should be tested in comparison with SSEs in women with HSDD for relevance and for treatment sensitivity, and responder and functional and dysfunctional cutoffs should be determined before incorporation into large-scale clinical trials. **Pyke R and Clayton A. What Sexual Behaviors Relate to Decreased Sexual Desire in Women? A Review and Proposal for End Points in Treatment Trials for Hypoactive Sexual Desire Disorder. Sex Med 2017;5:e73—e83.**

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INTRODUCTION

To prove efficacy for female sexual dysfunction (FSD) and for hypoactive sexual desire disorder (HSDD) specifically, the US Food and Drug Administration (FDA) division of bone, reproductive, and urologic products has long recommended[1] as the primary end point a monthly count of satisfying sexual events (SSEs), although for HSDD it also has come to accept a validated measurement of sexual desire as a second, co-primary, end point.[2] SSEs have long been a stumbling block to showing efficacy because of large, right-skewed variance,[3] poor reflection of severity,[4] lack of a well-defined change score for improvement,[5,6] and poorly identified value as a measurement to patients and clinicians alike.[7,8]

The regulatory primacy of SSEs might be wavering. Experts convened by the FDA to address measurement issues in trials of women with HSDD have recommended demoting SSEs to a secondary end point.[9]

For HSDD, if the objective of treatment is to restore sexual desire and obviate distress about loss of desire, and thereby help a woman regain the sexual aspects of her primary relationship, then the evaluation of treatment needs to assess change in the quality and quantity of the sexual behavior that was affected by her loss of desire.

Measuring improvement in a particular form of sexual dysfunction (eg, HSDD) by measuring specific aspects of sexual behavior that relate closely to the dysfunction seems a basic requirement. However, this has been minimally explored apart from research into the male sexual disorders of erectile dysfunction and premature ejaculation.

In women with sexual dysfunctions, SSEs reflect a non-specific impairment. SSEs are as infrequent in those with female sexual arousal disorder (FSAD) as in those with HSDD.[10,11] Data on SSEs in women with orgasmic disorder are scarce, but a large clinical trial sample[12] showed rates similar to those in trials of women with HSDD.[3,13]

This review attempted to determine the closest sexual behavioral correlates of female HSDD by a review of the literature and to propose which are sufficiently validated to be incorporated into clinical trials.

METHODS

We conducted a Medline search from 2010 to March 2016 for all published reviews of well-validated rating scales relevant to assessment of low sexual desire in women. This disclosed two reviews.[14,15] We supplemented the search with a compendium of sex-related measurements published in 2011.[16] We updated the search for relevant measurements by conducting Medline searches for *scales of sexual desire* and *measures of sexual desire* for 2010 through March 2016. We reviewed the scales for items that are specific behavioral correlates of low sexual desire and can be used to measure such behavior in studies of FSD. The measurements of sexual desire had to apply to adult women in general, not only women with a specific disease. This eliminated sexual scales on depression,[17] breast cancer,[18] pelvic problems[19] or incontinence,[20] or validated only for postmenopausal women[21–23] or for postpartum women.[24]

Validation had to include discriminant validity between women diagnosed with low sexual desire and sexually functional women. This eliminated three otherwise extremely detailed and well-characterized scales, the Sexual Arousal and Desire Inventory (SADI),[25] a partner-specific scale of the Sexual Wanting and Liking Scale,[26] and the Sexual Interaction System Scale.[27]

