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PSYCHOMETRICS

The Sexual Event Diary (SED): Development and Validation of a Standardized Questionnaire for Assessing Female Sexual Functioning During Discrete Sexual Events

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ABSTRACT

Background: The efficacy of on-demand drugs for hypoactive sexual desire disorder (HSDD) or female sexual interest/arousal disorder (FSIAD) should be assessed using a validated instrument that assesses the discrete sexual events during which the on-demand drug is taken.

Aim: To develop and validate an event log for measuring sexual satisfaction and sexual functioning of discrete sexual events.

Methods: Psychometric assessment was carried out on data of 10,959 Sexual Event Diaries (SEDs) collected during three clinical trials in a total of 421 women with HSDD. Cognitive debriefing interviews were held with 16 women with HSDD.

Outcomes: Item scores of the SED at the event level and at the subject level, summarized item scores of women during the baseline establishment and active treatment periods, and score changes in women from baseline establishment to active treatment.

Results: Several items of the initial 16-item SED items showed weak validity. The 16-item SED was refined to the 11-item SED. The reliability, content, and convergent validity of the 11-item SED were confirmed. For most 11-item SED item scores, the ability to discriminate between known groups was confirmed. Larger mean score changes from the baseline establishment period were found in those with than in those without known benefit from the medication, and Guyatt effect sizes ranged from 0.73 to 1.58, thereby demonstrating the ability to detect change.

Clinical Translation: The SED is a good tool for assessing sexual function during a discrete sexual event and for assessing the sexual function of women over longer periods.

Strengths and Limitations: The validation of the SED was performed on data from nearly 11,000 sexual events, gathered as part of a drug development program for HSDD and FSIAD. This amount of data provides very robust results when related to drug use for HSDD and FSIAD, but caution is advised when generalizing the validity of the SED directly to other areas of research (eg, recreational drug use and sexual risky behaviors), because such data were not used in this validation.

Conclusions: The 11-item SED is a reliable, valid, and responsive instrument and suitable for use in evaluating the effects of on-demand drugs in women with HSDD or FSIAD. **van Nes Y, Bloemers J, van der Heijden PGM, et al. The Sexual Event Diary (SED): Development and Validation of a Standardized Questionnaire for Assessing Female Sexual Functioning During Discrete Sexual Events. J Sex Med 2017;14:1438–1450.**

Key Words: Patient Reported Outcome; Questionnaire; Validation; Reliability; Satisfactory Sexual Event; Sexual function; Female Sexual Interest/Arousal Disorder; Female Sexual Dysfunction; Hypoactive Sexual Desire Disorder

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INTRODUCTION

Low sexual desire and arousal are the most common sexual complaints among women and commonly cause sexual dissatisfaction and personal distress.[1] These conditions were classified in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision* (DSM-IV-TR) as hypoactive sexual desire disorder (HSDD) and female sexual arousal disorder,[2] respectively, but have been merged in the fifth edition of the DSM as female sexual interest/arousal disorder (FSIAD).[3]

The pharmacotherapeutic options for HSDD and FSIAD are limited, with only one approved drug on the market in the United States.[4] This drug, flibanserin, is taken daily to increase overall sexual desire. There are other therapies in the late stages of clinical development[5–8] that are not taken daily but instead are taken on demand (ie, when a woman with HSDD or FSIAD *wants* to have sex). These medications are not intended to increase sexual desire continuously, but only before and during sexual activity. Measuring the efficacy of such an on-demand drug necessitates a different approach.

The efficacy of flibanserin was assessed using the Female Sexual Function Index (FSFI). The FSFI assesses different dimensions of female sexual functioning during the preceding 4 weeks.[9] The efficacy of an on-demand drug for HSDD and FSIAD is best determined by assessing the quality of a sexual event during which the drug was taken. Assessing sexual functioning retrospectively over a longer period, for example, during 4 weeks as in the FSFI, yields a more distal estimation of an on-demand drug's influence on sexual functioning than assessing sexual functioning during the actual events during which the drug was taken. However, to determine an on-demand drug's efficacy, an estimation of long-term effects is necessary. This can be operationalized by evaluating the change in the number of satisfactory sexual events from a baseline establishment period (BLE) to an active treatment period (ATP) during which the on-demand therapy was used. The primary end point in such trials is the difference between active treatment and placebo treatment arms in the change in the number of satisfactory sexual events from baseline to the end of treatment, which is one of the US Food and Drug Administration's preferred primary end points for the indication of HSDD and FSIAD.[10] For this, a standardized and validated sexual event questionnaire is necessary.

The aim of this research was to develop and validate a standardized event log for assessing sexual satisfaction and sexual functioning of a single sexual event. This patient-reported outcome instrument, the Sexual Event Diary (SED), underwent three cycles of development, starting with a 58-item version, followed by a 16-item version, and then an 11-item version. This patient-reported outcome instrument was developed to gather primary and (key) secondary end-point data in clinical trials assessing the efficacy of on-demand drugs in women with HSDD or FSIAD.

METHODS

Questionnaire Development

The first version of the SED included 58 items, which were selected based on literature review, expert opinion, and information from more than 250 clinical interviews that were conducted at our laboratory with women having sexual problems. The items that were included were selected to provide a comprehensive representation of sexual functioning and sexual satisfaction of a sexual event. 3 focus groups, 2 with 5 premenopausal women and 1 with 5 postmenopausal women, with (predominantly) sexual problems were formed to discuss what constituted sexual satisfaction and whether the 58-item SED adequately measured satisfaction and all other relevant aspects of sexual functioning.

The Dutch pilot version of the 58-item SED was tested in 156 women with ($n = 89$) and without ($n = 67$) sexual problems. These data were used for the initial validation and item reduction. Aside from completing the SED at their most recent sexual event, subjects were asked to select those 15 SED items that were most relevant to them in capturing sexual satisfaction and sexual functioning during an event. Principal components analysis was performed to determine the factors underlying the SED. Correlations of the items with global sexual satisfaction and Cronbach α coefficients were calculated to assess internal consistency (reliability).

