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# Prospective Cohort of Deep Dyspareunia in an Interdisciplinary Setting

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## ABSTRACT

**Introduction:** Deep dyspareunia is a common symptom in women, including in half of women with endometriosis, but little is known about its response to treatment and predictors of persistent deep dyspareunia over time.

**Aim:** To follow up deep dyspareunia severity over a 1-year prospective cohort at an interdisciplinary center, and to identify baseline predictors of more persistent deep dyspareunia at 1 year.

**Methods:** Prospective 1-year cohort study at a tertiary referral center for pelvic pain and endometriosis, where a range of interdisciplinary treatments are provided at a single center (surgical, hormonal, physical, and psychological therapies). Exclusion criteria were menopause, age >50 years, and never previously sexually active. Primary outcome (deep dyspareunia severity) and secondary outcome (sexual quality of life) were followed up over 1 year. Ordinal logistic regression was performed, controlling for baseline severity of deep dyspareunia, to identify baseline predictors of deep dyspareunia severity at 1 year.

**Main Outcome Measure:** Primary outcome was severity of deep dyspareunia on an 11-point numeric rating scale (0−10), categorized into absent-mild (0−3), moderate (4−6), and severe (7−10); secondary outcome was sexual quality of life measured by the Endometriosis Health Profile-30.

**Results:** 1-year follow-up was obtained for 278 subjects (56% response rate at 1 year; 278/497). Severity of deep dyspareunia improved over the 1 year (McNemar test, $P < .0001$): the proportion of patients in the severe category decreased from 55.0% to 30.4%, the moderate category remained similar from 17.7% to 25.0%, and the absent-mild category increased from 27.3% to 44.6%. Sexual quality of life also improved (56% to 43% on the sex subscale of the Endometriosis Health Profile-30) (Welch $t$ test, $P < .001$). On ordinal regression, severity of deep dyspareunia at 1 year was independently associated with younger age (OR = 0.94, 95% CI = 0.91−0.97, $P = .008$), and with a higher baseline depression score on the Patient Health Questionnaire-9 (OR = 1.07, 95% CI = 1.03−1.11, $P = .01$).

**Clinical Implications:** Clinicians should consider employing an interdisciplinary approach for deep dyspareunia, and screening for and treating depression symptoms in these women.

**Strength & Limitations:** Strengths of the study include its prospective nature, and assessment of deep dyspareunia specifically (as opposed to superficial dyspareunia). Limitations include non-randomized design, and the patients lost to follow-up over the 1 year.

**Conclusion:** Over 1 year in an interdisciplinary setting, improvements were observed in deep dyspareunia and sexual quality of life, but younger women and those with more severe depression at baseline had more persistent deep dyspareunia at 1 year. **Yong PJ, Williams C, Bodmer-Roy S, et al. Prospective Cohort of Deep Dyspareunia in an Interdisciplinary Setting. J Sex Med 2018;XX:XXX−XXX.**



**Key Words:** Deep Dyspareunia; Depression; Endometriosis; Interdisciplinary; Prospective Cohort; Superficial Dyspareunia; Quality of Life

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## INTRODUCTION

Dyspareunia can be divided into superficial (occurring at the introitus with initial penetration of the vagina) or deep (occurring with deep penetration of the vagina).[1] Deep dyspareunia is thought to have a variety of contributors, such as endometriosis, interstitial cystitis (IC)/bladder pain syndrome (BPS), and pelvic floor dysfunction.[2] In particular, deep dyspareunia occurs in approximately half of women with endometriosis.[3,4] Deep dyspareunia can be directly caused by endometriosis, for example due to deep infiltrating endometriosis[5] (which may be related in part to somatic driver mutations[6]) or to local neurogenesis surrounding endometriosis lesions[7] (which may be mediated by nerve growth factor[8]). Deep dyspareunia may also be the result of bladder or pelvic floor tenderness, not directly due to endometriosis lesions, but possibly related to comorbid conditions such as IC/BPS, myofascial pelvic pain, and depression, or related to central nervous system sensitization.[9] Thus, we recently proposed a multifactorial framework for deep dyspareunia in endometriosis, where deep dyspareunia can be due to gynecologic pathology (eg, endometriosis), or other comorbidity, central sensitization, or a combination of these causes.[10]

In women with endometriosis, observational cohort studies show that standard surgical or hormonal treatment is associated with improvements in deep dyspareunia intensity on average.[11,12] However, given the multifactorial origins of deep dyspareunia in endometriosis, not all patients respond to these standard gynecologic treatments.[10] Therefore, a multidisciplinary approach to deep dyspareunia in endometriosis has been proposed, which includes gynecologic treatments in combination with pain education, physical therapy, and psychological therapies.[10] Gynecologic treatments include minimally invasive surgery such as laparoscopic treatment of endometriosis, or hormonal therapy to suppress endometriosis lesions or the gynecologic organs (uterus, ovaries). Pain adjuvants can also be utilized, such as anti-epileptics or tricyclics. Pain education involves providing information to patients about pain generators beyond gynecologic sources, including non-gynecologic factors such as the bladder, bowel, pelvic musculature, and/or the central nervous system. Physiotherapy at our center has a particular focus on biofeedback for pelvic floor control and relaxation, while psychological therapies include cognitive behavioral therapy and mindfulness-based therapy. This multidisciplinary approach has a strong theoretical basis for addressing sexual pain in general,[13] and has been evaluated in women with superficial dyspareunia due to vulvodynia.[14]

However, studies evaluating the impact of a multidisciplinary approach on deep dyspareunia are sparse.[15] Prospective observational cohorts of multidisciplinary care for chronic pelvic pain have not included deep dyspareunia as an outcome.[16,17] 2 randomized controlled trials of multidisciplinary care for chronic pelvic pain also did not evaluate deep dyspareunia.[18,19] A recent randomized controlled trial of psychotherapy and somatosensory stimulation for chronic pelvic pain did evaluate dyspareunia (deep or superficial not specified) as a secondary outcome[15]; however, the study lacked power for the dyspareunia secondary outcome (n = 9 in intervention arm, n = 17 in wait-list control arm).[10,15]

