

Validation of the Sexual Activity Questionnaire in women with endometriosis

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STUDY QUESTION: Is the Sexual Activity Questionnaire (SAQ) a valid tool for patients treated for symptomatic endometriosis?

SUMMARY ANSWER: For women having surgical treatment for endometriosis, we determined that the SAQ is a valid and responsive tool.

WHAT IS KNOWN ALREADY: Endometriosis adversely affects sexual quality of life. Suitable validated sexual quality of life instruments for endometriosis are lacking both in clinical practice and for research.

STUDY, DESIGN, SIZE, DURATION: A total of 367 women with proven endometriosis undergoing medical or surgical treatment were included in an observational study conducted between 1 January 2012 and 31 December 2014 in two French tertiary care centers. Both hospitals are reference centers for endometriosis treatment. Of these 367 women, 267 were sexually active and constituted the baseline population.

PARTICIPANTS/MATERIALS, SETTINGS, METHODS: Women >18 years old with histological or radiological proven endometriosis, consulting for painful symptoms of at least 3 months duration, infertility, or other symptoms (bleeding, cysts) were invited to complete self-administered questionnaires before (T0) and 12 months after treatment (T1). Tests of data quality included descriptive statistics of the data, missing data levels, floor and ceiling effects, structural validity and internal consistency.

The construct validity was obtained by testing presupposed relationships between previously established SAQ scores and prespecified characteristics of the patients by comparing different subgroups of patients at T0. Sensitivity to change was subsequently calculated by comparing the SAQ score between T1 and T0 overall and for different subgroups of treatment. Effect sizes (to T1) were calculated according to Cohen's method. The minimally important difference was estimated by a step-wise triangulation approach (including anchor-based method).

MAIN RESULTS AND THE ROLE OF CHANCE: In total, 267 sexually active patients (204 surgical and 63 medical treatment) completed the SAQ at T0 and 136 (50.9%) at T1. The SAQ score ranged from 2.0 to 28.0 (mean \pm SD: 16.8 \pm 5.7).

The SAQ score was one-dimensional according to the scree plot with good internal consistency (*Cronbach alpha* = 0.78, 95% CI 0.74–0.81) and had good discriminative ability according to pain descriptors and quality of life in endometriosis. The SAQ was responsive in patients treated by surgery but the effect size was low (0.3, 95% CI (0.0–0.6), *P* = 0.01). The minimally important difference was determined at 2.2.

LIMITATIONS, REASONS FOR CAUTION: The effect size for medical treatment was non-significant. Other effect sizes were low but statistically significant. This could be explained by lower libido due to progestin intake, which was used for both surgically and medically treated patients.

WIDER IMPLICATIONS OF THE FINDINGS: The SAQ is easy to use, valid and effective in assessing sexual quality of life in patients with endometriosis. This patient-reported score could be used as a primary outcome for future clinical studies. The minimally important difference estimation will be useful for future research. We recommend using 2.2 for the minimally important difference of the SAQ.

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Key words: endometriosis / sexual quality of life / responsiveness / sexual activity questionnaire / minimally important difference

Introduction

Endometriosis is a chronic gynecological disease which occurs in 5–10% of women of reproductive age (Barbara *et al.*, 2017b). It is one of the most frequent causes of deep dyspareunia (Ferrero *et al.*, 2008; Vercellini *et al.*, 2011, 2013) and is associated with higher rates of interrupted intercourse (3.7 ± 1.9 over 3 months for women with endometriosis versus 2.6 ± 1.9 over 3 months for control group ($P < 0.05$)) and reduced frequency of sexual intercourse (Ferrero *et al.*, 2005). Dyspareunia negatively affects different domains of sexual functioning leading to psychological disorders and relational distress (Meana and Lykins, 2009), and has an unfavorable emotional impact on partners (Fernandez *et al.*, 2006). In a recent review (Barbara *et al.*, 2017a), it was reported that two-thirds of women with endometriosis have sexual dysfunction. It is not only limited to deep dyspareunia and pain but also has a psychological component and relational dimensions including the partner's sexual functioning (that has to be taken into account in a multidimensional perspective of endometriosis treatment). This dysfunction could alter sexual quality of life and consequently negatively impact health-related quality of life (Orley and Kuyken, 1994; Garratt *et al.*, 1995). Sexual function endpoints should thus be included in the evaluation of treatments of endometriosis. However, while several studies have demonstrated the effectiveness of medical and surgical treatment on dyspareunia (Chapron *et al.*, 1999; Garry *et al.*, 2000; Abbott *et al.*, 2004; Thomassin *et al.*, 2004), there is a paucity of data about sexual function in this setting (Fauconnier *et al.*, 2017).

The Sexual Activity Questionnaire (SAQ) was initially developed by Thirlaway (Thirlaway *et al.*, 1996a) to investigate the impact of long-term tamoxifen on the sexual function of women at high risk of developing breast cancer. The psychometric soundness of the questionnaire has since been validated in this population and it has been extensively used in studies of cancer therapy (Fallowfield *et al.*, 2001; Ganz *et al.*, 2002; Carmack Taylor *et al.*, 2004; Wenzel *et al.*, 2005). The SAQ has also been used and validated in the general population in Norway (Vistad *et al.*, 2007) with good psychometric properties (good internal consistency [Cronbach's coefficient alpha of 0.86] and confirmed construct validity). In 2000, Garry *et al.* used the SAQ to assess the effect of endometriosis and radical laparoscopic excision on sexual quality of life (among other quality of life questionnaires) but did not provide validation of the SAQ in this population. Thus to date, the SAQ has not been validated for patients with endometriosis.

The purpose of this study was to assess the psychometric validity of the SAQ in a population of patients treated for symptomatic endometriosis. We also examined responsiveness (ability to change) and the minimally important difference (MID) (smallest difference perceived by the patient as beneficial or harmful) of the SAQ in this population.

Materials and Methods

Recruitment sites and treatment

The data came from a French prospective observational study (Fauconnier *et al.*, 2017) conducted in two hospitals (Centre Hospitalier de Versailles and Centre Hospitalier Intercommunal de Poissy-Saint-Germain) between 1 January 2012 and 31 December 2014. Both these hospitals are reference centers for endometriosis treatment with extensive experience in surgery for deep infiltrating endometriosis (DIE) including intestinal and bladder resection. The two centers work together, follow the same treatment guidelines and apply similar preoperative assessments: standardized questionnaires for pelvic pain symptoms and quality-of-life, systematic ultrasound (US) examination, and magnetic resonance imaging (MRI). The choice of treatment – medical or surgical – is the result of a joint decision between physician and patient. Details of both treatments are provided below. A descriptive sheet is systematically used to report the location of the endometriosis implants and the subtype (endometriosis with or without DIE and the depth of infiltration) (Chapron *et al.*, 2003). This information leads to the classification of patients according to the American Fertility Society (AFS). The patient may also receive a medical hormonal treatment before or after surgery at the surgeon's discretion.