The goal was to develop a comprehensive and compact questionnaire that could adequately assess the quality of a sexual event without burdening the subject. Based on the gathered qualitative and psychometric assessments, the 58-item SED was reduced to a 16-item version. This 16-item version was subsequently translated into US English by a certified medical translation office in the Netherlands (Wilkens cs, Medical Translations, Leiden, The Netherlands). Two female interviewers with experience in women's sexual medicine (RTI Health Solutions, Research Triangle Park, NC, USA) performed cognitive debriefing interviews with 5 native US English-speaking women to test the adequacy of the translated version.

All participants of the focus groups, debriefing interviews, and observational study described earlier provided written informed consent.

The first versions of the SED were called the Satisfaction of an Event Questionnaire, but it was later renamed to the SED because this name covered the content of the questionnaire more adequately. In the present article, only the name SED is used (and to refer to prior versions) for clarity.

Data

Clinical Studies

The reliability, validity, and responsiveness of the 16-item US version of the SED were assessed using data collected during two

clinical studies in the United States. Study 1 (clinical trial identifier NCT01432665) investigated the efficacy and safety of on-demand use of 4 doses of the combined administration of sublingual testosterone (0.25 or 0.5 mg) and sildenafil (25 or 50 mg) compared with placebo and monotherapies in women with HSDD with low sensitivity for sexual cues. Study 2 (NCT01743235) investigated the efficacy and safety of on-demand use of 4 doses of the combined administration of sublingual testosterone (0.25 or 0.5 mg) and buspirone (5 or 10 mg) compared with placebo and monotherapies in women with HSDD and dysfunctional over-activation of sexual inhibitory mechanisms.[5] After subsequent qualitative and quantitative validation, the 16-item SED was modified to the 11-item SED (Appendix). Then, the reliability, validity, and responsiveness of the 11-item SED were assessed using data collected in a 3rd US study (NCT02101203),[5] in which the efficacy and safety of on-demand use of sublingual testosterone (0.5 mg) combined with buspirone (10 mg) were compared with placebo in women with HSDD and dysfunctional over-activation of sexual inhibitory mechanisms. A total of 5,281 16-item SEDs were completed by 188 women who were in the intention-to-treat population of study 1. A total of 4,604 16-item SEDs were completed by 183 women who were in the intention-to-treat population of study 2. A total of 1,074 11-item SEDs were completed by 50 women of study 3. The intention-to-treat population contained 52 women, but data from 2 women were excluded because 1 had only incomplete SEDs and 1 completed her SEDs too long after the sexual events occurred. All completed questionnaires were used for statistical analyses.

All 3 studies consisted of a 4-week BLE, 2 4-week placebo run-in periods, and 2 4-week ATPs. These studies investigated the effect of on-demand therapies on discrete sexual events. Because frequency of sexual events varies per individual, the number of sexual events for each subject in each study and each 4-week period varied, and thus the number of collected SEDs varied for each subject.

The SED was filled out on a secure web-based system (Viedoc Me, Pharma Consulting Group, Uppsala, Sweden) that the participants could access at home through their computer or portable device.

All participants of the three trials provided written informed consent.

Levels of Assessment

The reliability and validity of the 16- and 11-item SEDs were assessed at the event level and the subject level. Analyses were performed on the event level to establish the reliability and validity of the questionnaire in its ability to assess sexual function during a discrete sexual event and on the subject level to assess the sexual function of an individual. Thus, subject level can be used to establish the reliability and validity of the primary endpoint change in the number of satisfactory sexual events from BLE to ATP. For event-level analyses, SEDs filled out by the same woman were treated as independent events. For subject-level analyses, the validity and reliability of subject mean scores were assessed over 4-week periods. The SED mean scores at the BLE and at the ATP were calculated separately. The placebo run-in period mean scores were not included in the analyses at the subject level.

For assessing known-groups validity, SED mean scores for satisfying sexual events were compared with those for unsatisfying sexual events as reported by SED item 4 only on the event level. For evaluating responsiveness on the subject level, SED mean change scores from baseline in those subjects reporting study medication-dependent improvement could be compared with those reporting no study medication-dependent improvement. Medication-dependent improvement was assessed by the Subjective Evaluation of Gain Questionnaire (SEG). This questionnaire also was administered in the 3 studies, and item 1 asked whether subjects had experienced improvement in their sexual functioning attributable to the study medication in the preceding 4 weeks.

List-wise deletion was used to handle missing data and this resulted in the deletion of 13 of 5,281 events for study 1, 1 of 4,604 events in study 2, and 10 of 1,074 events in study 3. At the subject level, this resulted in the deletion of 23 of 376 observations in study 1, 48 of 366 observations in study 2, and 17 of 100 observations in study 3, mostly owing to no events being reported at the BLE or ATP.

Quantitative Assessment

Factor Analysis

Exploratory factor analysis was used to assess underlying dimensions of Likert scale items (items 5−15 for studies 1 and 2 and items 5−10 for study 3) at the event and subject levels. At the event level, exploratory factor analysis was conducted on the polychoric correlation matrices of the Likert scale items, because these data are ordinal. At the subject level, Pearson correlation matrices of the average Likert scale items were used. Factor analysis was estimated using the maximum likelihood (ML) method. The number of factors to be retained was determined by inspecting the eigenvalues and scree plots. Furthermore, parallel analyses (PAs) based on a minimum rank factor analysis[11] were conducted to find the number of factors under possible violations of the multivariate normality assumption.

Reliability

Internal consistency was assessed using the Cronbach α coefficient, which provides a lower bound for reliability. Inter-item and item-rest correlations were assessed using Pearson correlation coefficients. Inter-item correlations were used to assess the relation between individual items within the SED. Item-rest correlations were used to assess the relation between individual items and the total item sum score of the remaining items. 2 different sum scores were used: an unweighted sum score of all SED Likert

scale items, referred to as the SED total score, and an unweighted SED sexual function sum score, consisting of all relevant SED Likert scale items based on the results of the factor analyses and/or theoretical arguments. For the calculation of the SED sum score(s) and all statistical analyses, the answer categories of 16-item SED items 11 ("afraid of pain"), 12 ("disgust"), and 13 ("distracting thoughts") and 11-item SED item 8 ("distracting thoughts") were reversed, so that the answer categories of all items had the same direction.

Validity

At the event level, construct validity was assessed by comparing the means of the SED item scores that were included in the scale with the dichotomous items assessing satisfaction, gratification, and orgasm (answer options = yes or no).

