



# NILDE

Network Inter-Library Document Exchange

Il presente documento viene fornito attraverso il servizio NILDE dalla Biblioteca fornitrice, nel rispetto della vigente normativa sul Diritto d'Autore (Legge n.633 del 22/4/1941 e successive modifiche e integrazioni) e delle clausole contrattuali in essere con il titolare dei diritti di proprietà intellettuale.

**La Biblioteca fornitrice** garantisce di aver effettuato copia del presente documento assolvendo direttamente ogni e qualsiasi onere correlato alla realizzazione di detta copia.

**La Biblioteca richiedente** garantisce che il documento richiesto è destinato ad un suo utente, che ne farà uso esclusivamente personale per scopi di studio o di ricerca, ed è tenuta ad informare adeguatamente i propri utenti circa i limiti di utilizzazione dei documenti forniti mediante il servizio NILDE.

**La Biblioteca richiedente** è tenuta al rispetto della vigente normativa sul Diritto d'Autore e in particolare, ma non solo, a consegnare al richiedente un'unica copia cartacea del presente documento, distruggendo ogni eventuale copia digitale ricevuta.

**Biblioteca richiedente:** Biblioteca del Polo universitario di Novara  
**Data richiesta:** 18/10/2024 13:13:27  
**Biblioteca fornitrice:** Ufficio Servizi informatici ed interbibliotecari - Sistema Bibliotecario di Ateneo  
**Data evasione:** 18/10/2024 13:25:55

---

**Titolo rivista/libro:** Minerva obstetrics and gynecology Online  
**Titolo articolo/sezione:** Sexual function and quality of life in women with endometriosis  
**Autore/i:** Libera Troia 1, Stefano Luisi 2  
**ISSN:** 2724-6450  
**DOI:** 10.23736/S2724-606X.22.05033-3  
**Anno:** 2022  
**Volume:** 74  
**Fascicolo:** 3  
**Editore:**  
**Pag. iniziale:** 203  
**Pag. finale:** 221

## REVIEW

FEMALE SEXUALITY IN HEALTH AND DISEASE:  
A JOURNEY ALONG A WOMAN'S LIFESexual function and quality of life  
in women with endometriosisLibera TROIA<sup>1</sup>, Stefano LUISI<sup>2</sup> \*<sup>1</sup>Department of Obstetrics and Gynecology, San Donato Hospital, Arezzo, Italy; <sup>2</sup>Unit of Gynecology, Department of Molecular and Developmental Medicine, University of Siena, Siena, Italy\*Corresponding author: Stefano Luisi, Unit of Gynecology, Department of Molecular and Developmental Medicine, University of Siena, Viale Bracci, 53100 Siena, Italy. E-mail: [stefano.luisi@unisi.it](mailto:stefano.luisi@unisi.it)

## ABSTRACT

Endometriosis may exert a profound negative influence on the lives of individuals with the disorder, adversely affecting quality of life, participation in daily and social activities, physical and sexual functioning, relationships, educational and work productivity, mental health, and well-being. Symptoms of endometriosis represent a great source of stress and cause a substantial negative impact on the psychological parameters, on the daily life and on the physical functioning of patients. The impact of endometriosis on work attendance has very significant economic consequences, as lost productivity has an associated cost, as do career changes resulting from a decline in education due to symptoms. Endometriosis is a pathology that affects all aspects of women's lives and that thus, it must be treated with a multidisciplinary vision that includes not only a medical approach but also psychological, work, and economic support. In this specific long-term vision of patient-centered endometriosis care, aspects of quality of life and sexual health play a key role and should always be evaluated with any patient as part of a multidisciplinary management.

(Cite this article as: Troia L, Luisi S. Sexual function and quality of life in women with endometriosis. *Minerva Obstet Gynecol* 2022;74:203-21. DOI: 10.23736/S2724-606X.22.05033-3)

KEY WORDS: Quality of Life; Endometriosis; Infertility.

Endometriosis is a chronic inflammatory disease that affects approximately 10% of women of reproductive age and up to 50% of infertile women. As a consequence of inflammatory reaction and infiltration of anatomic structures, endometriosis can cause "pain symptoms" including dysmenorrhea, dyspareunia, dyschezia, dysuria, and chronic pelvic pain.<sup>1</sup> Endometriosis may exert a profound negative influence on the lives of individuals with the disorder, adversely affecting quality of life (QoL), participation in daily and social activities, physical and sexual functioning, relationships, educational and work productivity, mental health, and well-being. Over the course

of life, these daily challenges can result in limitations in achieving life goals such as pursuing or completing educational opportunities, making career choices or advancing in a chosen career, forming stable and fulfilling relationships, or starting a family.<sup>1,2</sup> This is a major issue considering that endometriosis mainly affects women in the reproductive period and that the onset of symptoms generally occurs at a time of life (from menarche to menopause, adolescence to middle age) when multiple life-changing and trajectory-defining decisions are made.<sup>2,3</sup> Pain is consistently reported as a central and destructive feature of life with endometriosis, and sev-

eral studies report a negative correlation between pain and QoL. The psychological and emotional distress resulting from endometriosis symptoms (chronic pelvic pain and infertility) may affect pain perception in these patients, who also have high rates of somatization, anxiety and depression.<sup>4, 5</sup> There is evidence that pelvic pain is the main driver of depressive symptoms; however, it is also possible that the presence of a mental health condition increases pain perception. Indeed, the personal experience of pelvic pain affects emotional functioning and high levels of anxiety and depression can amplify the severity of the pain.<sup>6</sup>