Endometriosis treatment

In both treatment centers, the medical hormonal treatment consisted of the elimination of menses by progestin pills, combined oral contraceptive pills or a GnRH agonist. Surgical treatment consisted, whenever possible, of complete excision of endometriosis lesions in one or two surgical steps. Surgery depended on the characteristic of the implants and included excision or fulguration of superficial peritoneal implants, excision of endometriomas, excision of deep endometriosis lesion with bowel resection and partial cystectomy when indicated with the help of a specialized surgeon if needed.

Study population

The study included women over 18 years old with proven endometriosis consulting for painful symptoms of at least 3 months' duration, infertility or other symptoms (bleeding, cysts).

To assess the psychometric properties of the SAQ, we focused on sexually active patients defined as 'involved in sexual relationship' (i.e. patients who responded 'yes' to the question 3 [*Do you engage in sexual activity with anyone at the moment?*] of Section I of the SAQ, see details of SAQ questionnaire 'design and data collection' section).

For patients receiving surgical treatment, a typical macroscopic black-bluish nodule or a histological examination with ectopic endometrial glands and stroma outside the endometrial cavity were considered as proof of endometriosis.

For patients receiving medical treatment, proof of endometriosis was based on clinical examination (posterior vaginal fornix macroscopic nodules),

or MRI (hyperintense foci on T1-weighted images, small hyperintense cavities on T2-weighted images) or US performed by an expert physician (abnormal hypoechoic linear thickening and nodules or masses with or without regular contours) (Vercellini et al., 1996; Bazot et al., 2007, 2009).

The exclusion criteria were the following: inability to read French, presence of another pelvic pathology, chronic pain other than endometriosis, sexual inactivity. The exclusion of sexual inactive women was motivated by the fact that several questions of Section 3 of the SAQ (SAQ-F) would make no sense for them (for instance: 'Was 'having sex' an important part of your life this month?').

Design and data collection

At the first visit before treatment (T0), each patient who agreed to participate completed T0 self-administered questionnaires, which had been developed to evaluate pain symptoms related to endometriosis (Chapron et al., 2005).

These questionnaires included the French version of the SAQ which has already been used in the field of oncology (Brédart et al., 2011). It consists of three basic sections, the first of which assesses whether the woman is sexually active (items 1 to 3). Those who are not sexually active go on to complete Section 2 (but not Section 3) which lists the eight reasons for her sexual inactivity (e.g. 'I have no partner', 'I am too tired', 'my partner is too tired', 'I am not interested in sex'). Women who are sexually active complete Section 3 of the SAQ, the function scale (SAQ-F), which contains 10 questions (items 4 to 13) designed to assess several aspects of sexual function: pleasure, desire, satisfaction, vaginal dryness, penetration pain, frequency of intercourse (e.g. 'Was 'having sex' an important part of your life this month?'; 'Did you enjoy sexual activity this month?'; 'During sexual relations, how frequently did you notice dryness of your vagina this month?') (Supplementary Data 1 for all 10 items). The patient is asked to respond to each item using a 4-point Likert scale (e.g. 'very much', 'somewhat', 'a little', 'not at all') (Supplementary Data 1).

For the analyses, we included all sexually active patients. For the calculation of the SAQ score, we included patients who completed more than 50% of SAQ-F. This cut-off (50%) has been previously used in the scoring of other quality of life questionnaires in women with endometriosis (Aubry et al., 2017).

The T0 questionnaires also included: a 10 cm visual analog scale (VAS) ranging between 0 for 'no pain' and 10 cm for 'unbearable pain' to assess the intensity of each pain symptom; the French version of the Endometriosis Health Profile-5 (EHP-5); and the French version of the EuroQoL Group 5D (EQ-5D) (Chevalier and Pouvourville, 2013; Aubry et al., 2017). We also collected data about the women's socio-demographic status, height, weight, gravidity, parity, infertility, menstrual cycle characteristics, sexual activity and previous pelvic surgery.

Follow-up was performed 12 months after treatment (second visit 'T1') when the patients were asked to complete the same self-administered questionnaires. The patients were also asked to complete a sexual Clinical Global Impression Improvement scale (sexual CGI-I), which assesses the progression of symptoms during sexual relations including the question 'current sexual symptoms are' (one of five answers possible: 'not concerned', 'recovered', 'improved', 'persistent' or 'worse') (Supplementary Data 2).

Statistical analysis

Baseline characteristics were analyzed as frequencies and percentages for categorical variables and as means and SD for continuous variables. These characteristics are described for all patients who completed the SAQ.

In the first step, descriptive statistics, score distribution and structural validity of the SAQ were assessed. We searched floor and ceiling effects (defined as >95% of respondents who answered the lowest or highest

category respectively) for the 10 items of SAQ-F. A scree plot with parallel analysis was conducted to examine the structure and determine the dimensions of the SAQ (Falissard, 2008). Internal consistency was assessed with the Cronbach's alpha (considered acceptable if >0.7).

As recommended by Thirlaway in their original description (Thirlaway et al., 1996b), we planned to calculate the SAQ score by simply summing up the responses to the 10 items of the SAQ-F. However, in the original description, Thirlaway found a three-dimensional structure of the SAQ that led to three separate factor scores. In the present study, the SAQ was found to be one-dimensional (see Results section), and so we calculated an overall SAQ score. The items were rated on a 4-point Likert scale ranging from 0 (lowest sexual quality) to 3 (highest sexual quality) for all items (Supplementary Data 1). The total score ranged from 0 to 30.

Missing data had no influence because the corresponding items were omitted from the calculation and a score average was calculated with the other items. The original SAQ description does not provide instructions on how to deal with missing items when creating a total score (Thirlaway et al., 1996b). We chose to calculate a total score using an average score based on the individual's completed items with a view to minimizing loss of information. However, we performed a sensitivity analysis with a complete case analysis (i.e. including only patients who responded to all 10 items of SAQ-F).

In a second step, the construct validity was evaluated for all the sexually active women who answered more than 50% of the SAQ at T0. We tested the pre-established relationships between the SAQ score and the patient characteristics and endometriosis assessment. We hypothesized a lower SAQ score in patients with: 'pain as primary indication of endometriosis treatment', 'pelvic pain', 'dyspareunia' (Ferrero et al., 2007; Mabrouk et al., 2012), 'intromission pain', 'pain in all sexual positions', worse 'EHP-5' (EHP-5 measures health-related quality of life (HrQoL); 100 is the worst possible HrQoL score and 0 the best possible) (Jones, 2005, Montanari et al., 2013), 'endometriosis severity (revised AFS)', and 'presence of deep anterior or posterior endometriosis' (Chapron et al., 2003). In contrast, we hypothesized a higher SAQ score for patients with a higher 'EQ-5D' score (EQ-5D also measures the HrQoL (a higher EQ-5D means a higher HrQoL)) (Montanari et al., 2013).