Several measurements were rejected for this review because, although much of their coverage was similar to that for measurements relevant to low sexual desire in women, the aim of the measurement was different (eg, the Sexual Activity Questionnaire to measure partners' initiation of sexual activities but not to measure desire per se[28]; the Sexual Awareness Questionnaire covers items similar to desire scales but its thrust is to measure sexual consciousness, preoccupation, monitoring, and assertiveness, not desire per se).[29] Other measurements were rejected because published discriminant validation was lacking[30,31] or because the validation was limited to accuracy in use of the instrument to diagnose rather than measure low desire (Decreased Sexual Desire Screener,[32] Women's Sexual Interest Diagnostic,[33] the Sexual Complaints Screener for Women,[34] and a structured diagnostic method to enable diagnosis of FSD in postmenopausal women).[21] Other measurements were rejected because they covered sexual desire only in a single, generic item (the Arizona Sexual Experiences Scale,[35] the Massachusetts General Hospital Sexual Function Questionnaire,[36] and an unnamed measurement).[37] In addition, the measurement had to be available in English to be included in this review.

RESULTS

General Findings

Seven sets of items generated by expert clinicians were found: three criteria sets of symptoms required for disorders of low sexual desire and four rating scales. Seven well-validated scales generated from patient input were found. All desire-related items that were found in expert-recommended rating scales or patient-generated scales are presented in and Table 1 and Appendix A.

Clinician-Developed Sets of Criteria or Items

The three sets of criteria developed in this century for disorders of low sexual desire include the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision* (DSM-IV-TR) of 2000[38]; the International Consensus Criteria of 2003[39]; and the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5) criteria of 2013 for the newly defined disorder that subsumes HSDD (ie, female sexual interest-arousal disorder [FSIAD]).[40] The only symptoms in the DSM-IV-TR set are low desire, low sexual thoughts or fantasies, and distress related to the low desire. The International Consensus Criteria added low receptivity. The desire-related criteria in the DSM-5 added low initiations. Much clinical experience went into these criteria sets but little or no field evaluation.

Four multi-item measurements of sexual desire were developed by expert clinicians.

DeRogatis Interview for Sexual Functioning

The DeRogatis Interview for Sexual Functioning (DISF)[43] was created by a highly experienced clinician and validated as a clinician-rated instrument, although the matching DISF—Self-Report was not validated for content as a self-report measurement and thus does not meet the current FDA guidance for industry on development of patient-reported outcomes (PROs).[51] Developed in 1987 to 1989, the DISF includes five items on desire (sexual thoughts or fantasies, **wanting to be involved in sexual activities** [in this review, each unique item is in boldface], the highly related but more focused consideration of **how often you want to have sexual intercourse,** plus **how often and how strong was your sexual desire,** and **how receptive were you to your partner's sexual requests**).

Brief Interview of Sexual Functioning in Women

The Brief Interview of Sexual Functioning in Women (BISF-W)[52] was developed in 1993 by clinicians from highly detailed interviews of patients as a standardized interview to measure sexual function broadly in clinical trials. The BISF-W is a self-report measurement that did not undergo retesting in patient samples for item reduction, although psychometric evaluation was performed and concurrent validity was shown.[52] In its most recently recommended partition of items, it includes seven items apparently related to desire.[41] These include sexual thoughts; desire to engage in sexual activities, with seven types to be rated, one of which is so different as to be worth mentioning separately (ie, un-partnered sexual activity [**masturbation alone**]); **becoming anxious or inhibited during sexual activity** (not part of the desire item cluster but of interest here for possible interference with desire); initiations; response to sexual partner's initiations; and **frequency of partnered sexual activity compared with frequency of desire for same.** However, the BISF-W was reviewed recently as having a lesser level of validation, with only "moderate" test-retest reliability and concurrent validity.[14]

Sexual Interest and Desire Inventory—Female

The Sexual Interest and Desire Inventory—Female (SIDI-F)[42,53,54] was developed for clinical trial use in 2002 to 2005 by expert clinicians based on their overall experience with patients, because of perceived shortcomings in the breadth of coverage of the available measurement of HSDD.[53] This included all the previously mentioned items plus **physical affection, use of erotica, and satisfaction about desire.** Discriminant and concurrent validation were published on results from more than 200 women with HSDD and more than 200 women without HSDD, plus item reduction studies.[42,53,54] A small content validity study (seven subjects) found each of the scale's items sufficiently clear and relevant and recommended no more directly related items, but that negative effects on the sexual relationship also should be measured (Shumaker SA, Final report, sexual interest and desire inventory validation study, 2005, unpublished). The SIDI-F also includes an item on frequency of sexual activity, but as a background item only, not to be analyzed with the validated total score.