There are several reasons why multidisciplinary care may have a different impact on deep dyspareunia, compared to superficial dyspareunia or chronic pelvic pain. While superficial dyspareunia is often related to vulvar skin diseases or vulvodynia, deep dyspareunia is often seen with endometriosis. These conditions have markedly different treatment options, with hormonally suppressive drugs and laparoscopic surgery being commonly used for endometriosis. In addition, while chronic pelvic pain and deep dyspareunia can be both related to endometriosis, there are differences such as abdominal wall trigger points in chronic pelvic pain vs pelvic floor dysfunction in deep dyspareunia. The former can be managed with abdominal wall trigger point injections, while pelvic floor physiotherapy would be first-line in the latter case.

To address this gap in the literature, we assessed severity of deep dyspareunia in a 1-year prospective observational cohort, at an interdisciplinary center for pelvic pain and endometriosis where gynecologic, physiotherapy, and psychological therapies are integrated at a single center.[20,21] Baseline predictors of deep dyspareunia severity at 1 year were also identified. Based on a previous cross-sectional study at our center of variables associated with baseline deep dyspareunia severity, we identified the following potential predictors of deep dyspareunia severity at 1 year: depression symptom severity, presence/absence of IC/BPS or endometriosis, as well as patterns of tenderness on pelvic examination.[9] Furthermore, sexual quality of life was measured over the 1 year as a secondary outcome, to see whether reductions in deep dyspareunia pain severity also translate into more global improvements in sexual well-being.

## METHODS

### Setting, Cohort, and Study Criteria

This is a prospective cohort at a tertiary referral center for endometriosis and pelvic pain, which was designed to examine factors associated with baseline and prospective pain measures and was described in detail previously.[20–23] In summary, patients are consented for intake into the research cohort prior to their initial assessment at the center by the gynecologist. Following informed consent, patients complete baseline online questionnaires using the REDCap system and the gynecologist enters physical examination data in real time during the assessment. After the gynecologist assessment, a treatment plan is devised and interdisciplinary interventions (eg, gynecological, physiotherapy, and psychological therapies) are integrated at the center. Interventions are tracked, and for patients who undergo surgery, surgical data are entered in real time by the gynecologist on the day of surgery. After 1 year, follow-up online questionnaires are sent to the patients. For this cohort, we have previously

published baseline characteristics and 1-year follow-up for chronic pelvic pain severity for patients seen between December 2013 to December 2014.[22,23] Institutional ethics approval for this cohort was obtained (H11-02882).

For this study of 1-year prospective follow-up for deep dyspareunia, the inclusion criterion was new or re-referral seen between December 2013 to December 2014 and followed up or 1 year. Exclusion criteria were menopausal or age >50 years (because endometriosis, the main diagnosis at our center, is a disease of reproductive-aged women); no follow-up visits at the center (to exclude patients who were immediately referred to another center, eg, those with urologic or gastrointestinal pain alone); or never previously sexually active.

## Interdisciplinary Approach

The interventions offered at the center are interdisciplinary and individualized to each patient.[20–23] This may include any combination of minimally invasive surgery including excision of endometriosis, hormonal suppression or pain adjuvants, and/or a pain program consisting of a pain education workshop, physiotherapy, and psychological therapy. The decision whether to undergo monotherapy or multiple treatments was made between the physician and the patient, and personalized to the clinical situation. Patients who were thought to have an active endometriosis component of their pain, such as deep infiltrating endometriosis of the pouch of Douglas, would have been offered surgery. These patients would have also been offered hormonal therapy, unless they were trying to conceive or had a history of side effects on hormonal treatments. Pain adjuvants would have been offered to patients with a central component of their pain, manifesting as multiple comorbid diagnoses (eg, irritable bowel syndrome, BPS) and multiple tender sites on pelvic examination. The pain program would have been recommended to patients with central pain, significant pelvic floor dysfunction, a history of failure or intolerance of hormonal therapy or pain adjuvant, and/or persistent pain after previous surgery. Aspects of the pain program relevant to sexual pain included the following.

In the pain education workshop, the sexual response cycle was introduced, including the role of responsive desire.[24] Sexual pain was also discussed, as well as female genital and pelvic floor anatomy, and the role of the pelvic floor muscles in sexual function. Physiotherapy, cognitive behavioral, and mindfulness-based strategies were taught.[25]

The physiotherapy component of the pain program incorporated screening and treatment for central and local factors impacting sexual function.[13] Specific problems related to sexual interest, desire, and arousal were identified and discussed.[26] Physical exam included screening for pelvic girdle and hip pain, vestibular allodynia, and pelvic floor overactivity, pressure hyperalgesia, and poor relaxation skill.[27] Breathing patterns and body tension at rest and during exam were noted.[26] Treatment included education about the helpful role of arousal,[24] pelvic floor relaxation techniques, and strategies to address pelvic girdle/hip pain and bladder and/or bowel concerns. Factors that reinforced up-regulation of central nervous system protection,[13] eg, unhelpful self-talk, rapid apical breathing, and increased overall body tension, were addressed with relaxation techniques, diaphragmatic breathing, helpful self-talk, and graded exposure techniques. Sensate focus[26] was often initially recommended, as well as modification of sexual positions as appropriate.

The psychological component of the pain program consisted of emotional support, as well as psychotherapeutic interventions individualized to the patient (eg, cognitive behavioral or mindfulness-based strategies). Meditation and guided imagery were utilized with the goal of activating the parasympathetic nervous system's relaxation response. As required, the role of mood, pain avoidance, communication skills, and relationship dynamics were discussed. A self-management plan was developed, and patients were referred to appropriate community mental health resources if longer term psychotherapy was seen as beneficial.