Pearson correlation coefficients and ANOVA were used to test the relationships between the SAQ scores and continuous and categorical variables, respectively. For variables correlated to the SAQ score, we estimated the effect size according to Cohen's method and his confidence interval (Kazis et al., 1989): a standardized difference in the mean SAQ score between two groups of around 0.2 was considered a small effect, around 0.5 a moderate effect, and 0.8 or higher a large effect (Rosnow and Rosenthal, 1996). For continuous variables, the cut-off to define groups was the median score for the quality of life scale (EH-P5 and EQ-5D) and 7 on the VAS scale (corresponding to severe pain) for pelvic pain, and dyspareunia. A positive effect size indicated that the variable was associated with an increase in SAQ score, i.e. improvement in sexual quality of life.

In a third step, SAQ score responsiveness was evaluated by comparing responses before and after treatment (T0 versus T1 self-questionnaires) by paired data Student's t-test and by using effect size in all patients and in different subgroups (patients with intestinal endometriosis, patients with surgical treatment, patients with medical treatment).

The MID is the smallest difference perceived by patients as beneficial or harmful in the score of an instrument's measure (Jaeschke et al., 1989). Because there is no 'gold standard' methodology for estimating the MID (Brozek et al., 2006), we used a step-wise triangulation to establish a MID for the SAQ score, including:

- an anchor-based method using the sexual clinical global impression of improvement (CGI-I) (Crosby et al., 2003; Gerlinger et al., 2010).
- a distribution-based approach among women who answered the SAQ questionnaire at T0 and T1 (Stull et al., 2014).

– use of receiver operating characteristic (ROC) curves to look at sensitivity and specificity for different cut-off points when comparing patients who improved versus those who did not ('persistent' and 'worse') on the SAQ T0 and T1 questionnaires. The final cut-off was the point with the best balance between sensitivity and specificity (Farrar *et al.*, 2001; Gerlinger and Schmelter, 2011) to show patients who improved, and was assessed by the Youden method or ROC 0.1 method (Youden, 1950; Metz, 1978).

Details about the estimation of the MID by step-wise triangulation are provided in the Supplementary Data 3.

The evaluation of responsiveness and the estimation of MID were based on the population of patients who answered SAQ-F at T0 and T1.

All tests were bilateral and a P -value <0.05 was considered significant.

All data were collected in a computed database and were analyzed by R software (Version 3.4.0; <https://cran.r-project.org/bin/macosx/>).

Ethics

The present study was purely observational and involved no intervention. As such, no written informed consent was required by French law (Huriet-Serusclet

Law, 20 December 1998). However, all patients received information about the study and were free to participate. Patient data, confidentiality and restrictions were respected. The study was approved by the Ethics Committee of Ile-de-France (modified version of Law 2004-806, dated 9 August 2004) and the French National Committee for Information Technology and Individual Liberties (N°906 253).

Results

Participants

Among the 367 women with confirmed endometriosis, 267 patients were sexually active and complete the SAQ at T0 (response rate: 72.8%) (Fig. 1). These 267 patients were included in the study and their data were used for descriptive analyses (Table 1). Of these women, 261 completed more than 50% of the SAQ-F. These 261 patients were used for the calculation of the SAQ score and to evaluate the SAQ construct validity. Among these 261 patients, 132 were sexually active and completed more than 50% of the SAQ-F at

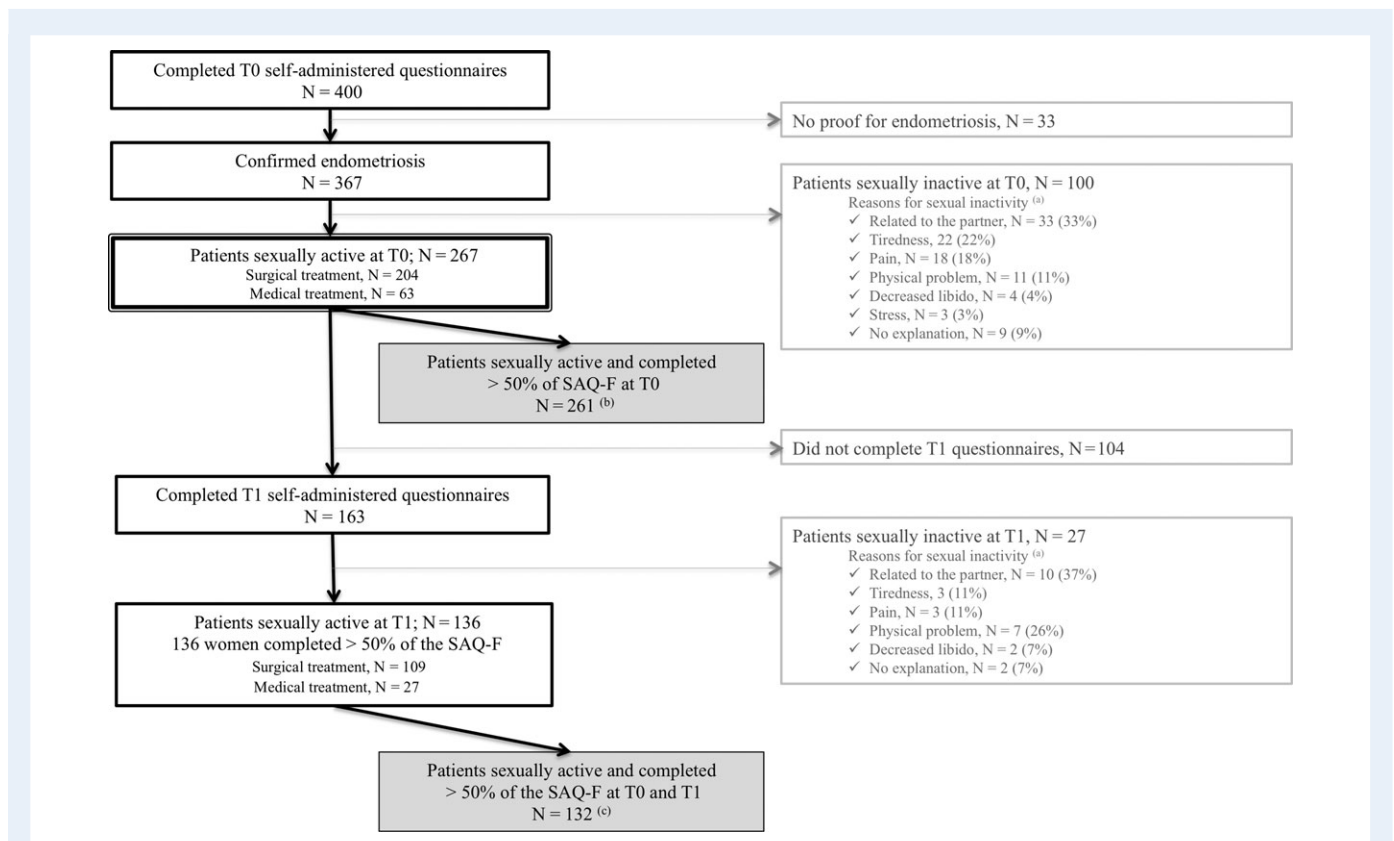


Figure 1 Flow-chart for the validation of the Sexual Activity Questionnaire in women with endometriosis.

