

Sexual function in endometriosis patients and their partners: effect of the disease and consequences of treatment

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BACKGROUND: Sexual function is an important aspect of health and quality of life and is influenced by both medical conditions and health-care interventions, especially when gynecologic disorders are involved. Coital pain is among the main factors that affect sexual functioning, and this symptom is reported by almost half of women suffering from endometriosis. However, sexuality is a complex phenomenon driven by social, psychological and biological/hormonal factors and the presence of endometriosis might further affect domains of sexual function and the quality of a sexual relationship.

OBJECTIVE AND RATIONALE: The objective of this report is to review the current state of knowledge on the impact that endometriosis and its treatments have on the sexual function of women and their sexual partners.

SEARCH METHODS: A systematic literature search was performed to identify studies evaluating sexual function in endometriosis patients, and a narrative analysis of results is presented. The review discusses relevant quantitative and qualitative studies analyzing the effect of endometriosis and its hormonal and surgical treatments on measures of sexual function and quality of sexual relationship.

OUTCOMES: Endometriosis negatively affects different domains of sexual function, and the presence of dyspareunia is not the only determinant of sexual health in these women. Chronic pelvic pain, advanced stages of disease and the presence of physical and mental comorbidities affect sexual function, as well as personality traits and women's expectations. Although a number of studies have evaluated

the effect of surgery and hormonal treatment on deep dyspareunia, overall sexual function and quality of the relationship with the partner are often under-investigated.

WIDER IMPLICATIONS: Multiple clinical and personal determinants affect sexual function in women with endometriosis, with potentially negative consequences on the sexual function of partners and quality of the relationship. Additional prospective and longitudinal investigations are warranted using specific instruments to analyze biopsychosocial variables of sexual pain in endometriosis patients and the effects that actual treatments have on measures of quality of sexual function and relationship.

Key words: endometriosis / sexual function / surgery / hormonal treatment

Introduction

Human sexuality is a complex phenomenon driven by social, psychological and biological/hormonal factors. Sexual health is a critical aspect of quality of life and is also influenced by medical conditions and health-care interventions, particularly when gynecological disorders are involved, such as gynecological cancer, breast cancer or infertility (Langer et al., 2015; Lindau et al., 2015; Candy et al., 2016). Although there has been great progress in understanding human sexuality and improving sexual health in recent years, health-care providers should accelerate and promote this progress to be more inclusive and comprehensive. Sexual and reproductive health are mentioned in the United Nations Sustainable Development Goals, and they represent a target in the post-2015 agenda (United Nations General Assembly, 2015), a sign of increasing global awareness and initiative in moving forward on global sexual health issues, including education, care and rights (Hawkes, 2014; Temmerman et al., 2014; Khosla et al., 2015).

Endometriosis is a global disease affecting 5–15% of women during their reproductive years. According to main international guidelines, endometriosis should be viewed as a chronic disease that requires a life-long individualized management plan with the aim of avoiding repeated surgical procedures. General principles that should guide medical management of endometriosis are not different from those applicable to other chronic inflammatory disorders (Vercellini et al., 2011a; ASRM Practice Committee, 2014; Dunselman et al., 2014). However, endometriosis is also a disease that affects young, sexually active women during different phases of their sexual life and during development of their sexual behavior. Consequently, sexual health is a major concern for endometriosis patients and should also be a primary concern in endometriosis care and research. Because endometriosis is viewed as a chronic disease that affects young women during their reproductive years, it is absolutely necessary to bridge the artificial divide between reproductive and sexual health in endometriosis patients and their partners.

However, the international consensus on future research priorities following the 10th World Congress on Endometriosis did not consider sexual health among symptoms and treatment outcomes (Rogers et al., 2009). Three years later, recommendations for future directions for endometriosis research following the 11th World Congress on Endometriosis underlined the need to better identify clinical features of pain and quality of life, although the notion of sexual functioning did not clearly emerge (Rogers et al., 2013). The importance of analyzing overall sexual function in endometriosis patients gained direct attention only recently in an article published in

2014 by members of the World Endometriosis Society, although the importance of sexual health has been argued since 2011 (Vercellini et al., 2011b; Hummelshoj et al., 2014).

Physical, mental and social dimensions characterize sexual health. The inability to engage in sexual activity in a fulfilling way may affect self-esteem, self-worth and relationships with partners (Basson, 2008). This issue deserves particular attention in the case of endometriosis, in which the decision-making process for treatment is mainly based on patients' symptoms and priorities.

The objective of this review is to analyze the current state of knowledge on the impact that endometriosis and its treatments (medical and surgical) have on sexual function and to provide insights into women's perspectives of sexual pain and consequences for the sexual partner.

Determinants of female sexual function and dysfunction, with special reference to genital pain

The sexual response is a psychophysiological experience. It is a sequence of physiological events, including sexual desire, arousal and genital responses (Bianchi-Demicheli and Ortigue, 2007; Ortigue et al., 2009). Basson conceptualized sexual response as a motivation-/incentive-based cycle comprising phases of physiological response and subjective experience (Basson, 2015). Phases of this cycle may overlap, and their order may vary. Psychological and biological factors influence the processing of sexual stimuli to allow or preclude subsequent arousal, and the type of outcome (sexual or non-sexual) influences future sexual motivation. Multiple factors, including stage of life cycle, age, relationship duration, mental health and relationship happiness, influence the sexual response between individuals and within a person's own sexual life (Basson, 2015).

Female sexual dysfunction includes a range of disorders, namely, hypoactive sexual desire, reduced subjective and/or physical genital arousal (poor sensation, vasocongestion, lubrication), sexual pain and inability to achieve orgasm/satisfaction, which are multidimensional by nature and often coexisting (Basson et al., 2004; van Lankveld et al., 2010). Therefore, a global approach has been proposed in the DSM-5 diagnostic criteria, which combine desire and arousal disorders into one disorder, namely female sexual interest/arousal disorder. Similarly, diagnosis of vaginismus, vulvodynia and dyspareunia were merged into a new genito-pelvic pain/penetration disorder (GPPPD) (<http://www.dsm5.org>). GPPPD is characterized by persistent or recurrent difficulties for 6 months or more with at least

one of the following symptoms: (1) inability to have vaginal intercourse/penetration, (2) marked genito-pelvic pain during vaginal intercourse/penetration attempts, (3) fear of pain as a result of vaginal penetration or (4) marked tensing or tightening of the pelvic floor muscles during attempted vaginal penetration (<http://www.dsm5.org>).

The association between coital pain and sexual dysfunction is the result of repeated experiences of sex associated with pain and fear of pain. The fearful reaction in turn negatively affects desire, arousal, reward, lubrication, loss of genital congestion and heightened pelvic floor tone in a circular model (Payne *et al.*, 2005; Thomten *et al.*, 2011; Thomten and Linton, 2013). Furthermore, emotional elaboration (anxiety, bitterness or frustration during or after sexual engagement, feelings of guilt, distress) and cognitive elaboration of pain (hypervigilance, catastrophizing) negatively affect sexual motivation and desire/arousal. Finally, central sensitization leads to hyperalgesia and allodynia and secondary hyperalgesia, worsening pain perception (Basson, 2012; Thomten and Linton, 2013; Thomten *et al.*, 2014).

However, while endometriosis-associated sexual pain is classically deep dyspareunia, the majority of studies investigating sexual pain in women have assessed patients affected by superficial dyspareunia/provoked dyspareunia (Basson, 2012; Thomten *et al.*, 2014). Therefore, their conclusions cannot be directly translated into the clinical setting of endometriosis patients, despite the occurrence of symptoms and emotional/cognitive elaboration shared with other causes of sexual pain. Specific features of endometriosis, namely the evolution of disease/symptoms over time, the presence of chronic pelvic pain, long-term hormonal treatment, fertility concerns, extensive pelvic surgery at a young age and risk of recurrence, might affect sexual response and exacerbate the emotional/cognitive elaboration of pain.

Methods

A systematic literature search was performed to identify studies evaluating sexual function in endometriosis patients. Articles were identified through the following electronic databases: MEDLINE, EMBASE, Google Scholar and The Cochrane Library (until December 2015) databases for all the prospective and retrospective studies with no date limits. We used the following combination of Medical Subject Headings (MeSH): endometriosis, dyspareunia, sexual function, sexuality, libido, arousal, desire, orgasm, satisfaction, pleasure, pain, quality of life, marital status and relationship. All relevant articles were examined, and their reference lists were systematically reviewed to identify other studies for potential inclusion in this review. Selection criteria included retrospective and prospective studies and the analysis of qualitative and quantitative variables. Only studies investigating sexual function in endometriosis patients were included. Studies investigating pelvic pain and dyspareunia without the concomitant analysis of sexual, psychological and social variables were arbitrarily excluded. Additional cross-references were identified during the review search.

Dyspareunia as a major reported sexual symptom in endometriosis patients

Pain during sexual intercourse is one of the main symptoms among endometriosis patients, and women with endometriosis are at an increased risk of experiencing sexual pain compared with the normal population. In a large case-control study evaluating more than 5000 women with

endometriosis, symptoms associated with sexual intercourse occurred in 11.5% of cases, with an OR of 7.4 (CI 6.5–8.5) compared with controls (Ballard *et al.*, 2006). Specifically, the presence of dyspareunia is an independent risk considered to be affected by endometriosis, with an adjusted OR of 6.8 (CI 5.7–8.2). Interestingly, this risk estimate was in the same range as that of the occurrence of dysmenorrhea and subfertility/infertility (Ballard *et al.*, 2008). More recently, the WERF EndoCost study showed that 47% of endometriosis patients suffer from dyspareunia (dysmenorrhea was reported by 57% and chronic pelvic pain by 60% of the women; De Graaff *et al.*, 2013). In the same study, multivariate regression analysis showed that sexual pain and chronic pelvic pain (but not dysmenorrhea) negatively affected both the physical health and mental health domains in the SF36 questionnaire (De Graaff *et al.*, 2013). Patients enrolled in that study experienced multiple medical treatments, including hormonal and fertility treatments and in most cases, at least one surgical intervention (De Graaff *et al.*, 2013).

A retrospective qualitative study evaluating the long-term consequences of endometriosis over 15 years showed that 48.5% of patients reported that endometriosis had caused problems with their sex life, but one-third of those patients experienced pain only during certain parts of their menstrual cycle. A significant correlation between dyspareunia and a negative influence on relationships was clearly evidenced (Fagervold *et al.*, 2009). In another cross-sectional study among patients, sexual pain occurred 'most of the time' and 'some of the time' in 27.2% and 35.2% of women, respectively (Lemaire, 2004). A similar prevalence of sexual pain was reported in two additional studies (Jones *et al.*, 2004; Denny and Mann, 2007).