## Data Collection

The data collected from the cohort, via the baseline patient questionnaire, gynecologist assessment, tracking of interventions including surgery, and the 1-year follow-up questionnaire, have been described previously.[22,23] Variables from the patient questionnaire and gynecologist assessment include self-reported pain scores on an 11-point numeric rating scale (0–10); the Endometriosis Health Profile (EHP)-30, a validated scale for quality of life[28]; physical exam data (eg, endovaginal ultrasound-assisted palpation of tender sites on pelvic exam[29]); diagnosis of endometriosis (defined as "present" if prior surgical diagnosis/treatment or current nodule or endometrioma, "clinically suspected" if no previous surgery but suspected based on history and exam tenderness, or "absent"); diagnosis of irritable bowel syndrome (Rome III criteria)[30]; diagnosis of BPS (American Urological Association[31] or International Continence Society[32]); and for psychological variables, we assessed depression (Patient Health Questionnaire [PHQ]-9)[33] as our previous data has implicated depression in severity of deep dyspareunia, and for comparison, we also assessed anxiety (Generalized Anxiety Disorder-7)[34] and catastrophizing by the Pain Catastrophizing Scale.[35] For interventions, we tracked the types of interdisciplinary interventions for each patient, and surgical variables were according to the Endometriosis Phenome and Biobanking Project.[36] For the 1-year follow-up questionnaire, the self-reported pain scores and the EHP-30 were repeated, which allowed comparison to the baseline questionnaire.

## Data Analyses

### Comparison of Severity of Deep Dyspareunia Between Baseline and 1-Year Follow-Up

Primary outcome was severity of deep dyspareunia (0–10), with scores categorized into none-mild (0–3), moderate (4–6), and severe (7–10). Deep dyspareunia was differentiated from

**Table 1.** Clinical characteristics of the study sample

| Baseline variables | Total sample n = 497 | Baseline data | | *P* value |
|---|---|---|---|---|
| | | Among those who were followed up at 1 y n = 278 | Among those lost to follow-up n = 219 | |
| Sexual outcomes | | | | |
| Deep dyspareunia severity, 0–10 | | | | |
| Absent-mild, 0–3 | 127 (25.6%) | 77 (27.7%) | 50 (22.8%) | .44 |
| Moderate, 4–6 | 183 (37.9%) | 48 (17.3%) | 43 (19.6%) | |
| Severe, 7–10 | 183 (37.9%) | 153 (55.0%) | 126 (57.5%) | |
| Sexual quality of life, EHP-30, 0–100% | | | | |
| Median (IQR) | 63% (40–80%) | 55% (38–80%) | 65% (40–85%) | .12 |
| Demographics | | | | |
| Age, y | | | | |
| Median (IQR) | 34.0 (28.0–41.0) | 35.0 (29.0–42.0) | 33.0 (28.0–39.0) | .009 |
| Parity | | | | |
| No previous birth | 300 (62.1%) | 164 (60.1%) | 136 (64.8%) | .30 |
| Previous births | 183 (37.9%) | 109 (39.9%) | 74 (35.2%) | |
| BMI | | | | |
| Median (IQR) | 23.9 (21.2–28.1) | 23.9 (21.8–28.2) | 23.7 (20.7–28.0) | .16 |
| Smoking | | | | |
| No | 410 (84.9%) | 233 (85.3%) | 177 (84.3%) | .80 |
| Yes | 73 (15.1%) | 40 (14.7%) | 33 (15.7%) | |
| Referral | | | | |
| New referral | 379 (76.3%) | 217 (78.1%) | 162 (74.0%) | .29 |
| Re-referral | 118 (23.7%) | 61 (21.9%) | 57 (26.0%) | |
| Geography | | | | |
| Metro Vancouver | 334 (68.6%) | 190 (69.6%) | 144 (67.3%) | .62 |
| Outside | 153 (31.4%) | 83 (30.4%) | 70 (32.7%) | |
| History of adult sexual assault | | | | |
| No | 367 (76.9%) | 214 (79.3%) | 153 (73.9%) | .16 |
| Yes | 70 (14.1%) | 39 (14.4%) | 31 (15.0%) | |
| No answer | 40 (8.4%) | 17 (6.3%) | 23 (11.1%) | |
| History of child sexual abuse | | | | |
| No | 351 (73.6%) | 201 (74.2%) | 150 (72.8%) | .053 |
| Yes | 86 (18.0%) | 54 (19.9%) | 32 (15.5%) | |
| No answer | 40 (8.4%) | 16 (5.9%) | 24 (11.7%) | |
| Marital status | | | | |
| Not currently married | 257 (53.3%) | 139 (50.9%) | 118 (56.5%) | .23 |
| Currently married | 225 (46.7%) | 134 (43.5%) | 91 (43.5%) | |
| Sexual orientation | | | | |
| Other | 30 (6.2%) | 15 (5.5%) | 15 (7.1%) | .57 |
| Heterosexual | 454 (93.8%) | 258 (94.5%) | 196 (92.9%) | |
| Comorbidities and physical examination | | | | |
| Endometriosis | | | | |
| None | 91 (18.3%) | 42 (15.1%) | 49 (22.4%) | .06 |
| Present | 284 (57.1%) | 160 (57.6%) | 124 (56.6%) | |
| Suspected | 122 (24.5%) | 76 (27.3%) | 46 (21.0%) | |
| Stage, for endometriosis present | | | | |
| I–II | 113 (43.6%) | 57 (39.0%) | 56 (49.6%) | .15 |
| III–IV | 117 (45.2%) | 69 (47.3%) | 48 (42.5%) | |
| Unknown | 29 (11.2%) | 20 (13.7%) | 9 (8.0%) | |
| Irritable bowel syndrome | | | | |
| No | 230 (46.3%) | 123 (44.2%) | 107 (48.9%) | .32 |
| Yes | 267 (53.7%) | 155 (55.8%) | 112 (51.1%) | |