– « Related to the partner » refers to 3 items of section 2 of the Sexual Activity Questionnaire (SAQ): 'I do not have a partner at the moment', 'My partner is too tired' and 'My partner is not interested in sex'

– Among the 267 patients, six patients did not complete more than 50% of SAQ-F (four completed only two items of SAQ-F and two patients no item). The remaining 261 patients (who completed more than 50% of SAQ-F) represent the population used for the calculation of SAQ score and the evaluation of SAQ construct validity.

– Among these 261 patients, 198 received surgical treatment and 63 medical treatment.

The 132 who responded to SAQ-F at T0 (before treatment) and T1 (after treatment) represent the population used for the analysis of the responsiveness and the calculation of the minimally important difference (MID). Among these 132 patients, 105 received surgical treatment and 27 medical treatment.

Table I Baseline characteristics of all sexually active patients with endometriosis and according to response to the sexual activity questionnaire.

	All sexually active patients N = 267	Women who completed SAQ at T1 N = 136	Women who did not complete SAQ at T1 N = 131	P value ^a
Center. n (%)				
Poissy	105 (39.3)	48 (35.3)	57 (43.5)	0.169
Versailles	162 (60.7)	88 (64.7)	74 (56.5)	
Main indications for endometriosis treatment. n (%)				
Pain	192 (71.9)	96 (70.6)	96 (73.3)	0.752
Infertility	54 (20.2)	28 (20.6)	26 (19.9)	
Bleeding	3 (1.1)	1 (0.7)	2 (1.5)	
Others ^b	18 (6.7)	11 (8.1)	7 (5.3)	
Age. years. mean (SD)	33.1 (6.5)	33.3 (6.2)	33.0 (6.7)	0.696
BMI. kg/m ² . mean (SD)	23.1 (4.4)	23.0 (4.1)	23.4 (4.8)	0.590
Parity. mean (SD)	0.5 (0.9)	0.5 (0.8)	0.6 (0.9)	0.437
Gravidity. mean (SD)	0.8 (1.2)	0.8 (1.0)	0.9 (1.4)	0.367
Main pain (VAS). mean (SD)	6.1 (2.5)	5.9 (2.7)	6.2 (2.3)	0.349
Dyspareunia (VAS). mean (SD)	4.3 (2.9)	4.2 (2.8)	4.5 (2.9)	0.399
Medical treatment only. n (%)	63 (23.6)	27 (19.9)	36 (27.5)	0.142
Surgical treatment. n (%)	204 (76.4)	109 (80.1)	95 (72.5)	
rAFS stage (surgical treatment ^c). n (%)				
1	38 (18.6)	20 (18.3)	18 (18.9)	0.974
2	32 (15.7)	16 (14.7)	16 (16.8)	
3	55 (27.0)	30 (27.5)	25 (26.3)	
4	79 (38.7)	43 (39.5)	36 (37.9)	
Anterior DIE ^c . n (%)				
A0 (None)	194 (72.7)	92 (67.6)	102 (77.9)	0.009
A1 (Anterior DIE without bladder)	54 (20.2)	28 (20.6)	26 (19.8)	
A2 (Bladder)	19 (7.1)	16 (11.8)	3 (2.3)	
Posterior DIE ^d . n (%)				
P0 (None posterior DIE)	14 (5.2)	7 (5.1)	7 (5.3)	0.956
P1 (USL)	108 (40.5)	57 (41.9)	51 (38.9)	
P2 (vagina without intestine)	21 (7.9)	11 (8.1)	10 (7.6)	
P3 (Intestine DIE)	124 (46.4)	61 (44.9)	63 (48.1)	

SAQ: sexual activity questionnaire, VAS: Visual analogical scale; AFS stage: stage of American Fertility Society; rAFS: revised American Fertility Society; DIE: deep infiltrating endometriosis, USL: uterosacral ligaments.

^aStudent's t-test for quantitative variables and Chi square test for qualitative variables (comparison of patients).

^bOvarian cyst. endometriosis on magnetic resonance imaging discovery. urinary problem. Missing data.

^cFor 204 patients with surgical treatment in the whole population study; for 109 patients who answered SAQ at T1 (12 months after treatment) and 95 who did not answer.

^dDIE classification according to DIE Chapron classification (Chapron et al. 2003).

T1 (Fig. 1). They represented the population used for the analysis of responsiveness and MID calculation.

At T0, sexually inactive women ($n = 100$) differed from sexually active women ($n = 267$) in having more pelvic pain (6.3 ± 2.4 versus 5.4 ± 2.4 , $P = 0.006$) and dyspareunia (5.5 ± 3.1 versus 4.3 ± 2.9 , $P = 0.004$) (Supplementary Table S1).

The patients' baseline characteristics are listed in Table I. There was no significant difference between the 136 patients who completed SAQ questionnaire at T1 and the 131 who did not (Table I), except for anterior DIE characteristics (less bladder injury in the group of patients who did not complete the SAQ at T1).

Descriptive statistics, score distributions and structural validity of the SAQ

The descriptive analyses of the SAQ are listed in Table II. The proportion of missing data was low (<5% for all items except for the item 'Frequency satisfaction' [5.2%]). There were no floor or ceiling effects.

All items of the SAQ were one-dimensional according to the scree plot (Supplementary Fig. S1). The internal consistency was good (Cronbach alpha = 0.78, 95% CI 0.74–0.81).

The distribution of the SAQ score (0–30) ranged from 2.0 to 28.0 (mean 16.8 ± 5.7).

Table II Descriptive analyses of the 10 items of SAQ-F.

Items	Mean (SD)	Response 0 n (%)	Response 1 n (%)	Response 2 n (%)	Response 3 n (%)	Skewness	Missing data n (%)
Importance	1.5 (0.9)	38 (14.2)	81 (30.3)	109 (40.8)	30 (11.2)	-0.2	9 (3.4)
Pleasure	2.1 (0.9)	17 (6.4)	48 (18.0)	98 (36.7)	98 (36.7)	-0.6	6 (2.3)
Tiredness	1.6 (1.0)	48 (18.0)	56 (21.0)	103 (38.6)	51 (19.1)	-0.3	9 (3.4)
Sexual desire	1.9 (0.9)	14 (5.2)	64 (24.0)	106 (40.0)	77 (28.8)	-0.4	6 (2.3)
Vaginal dryness	1.8 (1.1)	50 (18.7)	41 (15.4)	70 (26.2)	99 (37.1)	-0.5	7 (2.6)
Pain	1.4 (1.1)	74 (27.7)	51 (19.1)	86 (32.2)	50 (18.7)	-0.0	6 (2.3)
Sexual satisfaction	2.0 (1.0)	24 (9.0)	47 (17.6)	87 (32.6)	100 (37.5)	-0.6	9 (3.4)
Frequency	2.1 (0.8)	6 (2.3)	63 (23.6)	99 (37.1)	93 (34.8)	-0.4	6 (2.3)
Frequency variation	0.8 (0.8)	99 (37.1)	124 (46.4)	26 (9.7)	9 (3.4)	0.8	9 (3.4)
Frequency satisfaction	1.6 (1.1)	59 (22.1)	49 (18.4)	91 (34.1)	54 (20.2)	-0.2	14 (5.2)

N = 267 women. Response 0 = lowest sexual quality and response 3 = highest sexual quality.
SAQ-F: women who are sexually active complete Section 3 of the SAQ, the function scale.