The presence of deep dyspareunia caused by endometriosis is mostly associated with deep lesions infiltrating the utero-sacral ligaments, the pouch of Douglas, the posterior vaginal wall, and the rectum and is less frequently associated with ovarian and bladder lesions (Fauconnier *et al.*, 2002). The association of dyspareunia with adenomyosis is more controversial, although the co-existence of adenomyosis and deep endometriosis (50% of patients) may further worsen sexual pain (Lazzeri *et al.*, 2014).

Reviewing the anatomical and biological causes of dyspareunia in endometriosis is beyond the scope of this review, and many other articles have extensively examined pain symptoms (Fauconnier and Chapron, 2005; Brawn *et al.*, 2014; Morotti *et al.*, 2014b). However, some considerations are critical for the analysis of the effects of chronic sexual pain on overall sexual function, specifically in endometriosis: (1) Dyspareunia may be particularly harmful because it usually occurs whenever intercourse is attempted, whereas dysmenorrhea typically afflicts women during menstruation (Vercellini *et al.*, 2011b). (2) Endometriosis is a risk factor (OR 4.30; CI 1.16–15.90) for the concurrent presence of deep dyspareunia and superficial dyspareunia/provoked vestibulodynia. The presence of these symptoms is also associated with a higher prevalence of depression symptoms (OR 1.07; CI 1.02–1.12) (Yong *et al.*, 2015). Furthermore, the prevalence of pelvic floor tenderness was 40% in a cohort of patients with pelvic pain (OR 4.61; CI 1.55–13.7). In this cohort, dyspareunia was independently associated with pelvic floor tenderness in a multiple logistic regression analysis (OR 4.45; 95% CI 1.86–10.7) (Yong *et al.*, 2014). (3) Other conditions may overlap (10–50% of cases) with endometriosis contributing to painful sex, mostly interstitial cystitis/bladder pain syndrome (Cervigni and Natale, 2014; Yong *et al.*, 2014). (4) Endometriosis lesions are associated with central and peripheral hyperalgesia caused likely by local neuroinflammation, neuroangiogenesis and dysregulation of sensory and autonomic fibers. (5) Dyspareunia in endometriosis is often associated with chronic pelvic pain. The latter is correlated with modifications in the behavioral and functional brain response to noxious stimuli, changes in brain structure, activity of hypothalamic–pituitary–adrenal axis and autonomic nervous system and consequently personal distress (Morotti *et al.*, 2014b).

Female sexual function in endometriosis patients: not only deep dyspareunia

Although the prevalence of deep dyspareunia and chronic pelvic pain have been widely investigated in endometriosis, female sexual function and the relationship with the sexual partner have been scantily examined in the last decades. Indeed, deep dyspareunia occurrence and intensity has been considered for long time the only instrument to assess sexual functioning in endometriosis.

One of the first assessments of sexual function in endometriosis was done in 1995, where the analysis of 17 patients with minimal or mild symptomatic endometriosis showed an increased rate of sexual avoidance using the Golombok Rust Inventory of Sexual Satisfaction questionnaire, in comparison to controls (Waller and Shaw, 1995). Avoidance was also confirmed in other qualitative studies where the majority of women who suffered dyspareunia avoided or reduced sexual intercourse (Jones et al., 2004; Denny and Mann, 2007).

In 2005, sexual health was evaluated among a cohort of patients suffering from deep dyspareunia caused by different genital diseases. Patient with deep endometriosis infiltrating the utero-sacral ligaments showed more pain based on visual analog scale (VAS) and lower scores in the Global Sexual Satisfaction Index (GSSI) than patients with peritoneal endometriosis and non-endometriosis patients (Ferrero et al., 2005). In addition, sexual pain of patients with deep implants affected the intensity of the orgasm and satisfaction, causing a less relaxed and fulfilled state compared with controls. The presence of endometriosis (any type) was also associated with a reduction of the quality of communication with the partner about sex (Ferrero et al., 2005).

Vercellini et al. confirmed the complexity of the relationship between endometriosis, pain and sexual function (Vercellini et al., 2012). Although patients with deep rectovaginal lesions had poorer sexual function compared to non-endometriosis controls, differences in sexual function domains between women with different types of endometriosis (deep versus peritoneal/ovarian) were only marginal, suggesting that the diagnosis/presence of endometriosis, has a role in determining overall sexual health. Indeed, no significant correlation was observed between deep dyspareunia VAS scores and sexual rating scale. Specifically, rectovaginal endometriosis negatively affects current sexual interest and activity, and previous sexual satisfaction, sexual pleasure, and ability to reach orgasm, with ORs ranging from 2.32 (previous sexual activity) to 5.58 (current sexual interest) on the Sabbatsberg Sexual Self-Rating Scale. This is a 12-item questionnaire suitable for self-assessment of sexual functioning that evaluates six subdomains separately, including sexual interest, sexual activity, satisfaction of sexual life, experience of sexual pleasure, orgasm capacity and sexual relevancy (Garratt et al., 1995). In the rectovaginal endometriosis group, the risk of being sexually unsatisfied or feeling little or no sexual pleasure was three times higher, and the risk of engaging in limited or no sexual activity and of reduced capacity to reach orgasm was approximately two times higher, compared with subjects in the non-endometriosis group (Vercellini et al., 2012). Interestingly, the retrospective assessment of sexual functioning in the years immediately following coitarche did not show any differences, suggesting that sexual impairment in women with rectovaginal endometriosis arose and increased over time, most likely as a result of the development of lesions/symptoms.

A recent multicenter cohort study conducted in Austria and Germany assessed sexual function using two common and validated instruments, the Female Sexual Function Index (FSFI) and the Female Sexual Distress Scale revised (FSDS) (Fritzer et al., 2013). The FSFI is a 19-item questionnaire that has been developed as a brief, multidimensional self-report instrument for assessing the key dimensions (desire, arousal, lubrication, orgasm, satisfaction and pain) of sexual function in women. This test has the advance to investigate pain symptoms and provide a cut score for

differentiating women with and without sexual dysfunction (Wiegel et al., 2005). The FSFI has been widely tested and validated in different cultural environments and medical conditions and it has been also proposed as valid instrument to assess sexual function in endometriosis in a recent consensus paper (Vercellini et al., 2012; Vanhie et al., 2016). The FSDS was developed to provide a standardized, quantitative measure of sexually related personal distress in women with sexual dysfunction (Derogatis et al., 2008).

The cumulative prevalence of sexual dysfunction using the FSFI and FSDS were 32% and 78%, respectively, with a significant correlation between stage of disease, dyspareunia and score on both questionnaires (56% of patients had sexual dysfunction at AFS stage 4). In this cohort, more than half of women (66%) were afraid of pain before or during sexual intercourse. When sexual dysfunction was diagnosed, patients also had a significantly fewer episodes of sexual intercourse per month and greater fear of separation because of coital pain than patients without sexual dysfunction (Fritzer et al., 2013). These results are consistent with those reported in two other studies using the FSFI (Jia et al., 2013; Evangelista et al., 2014) that showed a crude prevalence 70–75% of sexual dysfunction among endometriosis patients. Specifically, compared with the patients with no to mild pelvic pain, those with moderate-to-severe pelvic pain had a 3.4-fold (CI 1.3–8.8) higher risk of sexual dysfunction. Patients with stage III or IV had a 4.4-fold (CI 1.3–15.5) higher risk than those with stage I or II (Jia et al., 2013). The presence of advanced states of disease also affected the desire domain, in addition to sexual satisfaction, orgasm and pain, when analyzed separately using the Sexual Health Outcomes in Women Questionnaire (SHOW-Q) (Montanari et al., 2013; Di Donato et al., 2014). The SHOW-Q is a recently developed 12-item scale for the assessment of four domains of sexual function: satisfaction, orgasm, desire and pelvic problem interference (Learnman et al., 2008).

In conclusion, based on available, although limited evidence, endometriosis appears to impact all domains of sexual function, desire/arousal, orgasm, satisfaction, and pain, leading to sexual dysfunction and distress in 70–75% of patients, at least in advanced/chronic cases. According to the motivation/incentive-based cycle of sexual response, repetitive painful experiences and the absence of reward (negative outcome) likely shift sexual response from motivation/arousal to hypervigilance and from desire to fear and avoidance, leading to sexual distress in symptomatic endometriosis patients (Fig. 1).

Specific biological and psychosocial variables associated with sexual dysfunction in endometriosis

Although dyspareunia can be considered the first step in the development of sexual dysfunction, additional factors characterize the evolution towards an impairment of sexual health. According to the fear-avoidance model, multiple biopsychosocial variables influence sexual distress (Fenton, 2007; Desrochers et al., 2009; Basson, 2012; Crombez et al., 2012; Thomten and Linton, 2013).