(continued)

**Table 1.** Continued

| Baseline variables | Total sample n = 497 | Baseline data: Among those who were followed up at 1 y n = 278 | Baseline data: Among those lost to follow-up n = 219 | *P* value |
|---|---|---|---|---|
| Painful bladder syndrome | | | | |
| No | 287 (57.7%) | 161 (57.9%) | 126 (57.5%) | 1.00 |
| Yes | 210 (42.3%) | 117 (42.1%) | 93 (42.5%) | |
| Depression—PHQ-9 | | | | |
| Median (IQR) | 7.0 (3.0–13.0) | 7.0 (3.0–11.25) | 8.0 (4.0–13.75) | .011 |
| Anxiety—GAD-7 | | | | |
| Median (IQR) | 5.0 (5.0–9.0) | 4.0 (2.0–9.0) | 5.0 (3.0–10.0) | .029 |
| Pain catastrophizing—PCS | | | | |
| Median (IQR) | 15.0 (15.0–30.0) | 15.0 (7.0–30.0) | 15.0 (8.0–29.0) | .84 |
| Abdominal wall pain | | | | |
| Carnett negative | 357 (71.8%) | 208 (74.8%) | 149 (68.0%) | .11 |
| Carnett positive | 140 (28.2%) | 70 (25.2%) | 70 (32.0%) | |
| Pelvic floor myalgia, levator ani tenderness | | | | |
| Non-tender | 334 (69.0%) | 197 (71.6%) | 137 (65.8%) | .17 |
| Tender | 150 (31.0%) | 78 (28.4%) | 72 (34.4%) | |
| Bladder tenderness | | | | .91 |
| Non-tender | 98 (19.7%) | 220 (80.0%) | 166 (79.4%) | |
| Tender | 350 (68.8%) | 55 (20.0%) | 43 (20.6%) | |
| Uterine-cervix tenderness | | | | .47 |
| Non-tender | 304 (68.6%) | 174 (70.2%) | 130 (66.7%) | |
| Tender | 139 (28.0%) | 74 (29.8%) | 65 (33.3%) | |
| Cul-de-sac tenderness | | | | .63 |
| Non-tender | 185 (41.8%) | 101 (40.7%) | 84 (43.1%) | |
| Tender | 258 (58.2%) | 147 (59.3%) | 111 (56.9%) | |
| Sum of tender pelvic sites* | | | | .81 |
| 0 | 128 (28.9%) | 72 (29.0%) | 56 (28.7%) | |
| 1 | 148 (33.4%) | 83 (33.5%) | 65 (33.3%) | |
| 2 | 70 (15.8%) | 43 (17.3%) | 27 (13.8%) | |
| 3 | 60 (13.5%) | 31 (12.5%) | 29 (14.9%) | |
| 4 | 37 (8.4%) | 19 (17.7%) | 18 (9.2%) | |

*P* values are from Wilcoxon rank sum tests for continuous variables and Fisher exact tests for categorical variables.
BMI = body mass index; EHP = Endometriosis Health Profile; GAD = Generalized Anxiety Disorder; IQR = interquartile range; PCS = Pain Catastrophizing Scale; PHQ = Patient Health Questionnaire.
*For cases where each pelvic exam finding is informative (levator ani, bladder, uterus-cervix, cul-de-sac).

superficial dyspareunia in our questionnaire.[22] Deep dyspareunia severity categories were compared between baseline and 1-year follow-up, using the McNemar test. Deep dyspareunia severity was categorized, because linear regression assumptions were not met when the raw pain score (0–10) was used, thereby necessitating ordinal regression for subsequent analyses (see below).

Secondary outcome was sexual quality of life derived from the sex subscale of the EHP-30 (0–100%, with a higher score indicating worse sexual quality of life).[28] The EHP-30 sex subscale includes questions about pain, guilt, frustration, worry, and avoidance with respect to sexual activity, and was compared between baseline and 1 year using a Wilcoxon signed-rank test.

### Predictors of Deep Dyspareunia Severity at 1 Year

Ordinal regression was performed between deep dyspareunia severity at 1 year and each baseline predictor in Table 1, controlling for baseline deep dyspareunia severity.[37] A separate ordinal regression model was developed for each baseline predictor (eg, 1 model for age and 1 model for depression). *P* values were corrected for multiple testing using the Benjamini-Hochberg false discovery rate method,[38] with alpha set to 0.05. *P* values were calculated via likelihood-ratio tests, and 95% CI calculated using likelihood profiling. As well, the proportional odds assumption was assessed for every model by comparing model fit with non-proportional odds. Ordinal regression modeling utilized R vector generalized linear and additive models.

**Table 2.** Outcome variables at baseline and follow-up

| Outcomes | N | Baseline | Follow-up | *P* value |
|---|---|---|---|---|
| Primary* | 260 | | | |
| Deep dyspareunia severity, severe 7–10, n [%] | | 143 [55.0%] | 79 [30.4%] | |
| Deep dyspareunia severity, moderate 4–6, n [%] | | 46 [17.7%] | 65 [25.0%] | |
| Deep dyspareunia severity, none-mild 0–3, n [%] | | 71 [27.3%] | 116 [44.6%] | <.0001 |
| Secondary | | | | |
| Sexual quality of life: EHP-30 sex subscale, 0–100%, mean (SD)† | 158 | 56% (29%) | 43% (32%) | <.0001 |

*P* values are from Welch paired sample *t* tests for paired numerical data and McNemar tests for paired categorical data.
EHP = Endometriosis Health Profile.
*N = 260 Subjects who were informative for deep dyspareunia severity at baseline and follow-up.
†N = 158 Subjects who were informative for the EHP-30 sex subscale at baseline and follow-up. A higher EHP-30 sex subscale indicates a lower sexual quality of life (ie, 100% centile indicative of worst quality of life).