Sexual Desire Inventory

The Sexual Desire Inventory[44,55] was developed from considerations of theoretical models of desire and from clinical experience. Content validity was confirmed in a sample of 20 patients. Factor analytic data were obtained from a total of 800 men and women students, geriatric care facility residents, and couples. It consists of 14 items. Most items are on specific aspects of desire for sexual activity (with a partner, with an attractive person, in a romantic situation, by oneself). Three items are novel to the scale**: importance of fulfilling sexual desire through activity (solitary and partnered items); compare with others your desire to behave sexually;** and **how long could you be abstinent comfortably.**[44,55]

Patient-Evoked Scales

Seven self-rated scales with sufficient validation were found. Each was designed or refined through patient interviews, generally following the steps recommended in the FDA's guidance for development of PROs,[51] namely that patients rather than clinicians should be relied on (in focus groups and/or polled) to determine what symptoms are relevant. Such exploration disclosed some other directly related considerations relevant for women with HSDD.

Female Sexual Function Index—Desire Subscale

The Female Sexual Function Index (FSFI),[46,56,57] the rating scale most commonly used to assess the severity of FSD,[56] has as its subscale on sexual desire only one directly related

Table 1. Sexual desire-related items present in recent diagnostic criteria and validated rating scales*

	Expert clinician sets							Scales developed with direct patient input							All 14 sets
	Criteria			Scales											
Symptom list and item	DSM-IV-TR[38]	International consensus[39]	DSM-5[40]	BISF-W[41]	SIDI-F[42]	DISF (SR)[43,†]	SDI[44]	GRISS[45]	FSFI[46]	CSFQ-F[47]	B-PFSF[48]	SFQ28[49]	PROMIS[50]	FSDQ[15]	Overall frequency, n (%)
Rater: C or S				S	C	C or S	S	S	S	S	S	S	S	S	
Desire or interest in sexual activity (level, frequency)	X	X	X	X	X	X	X[§]	X	X	X[§]	X	X	X	X[§]	14 (100)
Sexual thoughts or fantasies	X	X	X	X	X	X	X			X			X	X	10 (71)
Receptivity		X	X	X	X	X		X						X	7 (50)
Frequency of sexual activity					X[‡]			X[‡]		X		X	X[‡]	X	6 (43)
Initiations			X	X	X							X	X	X	6 (43)
Becoming anxious or inhibited during sex				X				X						X	3 (21)
Pleasure from sexual thoughts										X		X		X	3 (21)
Desire for masturbation				X			X							X	3 (21)
Distress about your level of sexual desire					X						X			X	3 (21)
Physical affection; wanting sensual touch and caresses					X							X			2 (14)
Erotica					X					X					2 (14)
Frequency of partnered sexual activity compared with frequency of desire for same				X											1 (7)
How often you want to have sexual intercourse						X									1 (7)

(continued)

Table 1. Continued

	Expert clinician sets															All 14 sets
	Criteria			Scales				Scales developed with direct patient input								
Symptom list and item	DSM-IV-TR[38]	International consensus[39]	DSM-5[40]	BISF-W[41]	SIDI-F[42]	DISF (SR)[43,†]	SDI[44]	GRISS[45]	FSFI[46]	CSFQ-F[47]	B-PFSF[48]	SFQ28[49]	PROMIS[50]	FSDQ[15]	Overall frequency, n (%)
Pleasure from masturbation														X	1 (7)
Satisfaction about desire					X										1 (7)
Felt like having sex											X				1 (7)
Felt sexually numb											X				1 (7)
Looking forward to sexual activity												X			1 (7)
Frequency of partnered sexual activity because of feeling desire for him														X	1 (7)
Avoiding sex with partner								X							1 (7)
Emotional closeness														X	1 (7)
Important to fulfill sexual desire through activity							X[§]								1 (7)
Compare with others your desire to behave sexually							X								1 (7)
How long could you be abstinent comfortably							X								1 (7)