Some of them may be related to the evolution of disease toward advanced stages and worsening of pain intensity or duration and the development of chronic pelvic pain (Tripoli et al., 2011); others may be related to the hallmarks of endometriosis, namely fertility concerns (up to 30–50% of cases), diagnostic delay and recurrence of symptoms after treatment. Infertility can affect an intimate relationship in a range of ways (Glover et al., 2009): sexual self-esteem may be deflated, paired with a perceived failure to fulfill traditional gender roles and/or external pressures to conceive (Monga et al., 2004; Bayley et al., 2009). Evidence also indicates that infertility status, length of infertility and IVF are associated with worse scores in all domains of the FSFI (Ashraf et al., 2015; Smith et al., 2015). How do fertility concerns and infertility treatment affect

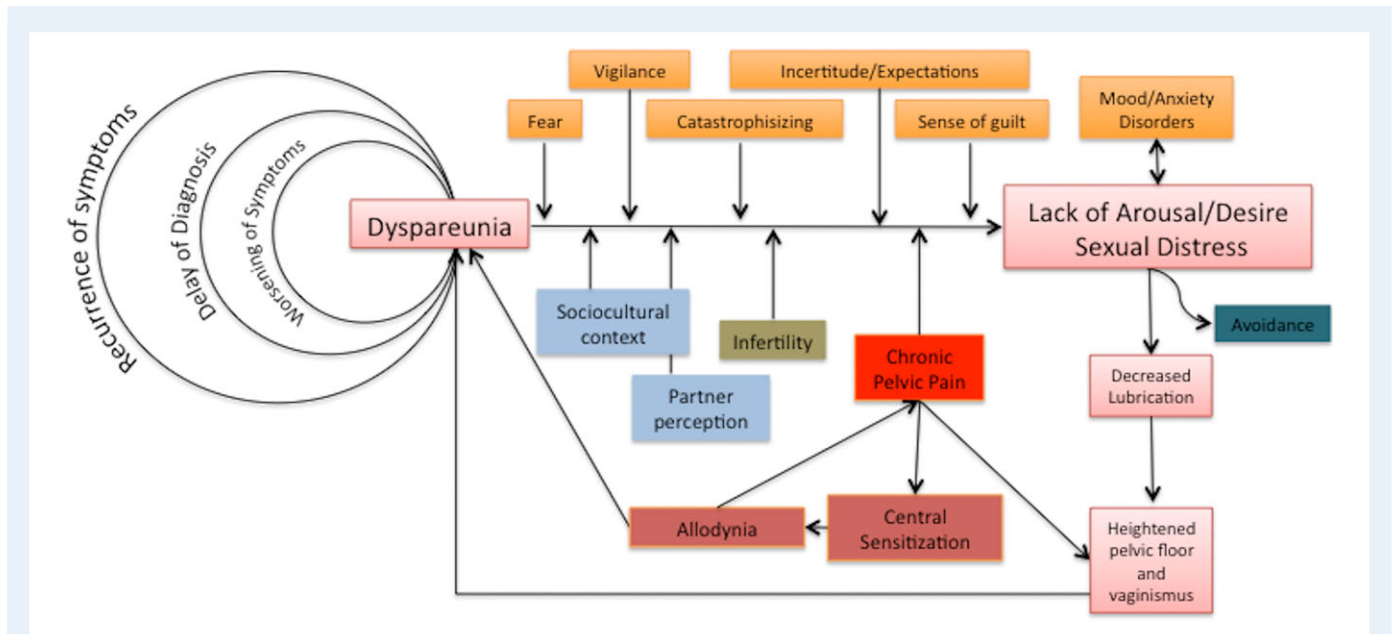


Figure 1 Adaptation of the fear-avoidance model in endometriosis patients. Sexual pain in endometriosis patients induces a fear-avoidance reaction, leading to arousal/desire disorder and sexual distress in the majority of patients. Biopsychosocial variables of sexual pain play a critical role in the fear-avoidance model. Senses of incertitude, fear, expectations and guilt are often reported in qualitative studies. Similarly, personality traits, coping strategies (catastrophizing) and the occurrence of mood/anxiety disorders are crucial in the evolution from coital pain to sexual dysfunction and distress. The partner's perception of sexual pain and the sociocultural context in which sexual pain and fertility concerns are experienced may exacerbate sexual distress, lack of arousal/desire and avoidance. As result, decreased lubrication and loss of genital congestion (also worsened by pharmacological hypogonadism) heighten pelvic floor tone, risk of vaginismus and pain. Central sensitization caused by chronic pelvic pain leads to hyperalgesia and allodynia, worsening dyspareunia in a circular model. Hallmarks of endometriosis, such as delay of diagnosis and worsening and recurrence of pain, exacerbate dyspareunia and dysfunctional behavior, prolonging the distress.

sexual health in endometriosis patients and their partners? Does the length of infertility (and sexual pain) play a role in predicting the worsening of sexual functioning? What is the effect of getting pregnant on sexual functioning? The available evidence, unfortunately, does not address these questions.

Endometriosis patients suffering from dyspareunia experience a sense of guilt towards their partner, lower feelings of femininity, alteration of body image and alexithymia, which, in turn, exacerbate sexual dysfunction (Fritzer *et al.*, 2013; Melis *et al.*, 2014, 2015) in endometriosis (Fig. 1). In a cohort of patients with chronic pelvic pain due to endometriosis, catastrophizing, a well-known pain-coping mechanism, played a pivotal role in pain experience, severity and recurrence (Martin *et al.*, 2011). Although dyspareunia and sexual health was not assessed in this cohort, catastrophizing was a significant predictor of pain at 1 year of follow-up, and women who showed severe catastrophizing at baseline had higher pain at follow-up (Martin *et al.*, 2011). Interestingly, across control subjects and the chronic pain population, patients with high levels of catastrophizing show augmented musculoskeletal tenderness and intensified pain sensitivity. This population has a higher risk of developing post-surgical and persistent pain syndromes (Turner *et al.*, 2002; Granot and Ferber, 2005).

The long delay between the first onset of symptoms of the disease and diagnosis may also play a role in sexual functioning. Painful sex is rarely brought up to medical attention, and physician awareness/education/sympathy is often inadequate in evaluating the symptom (Jones *et al.*, 2004). Coupled with the delay in endometriosis diagnosis, the perpetuation of painful sexual episodes in young women may exacerbate fear, catastrophizing and avoidance (Fig. 1). Symptomatic patients have frequently reported that they felt a sense of relief, legitimization, liberation

and empowerment, when the nature of disease is identified, replacing incertitude and frustration (Cox *et al.*, 2003a; Ballard *et al.*, 2006; Culley *et al.*, 2013).

An association between endometriosis and psychiatric disturbances such as depression, anxiety and increased stress has also been identified and widely described (Cheong *et al.*, 2008; Lagana *et al.*, 2015; Pope *et al.*, 2015; Chen *et al.*, 2016). Younger patients have an elevated likelihood of developing major depression, any depression disorders and anxiety disorders (Chen *et al.*, 2016). Depression is often associated with chronic illness and independently leads to a higher prevalence of sexual dysfunction (Piazza *et al.*, 1997; Basson *et al.*, 2010). However, whether mood disorders predict sexual dysfunction in endometriosis patients is unknown, and no study has specifically addressed this issue. Thus, the presence of a causal effect, although likely, can only be hypothesized.

Effect of endometriosis on sexual function of partner and relationship quality

The effects of endometriosis on relationships have not been featured prominently in the available literature. Dyspareunia, female sexual dysfunction and associated infertility (or concerns about possible infertility) may disrupt the relationship with the partner and his/her sexual functioning, especially in young couples. Moreover, the social (and relationship) dimension of pain constantly influences the changing dynamic of pain.

A reduction in the quality of communication about sex with the partner has been assessed in different studies on endometriosis. (Ferrero *et al.*, 2005; Vercellini *et al.*, 2012; Fritzer *et al.*, 2013). In the WERF

Endocost study, among women with affected relationships, 67% declared significant problems with their partner caused by endometriosis (34% of women) and 19% of women considered endometriosis as a cause of their divorce (of 10% of women) (De Graaff et al., 2013). In the retrospective qualitative study by Fagervold et al., 15% of women with endometriosis reported that, over a period of 15 years, they had serious problems in their relationships and 7.7% suffered from a broken relationship due to the symptoms of endometriosis (Fagervold et al., 2009). Previous qualitative studies have documented a strain on social relationships, including reduced social support and several relational difficulties (Cox et al., 2003a,b; Strzempko Butt and Chesla, 2007; Denny, 2009). Decreased socialization due to disease/illness and the incapacity of partners to tolerate chronic symptoms has been attributed to relational breakups or divorce. However, in most cases, the overlap of sexual symptoms with chronic pelvic pain does not allow for any conclusions to be made specifically on sexual complaints. Similarly, the consequences of chronic dyspareunia with or without associated sexual dysfunction for the sexual partner are largely unknown in endometriosis couples. Male partners of women with provoked vestibulodynia also suffer from the consequences of the partner's pain, showing increased rates of psychological distress, increased prevalence of sexual difficulties (e.g. erectile dysfunction), and decreased sexual satisfaction (Jodoin et al., 2008; Smith and Pukall, 2014; Boerner and Rosen, 2015). In the same setting, the quality of the couple relationship, male psychosocial functioning and male self-reported response to pain have all been linked to pain, sexual functioning and emotional/cognitive elaboration of pain among women (Boerner and Rosen, 2015).

Effects of endometriosis surgery on sexual function

Given the multifaceted aspects of sexual health in endometriosis patients, the question regarding whether surgery might affect sexual function is highly pertinent. Extensive surgery for endometriosis is feasible and effective, but it may be associated with significant complication rates (Dunselman et al., 2014; Pluchino et al., 2015). The potential beneficial effect of extensive surgery on deep dyspareunia has been extensively described in retrospective and prospective studies (Koninckx et al., 1991, 2012; Vercellini et al., 2006, 2009; Meuleman et al., 2009, 2011, 2014; Dunselman et al., 2014). However, three RCTs comparing diagnostic versus operative laparoscopy on dyspareunia changes did not note any significant outcome difference when the two procedures were compared in case of mild or moderate endometriosis (although the evidence was low quality) (Jacobson et al., 2014).

The assessment of sexual health in the surgical management of endometriosis has not received the same attention as dyspareunia (Fritzer et al., 2014). The paucity of data, methodological limits and inconsistencies of studies compromise the analysis of sexual health in women who have undergone endometriosis surgery.

Conservative surgery was shown to improve dyspareunia and sexual symptoms using the Revised Sabbatsberg Sexual Rating Scale at 1-year follow-up in an RCT comparing the effect of resection with that of non-resection of utero-sacral ligaments on symptom recurrence (Vercellini et al., 2003). Although the presence of deep lesions was not assessed in this trial, the resection of utero-sacral ligaments did not provide any additional advantage in improving sexual health (Vercellini et al., 2003). Similarly, a significant improvement in pleasure and habit and a decrease in discomfort with intercourse was reported 4 months after surgery (Garry et al., 2000), and was maintained for up to 5 years (median follow-up 3.2 years) (Abbott et al., 2003). Interestingly, in the latter study, dyspareunia was the main indication for surgery in only 3.5% of cases and

the second indication in less than 1% of cases (Abbott et al., 2003). A more detailed analysis showed that, 1 year following surgery, patients had an increased variety in sexual life, an increased frequency of intercourse, a relaxed disposition during sex, and more satisfying orgasms and were more relaxed and fulfilled after sex (Ferrero et al., 2007; Dubuisson et al., 2013). Vaginal resection in the case of deep lesions did not impair the recovery of sexual activity and was associated with an improvement in some domains of sexual function in the McCoy Female Sexuality Questionnaire (sexual satisfaction and sexual problems but not satisfaction with partner) (Setala et al., 2012).