## Statistics

We utilized R (Version 3.3.2; R Foundation for Statistical Computing, Vienna, Austria) or SPSS 22.0 (IBM Corp, Armonk, NY, USA). Means are shown ± 1 SD, and medians with interquartile range; alpha = 0.05 (2-tailed). Missing data were excluded.

## Pilot Study and Sample Size

We initially performed a retrospective pilot study (n = 22) of deep dyspareunia over 1 year at our center. Severe deep dyspareunia (7–10/10) decreased from 64% (14/22) to 41% (9/22); moderate deep dyspareunia (4–6/10) was unchanged (23%; 5/22) and absent-mild deep dyspareunia (0–3/10) increased from 14% (3/22) to 36% (8/22) (McNemar test, $P = .22$). Based on these findings, we conducted this prospective study. Since each ordinal regression model consisted of 2 predictors (1 baseline predictor variable, plus baseline deep dyspareunia severity), at least 20 subjects were required for each category of the primary outcome (deep dyspareunia at 1 year of 0–3, 4–6, 7–10).[23] This sample size requirement was met (Table 2).

# RESULTS

## Study Description

In all, 497 patients met the study criteria of which 278 completed the 1-year follow-up (56% response rate; 278/497) (Figure 1). Baseline clinical characteristics of those who were followed up and those lost to follow-up are illustrated in Table 1. There was no difference between the 2 groups in the primary outcome (ie, deep dyspareunia severity) or secondary outcome (EHP-30 sex subscale for sexual quality of life). However, those lost to follow-up were on average 1.8 years younger ($P = .009$), were a median 1 point higher on the depression scale (PHQ-9; total 27) ($P = .011$), and a median 1 point higher on the anxiety scale (Generalized Anxiety Disorder-7; total 21) ($P = .029$). Other demographic variables, comorbid diagnoses, and physical findings were similar between those who were followed up and those lost to follow-up (Table 1).

For those who were followed up, the baseline and 1-year scores for the primary and secondary outcomes are shown in Table 2. During the 1 year, interventions at the center involved laparoscopic surgery (n = 121), hormonal suppressive therapy (n = 33 taking at both baseline and 1 year), pain adjuvant medication (n = 29 taking

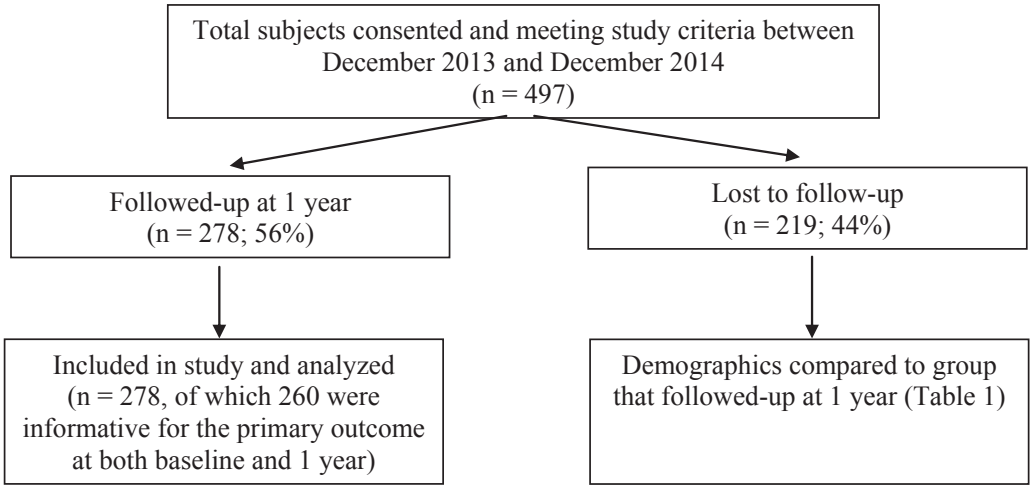


**Figure 1.** Flow chart.

**Table 3.** Treatment effects on deep dyspareunia severity at 1 year

| Intervention | N* | OR† | 95% CI | *P* value | Adjusted OR‡ | 95% CI | *P* value |
|---|---|---|---|---|---|---|---|
| Surgery | | 0.60 | 0.37–0.97 | .04 | 0.58 | 0.35–0.96 | .03 |
| No | 139 | | | | | | |
| Yes | 121 | | | | | | |
| Use of hormonal medication (baseline, follow-up) | | | | .04 | | | .11 |
| None | 161 | Reference | Reference | | Reference | Reference | |
| Started after baseline, and continued to follow-up | 25 | 1.08 | 0.47–2.47 | | 0.80 | 0.33–1.90 | |
| Taking at baseline, but discontinued before follow-up | 41 | 0.66 | 0.33–1.30 | | 0.61 | 0.30–1.24 | |
| Taking at both baseline and follow-up | 33 | 2.36 | 0.15–4.94 | | 1.88 | 0.88–4.08 | |
| Use of pain adjuvant (baseline, follow-up) | | | | .30 | | | .38 |
| None | 198 | Reference | Reference | | Reference | Reference | |
| Started after baseline, and continued to follow-up | 13 | 3.20 | 1.08–10.01 | | 2.63 | 0.82–8.69 | |
| Taking at baseline, but discontinued before follow-up | 18 | 0.77 | 0.29–1.93 | | 0.55 | 0.19–1.48 | |
| Taking at both baseline and follow-up | 29 | 1.35 | 0.63–2.92 | | 0.87 | 0.38–1.98 | |
| Pain program (pain educational workshop, physiotherapy, psychotherapy) | | 1.26 | 0.68–2.36 | .46 | 1.00 | 0.52–1.94 | 1.00 |
| No | 215 | | | | | | |
| Yes | 45 | | | | | | |
| No. of interventions§ | | 1.49 | 0.90–2.50 | .13 | 1.13 | 0.65–1.95 | .67 |
| ≤1 | 183 | | | | | | |
| ≥2 | 77 | | | | | | |
| Time between pain workshop and follow-up questionnaire,‖ d, median (IQR) | 389 (328–488) | 1.00 | 1.00–1.01 | .61 | – | – | – |