At the subject level, construct validity was assessed using Pearson correlation coefficients of the total score and domain scores of the Sexual Function Questionnaire[9] (SFQ; studies 1 and 2) and the FSFI[12] (study 3) with the sum scores and related domain items of the SED. The SFQ is a 34-item self-report questionnaire that assesses 7 domains of sexual function during the preceding 4 weeks: desire, arousal-sensation, arousal-lubrication, enjoyment, orgasm, pain, and partner relationship. The FSFI is a 19-item self-report questionnaire that assesses six domains of sexual function during the preceding 4 weeks: desire, arousal, lubrication, orgasm, satisfaction, and pain.

Also at the subject level, known-groups validity was assessed by comparing the mean SED scores during the ATP between responders and non-responders using independent-sample t-test statistics. Responders were defined as those subjects who indicated improvement in the past 4 of the 8 weeks of treatment using the SEG. Responders were subjects who answered yes to the question asking whether they had experienced benefit from the medication during the past 4 weeks, and non-responders were those who answered no. The responder classification was independent of study medication used.

Responsiveness

Responsiveness is the ability of the instrument to detect change when there is a known change in the measurement of interest. Responsiveness was assessed by comparing the mean changes from BLE to ATP in SED scores between responders and non-responders by calculating independent-sample t-test statistics.

Responsiveness also was assessed by determining the effect size statistics of the ability of the SED to measure change in sexual functioning using the Guyatt responsiveness index.[13,14]

$$Guyatt\ index = \frac{(change\ in\ SED\ scores\ for\ responders) - (change\ in\ SED\ scores\ for\ non-responders)}{SD\ of\ change\ in\ SED\ scores\ for\ non-responders}$$

Effect sizes of approximately 0.20 represent small effects, those of approximately 0.50 represent moderate effects, and those of at least 0.80 represent large effects.[13]

A two-sided 5% significance level was adopted for all statistical tests.

Qualitative Assessment

2 iterative sets of cognitive debriefing interviews were held with women with HSDD in the United States by RTI Health Solutions. Each set of cognitive interviews was held with 8 women. The purpose of the first set of interviews was to assess the content validity of the 16-item SED. The second set of interviews was carried out after SED adaptation to confirm content validity and finalize the 11-item SED

Population Cognitive Debriefing Interviews

All women had clinician-diagnosed HSDD. Comorbidity with female sexual arousal disorder and/or female orgasmic disorder (only as secondary diagnosis) was allowed. The participants were 21 to 70 years old and had been sexually active (ie, vaginal penetration, sexual intercourse) in the past 3 months. They could read and speak English and all provided written consent before study entry. Women were excluded if they were pregnant or lactating, had other unexplained gynecologic complaints such as clinically relevant abnormal uterine bleeding patterns, and/or had current sexual disorder of vaginismus or dyspareunia according to the DSM-IV or DSM-IV-TR.

Patients were recruited from a clinical site in West Palm Beach, Florida for the first round of interviews and from a clinical site in Houston, Texas for the second round. All patients provided written consent and received $100 reimbursement. All study materials were reviewed and approved by RTI Health Solutions' institutional review board before any participants were recruited for the study.

Debriefing Interview Methods

The 1-hour interviews in the 2 rounds were led by the same 2 female interviewers (RTI Health Solutions) with experience in women's sexual medicine using a semistructured interview guide. At the start of each interview in round 1, participants were asked to engage in a brief open-ended discussion describing their definitions of sexual desire and of satisfaction with sexual activity. Then, participants were asked to provide feedback on the 16-item SED items while describing their thought processes out loud. The interviewers also asked targeted questions to obtain further information about the way in which the participants interpreted the items and thought about the response options. At the close of the

Table 1. Baseline characteristic and demographics of study participants

	Psychometric assessment			Qualitative assessment	
	Clinical study			Debriefing interviews	
	1 (n = 188)	2 (n = 183)	3 (n = 50)	Round 1 (n = 8)	Round 2 (n = 8)
Menopausal status, n (%)*					
Premenopausal	134 (71.3)	132 (72.1)	30 (60.0)	2 (25.0)	0 (0.0)
Postmenopausal	54 (28.7)	51 (27.9)	20 (40.0)	6 (75.0)	8 (100)
Age (y), mean (range)	44.2 (22–65)	43.7 (24–67)	46.1 (23–66)	50.0 (29–62)	61.8 (54–69)
Race, n (%)					
Caucasian	152 (80.9)	112 (61.2)	31 (63.0)	3 (37.5)	5 (62.5)
Black	18 (9.6)	56 (30.6)	14 (28.0)	3 (37.5)	2 (25.0)
Asian	4 (2.1)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Other	14 (7.4)	14 (7.7)	5 (10.0)	2 (25.0)	1 (12.5)
Clinician secondary diagnosis, n (%)					
FSAD	25 (13.3)	36 (19.7)	13 (26.0)	2 (25.0)	1 (12.5)
FOD	18 (9.6)	19 (10.4)	4 (8.0)	5 (62.5)	0 (0.0)
FSAD and FOD	27 (14.4)	30 (16.4)	12 (24.0)	0 (0.0)	0 (0.0)
None	118 (62.8)	98 (53.6)	21 (42.0)	1 (12.5)	7 (87.5)

FSAD = female sexual arousal disorder; FOD = female orgasmic disorder.
*Perimenopausal women were not included in the three clinical trials because the variable nature of their hormonal status could affect the study results in an unpredictable manner.

debriefing interview, the interviewers asked whether the 16-item SED missed any important concept that participants deemed critical to measuring satisfaction with a sexual event and whether any items included in the SED seemed irrelevant to participants for inclusion in an SED. In round 2, at the start of each interview, participants were asked to engage in a brief open-ended discussion describing their definitions of satisfaction with sexual activity. Cognitive debriefing of the 11-item SED was conducted using a similar "think-aloud" procedure and directed probes to delve further into the question-answering process. At the end of each interview, participants were asked whether the 11-item SED missed any important concept that participants deemed critical to measuring satisfaction with a sexual event and whether any items included in the 11-item SED seemed irrelevant to participants for inclusion in an SED. From the concepts contained in the 11-item SED, participants were asked to select the three concepts that were most important to them in determining satisfaction with sexual activity.