Extensive surgical procedures, including bowel resection and/or deep parametrial excision are associated with higher morbidity (rectal, ureteral and bladder fistula, atonic bladder and anal incontinence) and may require additional procedures such as ileostomy and colostomy (Ret Davalos et al., 2007; Vercellini et al., 2009; Ceccaroni et al., 2012). Short- and long-term consequences for personal and couple distress, body image and sexual functioning are therefore expected. Nerve-sparing surgery may provide some advantages over conventional surgery (Ceccaroni et al., 2012; Che et al., 2014). The latter is associated with an increased post-operative sexual impairment (72.3% of patients had neither sexual sensations nor orgasmic pleasure at all), although altered sexual pleasure or reduced sexual pleasure and orgasm frequency have been observed in 47.5% and 11.8% of cases, respectively, also after nerve-sparing surgery (Ceccaroni et al., 2012). Additional studies investigated the effect of bowel resection on sexual function in endometriosis patients. The results were consistent to a certain extent with a reduction in sexual pain but inconsistent among all other domains of sexual function investigated (Kossi et al., 2013; Che et al., 2014; Morelli et al., 2015). A multidisciplinary approach in case of extensive surgery appears to improve functional results in terms of personal distress and sexual health, without significant differences between conservative management and bowel resection (Van den Broeck et al., 2013). Specifically, surgery improved all assessed domains (arousal, sexual desire, orgasm problems and pain during intercourse) and these remained stable over the 18-month follow-up period. Interestingly, relationship satisfaction was not affected by surgery or by the type of surgery (bowel resection versus no bowel resection) (Van den Broeck et al., 2013). Similarly, two studies conducted in the same institution involving 103 and 250 patients with mixed lesions and mixed types of surgical procedures (including bowel resection), respectively, showed an improvement in SHOW-Q scores in all sexual domains at 6 months follow-up without a marked effect of post-operative administration of an oral contraceptive (Mabrouk et al., 2012; Di Donato et al., 2015). However, if not adequately analyzed, the use of post-operative hormonal treatment may represent a limit for the correct interpretation of surgical outcomes. As shown in Table 1, surgical findings of five studies are not properly controlled for the use of post-operative hormones, limiting the interpretation of the real contribution of surgery in improving symptoms (Setala et al., 2012; Dubuisson et al., 2013; Kossi et al., 2013; Di Donato et al., 2015; Morelli et al., 2015). In a recent multicentre study, sexual function (FSFI total score) did not improve after surgery and FSD improved only in patients with symptomatic deep lesions (Fritzer et al., 2016). However, the emotional elaboration of pain (fear, feeling of guilt and physical tension) and the frequencies of interrupted sexual intercourse improved independently of the severity of disease and type of the associated surgical procedure (Fritzer et al., 2016).

The reported recurrence rate of endometriosis has been estimated to be between 5% and 21.5% at 2 years and between 5% and 40% at 5 years (Guo, 2009; Meuleman et al., 2011). Severe deep dyspareunia associated with persistent or recurrent endometriosis after unsuccessful first-line conservative surgery is associated with low scores on FSFI, below the cut-off for normal sexual function (Vercellini et al., 2013). The second-line surgery in this cohort improved all domains of sexual function relative

Table 1 List of studies investigating the effect of surgical management of endometriosis on sexual function.

Reference	Type of study	Number of patients	Type of lesion	Follow-up	Measuring instrument	Result	Note
Garry <i>et al.</i> (2000)	Prospective, Observational	57	AFS I-IV	4 months	The sexual Activity Questionnaire	Improved pleasure, habit, discomfort	
Vercellini <i>et al.</i> (2003)	RCT	37 without USL resection + 28 with USL resection	AFS I-IV	1 year	Revised Sabbatsberg Sexual Rating Scale	Index score improved in both groups	No effect of USL resection
Abbott <i>et al.</i> (2003)	Prospective, Observational	125	AFS I-IV and mixed deep lesions	2–5 (3.2) years	The Sexual Activity Questionnaire	Improved pleasure, habit, discomfort	Results are not controlled for type of procedure
Ferrero <i>et al.</i> (2005)	Prospective, Observational	34	AFS I-IV and mixed deep lesions	1 year	Sexual Satisfaction Subscale of the Derogatis Sexual Functioning Inventory	Improved variety in sexual life, frequency of intercourse, relaxed more easily during sex; more satisfying orgasms and more relaxed and fulfilled after sex	
Setälä <i>et al.</i> (2012)	Prospective, Observational	22	Deep Lesion involving the vagina	1 year	McCoy Female Sexuality Questionnaire	Improved sexual satisfaction and sexual problems; satisfaction with partner unchanged	Results are not controlled for hormone use
Mabrouk <i>et al.</i> (2012)	Prospective Observational	103	Mixed deep lesions	6 months	SHOW-Q	Improved satisfaction, desire, pelvic pain. Orgasm unchanged	All patients received post-operative COC.
Meuleman <i>et al.</i> (2011)	Retrospective, Observational	30	Deep lesions involving the bowel (bowel resection)	27 (range: 16–40) months	The Sexual Activity Questionnaire	Improved pleasure, habit, discomfort	
Dubuisson <i>et al.</i> (2013)	Prospective	20	Mixed deep lesions	23.3 months	Brief Index of Sexual Functioning for Women	Improved desire, arousal, pleasure, orgasm, relational satisfaction	Results are not controlled for hormone use and type of procedure (bowel resection)
Kossi <i>et al.</i> (2013)	Prospective, Observational	26	Deep lesions involving the bowel (bowel resection)	1 year	McCoy Female Sexuality Questionnaire	Improved sexual satisfaction; sexual problems and satisfaction with partner unchanged	Results are not controlled for hormone use
Vercellini <i>et al.</i> (2013)	Prospective	51	AFS I-IV and mixed deep lesions Second-line surgery	1 year	FSFI	Improved all domains. Score remained below the threshold for sexual dysfunction	
Van den Broeck <i>et al.</i> (2013)	Prospective	76 with bowel resection + 127 without bowel resection	AFS III-IV and deep lesions	18 months	Short sexual functioning Scale	Improved arousal, sexual desire, orgasm problems and pain during intercourse. Relationship satisfaction unchanged	
Morelli <i>et al.</i> (2015)	Retrospective	10	Deep lesions involving the bowel	1 year	FSFI	Improved pain; other domains unchanged	Results are not controlled for hormone use

Continued

Table I Continued

Reference	Type of study	Number of patients	Type of lesion	Follow-up	Measuring instrument	Result	Note
Di Donato et al. (2015)	Prospective	250	(bowel resection) Mixed deep lesions	6 months	SHOW-Q	Improved all domains	Results are not controlled for hormone use
Fritzer et al. (2016)	Prospective, multicenter	96	AFS I-IV and mixed deep lesions	10 months (9–12)	FSFI and FSD	FSFI unchanged FSD improved only in deep lesions	

FAFS: American Fertility Society; USL: utero-sacral ligaments; COC: combined oral contraceptive; FSFI: Female Sexual Function Index; FSD: Female Sexual Distress; SHOW-Q: Sexual Health Outcomes in Women Questionnaire.

to the baseline, but the FSFI score remained below the threshold for normal sexual function over the entire study period (1 year). Interestingly, the score improved substantially in the short term after surgery; it then deteriorated after 6–9 months (Vercellini et al., 2013) (Table I).

Effects of hormonal treatment on sexual function

Currently, hormonal contraceptives, progestins, danazol, GnRH agonists and antagonists and aromatase inhibitors are used in clinical settings for the medical management of endometriosis-associated pain and for secondary prevention (Rocha et al., 2012; Dunselman et al., 2014; Brown and Farquhar, 2015; Pluchino et al., 2016). Although they reduce or counteract the effects of estrogens on endometriosis growth and inflammation, endogenous and exogenous sex steroids interact with nociceptive processes at multiple levels of the peripheral and central nervous system (Martin, 2009; Pluchino et al., 2013a; Morotti et al., 2014b). Pharmacological hypogonadism and hormonal therapy affect brain areas involved in sexual response (desire, arousal, libido), in emotional and behavioral changes (mood, anxiety, fear) as well as in peripheral genital response to sexual stimuli (Fenton, 2007; Pluchino et al., 2009; Pletzer et al., 2015). Use of GnRH analogs in adults with endometriosis is associated with menopausal side effects including hot flashes, mood changes, and sleep disturbance (DiVasta and Laufer, 2013). Depression is also reported as an adverse event in 23% of adult women treated with GnRH analogs (DiVasta and Laufer, 2013). There are no available data on the effect of GnRH agonists on sexual function in endometriosis patients, although studies are consistent with a reduction in deep dyspareunia but also a significant decline in libido and vaginal lubrication. Follow-ups were no longer than 6 months (Henzi et al., 1988; Mettler et al., 1991; Cirkel et al., 1995). Furthermore, there were no data indicating that add-back therapy (any type) would reverse adverse effects on libido in endometriosis patients treated by a GnRH agonist. In contrast, fewer women experienced a loss of libido when NETA, instead of triptorelin, was associated with letrozole (Ferrero et al., 2011).

All combined oral contraceptives (COC) and progestins are effective in relieving pelvic pain and deep dyspareunia in endometriosis patients in several studies, although comparisons between different progestins or COC are lacking (Razzi et al., 2007; Momoeda et al., 2009; Brown et al., 2012; Pluchino et al., 2013b; Berlanda et al., 2016). Nevertheless, only a few studies have investigated the effect of these agents on sexual function in endometriosis. The use of hormonal contraception in healthy women

may be associated with the experience of negative sexual side effects in different domains (sexual activity, arousal, pleasure and orgasm and more difficulty with lubrication) (Davis et al., 2013; Smith et al., 2014). Similarly, certain personality traits (somatic anxiety and stress susceptibility) in healthy women may predict the development of mood disorders during COC use, reducing long-term compliance (Borgstrom et al., 2008). The occurrence of mood disorders and anxiety-like behavior has been also described during progestins treatment, although the bulk of this evidence is not consistent among different studies and can vary according to the class and chemical profile of progestins (Smith et al., 1994; Panay and Studd, 1997; van Wingen et al., 2008; Pluchino et al., 2009; Pluchino et al., 2013b).

At any rate, the occurrence of mood and anxiety changes during hormonal treatment may have far-reaching implications in endometriosis patients, in whom pain, personal distress and sexual function are strongly interrelated and it may also represent an important aspect for long-term treatment compliance.