*P* values are from likelihood ratio tests.
IQR = interquartile range.
*N = 260 With deep dyspareunia severity scores at baseline and 1 y.
†Ordinal regression, adjusted for baseline deep dyspareunia severity.
‡Ordinal regression, adjusted for baseline deep dyspareunia severity, age, and depression.
§≤1 Intervention (surgery, hormonal, or pain adjuvant); ≥2 interventions: pain program (ie, pain workshop, physiotherapy, psychotherapy) or combination of other treatments.
‖Among women who did the pain program, the number of days between the pain workshop attendance and the follow-up questionnaire time stamp; there were too few women in this analysis to include covariates.

at both baseline and 1 year), and the pain program (pain education, physiotherapy, psychological therapy) (n = 45) (Table 3).

## Comparison of Deep Dyspareunia Severity Between Baseline and 1-Year Follow-Up

For the cohort as a whole, the primary outcome (deep dyspareunia) and secondary outcome (sexual quality of life from EHP-30 sex subscale) are statistically compared between baseline and 1 year in Table 2. We observed a significant improvement in both deep dyspareunia severity ($P < .0001$) and sexual quality of life ($P < .0001$) (Table 2).

## Predictors of Deep Dyspareunia Severity at 1 Year

Ordinal regression was performed between each potential baseline predictor variable and deep dyspareunia at 1 year, controlling for baseline deep dyspareunia severity and with false-discovery rate correction (Table 4). 2 baseline features were significantly associated with deep dyspareunia severity at 1 year: younger age (OR = 0.94, 95% CI = 0.91–0.97, $P = .008$) and higher depression score (PHQ-9) (OR = 1.07, 95% CI = 1.03–1.11, $P = .01$) both predicted more persistent deep dyspareunia at 1 year (Table 4). Other baseline features did not predict deep dyspareunia severity at 1 year, including other comorbid diagnoses (eg, endometriosis, IC/BPS, or irritable bowel syndrome), anxiety or pain catastrophizing, or physical examination findings (eg, distribution or number of tender anatomic sites on pelvic examination) (Table 4). Among the interventions, a treatment effect was detected for surgery after adjustment for baseline age and depression ($P = .03$) (Table 3). There was no detectable difference between those who did ≥2 interventions compared to those who had monotherapy (≤1 intervention) (Table 3).

**Table 4.** Features at baseline associated with deep dyspareunia severity at 1 year (0–3, 4–6, 7–10)

| Features | Deep dyspareunia severity OR (95% CI) | *P* value | *P* adjusted* |
|---|---|---|---|
| Age | 0.94 (0.91–0.97)† | .0004 | .008 |
| BMI | 0.97 (0.92–1.01)† | .44 | .63 |
| Parous | 0.75 (0.46–1.22) | .25 | .51 |
| Heterosexual orientation | 0.91 (0.27–2.86) | .34 | .57 |
| Currently married | 0.70 (0.43–1.13) | .20 | .51 |
| Metro Vancouver | 1.64 (0.98–2.76) | .27 | .51 |
| Adult sexual assault | 1.89 (0.98–3.69) | .15 | .51 |
| Child sexual abuse | 0.76 (0.42–1.37) | .28 | .51 |
| Pain catastrophizing, PCS | 1.02 (1.00–1.03)† | .26 | .51 |
| Depression symptoms, PHQ-9 | 1.07 (1.03–1.11)† | .001 | .01 |
| Anxiety symptoms, GAD-7 | 1.06 (1.01–1.11)† | .02 | .13 |
| Endometriosis | | | |
| None | Reference | .18 | .51 |
| Confirmed | 0.52 (0.26–1.04) | | |
| Suspected | 0.64 (0.30–1.38) | | |
| Irritable bowel syndrome | 1.40 (0.87–2.27) | .17 | .51 |
| Painful bladder syndrome | 1.22 (0.75–1.97) | .43 | .63 |
| Bladder tenderness | 1.33 (0.74–2.38) | .58 | .68 |
| Pelvic floor tenderness | 1.32 (0.78–2.21) | .56 | .68 |
| Bladder or pelvic floor tenderness | 1.32 (0.79–2.18) | .55 | .68 |
| Cervix-uterine tenderness | 0.98 (0.57–1.70) | .73 | .77 |
| Cul-de-sac tenderness | 1.13 (0.68–1.90) | .72 | .77 |
| Sum of tender sites, 0–4 | | | |
| 0 | Reference | .77 | .77 |
| 1 | 1.13 (0.59–2.17) | | |
| 2 | 1.20 (0.53–2.75) | | |
| 3 | 0.99 (0.43–2.28) | | |
| 4 | 1.77 (0.67–4.76) | | |

BMI = body mass index; GAD = Generalized Anxiety Disorder; PCS = Pain Catastrophizing Scale; PHQ = Patient Health Questionnaire.
*False-discovery rate correction.
†Odds ratios reflect each unit increase in the measure (eg, each 1-y increase in age, or each 1-point increase in the PHQ-9 scale).

## DISCUSSION

We observed a reduction in severity of deep dyspareunia in a prospective observational 1-year cohort, at an interdisciplinary center for pelvic pain and endometriosis that combines conventional gynecological treatment with interdisciplinary care. Younger age and baseline depression score predicted more persistent deep dyspareunia at 1 year. We also observed an improvement in sexual quality of life. It should be emphasized that these are findings from a non-randomized observational cohort, and cannot prove causation as in a randomized study.