BISF-W = Brief Interview of Sexual Functioning in Women; B-PFSF = Brief Profile of Female Sexual Function; C = clinician; CSFQ-F = Changes in Sexual Functioning Questionnaire—Female; DISF (SR) = DeRogatis Interview for Sexual Functioning (Self-Rated); *DSM-IV-TR = Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision*; *DSM-5 = Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*; FSDQ = Female Sexual Desire Questionnaire; FSFI = Female Sexual Function Index; GRISS = Golombok Rust Inventory of Sexual Satisfaction; PROMIS = Patient Reported Outcomes Measurement Information System; S = self; SDI = Sexual Desire Inventory; SFQ28 = Sexual Function Questionnaire 28-item version; SIDI-F = Sexual Interest and Desire Inventory—Female; X = present.

*Criteria sets for female sexual desire disorders published since 2000 and well-validated rating scales of female sexual desire have included 1 to 16 symptoms related to desire. All or most clinician-specified criteria sets and scales have included desire for sexual activity, sexual thoughts, receptivity, and initiations, but patient-derived scales have consistently included no items other than desire for sexual activity.

†Items from the Self-Rated version of the DISF are included.

‡Clustered separately from sexual desire.

§By oneself and partnered.

consideration: desire or interest in having sexual activity in an item on frequency of interest (item 1) and an item on level of interest (item 2).[46] Content validation of the FSFI desire subscale was conducted in 76 patients[57] and pre- or postmenopausal women (45 premenopausal, 31 postmenopausal) with HSDD said that no other considerations were needed to describe their experience of low desire. However, as noted earlier, the three 21st century sets of criteria for disorders of low sexual desire according to expert clinicians added other considerations: for the definition of HSDD in the DSM-IV-TR, to add deficient or absent sexual fantasies; for the 2003 consensus statement, to add decreased sexual receptivity; and for the DSM-5 in 2013, to add no or decreased initiation of sexual activity.

Changes in Sexual Functioning Questionnaire

The next most popular scale for FSD is the Changes in Sexual Functioning Questionnaire—Female (CSFQ-F)[47,58] used in more than 70 studies, mainly of depressed patients. It was, in its final 14-item self-report form, reduced to five items on desire, two on desire and frequency, and three on desire and interest. Three items were previously mentioned as recommended by experts: one is frequency of sexual activity (partnered or solitary), which specifically mentions masturbation; one is frequency of desire for sexual activity; and one item is novel, **pleasure from sexual thoughts or fantasies.**

Brief Profile of Female Sexual Function

The patient-centered development of the Brief Profile of Female Sexual Function[48,59,60] found desire encompassed by five items. Two, lacked sexual desire and felt like having sex, appear to be opposite forms of the same consideration. The novel item, **felt sexually numb,** appears ambiguously referable to desire or to subjective arousal but might actually pertain to distress about low sexual desire. The two other items are identifiable as indirectly related to desire (ie, unhappy about my low interest in sex and I felt disappointed by my lack of interest in sex) and thus are more relevant to sexual distress scales.