Table 2. Maximum likelihood factor analyses: factor loadings of the one-factor solution for the SED items*

	1-Factor solution						
	Study 1		Study 2			Study 3	
16-Item SED	Event	Subject	Event	Subject	11-Item SED	Event	Subject
5. Pleasurable	0.918	0.915	0.924	0.933	5. Sexual desire	0.953	0.934
6. Letting go	0.848	0.850	0.856	0.841	6. Mentally aroused	0.966	0.981
7. In the mood for sex	0.851	0.856	0.855	0.830	7. Physically aroused	0.960	0.962
8. Vaginal arousal	0.893	0.920	0.939	0.928	8. Distracting thoughts†	0.668	0.594
9. Sexually aroused	0.951	0.960	0.964	0.956	9. Letting go	0.884	0.803
10. Body image	0.566	0.484	0.546	0.526	10. Pleasurable	0.947	0.952
11. Afraid pain†	0.125	0.087	0.176	0.120			
12. Disgust†	0.420	0.338	0.397	0.283			
13. Distracting thoughts†	0.410	0.370	0.490	0.442			
14. Partner attractiveness	0.500	0.466	0.451	0.420			
15. Partner's actions	0.749	0.796	0.709	0.703			

SED = Sexual Event Diary.
*Dichotomous items 1 to 4 and items 11 and 16 were not included in the factor analyses. Items 11 and 16 are the same item (orgasm), but numbered 11 in the 11-item SED and 16 in the 16-item SED.
†Reversed variable.

Table 3. Cronbach α coefficients of all items on event level and subject level

		Internal consistency*		
Level of analysis	Items	Study 1	Study 2	Study 3
Event level	5–15	0.89	0.89	
	5, 6, 7, 8, 9, 10, 13‡, 14, 15†	0.91	0.91	
	5–10†			0.95
Subject level	5–15	0.90	0.90	
	5, 6, 7, 8, 9, 10, 13‡, 14, 15†	0.92	0.92	
	5–10†			0.95

*Cronbach α (range = −1.00 to +1.00).
†Items that loaded on factor 1 and/or were theoretically important for measuring sexual function.
‡Reversed variable.

RESULTS

Participant Characteristics

Baseline characteristics and demographics of women with HSDD who were included in the psychometric assessments and who participated in the debriefing interviews are listed in Table 1.

16-Item SED (Studies 1 and 2)

Event Level

Factor analysis. Inspection of the eigenvalues and scree plots of the ML factor analyses and results of the PAs showed that 1 factor should be retained. The first factor had an eigenvalue of 5.48, explaining 49.8% of the variance for study 1, and an eigenvalue of 5.56, explaining 50.5% of the variance for study 2. Items 5 through 10 and 15 had moderate (>0.50) to strong (>0.80) loadings, with weaker contributions from items 12, 13, and 14 (Table 2). The SED sexual function sum score was derived using items 5 through 10 and items 13 through 15. Items 11 and 12 were not included because overall they had the lowest factor loadings.

Reliability. Items 5 through 10 and 13 through 15 yielded a high Cronbach α coefficient for studies 1 and 2 (Table 3). Most inter-item Pearson correlation coefficients were higher than 0.30 (eTables A and B). Only items 11 ("afraid pain") and 12 ("disgust") in studies 1 and 2 and item 13 ("distracting thoughts") in study 1 had correlations below 0.30. Item-rest Pearson correlation coefficients between 16-item SED items 4 ("satisfied"), 3 ("gratified"), and 16 ("orgasms"), with answer options yes or no, and the sum scores were larger than 0.30 in studies 1 and 2. Here, the item-rest correlation coefficients between items 4 ("satisfied") and 3 ("gratified") and the sum scores were somewhat larger compared with item 16 ("orgasm") for studies 1 and 2. The item-rest Pearson correlation coefficients between 16-item SED Likert items 5 to 15 and the sum scores were mostly larger than 0.30, except for item 11 ("afraid of pain"), for studies 1 and 2.

Validity. All items that were included in the 16-item SED of studies 1 and 2 showed strong known-groups validity, because the mean differences in SED item and sum scores between yes and no responders on SED items measuring "gratified," "satisfied," and "orgasm" were highly significant ($P < .0001$ for all but one), all in the expected direction (Table 4).

Subject Level

Factor analysis. Inspection of the eigenvalues and scree plots of the ML factor analyses and results of the PAs showed that one factor should be retained. The first factor had an eigenvalue of 5.41, explaining 49.1% of the variance for study 1, and an eigenvalue of 5.28, explaining 48.0% of the variance for study 2. Items 5 to 9 and 15 had strong factor loadings, with weaker contributions from items 10, 13, and 14 (Table 2). Sexual function sum score was derived using the same items as for the event-level analyses.

Reliability. The items yielded a high Cronbach α coefficient for studies 1 and 2 (Table 2). Most inter-item Pearson correlation coefficients were larger than 0.30 (eTables C and D). Only items 11 ("afraid pain") and 12 ("disgust") for studies 1 and 2 and item 13 ("distracting thoughts") for study 1 had correlations lower than 0.30. Item-rest Pearson correlation coefficients between 16-item SED items 4 ("satisfied"), 3 ("gratified"), and 16 ("orgasms"), with answer options yes or no, and the sum scores were larger than 0.30 in studies 1 and 2. The item-rest Pearson correlation coefficients between 16-item SED Likert items 5 to 15 and the sum scores were mostly larger than 0.30, except for item 11 ("afraid pain"), for studies 1 and 2.