This is the first prospective longitudinal cohort for deep dyspareunia in an interdisciplinary setting of which we are aware. Strengths of the study include assessment of deep dyspareunia specifically (ie, differentiated from superficial dyspareunia), and use of validated psychological questionnaires and standard diagnostic criteria for endometriosis and comorbid pain conditions. The study is limited by the non-randomized design where patients and clinicians individualized the treatment plan. Also, the results may not be generalizable to centers where physiotherapy and psychological therapy are not offered with gynecologic treatment at a single interdisciplinary center. Further, patients lost to follow-up had slightly younger ages and more depression symptoms than those who were followed up at 1 year.

Depression severity was the only comorbidity that predicted more persistent deep dyspareunia at 1 year. This is consistent with our previous finding that depression was specifically associated with bladder and pelvic floor tenderness and baseline deep dyspareunia in this cohort.[9] This is in contrast to chronic pelvic pain at 1 year, where we found that pain catastrophizing was the significant baseline predictor.[23] Depression could have a specific negative impact on deep dyspareunia, via alterations in the sexual response cycle,[39,40] association with pelvic floor dysfunction,[9] impact on relationship dynamics, or emotional sensitization that amplifies pain centrally.[41] Further work is needed to elucidate the role of depression in deep dyspareunia, and to determine the ideal treatment of depression in this context (psychological, pharmacological, or a combination). While the relationship between depression and deep dyspareunia is likely to be some degree bi-directional, the fact that baseline depression score predicted deep dyspareunia at 1 year does support a potential causative role for depression in the pathophysiology of deep dyspareunia.

Younger age was also associated with more persistent deep dyspareunia at 1 year, which was also observed in our previous study on chronic pelvic pain at 1 year.[23] This may be related to younger women being more symptomatic and thus seeking care sooner, or perhaps age-related responses to the different interventions in the center.

This study provides initial evidence for an interdisciplinary approach to deep dyspareunia,[10] as has been advocated for superficial dyspareunia due to vulvodynia.[14] The rationale of this interdisciplinary approach is to address the multifactorial origins of deep dyspareunia[10] based on underlying pain mechanisms.[13] This includes sexual pain directly due to endometriosis lesions (treated with surgery or hormonal therapy), or due to comorbid conditions such as depression or IC/BPS (each with their own specific treatment approach), or due to central sensitization (addressed through pain education, and physical therapy and psychological strategies).[10] However, given the mixed interventions and non-randomized design, we do not think any firm conclusions can be made about specific interventions, other than an improvement in deep dyspareunia was observed in the center as a whole. We recommend a future randomized trial to determine more conclusively the impact of multidisciplinary care components on deep dyspareunia.

A treatment effect was detected for surgery, but because treatment was tailored to each patient, it is not possible to compare interventions as the populations undergoing each intervention are different. For example, patients undergoing surgery are more likely to have a specific peripheral nociceptive source (eg, pouch of Douglas endometriosis), while more morbid patients who have central nervous system or musculoskeletal sources of pain or who may have previously failed surgery would be less likely to be recommended surgery. In addition, while no treatment effect was detected for the pain program, the reason is likely because patients who required the program are much more morbid (eg, more chronic pain) than patients who did not require the pain program, which makes it less likely that a treatment effect could be detected. Furthermore, due to limited sample sizes, it was not possible to analyze subgroups of patients undergoing different combinations of interventions (eg, surgery and pain program vs surgery and pain adjuvant). In placebo-controlled randomized controlled trials of endometriosis surgery, impact on deep dyspareunia has been equivocal although this may be related in part to limited power to detect differences in sexual outcomes in these trials.[10]

Based on this study, we propose that there be greater recognition of the potential role of interdisciplinary care in deep dyspareunia, which warrants more study, similar to superficial dyspareunia. We also propose that clinicians screen for depression symptoms in women with deep dyspareunia, and to consider treatment of depression prior in conjunction with conventional gynecologic treatment. By better management of depression, it may be possible to reduce unnecessary gynecologic treatments for deep dyspareunia (eg, repeated surgical or hormonal interventions).

## CONCLUSION

While deep dyspareunia improved over a 1-year prospective cohort in an interdisciplinary setting, predictors of persistent deep dyspareunia included younger age and depression. Clinicians should consider screening and treatment of depression in women with deep dyspareunia.

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## REFERENCES

1. Steege JF, Zolnoun DA. Evaluation and treatment of dyspareunia. Obstet Gynecol 2009;113:1124-1136.
2. Ferrero S, Ragni N, Remorgida V. Deep dyspareunia: causes, treatments, and results. Curr Opin Obstet Gynecol 2008; 20:394-399.
3. De Graaff AA, D'Hooghe TM, Dunselman GA, et al. The significant effect of endometriosis on physical, mental and social well-being: results from an international cross-sectional survey. Hum Reprod 2013;28:2677-2685.