Moreover, the use of psychotropic treatments can further worsen sexual function in young women, perpetuating negative consequences of endometriosis on sexual function. Indeed, antidepressants with serotonergic activity and antipsychotics that increase prolactin and block dopamine signaling, frequently cause mild to severe sexual dysfunction (Basson et al., 2010; Montejo et al., 2015).

The investigation of sexual functioning in endometriosis following estrogen/progestin treatments commenced only after the year 2000. Table II summarizes the available evidence. A group of 90 patients with pain recurrence/persistence after surgery were randomized to receive cyproterone acetate (CA) or ethinyl estradiol (EE) (0.02 mg) and desogestrel (0.15 mg). The total score on the Sabbatsberg Sexual Rating Scale increased in both groups, without any inter-group difference after 6 months, although 16% of patients receiving CA reported lower libido (Vercellini et al., 2002). Patients with pain recurrence or persistence after surgery were also randomized to receive 1 mg norethisterone acetate (NETA) + 35 µg EE or Leuprolide acetate (LA) + 5 mg NETA daily (Guzick et al., 2011). The index of sexual satisfaction increased only in the LA group (10 patients) after 1-year follow-up despite the improvement in sexual pain in both groups (Guzick et al., 2011). In the case of persistence or recurrence of deep dyspareunia after previous surgery, daily administration of 2.5 mg NETA improved sexual functioning based on the FSFI total score, although the score remained below the cut-off of normal sexual function over the entire study period (1 year). In the same study, patients who opted for surgery instead of administration of NETA showed a better total FSFI score, desire, arousal and lubrication and a

Table II List of studies investigating the effect of hormonal management of endometriosis on sexual function.

Reference	Type of study	Number of patients (Intervention)	Type of lesion/ inclusion criteria	Follow-up	Measuring instrument	Result	Note
Vercellini <i>et al.</i> (2002)	RCT	45 (CA) + 45 (EE + DSG)	Pain recurrence/ persistence after surgery (<1 year)	6 months	Sabbatsberg Sexual Rating Scale	Improved in both groups. Libido decreased in 13% of CA group.	
Guzick <i>et al.</i> (2011)	RCT	26 (EE + NETA) + 21 (LA + NETA)	Pain recurrence/ persistence after surgery	1 year (19 patients)	Index of Sexual Satisfaction	Improved only in LA+NETA group after 1 year.	
Vercellini <i>et al.</i> (2013)	Prospective	103 (NETA)	Deep dyspareunia recurrence/persistence after surgery (mixed lesions)	1 year	FSFI	Improved all domains. Score remained below the threshold for sexual dysfunction.	
Morotti <i>et al.</i> (2014a)	Prospective	25 (DNG)	Rectovaginal lesions in patients not responsive to NETA	6 months	FSFI	Improved total score. Mean score remained below the threshold for sexual dysfunction.	Two doses of NETA had been used.
Vercellini <i>et al.</i> (2016)	Retrospective, before and after	90 (NETA) + 90 (DNG)	Mixed lesions	6 months	FSFI	Improved total score in both groups. Score remained below the threshold for sexual dysfunction in both groups.	Results are not adjusted for type of lesion.

CA: cyproterone acetate; LA: leuprolide acetate; NETA: norethindrone acetate; DNG: dienogest.

similar score for pain and satisfaction at 12 months follow-up. Interestingly, stratified analyses showed that the difference in lubrication, in favor of surgery, was limited to nulliparous women, whereas a benefit of NETA over surgery with respect to orgasm was observed in parous participants (Vercellini *et al.*, 2013). Dienogest (DNG) and NETA showed similar effects in controlling pain symptoms, including deep dyspareunia (Vercellini *et al.*, 2015). The total FSFI score increased in both groups after six months of treatment but was still lower than the threshold value for normal sexual function (Vercellini *et al.*, 2015). Similarly, the FSFI total score improved after switching from NETA to DNG in patients who were unsatisfied by the use of NETA, but it remained below the cut-off for normal sexual function (Morotti *et al.*, 2014a). Although switching to another progestin slightly improved chronic pain, the mean dyspareunia value on the 10 cm VAS scale still measured between 5.5 and 6 cm after 6 months of treatment with DNG in patients with deep rectovaginal lesions (Morotti *et al.*, 2014a) (Table II).

Discussion

Substantial evidence from qualitative and quantitative studies shows that symptomatic endometriosis negatively affects all domains of female sexual function causing distress. The presence and the assessment of deep dyspareunia provide only a partial clinical picture of the sexual health of the patient, her partner and the couple.

When sexual function is investigated, it does not represent the primary study end-point in most cases, limiting a comprehensive evaluation of sexual functioning. Therefore, evidence lacks quality in terms of research design, diagnostic instruments, study power or adjustment for confounding factors. Follow-ups are rarely longer than 1 year. Moreover, studies have often reported only the total score on questionnaires, hampering the analysis of specific domains of sexual response, such as arousal/desire, satisfaction or orgasm. In addition,

the modality of coital pain assessment limits the interpretation of results. Indeed, the analysis of pain through questionnaires completed by patients does not differentiate between deep dyspareunia, superficial dyspareunia/provoked vestibulodynia, vaginismus and pelvic floor tenderness or their co-existence. Furthermore, as recently described, recruitment strategy (tertiary referral center, community hospitals or patient associations) may also represent a bias in the analysis of outcomes of quality of life (De Graaff *et al.*, 2015).

Nevertheless, in any form of its manifestation, sexual pain in endometriosis patients induces a fear-avoidance reaction, leading to arousal/desire disorder in the majority of patients. Biopsychosocial variables of sexual pain are under-investigated in endometriosis, although they play a critical role in the fear-avoidance model. A sense of incertitude, fear, expectations and a changing self-image are often reported in qualitative studies, but they are neglected in quantitative studies. Similarly, personality traits, coping capacity (i.e. catastrophizing), and the occurrence of mood/anxiety disorders are crucial in the evolution from coital pain to sexual dysfunction and distress, although their risk estimation and predictive values are largely unknown. The social dimension of pain and long-term implications, crucial in the case of sexual pain, have been under-investigated, particularly from an ecological model perspective (Fig. 2). At the intimate level, the partner's perception of sexual pain and the sociocultural context in which pain (and sex) is experienced may exacerbate behavior associated with sexual pressure or withdrawal, perpetuating the distress (Jodoïn *et al.*, 2008). At the health-care providers level, the quality of interventions, such as a prompt diagnosis or a physicians' awareness of sexual pain severity, affect fear, incertitude and expectations (Fig. 2).

Although certain speculations emerge from clinical scenarios of other causes of painful sex, the role played by hallmarks of endometriosis (delay of diagnosis, extensive or repetitive surgeries, fertility

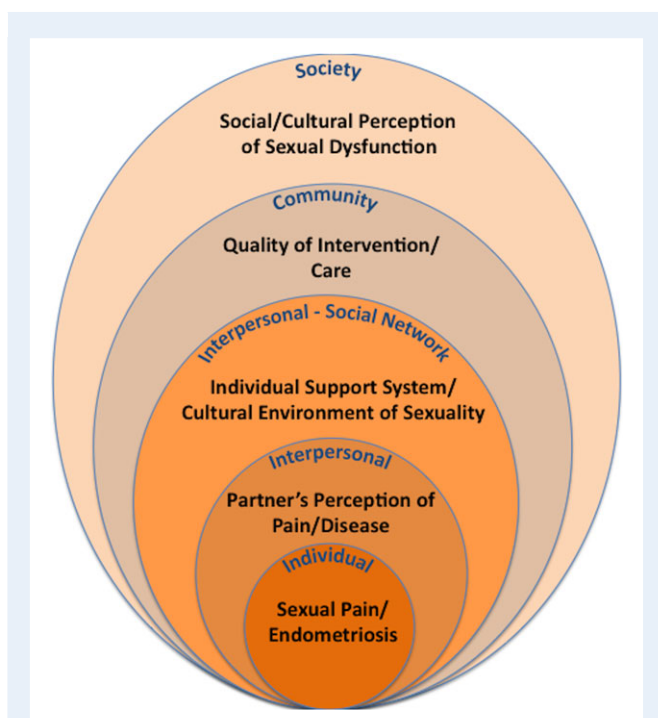


Figure 2 Ecological framework model describing multiple (and interacting) determinants of sexual function in endometriosis patients and their sexual partners, from an individual to a societal perspective. The social dimension of pain constantly influences the changing dynamic of pain, especially in case of sexual pain. At the intimate level, the partner's perception of sexual pain, relational difficulties and cultural environment exacerbate distress for the couple. At the health-care providers level, the quality of interventions, such as a timely diagnosis or a physicians' perceptions of sexual pain severity, affect fear and uncertainty. In a larger perspective, the social/cultural perception of sexual dysfunction influence expectations, attitudes and response to treatment. Long-term implications of sexual pain, from an ecological model perspective, have been largely under-investigated.

concerns) has been neglected. This lack of knowledge (and proper investigation) might explain the inconsistent findings obtained following treatment when the reduction of sexual pain does not necessarily aid the recovery of normal sexual function.

Surgical results are consistent with respect to the reduced sexual pain, but the effects on other domains of sexual function are less consistent. However, radical techniques involving the resection of pelvic nerves may worsen peripheral sexual functioning, and the evaluation of the long-term impacts of surgery may also be affected by other technical factors, mainly the absence of standardization of surgical procedures and quality of care (Pluchino et al., 2015). The persistence or recurrence of pain following surgery has harmful effects on sexual function. Indeed, the identification of psychosocial and biological variables contributing to pain is critical to predicting results and meeting the expectation of patients. Similarly, the effect of hormonal treatment on sexual functioning is less clear. Patients have reported reduced sexual pain, but other sexual function domains are only slightly affected or not affected, especially in case of rectovaginal lesions.

Sexual function in adolescents with endometriosis has also been under-investigated. Two-thirds of adolescent girls with severe dysmenorrhea show laparoscopic evidence of endometriosis, and the consequences of sexual pain in the development of sexual behavior and self-image in this specific population, are largely unknown (Janssen et al., 2013).