Construct validity

As expected, we found significant associations between the SAQ score and: VAS of pelvic pain ($P = 0.029$), VAS of dyspareunia ($P < 0.001$), pain as the main indication for endometriosis treatment ($P = 0.001$), EHP5 ($P < 0.001$), EQ5D ($P = 0.008$), and progestin intake ($P < 0.001$) (Table III and Supplementary Table SII). Unexpected findings emerged with the absence of association between SAQ score and the AFS severity score, and location or extension of the endometriosis (Table III). The results of Pearson correlation and the ANOVA are presented in Supplementary Tables SII and SIII, respectively.

Sensitivity analysis

The sensitivity analysis with complete case analysis confirmed the psychometric validity of the SAQ ($n = 243$). In this subpopulation the Cronbach alpha is good = 0.78 (IC 95%: 0.74–0.81). Supplementary Table SIV provides descriptive analyses of the 10 items of SAQ-F in the subpopulation of patients who completed all 10 items of the SAQ-F. Supplementary Fig. S2 provides the Scree plot of the 10 items of the SAQ-F in this subpopulation. The construct validity was attested by a correlation between the SAQ score and: VAS of dyspareunia ($P < 0.001$), EHP5 ($P < 0.001$) and EQ5D ($P = 0.001$).

Responsiveness and MID

As already mentioned, the 132 patients who completed SAQ-F at T0 and T1 represent the population used for the analysis of the responsiveness and the calculation of the MID.

The SAQ score significantly increased after treatment (Table III). The change in response for each item is detailed in Fig. 2.

In the subgroup of patients with surgical treatment, the SAQ score significantly increased between T0 and T1, while no significant change in SAQ score was observed in the subgroup of patients treated by medical treatment only (Table III). According to the anchor-based approach, the change in SAQ scores between T0 and T1 were significantly correlated with the response to the Sexual CGI-I ($r = -0.3$, $P = 0.003$, $n = 47$) leading to the use of the sexual CGI-I as anchor. Forty-

seven patients declared to be improved (on sexual CGI-I) after treatment. By this method, the MID value was 2.2.

According to the distribution-based approaches, the MID value was 3.0 and 2.6 and based on the half standard of deviation and SEM, respectively ($n = 132$).

The ROC curve with Youden method found a MID value of 4.0, which correctly classifies 75% of cases. The ROC curve using the ROC 0.1 method found a MID value of 2.0, which correctly classifies 75% of cases ($n = 72$, patients were classified as 'improved' or 'persistent or worse'). (Data not shown.)

Discussion

This prospective study supports the psychometric validity of the SAQ in patients with endometriosis. In this population, the SAQ was found to be of a one-dimensional structure and the internal consistency was satisfactory. The SAQ score was also found to be responsive to surgical treatment. We assessed the MID of the SAQ score, which should be useful for future trials with SAQ as the endpoint.

Strengths and weaknesses

Our database included patients with a wide range of endometriosis lesions (DIE and non-DIE in various locations). The rate of response to the SAQ was good (>70%) compared to other studies (Klee *et al.*, 1997; Fugl-Meyer and Fugl-Meyer, 2002; Vistad *et al.*, 2007) and the population was well distributed on the full scale of the instrument. However, only 51% of patients who answered SAQ at T0 completed it at T1. This response rate is comparable to those shown in other studies assessing sexual questionnaires (Clarkson *et al.*, 2001; Fauconnier *et al.*, 2012).

We acknowledge that the effect sizes for the responsiveness of the SAQ were low. However, statistical significance was reached except for the medical treatment group. This could be explained by the use of progestin intake in both subgroups (medical and surgical treatment), which may contribute to decreased libido, dryness and sexual discomfort leading to a lower SAQ score overall. The absence of

Table III Construct validity and responsiveness of the SAQ.

	N	Mean value of SAQ score \pm 1 SD	P-value	Effect size	95% CI Effect size
Predefined known groups (N = 261)					
Pain as main indication for endometriosis treatment					
Yes	186	16.1 \pm 5.7	0.001	0.5	0.2–0.8
No	75	18.7 \pm 5.4			
Pelvic pain (VAS) ^a					
>7	44	14.6 \pm 5.9	0.028	0.4	0.0–0.7
\leq 7	158	16.7 \pm 5.6			
Dyspareunia (VAS) ^a					
>7	42	13.4 \pm 5.3	<0.001	0.7	0.4–1.0
\leq 7	200	17.3 \pm 5.5			
Sexual intromission pain ^a					
Yes	11	19.2 \pm 5.6	0.073	0.6	–0.1–1.2
No	202	16.2 \pm 5.5			
EHP-5 ^{b,c}					
<50	124	18.5 \pm 5.0	<0.001	0.6	0.3–0.8
> or =50	131	15.4 \pm 5.8			
EQ-5D ^c					
>0.79	127	17.8 \pm 5.3	0.008	0.3	0.1–0.6
\leq 0.79	112	15.8 \pm 5.9			
rAFS stage ^d					
III–IV	129	16.8 \pm 5.8	0.243	0.2	–0.1–0.5
I–II	69	15.7 \pm 6.0			
Deep anterior endometriosis ^e					
Yes	69	18.0 \pm 5.9	0.055	0.3	0.01–0.5
No	192	16.4 \pm 5.6			
Deep posterior endometriosis with intestinal involvement ^e					
Yes	120	17.3 \pm 5.6	0.183	0.2	–0.1–0.4
No	141	16.4 \pm 5.7			
Progestin intake at T0					
Yes	80	15.0 \pm 5.8	<0.001	0.5	0.2–0.8
No	181	17.7 \pm 5.5			
Responsiveness (N = 132 who answered the SAQ at T1) ^f					
All patients					
T0		17.0 \pm 5.7	0.010	0.3	–0.1–0.6
T1		18.5 \pm 6.0			
Patients with intestinal endometriosis					
T0		17.7 \pm 5.2	0.044	0.3	–0.2–0.9
T1		19.5 \pm 5.4			
Patients with surgical treatment					
T0		16.5 \pm 5.9	0.010	0.3	–0.1–0.7
T1		18.4 \pm 6.2			
Patients with medical treatment only					
T0		18.8 \pm 4.4	0.638	0.1	–0.7–0.9
T1		19.3 \pm 5.6			

^aNumber of patients differs from 261 because some patients did not answer for dyspareunia, pelvic pain or sexual intromission pain.

^bFor the EHP-5 lower scores indicate better health status.