Validity. Convergent validity was deemed adequate, with correlation coefficients between the SFQ domains and their related 16-item SED items ranging from 0.33 to 0.77 for study 1 and from 0.22 to 0.80 for study 2 during the 2 periods (eTables E and F). These results provided support for adequate to strong convergence of the 16-item SED. The lower, but adequate, convergence of SFQ "orgasm" and SFQ34 "how satisfied have

Table 4. Known-groups validity: comparison between 16-item SED and sum score mean values (SEM) and "yes" and "no" answers on 16-item SED items 3, 4, and 11

	3. Did you find this sexual activity gratifying?						4. Were you satisfied with the sexual activity?						16. Did you have an orgasm?					
	Yes		No		Test statistics		Yes		No		Test statistics		Yes		No		Test statistics	
SED item	Mean	SEM	Mean	SEM	t value	*P* value*	Mean	SEM	Mean	SEM	t value	*P* value*	Mean	SEM	Mean	SEM	t value	*P* value*
Study 1‡																		
5. Pleasurable	3.68	0.02	1.86	0.02	78.18	<.0001	3.69	0.02	1.99	0.02	69.12	<.0001	3.80	0.02	2.47	0.02	49.12	<.0001
6. Letting go	3.62	0.02	2.08	0.03	49.80	<.0001	3.62	0.02	2.22	0.03	44.95	<.0001	3.74	0.02	2.56	0.02	39.58	<.0001
7. In the mood for sex	3.27	0.02	1.81	0.02	49.67	<.0001	3.26	0.02	1.95	0.03	42.17	<.0001	3.35	0.02	2.30	0.02	33.86	<.0001
8. Vaginal arousal	3.31	0.02	1.63	0.02	61.82	<.0001	3.32	0.02	1.74	0.02	55.87	<.0001	3.49	0.02	2.10	0.02	46.98	<0.0001
9. Sexually aroused	3.41	0.02	1.71	0.02	61.01	<.0001	3.42	0.02	1.84	0.02	53.67	<.0001	3.55	0.02	2.25	0.02	42.84	<.0001
10. Body image	3.67	0.02	2.97	0.03	19.38	<.0001	3.67	0.02	3.04	0.03	17.80	<.0001	3.73	0.02	3.19	0.02	16.97	<.0001
11. Afraid pain†	4.81	0.01	4.71	0.02	4.43	<.0001	4.80	0.01	4.72	0.02	3.72	.0002	4.84	0.01	4.72	0.02	6.48	<.0001
12. Disgust†	3.98	0.02	3.36	0.03	11.65	<.0001	4.83	0.01	4.55	0.02	11.83	<.0001	4.84	0.01	4.64	0.02	10.31	<.0001
13. Distracting thoughts†	3.98	0.02	3.36	0.03	18.01	<.0001	4.00	0.02	3.36	0.03	19.14	<.0001	4.08	0.02	3.5	0.02	19.91	<.0001
14. Partner attractiveness	3.89	0.02	3.33	0.03	15.83	<.0001	3.88	0.02	3.41	0.03	13.24	<.0001	3.83	0.02	3.63	0.02	5.99	<.0001
15. Partners actions	3.66	0.02	2.37	0.03	38.48	<.0001	3.65	0.02	2.50	0.03	33.59	<.0001	3.66	0.02	2.89	0.02	23.05	<.0001
SED Total	42.83	0.12	30.45	0.15	63.90	<.0001	42.86	0.12	31.43	0.16	56.17	<.0001	43.89	0.14	34.24	0.15	47.26	<.0001
SED sexual function	32.49	0.11	21.13	0.14	62.96	<.0001	32.51	0.11	22.05	0.15	55.05	<.0001	33.22	0.13	24.89	0.14	42.48	<.0001
Study 2§																		
5. Pleasurable	3.77	0.02	1.84	0.02	70.50	<.0001	3.76	0.02	1.87	0.02	70.07	<.0001	3.89	0.02	2.43	0.02	48.18	<.0001
6. Letting go	3.63	0.02	1.94	0.03	49.12	<.0001	3.64	0.02	1.95	0.03	50.35	<.0001	3.79	0.02	2.40	0.03	40.95	<.0001
7. In the mood for sex	3.34	0.02	1.76	0.03	47.99	<.0001	3.31	0.02	1.83	0.03	44.00	<.0001	3.45	0.02	2.23	0.03	35.18	<.0001
8. Vaginal arousal	3.46	0.02	1.66	0.02	62.10	<.0001	3.44	0.02	1.74	0.02	56.88	<.0001	3.64	0.02	2.14	0.02	46.85	<.0001
9. Sexually aroused	3.53	0.02	1.68	0.02	64.78	<.0001	3.51	0.02	1.75	0.02	59.50	<.0001	3.67	0.02	2.22	0.02	44.83	<.0001
10. Body image	3.83	0.02	3.08	0.04	18.62	<.0001	3.84	0.02	3.05	0.04	19.82	<.0001	3.94	0.02	3.24	0.03	19.91	<.0001
11. Afraid of pain†	4.76	0.01	4.61	0.03	5.74	<.0001	4.77	0.01	4.60	0.02	6.48	<.0001	4.78	0.01	4.65	0.02	5.85	<.0001
12. Disgust†	4.75	0.01	4.30	0.03	14.54	<.0001	4.76	0.01	4.28	0.03	15.37	<.0001	4.75	0.01	4.47	0.02	11.02	<.0001
13. Distracting thoughts†	4.09	0.02	3.16	0.04	22.92	<.0001	4.11	0.02	3.12	0.04	24.85	<.0001	4.14	0.02	3.46	0.03	19.55	<.0001
14. Partner attractiveness	4.04	0.02	3.47	0.04	13.87	<.0001	4.06	0.02	3.41	0.04	16.40	<.0001	4.00	0.02	3.72	0.03	8.01	<.0001
15. Partners actions	3.77	0.02	2.43	0.03	34.84	<.0001	3.79	0.02	2.41	0.03	37.46	<.0001	3.82	0.02	2.89	0.03	25.39	<.0001
SED total	43.69	0.13	30.01	0.17	63.76	<.0001	43.72	0.13	30.12	0.16	64.54	<.0001	44.86	0.15	33.86	0.17	48.12	<.0001
SED sexual function	33.47	0.12	21.03	0.15	63.54	<.0001	33.48	0.13	21.15	0.15	64.19	<.0001	34.34	0.15	24.74	0.16	44.58	<.0001

SED = Sexual Event Diary; SEM = standard error of the mean.
*Two-sided *P* values.
†Reversed variable.
‡Study 1: gratified = yes (n = 3,788) and no (n = 1,479); satisfied = yes (n = 3,649) and no (n = 1,618); orgasm = yes (n = 2,790; items 5 and 6, n = 2,789) and no (n = 2,479).
§Study 2: gratified = yes (n = 3,237) and no (n = 1,366); satisfied = yes (n = 3,220) and no (n = 1,383); orgasm = yes (n = 1,383) and no (n = 2,415).

you been" was expected, because the SFQ items assessed intensity on these concepts over a 4-week period, whereas their related SED variables represented the different concepts of frequency of satisfactory events and orgasms. Low correlations between SFQ "partner relation" and SED "partner" items also were expected, because the "partner" items were dissimilar. The SFQ assesses the fear of negative impact of sexual dysfunction on the relationship, whereas the SED assesses the partner's proficiency and attractiveness during the sexual event.