Conclusion

Sexual pain associated with endometriosis has the potential to affect sexual function in young women, leading to fear, a sense of uncertainty and relationship difficulties. Over a longer period of time, this pain may lead to a lack of desire, arousal difficulties and withdrawal. Social, cultural, psychological and biological factors may further exacerbate this clinical picture, particularly in the case of chronic painful disease. Surgical and hormonal treatments do not consistently allow for the recovery of normal sexual function, although they improve pain. However, obtaining consistent findings is hampered by several research limitations. A more inclusive and comprehensive analysis of sexual health in endometriosis is therefore required, including the use of proper instruments and quantitative assessments of pain symptoms, sexual function and distress, taking biological, psychological and socio-ecological variables into account.

Moreover, the value of early treatment (surgical or hormonal) of symptomatic patient requires more attention. At the same time, there is a need for better long-term measures of treatment, which incorporate social, physical and psychological outcomes. These improvements are essential for counseling, treating and meeting the expectations of young, sexually active women affected by endometriosis and their partners.

Authors' roles

N.P. and M.B. had roles in the study design, acquisition, analysis and interpretation of data and drafting of the article; J.-M.W., P.P., R.T., H.S.T. and F.B.-D. contributed to the analysis and interpretation of data, revision of the article and final approval of the version to be published.

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Conflict of interest

N.P., J.-M.W., P.P., R.T., M.B., and F.B.-D. have nothing to disclose. H.S.T. is a consultant for Pfizer and has received grants from Pfizer and OvaScience to support research.

References

- Abbott JA, Hawe J, Clayton RD, Garry R. The effects and effectiveness of laparoscopic excision of endometriosis: a prospective study with 2–5 year follow-up. *Hum Reprod* 2003;**18**:1922–1927.

- American Society for Reproductive Medicine, Practise Committee. Treatment of pelvic pain associated with endometriosis: a committee opinion. *Fertil Steril* 2014; **101**:927–935.
- Ashraf DM, Ali D, Azadeh DM. Effect of infertility on sexual function: a cross-sectional study. *J Clin Diagn Res* 2015; **9**:Qc01–Qc03.
- Ballard K, Lowton K, Wright J. What's the delay? A qualitative study of women's experiences of reaching a diagnosis of endometriosis. *Fertil Steril* 2006; **86**: 1296–1301.
- Ballard KD, Seaman HE, de Vries CS, Wright JT. Can symptomatology help in the diagnosis of endometriosis? Findings from a national case-control study – Part 1. *BJOG* 2008; **115**:1382–1391.
- Basson R. Women's sexual function and dysfunction: current uncertainties, future directions. *Int J Impot Res* 2008; **20**:466–478.
- Basson R. The recurrent pain and sexual sequelae of provoked vestibulodynia: a perpetuating cycle. *J Sex Med* 2012; **9**:2077–2092.
- Basson R. Human sexual response. *Handb Clin Neurol* 2015; **130**:11–18.
- Basson R, Althof S, Davis S, Fugl-Meyer K, Goldstein I, Leblum S, Meston C, Rosen R, Wagner G. Summary of the recommendations on sexual dysfunctions in women. *J Sex Med* 2004; **1**:24–34.
- Basson R, Rees P, Wang R, Montejó AL, Incrocci L. Sexual function in chronic illness. *J Sex Med* 2010; **7**:374–388.
- Bayley TM, Slade P, Lashen H. Relationships between attachment, appraisal, coping and adjustment in men and women experiencing infertility concerns. *Hum Reprod* 2009; **24**:2827–2837.
- Berlanda N, Somigliana E, Viganò P, Vercellini P. Safety of medical treatments for endometriosis. *Expert Opin Drug Saf* 2016; **15**:21–30.
- Bianchi-Demicheli F, Ortigue S. Toward an understanding of the cerebral substrates of woman's orgasm. *Neuropsychologia* 2007; **45**:2645–2659.
- Boerner KE, Rosen NO. Acceptance of vulvovaginal pain in women with provoked vestibulodynia and their partners: associations with pain, psychological, and sexual adjustment. *J Sex Med* 2015; **12**:1450–1462.
- Borgstrom A, Odland V, Ekselius L, Sundstrom-Poromaa I. Adverse mood effects of combined oral contraceptives in relation to personality traits. *Eur J Obstet Gynecol Reprod Biol* 2008; **141**:127–130.
- Brawn J, Morotti M, Zondervan KT, Becker CM, Vincent K. Central changes associated with chronic pelvic pain and endometriosis. *Hum Reprod Update* 2014; **20**: 737–747.
- Brown J, Farquhar C. An overview of treatments for endometriosis. *JAMA* 2015; **313**:296–297.
- Brown J, Kives S, Akhtar M. Progestagens and anti-progestagens for pain associated with endometriosis. *Cochrane Database Syst Rev* 2012; **3**:Cd002122.
- Candy B, Jones L, Vickerstaff V, Tookman A, King M. Interventions for sexual dysfunction following treatments for cancer in women. *Cochrane Database Syst Rev* 2016; **2**:Cd005540.
- Ceccaroni M, Clarizia R, Bruni F, D'Urso E, Gagliardi ML, Roviglione G, Minelli L, Ruffo G. Nerve-sparing laparoscopic eradication of deep endometriosis with segmental rectal and parametrial resection: the Negar method. A single-center, prospective, clinical trial. *Surg Endosc* 2012; **26**:2029–2045.
- Cervigni M, Natale F. Gynecological disorders in bladder pain syndrome/interstitial cystitis patients. *Int J Urol* 2014; **21**:85–88.
- Che X, Huang X, Zhang J, Xu H, Zhang X. Is nerve-sparing surgery suitable for deeply infiltrating endometriosis? *Eur J Obstet Gynecol Reprod Biol* 2014; **175**: 87–91.
- Chen LC, Hsu JW, Huang KL, Bai YM, Su TP, Li CT, Yang AC, Chang WH, Chen TJ, Tsai SJ *et al.* Risk of developing major depression and anxiety disorders among women with endometriosis: a longitudinal follow-up study. *J Affect Disord* 2016; **190**:282–285.
- Cheong Y, Tay P, Luk F, Gan HC, Li TC, Cooke I. Laparoscopic surgery for endometriosis: how often do we need to re-operate? *J Obstet Gynaecol* 2008; **28**:82–85.
- Cirkel U, Ochs H, Schneider HP. A randomized, comparative trial of triptorelin depot (D-Trp6-LHRH) and danazol in the treatment of endometriosis. *Eur J Obstet Gynecol Reprod Biol* 1995; **59**:61–69.
- Cox H, Henderson L, Andersen N, Cagliarini G, Ski C. Focus group study of endometriosis: struggle, loss and the medical merry-go-round. *Int J Nurs Pract* 2003a; **9**:2–9.
- Cox H, Henderson L, Wood R, Cagliarini G. Learning to take charge: women's experiences of living with endometriosis. *Complement Ther Nurs Midwifery* 2003b; **9**:62–68.
- Crombez G, Eccleston C, Van Damme S, Vlaeyen JW, Karoly P. Fear-avoidance model of chronic pain: the next generation. *Clin J Pain* 2012; **28**:475–483.
- Culley L, Law C, Hudson N, Denny E, Mitchell H, Baumgarten M, Raine-Fenning N. The social and psychological impact of endometriosis on women's lives: a critical narrative review. *Hum Reprod Update* 2013; **19**:625–639.
- Davis SR, Bitzer J, Giraldi A, Palacios S, Parke S, Serrani M, Mellinger U, Nappi RE. Change to either a nonandrogenic or androgenic progestin-containing oral contraceptive preparation is associated with improved sexual function in women with oral contraceptive-associated sexual dysfunction. *J Sex Med* 2013; **10**: 3069–3079.
- De Graaff AA, D'Hooghe TM, Dunselman GA, Dirksen CD, Hummelshoj L, Simoens S. The significant effect of endometriosis on physical, mental and social wellbeing: results from an international cross-sectional survey. *Hum Reprod* 2013; **28**:2677–2685.
- De Graaff AA, Dirksen CD, Simoens S, De Bie B, Hummelshoj L, D'Hooghe TM, Dunselman GA. Quality of life outcomes in women with endometriosis are highly influenced by recruitment strategies. *Hum Reprod* 2015; **30**:1331–1341.
- Denny E. I never know from one day to another how I will feel: pain and uncertainty in women with endometriosis. *Qual Health Res* 2009; **19**:985–995.
- Denny E, Mann CH. Endometriosis-associated dyspareunia: the impact on women's lives. *J Fam Plann Reprod Health Care* 2007; **33**:189–193.
- Derogatis L, Clayton A, Lewis-D'Agostino D, Wunderlich G, Fu Y. Validation of the female sexual distress scale-revised for assessing distress in women with hypoactive sexual desire disorder. *J Sex Med* 2008; **5**:357–364.
- Desrochers G, Bergeron S, Khalife S, Dupuis MJ, Jodoin M. Fear avoidance and self-efficacy in relation to pain and sexual impairment in women with provoked vestibulodynia. *Clin J Pain* 2009; **25**:520–527.
- Di Donato N, Montanari G, Benfenati A, Monti G, Bertoldo V, Mauloni M, Seracchioli R. Do women with endometriosis have to worry about sex? *Eur J Obstet Gynecol Reprod Biol* 2014; **179**:69–74.
- Di Donato N, Montanari G, Benfenati A, Monti G, Leonardi D, Bertoldo V, Facchini C, Raimondo D, Villa G, Seracchioli R. Sexual function in women undergoing surgery for deep infiltrating endometriosis: a comparison with healthy women. *J Fam Plann Reprod Health Care* 2015; **41**(4):278–283.
- DiVasta AD, Laufer MR. The use of gonadotropin releasing hormone analogues in adolescent and young patients with endometriosis. *Curr Opin Obstet Gynecol* 2013; **25**:287–292.
- Dubuisson J, Pont M, Roy P, Golfier F, Raudrant D. Female sexuality after surgical treatment of symptomatic deep pelvic endometriosis. *Gynecol Obstet Fertil* 2013; **41**:38–44.
- Dunselman GA, Vermeulen N, Becker C, Calhaz-Jorge C, D'Hooghe T, De Bie B, Heikinheimo O, Horne AW, Kiesel L, Nap A *et al.* ESHRE guideline: management of women with endometriosis. *Hum Reprod* 2014; **29**:400–412.
- Evangelista A, Dantas T, Zendron C, Soares T, Vaz G, Oliveira MA. Sexual function in patients with deep infiltrating endometriosis. *J Sex Med* 2014; **11**:140–145.
- Fagervold B, Jenssen M, Hummelshoj L, Moen MH. Life after a diagnosis with endometriosis – a 15 years follow-up study. *Acta Obstet Gynecol Scand* 2009; **88**: 914–919.
- Fauconnier A, Chapron C. Endometriosis and pelvic pain: epidemiological evidence of the relationship and implications. *Hum Reprod Update* 2005; **11**:595–606.
- Fauconnier A, Chapron C, Dubuisson JB, Vieira M, Dousset B, Breart G. Relation between pain symptoms and the anatomic location of deep infiltrating endometriosis. *Fertil Steril* 2002; **78**:719–726.
- Fenton BW. Limbic associated pelvic pain: a hypothesis to explain the diagnostic relationships and features of patients with chronic pelvic pain. *Med Hypotheses* 2007; **69**:282–286.
- Ferrero S, Abbamonte LH, Giordano M, Ragni N, Remorgida V. Deep dyspareunia and sex life after laparoscopic excision of endometriosis. *Hum Reprod* 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, Venturini PL, Gillott DJ, Remorgida V. Letrozole and norethisterone acetate versus triptorelin in the treatment of endometriosis related pain symptoms: a randomized controlled trial. *Reprod Biol Endocrinol* 2011; **9**:88.
- Fritzer N, Haas D, Oppelt P, Renner S, Hornung D, Wolfner M, Ulrich U, Fischerlehner G, Sillem M, Hudelist G. More than just bad sex: sexual