^cNumber of patients differs from 261, when no answer to other questionnaires such as EQ-5D and EHP-5.

^dConcerning the 198 patients with surgical treatment.

^eAccording to DIE Chapron classification (Chapron et al. 2003).

^fP value with paired data Student's t test.

Construct validity: N = 261, patients sexually active and who answered more than 50% of the SAQ-F at T0.

Responsiveness: N = 132, patients sexually active and who answered the SAQ-F at the first visit before treatment (T0) and 12 months after treatment (T1).

EQ-5D: self-administrated EuroQol 5D; EHP-5: self-administrated Endometriosis Health Profile 5.

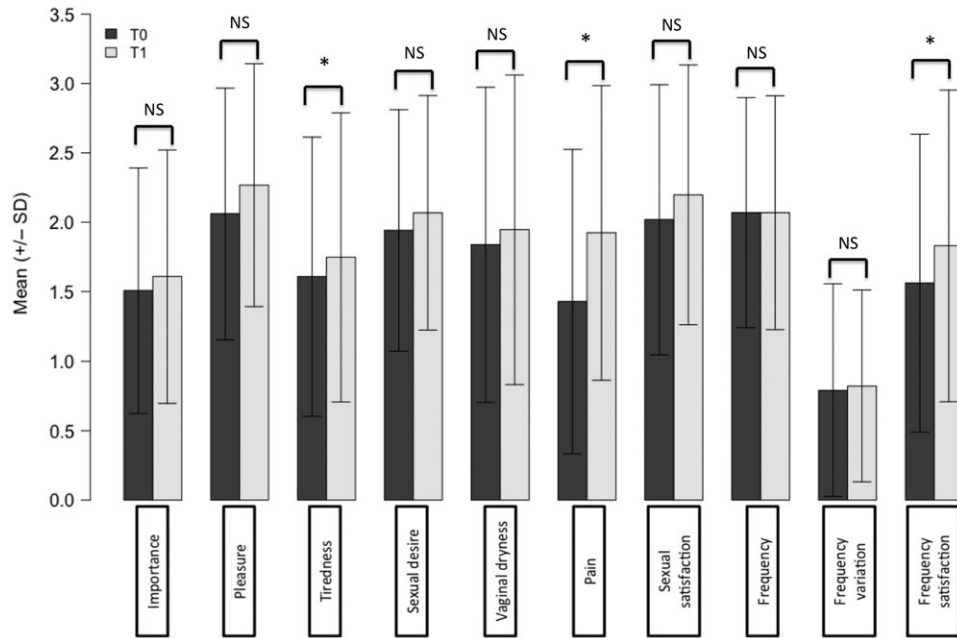


Figure 2 Change in response for each item (responsiveness) of the SAQ-F. Mean of the response for the 10 items of SAQ-F before (T0) and after treatment (T1). 0 = lowest sexual quality and 3 = highest sexual quality. Y-axis refers to the 10 items of SAQ-F. *Statistically significant ($P < 0.05$, paired Student's t -test).

responsiveness for patients who received medical treatment only may be explained by a lack of power with a small sample size. Further studies should be performed to answer this question.

We showed a wide variation in the MID according to the method used. One should note that there is currently no gold standard technique to estimate the MID (Brozek *et al.*, 2006). The assessment of a cut-off point on the ROC curves by Youden and ROC 0.1 methods appears invalid in this case because we observed a large measurement gap between the two methods (4 with Youden and 2 with ROC 0.1). As previously reported by experts, the anchor-based method is more relevant to determine the MID (Revicki *et al.*, 2008). We thus recommend using 2.2 for the MID of the SAQ in future studies in endometriosis populations.

In a non-prespecified complementary analysis, we found that the women who were not included in the study, because they were not sexually active (and did not complete the SAQ-F) ($n = 100$), had significantly more pelvic pain and dyspareunia (complementary analysis is provided in the Supplementary Table S1). This may lead to an overestimated SAQ score in the present study. To assess if the severity of dyspareunia impacts the MID value, we performed another non-prespecified complementary analysis. First, we identified a subgroup of patients with the most severe dyspareunia (defined as a VAS dyspareunia score >4 [4 was the median value of VAS dyspareunia in the population of patients responded to the SAQ-F at T0 and T1]). Second, we calculated the MID with the anchor-based method in this subpopulation. The MID score in most severe dyspareunia patients was 2.8 (P -value = 0.018, 95% CI: 0.52–5.11) and is very similar to the MID of 2.2 calculated in the whole population of the study.

Surprisingly, we did not find a relation between the SAQ score and endometriosis severity (AFS) or location/extension of the endometriosis. The pain was not associated with severity of the endometriosis (AFS and anterior or posterior DIE). However, this does not negatively impact the construct validity of the SAQ because another study (Aubry *et al.*, 2017) has previously demonstrated that endometriosis severity does not impact the patients' quality of life (EHP-5).

One should note that we found a one-dimensional SAQ structure in our study – as opposed to the three-dimensional structure found in the original study (Thirlaway *et al.*, 1996a) – which simplified the calculation of the overall score. This could be explained by the different populations in the two studies: patients with endometriosis in our study and oncology patients in that of Thirlaway *et al.*

Furthermore, the inclusion of two intervention centers may have induced a potential center effect. However both centers are reference centers for endometriosis treatment with extensive experience in surgery for DIE and both used standardized surgical procedures and medical treatment. On the contrary, the inclusion of two intervention centers could be viewed as a strength because it increases the external validity of our findings.

Implications

Sexual quality of life is frequently impaired by endometriosis. It was therefore important to validate a patient-reported outcome tool to assess sexual quality of life. Although the SAQ has previously been used in the field of endometriosis (Garry *et al.*, 2000), to date it has not been validated in this population. We now provide the validation of the SAQ in a large population of patients with endometriosis.

Other sexual quality-of-life questionnaires have been developed. One of the most popular is the female sexual function index (FSFI), developed by Rosen et al. (Rosen et al., 2000). In their scoring algorithm, 15 of the 19 items refer to sexual activity and the items are scored from 0 to 5 (with 0 for 'no sexual activity during the past 4 weeks'). However, a score of 0 could refer to the absence of sexual activity for a reason other than sexual dysfunction, e.g. the absence of a partner (Hevesi et al., 2017). This confusion could lead to bias. Moreover, in a study by Vercellini, the FSFI did not show good responsiveness as attested by a mean total FSFI score which never exceeded the normal cut-off limit of 26.55 (Vercellini et al., 2013).

The SAQ thus has the added benefit of differentiating between sexually active or inactive women and identifying the reasons for sexual inactivity. Moreover, the SAQ is brief, easy to use, and does not include intimidating questions that could limit the answers (fewer than 6% of missing answers).

Our study shows that the SAQ score is responsive in the context of surgical therapy. It could therefore be recommended to evaluate sexual function after surgical treatment for future clinical research evaluating therapeutic strategies in patients with endometriosis.