Responders, as defined by the SEG, had significantly higher 16-item SED item scores at ATP compared with non-responders on almost all items (eTable G). SED item scores for item 10 ("body image") for study 1 and items 11 ("afraid of pain") and 12 ("disgust") for studies 1 and 2 did not differ significantly between responders and non-responders.

Responsiveness. Responders had a significantly higher increase in change from BLE to ATP in 16-item SED scores compared with non-responders (Table 4). Only item 12 ("disgust") for studies 1 and 2 and item 11 ("afraid of pain") for study 1 did not differ significantly between responders and non-responders.

Guyatt effect size ranges were 0.80 to 1.23 for study 1 and 0.59 to 1.29 for study 2, indicating moderate to strong ability to detect changes in 16-item SED item scores (Table 5). Exceptions were items 11 ("afraid of pain"), 12 ("disgust"), and 13 ("distracting thoughts") for studies 1 and 2 and item 14 ("partner attractive") for study 1, because their effect sizes were small (0.07−0.44 and 0.05−0.41 for studies 1 and 2, respectively).

11-Item SED (Study 3)

Cognitive Debriefing Interviews and Item Reduction

Content validity of the SED was assessed by conducting 2 iterative sets of cognitive debriefing interviews. The 16-item SED was tested in round 1 and, after adaptation, the 11-item SED was tested in round 2. Each round included 8 women (Table 1) who met the inclusion and exclusion criteria. 6 interview participants were classified as having low sensitivity to sexual cues and 2 were classified as having dysfunctional overactivity of sexual inhibitory mechanisms. This subdivision is based on the dual control model of sexual response and is substantiated by cognitive,[15,16] psychophysiologic,[6,7,15–17] subjective,[6,7,16] neuroanatomic,[18,19] and pharmacologic[6,7,15,16,18] evidence. This information was collected to ascertain whether these groups differed in opinions or perceptions of what is important for satisfactory sex. No differences were observed. Based on the results of these interviews in round 1, revisions were made to the item set, including the removal of items addressing concepts less important to patients and the development of new items to capture concepts of greater importance to patients. SED item wording of the 2 versions, including a brief description of the type of change made, is presented in eTable H. In round 1, all patients found items 4 ("satisfied") and 16 ("orgasm") and most patients found items 5 ("pleasure"), 6 ("letting go"), and 13 ("distracting thoughts") clear, easy to understand and answer, and relevant for an SED. Therefore, these items were retained. Items 4 ("satisfied"), 6 ("letting go"), and 13 ("distracting thoughts") were not modified, and for items 5 ("pleasure") and 16 ("orgasm"), minor modifications to wording were made (eg, refinements to US English). Most patients indicated that the "gratified" item was measuring the same concept as the "satisfaction" item; half the patients preferred the item assessing "satisfaction," and several said the term "gratification" was not clear (38%). In consequence, the "gratified" item was deleted without replacement. Item 9 ("sexually aroused") was deleted and replaced because participants did not always interpret the question as asking about mental arousal. Item 7 ("in the mood for sex") was deleted and replaced, because participants found this item did not fully measure desire. Several patients indicated that overall physical arousal also was important to assess, instead of only vaginal arousal; as a result, item 8 ("vaginal arousal") was deleted and replaced. Items 10 ("body image"), 11 ("afraid of pain"), 12 ("disgust"), 14 ("partner attractiveness"), and 15 ("partner's actions") were deemed irrelevant to an SED by interview participants. Therefore, these items were deleted without replacement. The deletion of items 11 ("afraid of pain") and 12 ("disgust") also was justified by evaluating the quantitative assessment results. These two items overall had the lowest factor loadings. Then, the 11-item SED was tested in round 2, which resulted in strong content validity. Nearly all participants found that each item included in the SED was clear, easy to answer, and important to capture in an SED, so no changes were made to the final SED. An exception was the deletion of the "how would you rate" stem of SED items 6 to 9, because this item formulation generally did not perform well. The wording was changed to a more direct form (eg, "How physically aroused or excited did you become during the sexual activity?"). The psychometric data gathered in studies 1 and 2 supported the item selection for the SED.

Event Level

Factor analysis. Inspection of the eigenvalues and scree plots of the ML factor analyses and results of the PAs showed that one factor should be retained. The factor had an eigenvalue of 4.89, explaining 81.4% of the variance. The one-factor structure showed high loadings for all SED items (Table 2). Because of this finding, the SED total sum score and the SED sexual function sum score were equal and consisted of all Likert scale items.

Reliability. The Cronbach α coefficient was high (Table 3). Pearson correlation coefficients, which were calculated for assessing the SED inter-item and item-rest correlations, were larger than 0.30 ($P < .0001$; eTable I).

Validity. All SED items showed strong construct validity. The mean differences in SED scores between yes and no responders

Table 5. Known-groups responsiveness—mean change (SEM) in 16-item SED scores from baseline establishment to active treatment period in responders and non-responders as defined by the SEG