- dysfunction and distress in patients with endometriosis. *Eur J Obstet Gynecol Reprod Biol* 2013;**169**:392–396.
- Fritzer N, Tamma A, Haas D, Oppelt P, Renner S, Hornung D, Wolfer M, Ulrich U, Hudelist G. When sex is not on fire: a prospective multicentre study evaluating the short-term effects of radical resection of endometriosis on quality of sex life and dyspareunia. *Eur J Obstet Gynecol Reprod Biol* 2016;**197**:36–40.
- Fritzer N, Tamma A, Salzer H, Hudelist G. Dyspareunia and quality of sex life after surgical excision of endometriosis: a systematic review. *Eur J Obstet Gynecol Reprod Biol* 2014;**173**:1–6.
- 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* 2000;**107**:44–54.
- Glover L, McLellan A, Weaver SM. What does having a fertility problem mean to couples? *J Reprod Infant Psychol* 2009;**27**:401–418.
- Granot S, Ferber SG. The roles of pain catastrophizing and anxiety in the prediction of postoperative pain intensity: a prospective study. *Clin J Pain* 2005;**21**:439–445.
- Guo SW. Recurrence of endometriosis and its control. *Hum Reprod Update* 2009;**15**:441–461.
- Guzick DS, Huang LS, Broadman BA, Nealon M, Hornstein MD. Randomized trial of leuprolide versus continuous oral contraceptives in the treatment of endometriosis-associated pelvic pain. *Fertil Steril* 2011;**95**:1568–1573.
- Hawkes S. Sexual health: a post-2015 palimpsest in global health? *Lancet Glob Health* 2014;**2**:e377–e378.
- Henzl MR, Corson SL, Moghissi K, Buttram VC, Berqvist C, Jacobson J. Administration of nasal nafarelin as compared with oral danazol for endometriosis. A multicenter double-blind comparative clinical trial. *N Engl J Med* 1988;**318**:485–489.
- Hummelshoj L, De Graaff A, Dunselman G, Vercellini P. Let's talk about sex and endometriosis. *J Fam Plann Reprod Health Care* 2014;**40**:8–10.
- Jacobson TZ, Duffy JM, Barlow DH, Koninckx PR, Garry R. WITHDRAWN: laparoscopic surgery for pelvic pain associated with endometriosis. *Cochrane Database Syst Rev* 2014;**8**:Cd001300.
- Janssen EB, Rijkers AC, Hoppenbrouwers K, Meuleman C, D'Hooghe TM. Prevalence of endometriosis diagnosed by laparoscopy in adolescents with dysmenorrhea or chronic pelvic pain: a systematic review. *Hum Reprod Update* 2013;**19**:570–582.
- Jia SZ, Leng JH, Sun PR, Lang JH. Prevalence and associated factors of female sexual dysfunction in women with endometriosis. *Obstet Gynecol* 2013;**121**:601–606.
- Jodoin M, Bergeron S, Khalife S, Dupuis MJ, Desrochers G, Leclerc B. Male partners of women with provoked vestibulodynia: attributions for pain and their implications for dyadic adjustment, sexual satisfaction, and psychological distress. *J Sex Med* 2008;**5**:2862–2870.
- Jones G, Jenkinson C, Kennedy S. The impact of endometriosis upon quality of life: a qualitative analysis. *J Psychosom Obstet Gynaecol* 2004;**25**:123–133.
- Khosla R, Say L, Temmerman M. Sexual health, human rights, and law. *Lancet* 2015;**386**:725–726.
- Koninckx PR, Meuleman C, Demeyere S, Lesaffre E, Cornillie FJ. Suggestive evidence that pelvic endometriosis is a progressive disease, whereas deeply infiltrating endometriosis is associated with pelvic pain. *Fertil Steril* 1991;**55**:759–765.
- Koninckx PR, Ussia A, Adamyan L, Wattiez A, Donnez J. Deep endometriosis: definition, diagnosis, and treatment. *Fertil Steril* 2012;**98**:564–571.
- Kossi J, Setälä M, Mäkinen J, Harkki P, Luostarinen M. Quality of life and sexual function 1 year after laparoscopic rectosigmoid resection for endometriosis. *Colorectal Dis* 2013;**15**:102–108.
- Lagana AS, Condemi I, Retto G, Muscatello MR, Bruno A, Zoccali RA, Triolo O, Cedro C. Analysis of psychopathological comorbidity behind the common symptoms and signs of endometriosis. *Eur J Obstet Gynecol Reprod Biol* 2015;**194**:30–33.
- Langer A, Meleis A, Knäul FM, Atun R, Aran M, Arreola-Ornelas H, Bhutta ZA, Binagwaho A, Bonita R, Caglia JM et al. Women and Health: the key for sustainable development. *Lancet* 2015;**386**:1165–1210.
- Lazzeri L, Di Giovanni A, Exacoustos C, Tosti C, Pinzauti S, Malzoni M, Petraglia F, Zupi E. Preoperative and postoperative clinical and transvaginal ultrasound findings of adenomyosis in patients with deep infiltrating endometriosis. *Reprod Sci* 2014;**21**:1027–1033.
- Learman LA, Huang AJ, Nakagawa S, Gregorich SE, Kuppermann M. Development and validation of a sexual functioning measure for use in diverse women's health outcome studies. *Am J Obstet Gynecol* 2008;**198**:710 e711–710 e718; discussion 710 e718–719.
- Lemaire GS. More than just menstrual cramps: symptoms and uncertainty among women with endometriosis. *J Obstet Gynecol Neonatal Nurs* 2004;**33**:71–79.
- Lindau ST, Abramssohn EM, Matthews AC. A manifesto on the preservation of sexual function in women and girls with cancer. *Am J Obstet Gynecol* 2015;**213**:166–174.
- Mabrouk M, Montanari G, Di Donato N, Del Forno S, Frasca 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.
- Martin VT. Ovarian hormones and pain response: a review of clinical and basic science studies. *Gen Med* 2009;**6**:168–192.
- Martin CE, Johnson E, Wechter ME, Leserman J, Zolnoun DA. Catastrophizing: a predictor of persistent pain among women with endometriosis at 1 year. *Hum Reprod* 2011;**26**:3078–3084.
- Melis I, Agus M, Pluchino N, Di Spiezo Sardo A, Litta P, Melis GB, Angioni S. Alexithymia in women with deep endometriosis? A pilot study. *J Endometr Pelvic Pain Disord* 2014;**6**:26–33.
- Melis I, Litta P, Nappi L, Agus M, Melis GB, Angioni S. Sexual function in women with deep endometriosis: correlation with quality of life, intensity of pain, depression, anxiety, and body image. *Int J Sex Health* 2015;**27**:175–185.
- Mettler L, Steinmüller H, Schachner-Wunschmann E. Experience with a depot GnRH-agonist (Zoladex) in the treatment of genital endometriosis. *Hum Reprod* 1991;**6**:694–698.
- Meuleman C, D'Hoore A, Van Cleynenbreugel B, Beks N, D'Hooghe T. Outcome after multidisciplinary CO₂ laser laparoscopic excision of deep infiltrating colorectal endometriosis. *Reprod Biomed Online* 2009;**18**:282–289.
- Meuleman C, Tomassetti C, D'Hooghe TM. Clinical outcome after laparoscopic radical excision of endometriosis and laparoscopic segmental bowel resection. *Curr Opin Obstet Gynecol* 2012;**24**:245–252.
- Meuleman C, Tomassetti C, D'Hoore A, Van Cleynenbreugel B, Penninckx F, Vergote I, D'Hooghe T. Surgical treatment of deeply infiltrating endometriosis with colorectal involvement. *Hum Reprod Update* 2011;**17**:311–326.
- Meuleman C, Tomassetti C, Wolthuis A, Van Cleynenbreugel B, Laenen A, Penninckx F, Vergote I, D'Hoore A, D'Hooghe T. Clinical outcome after radical excision of moderate-severe endometriosis with or without bowel resection and reanastomosis: a prospective cohort study. *Ann Surg* 2014;**259**:522–531.
- Momoeda M, Harada T, Terakawa N, Aso T, Fukunaga M, Hagino H, Taketani Y. Long-term use of dienogest for the treatment of endometriosis. *J Obstet Gynaecol Res* 2009;**35**:1069–1076.
- Monga M, Alexandrescu B, Katz SE, Stein M, Ganiats T. Impact of infertility on quality of life, marital adjustment, and sexual function. *Urology* 2004;**63**:126–130.
- 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.
- Montejo AL, Montejo L, Navarro-Cremades F. Sexual side-effects of antidepressant and antipsychotic drugs. *Curr Opin Psychiatry* 2015;**28**:418–423.
- Morelli L, Perutelli A, Palmeri M, Guadagni S, Mariniello MD, Di Franco G, Cela V, Brundu B, Salerno MG, Di Candio G et al. Robot-assisted surgery for the radical treatment of deep infiltrating endometriosis with colorectal involvement: short- and mid-term surgical and functional outcomes. *Int J Colorectal Dis* 2016;**31**(3):643–652.
- Morotti M, Sozzi F, Remorgida V, Venturini PL, Ferrero S. Dienogest in women with persistent endometriosis-related pelvic pain during norethisterone acetate treatment. *Eur J Obstet Gynecol Reprod Biol* 2014a;**183**:188–192.
- Morotti M, Vincent K, Brawn J, Zondervan KT, Becker CM. Peripheral changes in endometriosis-associated pain. *Hum Reprod Update* 2014b;**20**:717–736.
- Ortigue S, Patel N, Bianchi-Demicheli F. New electroencephalogram (EEG) neuroimaging methods of analyzing brain activity applicable to the study of human sexual response. *J Sex Med* 2009;**6**:1830–1845.
- Panay N, Studd J. Progestogen intolerance and compliance with hormone replacement therapy in menopausal women. *Hum Reprod Update* 1997;**3**:159–171.
- Payne KA, Binik YM, Amsel R, Khalife S. When sex hurts, anxiety and fear orient attention towards pain. *Eur J Pain* 2005;**9**:427–436.
- Piazza LA, Markowitz JC, Kocsis JH, Leon AC, Portera L, Miller NL, Adler D. Sexual functioning in chronically depressed patients treated with SSRI antidepressants: a pilot study. *Am J Psychiatry* 1997;**154**:1757–1759.