The validated longer version of the overall scale, the Profile of Female Sexual Function, does not contain more items on its sexual desire subscale.[59] Originally for postmenopausal women only, it was recently validated in premenopausal women.[48]

Sexual Function Questionnaire—28-Item Version

The Sexual Function Questionnaire—28-tem version[49] has a desire subscale of six items: how often have you had pleasurable thoughts and feelings about sexual activity, the novel **how often you wanted to be sensually touched and caressed by your partner** (in Table 1 under physical affection), frequency of wanting sexual activity, initiations, frequency of sexual activity, and the novel **how often you look forward to sexual activity.**

Golombok Rust Inventory of Sexual Satisfaction

The Golombok Rust Inventory of Sexual Satisfaction,[45] although 30 years old, was recommended as sufficiently validated in the review by Lorenz et al[14] and in the most definitive previous (2006) review of patient-rated measurements of FSD.[61] However, this scale has no designated subscale on sexual desire. Among its 28 items for women, one is on interest (do you feel uninterested in sex?), one is on receptivity (do you refuse to have sex with your partner?), and one covers avoidance (**do you try to avoid having sex with your partner?**). The answer set strictly measures frequency: "never," "hardly ever," "occasionally," "usually," and "always." Frequency of sexual intercourse also is queried.

PROMIS Sexual Interest Scale

The Patient Reported Outcomes Measurement Information System (PROMIS)[50,62] project developed self-rating instruments for physical and sexual symptoms based on the FDA's guidance for development of PROs.[51] The number of women sampled was large (>800) but limited to those surviving cancer. Four items factored with sexual desire: frequency of desire for sexual activity, intensity of desire for sexual activity, thoughts or fantasies about sex, and initiation of sexual activity. In the PROMIS "profiles," frequency of sexual activity is included, although separately from sexual desire.[62] Recently, the scale was refined through validation studies in large, diverse populations (without cancer).[50]

Female Sexual Desire Questionnaire

Another scale on female sexual desire first published since 2010 is the Female Sexual Desire Questionnaire (FSDQ),[15] also developed in a large sample of women (>700). The full version of the scale includes 50 items, limiting its practical use in clinical trials, and the authors state that the scale's clinical utility remains to be determined. Discriminant validity was not tested, but the tested sample included 47% self-identified as having at least one sexual problem. The authors also created a short form of the instrument with the six highest-loading items from each domain. Desire for sexual activity is split into two domains, one on solitary desire and one on dyadic desire. One domain, resistance, is the opposite of receptivity (highest-loading item: **being approached by the partner when you were clearly not "in the mood"**). Feeling inhibited during sexual activity is categorized as sexual self-image (highest-loading item: **how often were you worried about your body looking unattractive when naked in front of your partner?**). Sexual distress is usually rated in separate scales, but in the FSDQ it is the concern domain (highest-loading item: **how often did your level of sexual desire cause you to feel distressed?**).[15]

Other items in the FSDQ of relevance to sexual behavior (rather than feelings) are within the domains of solitary desire or dyadic desire. Such items cover initiations (three items: When you were experiencing sexual desire, how often did you act on this by starting sexual activity with your partner?; When you

were having enjoyable sexual thoughts or fantasies, how often did these lead you to seek out a sexual encounter with a partner?; and How often did you plan a sexual encounter in advance?), receptivity (two items: How often did your partner stroking or touching you intimately start your feelings of sexual desire?; and How often did you have enjoyable sexual thoughts or fantasies once you had begun self-stimulation?), or frequency of sexual activity precipitated by desire (**How often did you participate in sex with partner because of feeling desire for him?**).

Comparison of Item and Criteria Sets

Across all 14 sets, 24 types of items relating to sexual desire were found. Only desire for sexual activity was represented in each set. Four other items were in approximately at least half the sets: sexual thoughts or fantasies, frequency of sexual activity, receptivity, and initiations. The sexual thoughts or fantasies item was in every expert-derived set but only three patient-derived sets. Receptivity was in five of the seven expert-derived sets versus two of the seven patient-derived sets. Frequency of sexual activity was in one of the seven expert-derived sets but in five of the patient-derived sets. Initiation was in three of the clinician-derived sets and in three of the patient-derived sets. All other items were on one to three sets each.