	Study 1					Study 2				
	Responder (n = 72*), mean change (SEM)	Non-responder (n = 76), mean change (SEM)	t value	*P* value†	Guyatt responsiveness	Responder (n = 76), mean change (SEM)	Non-responder (n = 48), mean change (SEM)	t value	*P* value†	Guyatt responsiveness
SED3 gratified‡	2.48 (0.40)	0.42 (0.27)	4.25	<.0001	0.87	2.14 (0.32)	0.73 (0.34)	2.89	.005	0.59
SED4: satisfied‡	2.56 (0.40)	0.32 (0.27)	4.65	<.0001	0.95	2.08 (0.33)	0.75 (0.32)	2.92	.004	0.60
SED5: pleasurable	1.12 (0.12)	0.19 (0.11)	5.83	<.0001	0.97	0.97 (0.11)	0.24 (0.16)	3.82	.0002	0.65
SED6: letting go	1.23 (0.11)	0.23 (0.11)	6.44	<.0001	1.08	1.16 (0.12)	0.13 (0.11)	6.10	<.0001	1.29
SED7: in the mood for sex	1.33 (0.12)	0.36 (0.11)	6.10	<.0001	1.04	1.10 (0.13)	0.25 (0.15)	4.22	<.0001	0.84
SED8: vaginal arousal	1.17 (0.12)	0.15 (0.11)	6.22	<.0001	1.02	1.11 (0.13)	0.33 (0.15)	3.91	.0002	0.75
SED9: sexually aroused	1.25 (0.13)	0.34 (0.11)	5.28	<.0001	0.96	1.17 (0.12)	0.23 (0.15)	4.90	<.0001	0.89
SED10: body image	0.75 (0.12)	0.08 (0.09)	4.62	<.0001	0.88	0.88 (0.14)	0.25 (0.13)	3.38	.001	0.72
SED11: afraid of pain‡	0.19 (0.06)	0.13 (0.08)	0.50	.616	0.07	0.29 (0.09)	−0.03 (0.12)	2.20	.030	0.38
SED12: disgust§	0.22 (0.06)	0.14 (0.06)	0.94	.350	0.15	0.32 (0.08)	0.29 (0.10)	0.26	.793	0.05
SED13: distracting thoughts‡	0.46 (0.12)	0.06 (0.11)	2.47	.015	0.44	0.82 (0.11)	0.39 (0.15)	2.32	.022	0.41
SED14: partner attractiveness	0.24 (0.12)	−0.11 (0.11)	2.23	.027	0.38	0.53 (0.11)	0.02 (0.12)	3.01	.003	0.60
SED15: partner's actions	0.86 (0.13)	0.10 (0.11)	4.51	<.0001	1.23	0.82 (0.13)	0.20 (0.14)	3.16	.002	0.62
SED16: orgasms‡	2.04 (0.28)	−0.11 (0.20)	6.28	<.0001	0.80	1.59 (0.27)	0.40 (0.26)	3.17	.002	0.66
SED total	8.83 (0.86)	1.69 (0.70)	6.45	<.0001	1.17	9.17 (0.84)	2.28 (1.00)	5.22	<.0001	0.99
SED sexual function	8.43 (0.82)	1.41 (0.67)	6.61	<.0001	1.20	8.56 (0.82)	2.03 (0.91)	5.17	<.0001	1.03

SED = Sexual Event Diary; SEG = Subjective Evaluation of Gain; SEM = standard error of the mean.
*Study 1 items 3 and 4 (n = 73).
†Two-sided tests were used.
‡Counts of yes answers on these items were used according to efficacy analyses.
§Reversed variable.

on SED items measuring "satisfied" and "orgasm" were highly significant ($P < .0001$) and the results were in the expected direction (Table 6).

Subject Level

Factor analysis. Inspection of the eigenvalues and scree plots of the ML factor analyses and results of the PAs showed that one factor should be retained. The factor had an eigenvalue of 4.66, explaining 77.7% of the variance. The one-factor structure showed high loadings for all items (Table 2). Also, the SED total sum score was equal to the SED sexual function sum score and consisted of all Likert scale items.

Reliability. The Cronbach α coefficient was high (Table 3). Most Pearson correlation coefficients, which were calculated for assessing the SED inter-item and item-rest correlations, were larger than 0.30 ($P < .0001$; eTable J).

Validity. Convergent validity was deemed adequate, with correlation coefficients between the FSFI domains with their related SED items ranging from 0.36 to 0.79 during the two periods (eTable K). These results provided support for adequate to strong convergence of the 11-item SED. The adequate convergence between FSFI item 16 ("how satisfied have you been") and SED item 4 ("satisfied") was expected, because FSFI item 16 measured intensity of satisfaction over a 4-week period, whereas the related SED item 4 ("satisfied") measured the different concept of frequency of satisfactory events.

Known-groups validity was good. Responders scored significantly higher compared with non-responders ($P < .05$; eTable L) on all items during the ATP, except on items 8 ("distracting thoughts"), 9 ("letting go"), and 11 ("orgasm").

Responsiveness. For responders the increase in SED item scores from BLE to ATP was significantly higher than for non-responders ($P < .05$; Table 7) with exception of items 8 ("distracting thoughts") and 11 ("orgasm"), showing strong known-groups responsiveness.

The Guyatt effect sizes ranged from 0.73 to 1.58, indicating a very good ability to detect changes in SED item scores (Table 7). An exception was item 8 ("distracting thoughts"), which had a small effect size (0.14).

DISCUSSION

A standardized event log, the SED, was developed for the assessment of sexual satisfaction and sexual functioning during a single sexual event. The questions in the SED are directed at a discrete sexual event instead of being directed at sexual functioning over a longer period (eg, 4 weeks). Measuring discrete sexual events provides a more valid assessment of efficacy of on-demand investigational drugs on sexual functioning of

Table 6. Mean (SEM) of 11-item SED scores separately for answering SED items 4 ("Were you satisfied with the sexual activity?") and 11 ("Did you have an orgasm?") with yes or no—study 3*

SED item	4. Were you satisfied with the sexual activity?						11. Did you have an orgasm?					
	Yes		No		Test statistics		Yes		No		Test statistics	
	Mean	SEM	Mean	SEM	t value	*P* value†	Mean	SEM	Mean	SEM	t value	*P* value†
5. How would you rate your level of sexual desire during the sexual activity?	2.61	0.04	0.83	0.05	30.74	<.0001	2.63	0.04	1.22	0.05	21.74	<.0001
6. How mentally aroused or excited did you become during the sexual activity?	2.56	0.04	0.78	0.05	29.73	<.0001	2.60	0.05	1.14	0.05	22.37	<.0001
7. How physically aroused or excited did you become during the sexual activity?	2.72	0.04	0.92	0.05	31.63	<.0001	2.80	0.04	1.25	0.05	25.56	<.0001
8. To what extent did you have distracting thoughts?‡	2.62	0.04	1.47	0.07	14.81	<.0001	2.65	0.05	1.70	0.06	12.96	<.0001
9. To what extent were you able to let yourself go?	2.66	0.04	0.83	0.05	27.50	<.0001	2.79	0.05	1.13	0.05	24.49	<.0001
10. How pleasurable was the sexual activity to you?	2.82	0.04	0.87	0.05	33.81	<.0001	2.89	0.04	1.25	0.05	26.01	<.0001
SED sexual function	15.99	4.71	5.70	5.15	32.85	<.0001	16.36	0.22	7.69	0.26	25.79	<.0001

SED = Sexual Event Diary; SEM = standard error of the mean.
*Satisfied = yes (n = 650) and no (n = 414); orgasm = yes (n = 527) and no (n = 537).
†Two-sided *P* values.
‡Reversed variable.