4. Hummelshoj L, De Graaff A, Dunselman G, et al. Let's talk about sex and endometriosis. **J Fam Plann Reprod Health Care 2014;40:8-10.**
5. Vercellini P, Fedele L, Aimi G, et al. Association between endometriosis stage, lesion type, patient characteristics and severity of pelvic pain symptoms: a multivariate analysis of over 1000 patients. **Hum Reprod 2007; 22:266-271.**
6. Anglesio MS, Papadopoulos N, Ayhan A, et al. Cancer-associated mutations in endometriosis without cancer. **N Engl J Med 2017;376:1835-1848.**
7. Williams C, Hoang L, Yosef A, et al. Nerve bundles and deep dyspareunia in endometriosis. **Reprod Sci 2016;23:892-901.**
8. Peng B, Zhan H, Alotaibi F, et al. Nerve growth factor is associated with sexual pain in women with endometriosis. **Reprod Sci 2018;25:540-549.**
9. Yong PJ, Yosef A, Wong F, et al. Anatomic sites and associated clinical factors in deep dyspareunia. **Sex Med 2017;5:e184-e195.**
10. Yong PJ. Deep dyspareunia in endometriosis: proposed framework based on pain mechanisms and genito-pelvic pain penetration disorder. **Sex Med Rev 2017;5:495-507.**
11. Ferrero S, Abbamonte LH, Giordano M, et al. Deep dyspareunia and sex life after laparoscopic excision of endometriosis. **Hum Reprod 2007;22:1142-1148.**
12. Vercellini P, Somigliana E, Consonni D, et al. Surgical versus medical treatment for endometriosis-associated severe deep dyspareunia: I. Effect on pain during intercourse and patient satisfaction. **Hum Reprod 2012;27:3450-3459.**
13. Vandyken C, Hilton S. Physical therapy in the treatment of central pain mechanisms for female sexual pain. **Sex Med Rev 2017;5:20-30.**
14. Brotto LA, Yong P, Smith KB, et al. Impact of a multidisciplinary vulvodynia program on sexual functioning and dyspareunia. **J Sex Med 2015;12:238-247.**
15. Meissner K, Schweizer-Arau A, Limmer A, et al. Psychotherapy with somatosensory stimulation for endometriosis-associated pain: a randomized controlled trial. **Obstet Gynecol 2016;128:1134-1142.**
16. Lamvu G, Williams R, Zolnoun D, et al. Long-term outcomes after surgical and nonsurgical management of chronic pelvic pain: one year after evaluation in a pelvic pain specialty clinic. **Am J Obstet Gynecol 2006;195:591-600.**
17. Martin CE, Johnson E, Wechter ME, et al. Catastrophizing: a predictor of persistent pain among women with endometriosis at 1 year. **Hum Reprod 2011;26:3078-3084.**
18. Peters AA, van Dorst E, Jellis B, et al. A randomized clinical trial to compare two different approaches in women with chronic pelvic pain. **Obstet Gynecol 1991; 77:740-744.**
19. Haugstad GK, Haugstad TS, Kirste UM, et al. Mensendieck somatocognitive therapy as treatment approach to chronic pelvic pain: results of a randomized controlled intervention study. **Am J Obstet Gynecol 2006;194:1303-1310.**
20. Yong PJ, Williams C, Houlihan E, et al. Development of a center for interdisciplinary care of patients with pelvic pain and endometriosis. **BMJ 2013;55:244-247.**
21. Allaire CAT, Bedaiwy M, Britnell S, et al. An interdisciplinary approach to endometriosis-associated persistent pelvic pain. **J Endo Pelvic Pain Disord 2017;9:77-86.**
22. Yosef A, Allaire C, Williams C, et al. Multifactorial contributors to the severity of chronic pelvic pain in women. **Am J Obstet Gynecol 2016;215:760.e1-760.e14.**
23. Allaire C, Williams C, Bodmer-Roy S, et al. Chronic pelvic pain in an interdisciplinary setting: 1-year prospective cohort. **Am J Obstet Gynecol 2018;218:114.e1-114.e12.**
24. Basson R. The female sexual response: a different model. **J Sex Marital Ther 2000;26:51-65.**
25. Rosenbaum TY. The role of physical therapy in female sexual dysfunction. **Curr Sex Health Rep 2008;5:97-101.**
26. Kammerer-Doak D, Rogers RG. Female sexual function and dysfunction. **Obstet Gynecol Clin North Am 2008;35:169-183; vii.**
27. Morin M, Carroll MS, Bergeron S. Systematic review of the effectiveness of physical therapy modalities in women with provoked vestibulodynia. **Sex Med Rev 2017;5:295-322.**
28. Jones G, Kennedy S, Barnard A, et al. Development of an endometriosis quality-of-life instrument: the Endometriosis Health Profile-30. **Obstet Gynecol 2001;98:258-264.**
29. Yong PJ, Sutton C, Suen M, et al. Endovaginal ultrasound-assisted pain mapping in endometriosis and chronic pelvic pain. **J Obstet Gynaecol 2013;33:715-719.**
30. Longstreth GF, Thompson WG, Chey WD, et al. Functional bowel disorders. **Gastroenterology 2006;130:1480-1491.**
31. Hanno PM, Burks DA, Clemens JQ, et al. AUA guideline for the diagnosis and treatment of interstitial cystitis/bladder pain syndrome. **J Urol 2011;185:2162-2170.**
32. Abrams P, Cardozo L, Fall M, et al. The standardization of terminology of lower urinary tract function: report from the standardization sub-committee of the International Continence Society. **Neurourol Urodyn 2002;21:167-178.**
33. Spitzer RL, Kroenke K, Williams JB. Validation and utility of a self-report version of PRIME-MD: the PHQ primary care study. Primary care evaluation of mental disorders. Patient Health Questionnaire. **JAMA 1999;282:1737-1744.**
34. Spitzer RL, Kroenke K, Williams JB, et al. A brief measure for assessing generalized anxiety disorder: the GAD-7. **Arch Intern Med 2006;166:1092-1097.**
35. Sullivan MJL, Bishop SR, Pivik J. The Pain Catastrophizing Scale: development and validation. **Psych Assess 1995;7:524-532.**
36. Becker CM, Laufer MR, Stratton P, et al. World Endometriosis Research Foundation endometriosis phenome and biobanking harmonization project: I. Surgical phenotype data collection in endometriosis research. **Fertil Steril 2014; 102:1213-1222.**

37. Barnett AG, van der Pols JC, Dobson AJ. Regression to the mean: what it is and how to deal with it. **Int J Epidemiol 2005;34:215-220.**

38. Benjamini Y, Hockberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. **J R Stat Soc Series B 1995;57:289-300.**

39. Basson R, Rees P, Wang R, et al. Sexual function in chronic illness. **J Sex Med 2010;7:374-388.**

40. Basson R. Sexuality in chronic illness: no longer ignored. **Lancet 2007;369:350-352.**

41. Kaya S, Hermans L, Willems T, et al. Central sensitization in urogynecological chronic pelvic pain: a systematic literature review. **Pain Physician 2013;16:291-308.**