Conclusion

Because endometriosis is a common disease and strongly impairs sexual quality of life, it is crucial to develop easy-to-use validated tools for clinical practice and therapeutic evaluation. The SAQ is now validated in this population and could be used as a patient-reported outcome in future studies. More investigations are needed to assess the responsiveness of the SAQ after medical treatment.

Supplementary data

Supplementary data are available at *Human Reproduction* online.

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Authors' roles

A.F. was coordinator of the project. A.F. and P.P. conceived and designed the study. A.O., A.F., P.P. and J.D.C. contributed to data collection. A.F. and P.P. performed surgical procedures and medical follow-up. A.O. analyzed and interpreted the data. A.O. wrote the manuscript. A.R. and X.D. reviewed the data analyses and the manuscript. All authors approved the final submitted version of the manuscript.

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Conflict of interest

None declared.

References

- Abbott J, Hawe J, Hunter D, Holmes M, Finn P, Garry R. Laparoscopic excision of endometriosis: a randomized, placebo-controlled trial. *Fertil Steril* 2004;**82**:878–884.
- Angst F, Aeschlimann A, Angst J. The minimal clinically important difference raised the significance of outcome effects above the statistical level, with methodological implications for future studies. *J Clin Epidemiol* 2017;**82**:128–136.
- Aubry G, Panel P, Thiollier G, Huchon C, Fauconnier A. Measuring health-related quality of life in women with endometriosis: comparing the clinimetric properties of the Endometriosis Health Profile-5 (EHP-5) and the EuroQol-5D (EQ-5D). *Hum Reprod* 2017;**32**:1258–1269.
- Barbara G, Facchin F, Buggio L, Somigliana E, Berlanda N, Kustermann A, Vercellini P. What is known and unknown about the association between endometriosis and sexual functioning: a systematic review of the literature. *Reprod Sci Thousand Oaks Calif* 2017a;**24**:1566–1576.
- Barbara G, Facchin F, Meschia M, Berlanda N, Frattaruolo MP, Vercellini P. When love hurts. A systematic review on the effects of surgical and pharmacological treatments for endometriosis on female sexual functioning. *Acta Obstet Gynecol Scand* 2017b;**96**:668–687.
- Bazot M, Lafont C, Rouzier R, Roseau G, Thomassin-Naggara I, Daraï E. Diagnostic accuracy of physical examination, transvaginal sonography, rectal endoscopic sonography, and magnetic resonance imaging to diagnose deep infiltrating endometriosis. *Fertil Steril* 2009;**92**:1825–1833.
- Bazot M, Malzy P, Cortez A, Roseau G, Amouyal P, Daraï E. Accuracy of transvaginal sonography and rectal endoscopic sonography in the diagnosis of deep infiltrating endometriosis. *Ultrasound Obstet Gynecol Off J Int Soc Ultrasound Obstet Gynecol* 2007;**30**:994–1001.
- Brozek JL, Guyatt GH, Schünemann HJ. How a well-grounded minimal important difference can enhance transparency of labelling claims and improve interpretation of a patient reported outcome measure. *Health Qual Life Outcomes* 2006;**4**:69.
- Brédart A, Dolbeault S, Savignoni A, Besancenet C, This P, Giami A, Michaels S, Flahault C, Falcou M-C, Asselain B et al. Prevalence and associated factors of sexual problems after early-stage breast cancer treatment: results of a French exploratory survey. *Psychooncology* 2011;**20**:841–850.
- Carmack Taylor CL, Basen-Engquist K, Shinn EH, Bodurka DC. Predictors of sexual functioning in ovarian cancer patients. *J Clin Oncol Off J Am Soc Clin Oncol* 2004;**22**:881–889.
- Chapron C, Barakat H, Fritel X, Dubuisson J-B, Bréart G, Fauconnier A. Presurgical diagnosis of posterior deep infiltrating endometriosis based on a standardized questionnaire. *Hum Reprod Oxf Engl* 2005;**20**:507–513.
- Chapron C, Dubuisson JB, Chopin N, Foulot H, Jacob S, Vieira M, Barakat H, Fauconnier A. Deep pelvic endometriosis: management and proposal for a 'surgical classification'. *Gynecol Obstet Fertil* 2003;**31**:197–206.
- Chapron C, Dubuisson JB, Fritel X, Fernandez B, Poncelet C, Béguin S, Pinelli L. Operative management of deep endometriosis infiltrating the uterosacral ligaments. *J Am Assoc Gynecol Laparosc* 1999;**6**:31–37.
- Chevalier J, De Pourville G. Valuing EQ-5D using time trade-off in France. *Eur J Health Econ HEPAC Health Econ Prev Care* 2013;**14**:57–66.
- Clarkson J, Newton C, Bick D, Gyte G, Kettle C, Newburn M, Radford J, Johanson R. Achieving sustainable quality in maternity services – using audit of incontinence and dyspareunia to identify shortfalls in meeting standards. *BMC Pregnancy Childbirth* 2001;**1**:4.