Table 7. Known-groups responsiveness—mean change (SEM) in SED scores from baseline establishment to active treatment period in responders and non-responders as defined by the SEG—study 3

	Responder (n = 18)		Non-responder (n = 10)				
	Mean change	SEM	Mean change	SEM	t value	*P* value*	Guyatt responsiveness
4. Were you satisfied with the sexual activity?†	1.17	0.52	−1.40	0.83	2.76	.011	0.97
5. How would you rate your level of sexual desire during the sexual activity?	1.06	0.21	0.06	0.26	2.92	.007	1.22
6. How mentally aroused or excited did you become during the sexual activity?	1.05	0.22	−0.37	0.28	3.89	.0006	1.58
7. How physically aroused or excited did you become during the sexual activity?	0.94	0.20	−0.21	0.27	3.41	.002	1.34
8. To what extent did you have distracting thoughts?‡	0.56	0.26	0.43	0.31	0.32	.751	0.14
9. To what extent were you able to let yourself go?	0.73	0.18	−0.07	0.35	2.29	.031	0.73
10. How pleasurable was the sexual activity to you?	0.91	0.22	−0.44	0.34	3.50	.002	1.25
11. Did you have an orgasm?†	0.83	0.48	−0.60	0.56	1.86	.074	0.81
SED sexual function	5.25	0.98	−0.60	1.30	3.59	.001	1.42

SED = Sexual Event Diary; SEG = Subjective Evaluation of Gain; SEM = standard error of the mean.
*Two-sided *P* values.
†Counts of yes answers on these items were used according to efficacy analyses.
‡Reversed variable.

women with HSDD or FSIAD compared with questionnaires that are directed at the assessment of sexual function over longer periods (eg, SFQ and FSFI). This is because the influence of on-demand medication is predominantly present during an event and therefore the data from event logs are more proximate estimations of an on-demand drug's efficacy than data from monthly questionnaires, providing the advantage of minimized recall bias and increased precision. The results of the present study show that the SED is a valid and reliable instrument for assessing female sexual function during discrete sexual events.

Reliability, validity, and responsiveness were confirmed for most items in the 11-item SED based on evidence from cognitive debriefing interviews and psychometrical assessments in patients with HSDD. These findings indicated that most items measured the same concept of interest, the construct we intended to measure, and changes in sexual functioning when change was reported. The primary end-point measurement, "change in the number of satisfying sexual events from baseline," proved to be an excellent measurement. This measurement was comprehensive and correlated strongly with, and has excellent discriminating ability in, all aspects of sexual functioning. Furthermore, the SED showed a clear one-factor structure, indicating that the resulting scale (sum score) measured the same concept, and this scale showed excellent reliability, validity, and responsiveness.

Discrepancies were found in our results regarding 11-item SED items 8 ("distracting thoughts"), 9 ("letting go "), and 11 ("orgasm"). These appeared to be less valid and/or responsive according to psychometric assessments, whereas debriefing interviews showed excellent content validity of all items included in the SED, indicating that they are appropriate and comprehensive relative to its intended measurement concept, population, and use. For item 11 ("orgasm") a lower validity than the other SED items was expected, because sexual satisfaction in women is less dependent on reaching orgasm than in men.[20] Nevertheless, for a substantial number of women, orgasm is an important aspect of sexual functioning[20] and therefore should be assessed in clinical trials that investigate the efficacy of drugs for HSDD and FSIAD. The main reason items 8 ("distracting thoughts") and 9 ("letting go") were included in the 11-item SED was to capture information on inhibition for the subtype of women in whom HSDD or FSIAD is caused by dysfunctional overactivity of sexual inhibitory mechanisms. These women's sexual excitation is hampered by overactivity of normal inhibitory processes in the brain,[18] which can be expressed behaviorally as excessive distraction or an inability to let oneself go during sexual activity.

A limitation of the present study is that the final focus groups and cognitive interviews were performed in predominantly postmenopausal women and predominantly women with low sensitivity to sexual cues. It is not expected that additional research in premenopausal and high inhibitory subjects would necessitate additional items or adjustment of items to

reach concept saturation. There is no literature that suggests a difference between these subgroups of women (pre- vs post-menopausal and low sensitive vs high inhibitory) with respect to which aspects of a sexual event are important. This will need to be confirmed in future research.

The SED was developed and validated as a part of a drug development program for HSDD and FSIAD. Development of and modifications to the SED were based on the premise that the instrument had to be a valid and reliable tool for use in such a program. The data that were used for the present described validation also were gathered in this program. Despite this focus, the SED also might show merit in the assessment of sexual functioning of discrete sexual events in other areas of research (eg, recreational drug use and sexual risky behaviors).

In conclusion, the 11-item SED proved to be an excellent tool for measuring sexual satisfaction and sexual functioning during a single sexual event and therefore is suitable for use in clinical trials assessing the efficacy of on-demand drugs in women with HSDD or FSIAD.

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Conflicts of Interest: Ms. Van Nes and Mr. Kessels are employees of Emotional Brain (EB). Dr Bloemers, Dr van Rooij, and Mr Gerritsen are employees of EB and own shares or share options in EB. Dr Van der Heijden is advisor to EB. Dr. Derogatis is a member of the scientific advisory board for Palatin Pharmaceuticals, S1 Biopharam, Emotional Brain, Acerus, and Endoceutics. Dr Tuiten is CEO of EB and a shareholder of EB.

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SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.jsxm.2017.09.008.