Items relating specifically and directly to sexual activity included frequency of sexual activity, receptivity, initiations, frequency of partnered sexual activity because of feeling desire for him (in one patient-derived set only), and frequency of partnered sexual activity compared with frequency of desire for same (in one of the seven expert sets only).

DISCUSSION

General Comments

Some validated questionnaires about low sexual desire list only desire, whereas others include up to 16 items. The paucity of items and considerations in the FSFI desire subscale has been repeatedly criticized by the applicable division of the FDA, most recently in its brief on the new drug application for flibanserin (2014 and 2015). It does seem reasonable to identify aspects of sexual desire that are important to women with dysfunctionally low sexual desire and then to choose, for the present purposes, the items that are about sexual behavior.

Despite undergoing the recommended item-finding and -refining process in large patient samples, the desire-related items on the self-rated scales validated to measure sexual desire are markedly different for each scale except for the item of desire for sexual activity.

Only two of the seven scales with patient input include receptivity, but receptivity is the only behavioral item that most (five of seven) of the expert criteria developers and expert scale developers recommended as discriminating disorders of low desire from other sexual disorders. Three of the seven clinician-generated sets and three of the seven patient-adduced scales include initiations.

This lack of uniformity calls into question not only the comprehensiveness of these self-rated scales but also the validity of the process by which self-rated scales have been developed for sexual disorders.

In any case, it appears moot, given that no directly related items besides desire for sexual activity were endorsed as relevant by women with sexual desire disorder,[57] and thus that no multi-item rating scale of sexual desire can be designated as superior to any other.

Behavioral Symptoms

Despite these negative findings about items relating to sexual desire in general, the *behavioral* aspects of HSDD of relevance to patients can still be considered. The disparity in content among validated scales disfavors selecting any one multi-item scale as the standard but also allows freedom of selection of items from any of the validated scales as co-equal in validity.

Frequency of sexual activity appears acceptable as a measurement of sexual desire because it is present in some form or other on approximately half the scales, if we include the item in the BISF-W item (frequency of partnered sexual activity compared with frequency of desire for same) and the non-scored item of the SIDI-F, and in approximately half the scales it factored with sexual desire. Some scale developers have found that the frequency of sexual activity clusters with desire symptoms.[15,49] However, a decrease in the frequency of sexual activity does not have any inherent specificity for loss of sexual desire; loss of arousal or orgasm, or sexual pain, also is associated with lower frequency of frequency of sexual activity, as noted in the Introduction.

Only two scales have more than one item on the frequency of sexual activity. The DISF covers frequency of sexual intercourse, masturbation, kissing and petting, and even the patient's ideal frequency of intercourse but is not validated as a self-rated instrument. The FSDQ (50-item version) has the item frequency of partnered sexual activity because of feeling desire for him, which intuitively seems appropriate for monitoring treatment of HSDD, at least in heterosexual women. The other item of the FSDQ relating to sexual activity, How often did you have a new or spontaneous sexual experience with your partner?, seems unlikely to differentiate treatment results in women in a long-term relationship unless they were quite creative. A domain of the scale is devoted to solitary desire, but no item covers frequency of masturbation. The CSFQ is the only scale with an item covering frequency of solitary and partnered sexual activity (How frequently do you engage in sexual activity [sexual intercourse, masturbation, etc] now?). Validation study data are available to determine responder and dysfunction cutoffs for the CSFQ item.

Beyond that, for HSDD, the two more recently recommended diagnostic requirement sets, the 2003 consensus of

experts and the DSM-5 (for FSIAD) include, for loss of desire, two behavioral criteria: loss of initiation of sexual activity and loss of receptivity to a partner's attempts to initiate. Items on the two are incorporated in the clinician-rated SIDI-F,[42] produced by expert clinicians from their overall experience of women with HSDD, and in the BISF-W,[41] a self-rated scale gleaned by a panel of expert clinicians from questionnaire responses from hundreds of women almost two decades before the FDA guidance on PRO development.[51] The SIDI-F is freely available, but the BISF-W is proprietary and is not licensed to be used in parts.