- Pletzer B, Kronbichler M, Kerschbaum H. Differential effects of androgenic and anti-androgenic progestins on fusiform and frontal gray matter volume and face recognition performance. *Brain Res* 2015;**1596**:108–115.
- Pluchino N, Cubeddu A, Giannini A, Merlini S, Cela V, Angioni S, Genazzani AR. Progestogens and brain: an update. *Maturitas* 2009;**62**:349–355.
- Pluchino N, Freschi L, Wenger JM, Streuli I. Innovations in classical hormonal targets for endometriosis. *Expert Rev Clin Pharmacol* 2016;**9**:317–327.
- Pluchino N, Petignat P, Wenger JM. Laparoscopic 'Successful' excision of deep endometriosis: a fertility-enhancing surgery. *Ann Surg* 2015;**262**:e26.
- Pluchino N, Russo M, Santoro AN, Litta P, Cela V, Genazzani AR. Steroid hormones and BDNF. *Neuroscience* 2013a;**239**:271–279.
- Pluchino N, Santoro A, Casarosa E, Wenger JM, Genazzani AD, Petignat P, Genazzani AR. Advances in neurosteroids: role in clinical practice. *Climacteric* 2013b;**16**:8–17.
- Pope CJ, Sharma V, Sharma S, Mazmanian D. A systematic review of the association between psychiatric disturbances and endometriosis. *J Obstet Gynaecol Can* 2015;**37**:1006–1015.
- Razzi S, Luisi S, Calonaci F, Altomare A, Bocchi C, Petraglia F. Efficacy of vaginal danazol treatment in women with recurrent deeply infiltrating endometriosis. *Fertil Steril* 2007;**88**:789–794.
- Ret Davalos ML, De Cicco C, D'Hoore A, De Decker B, Koninckx PR. Outcome after rectum or sigmoid resection: a review for gynecologists. *J Minim Invasive Gynecol* 2007;**14**:33–38.
- Rocha AL, Reis FM, Petraglia F. New trends for the medical treatment of endometriosis. *Expert Opin Investig Drugs* 2012;**21**:905–919.
- Rogers PA, D'Hooghe TM, Fazleabas A, Gargett CE, Giudice LC, Montgomery GW, Rombauts L, Salamonsen LA, Zondervan KT. Priorities for endometriosis research: recommendations from an international consensus workshop. *Reprod Sci* 2009;**16**:335–346.
- Rogers PA, D'Hooghe TM, Fazleabas A, Giudice LC, Montgomery GW, Petraglia F, Taylor RN. Defining future directions for endometriosis research: workshop report from the 2011 World Congress of Endometriosis In Montpellier, France. *Reprod Sci* 2013;**20**:483–499.
- Setälä M, Harkki P, Matomaki J, Makinen J, Kossi J. Sexual functioning, quality of life and pelvic pain 12 months after endometriosis surgery including vaginal resection. *Acta Obstet Gynecol Scand* 2012;**91**:692–698.
- Smith KB, Pukall CF. Sexual function, relationship adjustment, and the relational impact of pain in male partners of women with provoked vulvar pain. *J Sex Med* 2014;**11**:1283–1293.
- Smith NK, Jozkowski KN, Sanders SA. Hormonal contraception and female pain, orgasm and sexual pleasure. *J Sex Med* 2014;**11**:462–470.
- Smith NK, Madeira J, Millard HR. Sexual function and fertility quality of life in women using in vitro fertilization. *J Sex Med* 2015;**12**:985–993.
- Smith RN, Holland EF, Studd JW. The symptomatology of progestogen intolerance. *Maturitas* 1994;**18**:87–91.
- Strzempko Butt F, Chesla C. Relational patterns of couples living with chronic pelvic pain from endometriosis. *Qual Health Res* 2007;**17**:571–585.
- Temmerman M, Khosla R, Say L. Sexual and reproductive health and rights: a global development, health, and human rights priority. *Lancet* 2014;**384**:e30–e31.
- Thomten J, Linton SJ. A psychological view of sexual pain among women: applying the fear-avoidance model. *Womens Health (Lond Engl)* 2013;**9**:251–263.
- Thomten J, Lundahl R, Stigenberg K, Linton S. Fear avoidance and pain catastrophizing among women with sexual pain. *Womens Health (Lond Engl)* 2014;**10**:571–581.
- Thomten J, Soares JJ, Sundin O. The influence of psychosocial factors on quality of life among women with pain: a prospective study in Sweden. *Qual Life Res* 2011;**20**:1215–1225.
- Tripoli TM, Sato H, Sartori MG, de Araujo FF, Girao MJ, Schor E. Evaluation of quality of life and sexual satisfaction in women suffering from chronic pelvic pain with or without endometriosis. *J Sex Med* 2011;**8**:497–503.
- Turner JA, Jensen MP, Warms CA, Cardenas DD. Catastrophizing is associated with pain intensity, psychological distress, and pain-related disability among individuals with chronic pain after spinal cord injury. *Pain* 2002;**98**:127–134.
- United Nations General Assembly. *Transforming our World: The 2030 Agenda for Sustainable Development*. 2015. http://www.un.org/ga/search/view_doc.asp?symbol=A/RES/70/1&Lang=E.
- Van den Broeck U, Meuleman C, Tomassetti C, D'Hoore A, Wolthuis A, Van Cleynenbreugel B, Vergote I, Enzlin P, D'Hooghe T. Effect of laparoscopic surgery for moderate and severe endometriosis on depression, relationship satisfaction and sexual functioning: comparison of patients with and without bowel resection. *Hum Reprod* 2013;**28**:2389–2397.
- van Lankveld JJ, Granot M, Weijmar Schultz WC, Binik YM, Wessellmann U, Pukall CF, Bohm-Starke N, Achtrari C. Women's sexual pain disorders. *J Sex Med* 2010;**7**:615–631.
- van Wingen GA, van Broekhoven F, Verkes RJ, Petersson KM, Backstrom T, Buitelaar JK, Fernandez G. Progesterone selectively increases amygdala reactivity in women. *Mol Psychiatry* 2008;**13**:325–333.
- Vanhie A, Meuleman C, Tomassetti C, Timmerman D, D'Hoore A, Wolthuis A, Van Cleynenbreugel B, Dancet E, Van den Broeck U, Tsaltas J et al. Consensus on recording deep endometriosis surgery: the CORDES statement. *Hum Reprod* 2016;**31**:1219–1223.
- Vercellini P, Aimi G, Busacca M, Apolone G, Uglietti A, Crosignani PG. Laparoscopic uterosacral ligament resection for dysmenorrhea associated with endometriosis: results of a randomized, controlled trial. *Fertil Steril* 2003;**80**:310–319.
- Vercellini P, Bracco B, Mosconi P, Roberto A, Alberico D, Dhouha D, Somigliana E. Norethindrone acetate or dienogest for the treatment of symptomatic endometriosis: a before and after study. *Fertil Steril* 2016;**105**(3):734–743.
- Vercellini P, Crosignani P, Somigliana E, Vigano P, Frattaruolo MP, Fedele L. 'Waiting for Godot': a commonsense approach to the medical treatment of endometriosis. *Hum Reprod* 2011a;**26**:3–13.
- Vercellini P, Crosignani PG, Abbiati A, Somigliana E, Vigano P, Fedele L. The effect of surgery for symptomatic endometriosis: the other side of the story. *Hum Reprod Update* 2009;**15**:177–188.
- Vercellini P, De Giorgi O, Mosconi P, Stellato G, Vicentini S, Crosignani PG. Cyproterone acetate versus a continuous monophasic oral contraceptive in the treatment of recurrent pelvic pain after conservative surgery for symptomatic endometriosis. *Fertil Steril* 2002;**77**:52–61.
- Vercellini P, Fedele L, Aimi G, De Giorgi O, Consonni D, Crosignani PG. Reproductive performance, pain recurrence and disease relapse after conservative surgical treatment for endometriosis: the predictive value of the current classification system. *Hum Reprod* 2006;**21**:2679–2685.
- 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* 2013;**28**:1221–1230.
- Vercellini P, Meana M, Hummelshoj L, Somigliana E, Vigano P, Fedele L. Priorities for endometriosis research: a proposed focus on deep dyspareunia. *Reprod Sci* 2011b;**18**:114–118.
- Vercellini P, Somigliana E, Buggio L, Barbara G, Frattaruolo MP, Fedele L. 'I can't get no satisfaction': deep dyspareunia and sexual functioning in women with rectovaginal endometriosis. *Fertil Steril* 2012;**98**:1503–1511 e1501.
- Waller KG, Shaw RW. Endometriosis, pelvic pain, and psychological functioning. *Fertil Steril* 1995;**63**:796–800.
- Wiegel M, Meston C, Rosen R. The female sexual function index (FSFI): cross-validation and development of clinical cutoff scores. *J Sex Marital Ther* 2005;**31**:1–20.
- Yong PJ, Mui J, Allaire C, Williams C. Pelvic floor tenderness in the etiology of superficial dyspareunia. *J Obstet Gynaecol Can* 2014;**36**:1002–1009.
- Yong PJ, Sadownik L, Brotto LA. Concurrent deep-superficial dyspareunia: prevalence, associations, and outcomes in a multidisciplinary vulvodynia program. *J Sex Med* 2015;**12**:219–227.