- Crosby RD, Kolotkin RL, Williams GR. Defining clinically meaningful change in health-related quality of life. *J Clin Epidemiol* 2003;**56**:395–407.
- Falissard B Valider un instrument de mesure subjective. *Mes Subj En Santé Perspect Méthodologique Stat* 2008; Masson.
- Fallowfield L, Fleissig A, Edwards R, West A, Powles TJ, Howell A, Cuzick J. Tamoxifen for the prevention of breast cancer: psychosocial impact on women participating in two randomized controlled trials. *J Clin Oncol Off J Am Soc Clin Oncol* 2001;**19**:1885–1892.
- Farrar JT, Young JP, LaMoreaux L, Werth JL, Poole RM. Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale. *Pain* 2001;**94**:149–158.
- Fauconnier A, Goltzene A, Issartel F, Janse-Marec J, Blondel B, Fritel X. Late post-partum dyspareunia: does delivery play a role? *Progres En Urol J Assoc Francaise Urol Soc Francaise Urol* 2012;**22**:225–232.
- Fauconnier A, Huchon C, Chaillou L, Aubry G, Renouvel F, Panel P. Development of a French version of the Endometriosis Health Profile 5 (EHP-5): cross-cultural adaptation and psychometric evaluation. *Qual Life Res Int J Qual Life Asp Treat Care Rehabil* 2017;**26**:213–220.
- Fernandez I, Reid C, Dziurawiec S. Living with endometriosis: the perspective of male partners. *J Psychosom Res* 2006;**61**:433–438.
- Ferrero S, Abbamonte LH, Giordano M, Ragni N, Remorgida V. Deep dyspareunia and sex life after laparoscopic excision of endometriosis. *Hum Reprod Oxf Engl* 2007;**22**:1142–1148.
- Ferrero S, Esposito F, Abbamonte LH, Anserini P, Remorgida V, Ragni N. Quality of sex life in women with endometriosis and deep dyspareunia. *Fertil Steril* 2005;**83**:573–579.
- Ferrero S, Ragni N, Remorgida V. Deep dyspareunia: causes, treatments, and results. *Curr Opin Obstet Gynecol* 2008;**20**:394–399.
- Fugl-Meyer K, Fugl-Meyer AR. Sexual disabilities are not singularities. *Int J Impot Res* 2002;**14**:487–493.
- Ganz PA, Desmond KA, Leedham B, Rowland JH, Meyerowitz BE, Belin TR. Quality of life in long-term, disease-free survivors of breast cancer: a follow-up study. *J Natl Cancer Inst* 2002;**94**:39–49.
- Garratt AM, Torgerson DJ, Wyness J, Hall MH, Reid DM. Measuring sexual functioning in premenopausal women. *Br J Obstet Gynaecol* 1995;**102**:311–316.
- Garry R, Clayton R, Hawe J. The effect of endometriosis and its radical laparoscopic excision on quality of life indicators. *BJOG Int J Obstet Gynaecol* 2000;**107**:44–54.
- Gaunt DM, Metcalfe C, Ridd M. The Patient-Oriented Eczema Measure in young children: responsiveness and minimal clinically important difference. *Allergy* 2016;**71**:1620–1625.
- Gerlinger C, Schmelter T. Determining the non-inferiority margin for patient reported outcomes. *Pharm Stat* 2011;**10**:410–413.
- Gerlinger C, Schumacher U, Faustmann T, Colligs A, Schmitz H, Seitz C. Defining a minimal clinically important difference for endometriosis-associated pelvic pain measured on a visual analog scale: analyses of two placebo-controlled, randomized trials. *Health Qual Life Outcomes* 2010;**8**:138.
- Guyatt GH, Feeny DH, Patrick DL. Measuring health-related quality of life. *Ann Intern Med* 1993;**118**:622–629.
- Hevesi K, Mészáros V, Kövi Z, Márki G, Szabó M. Different Characteristics of the Female Sexual Function Index in a sample of sexually active and inactive women. *J Sex Med* 2017;**14**:1133–1141.
- Jaeschke R, Singer J, Guyatt GH. Measurement of health status. Ascertain the clinically important difference. *Control Clin Trials* 1989;**10**:407–415.
- Kazis LE, Anderson JJ, Meenan RF. Effect sizes for interpreting changes in health status. *Med Care* 1989;**27**:S178–S189.
- Klee M, Groenvold M, Machin D. Quality of life of Danish women: population-based norms of the EORTC QLQ-C30. *Qual Life Res Int J Qual Life Asp Treat Care Rehabil* 1997;**6**:27–34.
- Mabrouk M, Montanari G, Di Donato N, Del Forno S, Frascà C, Geraci E, Ferrini G, Vicenzi C, Raimondo D, Villa G et al. What is the impact on sexual function of laparoscopic treatment and subsequent combined oral contraceptive therapy in women with deep infiltrating endometriosis? *J Sex Med* 2012;**9**:770–778.
- Meana M, Lykins A. Negative affect and somatically focused anxiety in young women reporting pain with intercourse. *J Sex Res* 2009;**46**:80–88.
- Metz CE. Basic principles of ROC analysis. *Semin Nucl Med* 1978;**8**:283–298.
- Montanari G, Di Donato N, Benfenati A, Giovanardi G, Zannoni L, Vicenzi C, Solfrini S, Mignemi G, Villa G, Mabrouk M et al. Women with deep infiltrating endometriosis: sexual satisfaction, desire, orgasm, and pelvic problem interference with sex. *J Sex Med* 2013;**10**:1559–1566.
- Orley J, Kuyken W. The development of the World Health Organization Quality of Life assessment instrument (the WHOQOL). In: *Qual Life Assess Int Perspect*. Germany: Heidelberg, 1994, 41–60.
- Revicki D, Hays RD, Cella D, Sloan J. Recommended methods for determining responsiveness and minimally important differences for patient-reported outcomes. *J Clin Epidemiol* 2008;**61**:102–109.
- Rosen R, Brown C, Heiman J, Leiblum S, Meston C, Shabsigh R, Ferguson D, D'Agostino R. The Female Sexual Function Index (FSFI): a multidimensional self-report instrument for the assessment of female sexual function. *J Sex Marital Ther* 2000;**26**:191–208.
- Rosnow RL, Rosenthal R. Computing contrasts, effect sizes, and counter-nulls on other people's published data: general procedures for research consumers. *Psychol Methods* 1996;**4**:331–340.
- Stull DE, Wasiaik R, Kreif N, Raluy M, Colligs A, Seitz C, Gerlinger C. Validation of the SF-36 in patients with endometriosis. *Qual Life Res Int J Qual Life Asp Treat Care Rehabil* 2014;**23**:103–117.
- Thirlaway K, Fallowfield L, Cuzick J. The Sexual Activity Questionnaire: a measure of women's sexual functioning. *Qual Life Res* 1996a;**5**:81–90.
- Thirlaway K, Fallowfield L, Cuzick J. The Sexual Activity Questionnaire: a measure of women's sexual functioning. *Qual Life Res Int J Qual Life Asp Treat Care Rehabil* 1996b;**5**:81–90.
- Thomassin I, Bazot M, Detchev R, Barranger E, Cortez A, Darai E. Symptoms before and after surgical removal of colorectal endometriosis that are assessed by magnetic resonance imaging and rectal endoscopic sonography. *Am J Obstet Gynecol* 2004;**190**:1264–1271.
- Vercellini P, Frattaruolo MP, Somigliana E, Jones GL, Consonni D, Alberico D, Fedele L. Surgical versus low-dose progestin treatment for endometriosis-associated severe deep dyspareunia II: effect on sexual functioning, psychological status and health-related quality of life. *Hum Reprod Oxf Engl* 2013;**28**:1221–1230.
- Vercellini P, Meana M, Hummelshoj L, Somigliana E, Viganò P, Fedele L. Priorities for endometriosis research: a proposed focus on deep dyspareunia. *Reprod Sci Thousand Oaks Calif* 2011;**18**:114–118.
- Vercellini P, Trespidi L, De Giorgi O, Cortesi I, Parazzini F, Crosignani PG. Endometriosis and pelvic pain: relation to disease stage and localization. *Fertil Steril* 1996;**65**:299–304.
- Vistad I, Fosså SD, Kristensen GB, Mykletun A, Dahl AA. The sexual activity questionnaire: psychometric properties and normative data in a norwegian population sample. *J Womens Health* 2007;**16**:139–148. 2002.
- Wenzel L, DeAlba I, Habbal R, Kluhsman BC, Fairclough D, Krebs LU, Anton-Culver H, Berkowitz R, Aziz N. Quality of life in long-term cervical cancer survivors. *Gynecol Oncol* 2005;**97**:310–317.
- Wyrwich KW, Tierney WM, Wolinsky FD. Further evidence supporting an SEM-based criterion for identifying meaningful intra-individual changes in health-related quality of life. *J Clin Epidemiol* 1999;**52**:861–873.
- Youden WJ. Index for rating diagnostic tests. *Cancer* 1950;**3**:32–35.