Discriminant validation study data on items of the SIDI-F support that receptivity and initiations are specific functional impairments in women with HSDD. Three datasets have been published in validation studies: in North American women 18 to 65 years with HSDD only, FSAD only, or with no sexual dysfunction[42]; in European women with HSDD or no FSD[42]; and in North American women with HSDD, female orgasmic disorder, or no FSD.[53]

The validation study data on the SIDI-F showed much worse functionality in women with HSDD on the receptivity and initiations items than in women with FSAD, whereas functionality in women with FSAD was much worse on arousal frequency and arousal ease ($P < .001$ for all comparisons).

Thus, the validated behavioral measurements that might be used to test whether treatment for HSDD improves not only the emotional criteria for the disorder but also a woman's sex life include sexual activity, initiations, and receptivity. For the latter two items, the respective items of the BISF-W, the SIDI-F, or the FSDQ (50-item version) might serve the purpose.

Use of the items from the BISF-W seems precluded by the limitations on use of scale items that are imposed by the authors and publisher. Use of the items from the SIDI-F, which is freely available, is hampered by the fact that the scale is rated by a clinician. However, each item of the SIDI is to be read verbatim to the patient, so the items might be used directly by patients, after proper validation.

Use of the items from the FSDQ might be recommended, especially because multiple items loaded highly and multiple (two to three) items were validated per "construct" (receptivity or initiations), providing the potential for greater psychometric validity. For receptivity, How often did you participate in sexual activity with your partner because you felt sexual desire toward him? loaded at 0.69, just 0.01 below the loading for the highest-loading item in the domain of dyadic desire. How often did your partner stroking or touching you intimately start your feelings of sexual desire? loaded at 0.58.

For initiations, When you were experiencing sexual desire, how often did you act on this by starting sexual activity with your partner? loaded at 0.61. When you were having enjoyable sexual thoughts or fantasies, how often did these lead you to seek out a sexual encounter with a partner? loaded at 0.59. How often did you plan a sexual encounter in advance? loaded at 0.53.

However, neither the scale as a whole nor the items individually or grouped by "construct" have been tested for discriminant validity in women with a diagnosed disorder of low sexual desire and have not been used in clinical trials. Thus, there are no known cutoffs for dysfunction or for response to treatment. Clinicians experienced in treating women with low sexual desire might suspect that some of these five items (eg, planning sexual encounters in advance) are not relevant to women with even borderline-low desire. Further validation studies in women with diagnosed conditions of low sexual desire are needed. Validation research into such items should include comparison of the relevance (importance) to the patient of SSEs and of one of the validated versions of the item on frequency of sexual activity.

CONCLUSIONS

SSEs have been discredited as the primary measurement in clinical trials of women with HSDD, but it would be meaningful to include at least one sexual behavioral symptom specific to HSDD as an end point. Expert-recommended sexual behaviors specifically related to HSDD are irregularly represented in self-rating scales whether developed as in the FDA guidance on PROs or not. Six or seven items on sexual behavior in self-rated scales can be recommended for relevance to women with HSDD in clinical trials. The item on frequency of sexual activity in the Changes in Sexual Functioning—Female scale is the only item that covers frequency of dyadic and solitary sexual activity. An item in the FSDQ covers the intuitively relevant topic of frequency of sexual activity motivated by the woman's desire. Three FSDQ items on initiations and two items on receptivity reflect expert opinion on the sexual behaviors of most relevance to HSDD, but the FSDQ has not been validated in women with HSDD. Items on female sexual behavior should be tested in comparison with SSEs in women with HSDD for relevance and for treatment sensitivity, and a responder cutoff and a functional and dysfunctional threshold should be determined before incorporation into large-scale clinical trials.

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Category 3

(a) Final Approval of the Completed Article
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SUPPLEMENTARY DATA

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