Sexual health, *i.e.* physical, emotional, mental and social well-being in relation to sexuality, is a fundamental dimension of human life with important consequences on physical and psychological health and on the overall QoL.<sup>7</sup> This is particularly important considering that in women with endometriosis female sexual dysfunctions are relatively common and varies between 30% and 70%.<sup>7</sup> Endometriosis, with its physical symptoms of dyspareunia, chronic pelvic pain, fatigue and infertility, as well as psychological symptoms such as depression and anxiety, is known to have a significant negative influence on several aspects of female sexual functioning, such as desire, orgasm, and overall satisfaction with sex.<sup>7, 8</sup> These symptoms of sexual dysfunction reduce the frequency and quality of sexual intercourse, reduce arousal, worsen QoL with a negative impact on the psychological well-being of women and also on the couple's life.<sup>9</sup> Biopsychosocial variables of sexual pain play a critical role in the fear-avoidance model. Senses of uncertainty, 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. Sexual health matters and improving global sexual functioning, and not just reducing pain at intercourse, should be considered as a major clinical goal of endometriosis treatment. Although surgical and hormonal treatment of endometriosis can relieve symptoms related to endometriosis, it does not necessarily allow for normal sexual function.

Because of this sexual counselling should be offered as a standard component of medical support for endometriosis and knowledge of the associations between endometriosis, physical and psychosocial symptoms related to endometriosis and sexuality is mandatory.<sup>10</sup> The economic burden of endometriosis is considerable, also considering the negative impact of the disease on the professional activity of women, as well as the cost of treatment and hospitalization. Due to the chronicity of endometriosis, it can be associated with significant physical and emotional morbidity affecting the daily activities of affected women, leading to absenteeism or the inability to work for long hours. The impact of endometriosis on work attendance has very significant economic consequences, as lost productivity has an associated cost, as do career changes resulting from a decline in education due to symptoms.<sup>11</sup> Ultimately endometriosis is a pathology that affects all aspects of women's lives and that thus, it must be treated with a multidisciplinary vision that includes not only a medical approach but also psychological, work, and economic support.

### QoL instruments and measures for endometriosis

Health related quality of life (HRQoL) is a multidimensional concept that includes physical, psychological, and social aspects. Despite the importance of assessing the impact of endometriosis on QoL, there is still little consensus on which method to use. Several types of questionnaires have been proposed and used over the years and the most commonly used QoL tools were the Short Form 36 (SF 36), the Short Form 12 (SF 12), and the World Health Organization Quality of Life Assessment BREF (WHOQOL BREF).<sup>2, 12</sup>

The SF 36 consists of 36 items in eight domains: physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health.<sup>13</sup> Women with endometriosis had significantly lower SF 36 scores than the general population, especially in the domains: vitality, role-physical, and general health.<sup>14</sup> The SF 12 is made up of 12 items (taken from the SF 36) which produce two measures re-



lating to two different aspects of health: physical and mental health.<sup>15</sup> The WHOQOL BREF is a brief questionnaire comprising 26 items, including two items for overall QoL and general health, and another 24 items categorized in four domains (physical, psychological, social, and environmental health).<sup>16</sup>

The Nottingham Health Profile (NHP) is a questionnaire divided into two parts assessing the physical, social, and emotional health of women with endometriosis. Part I contains 38 objects (physical skills, pain, sleep, social isolation, emotional reactions, energy level). The second optional part provides a brief handicap indicator and considers the effect of health problems on personal relationships, social and sexual life, employment, housework, hobbies and holidays.<sup>17</sup>

The EuroQOL 5-dimension instrument (EQ 5D) is a generic test that includes five dimensions: mobility, self care, daily activities, pain, and emotional well being (depression or anxiety). Each item is scored based on a three-point scale, and the EQ 5D score is calculated by their sum, resulting in scores ranging from 0 (best possible status) to 10 (worst possible status).<sup>18</sup>

Endometriosis also affects employment because women are unable to manage a full-time job due to the difficulties associated with the disease and for this reason it is also important to evaluate this QoL domain.<sup>19, 20</sup> The Health-Related Productivity Questionnaire (HRPQ) is a 9-item measure of productivity, including absenteeism (work time missed, including household work) and presenteeism (reduced work effectiveness because of endometriosis, including household work).<sup>21</sup>

To evaluate and quantify chronic pelvic pain, dyspareunia, and dysmenorrhea, several scales are available. One of the main tools for interviewing patients about their pain level is the Visual Analogue Scale (VAS) for five components: dysmenorrhea, dyspareunia, dyschezia, chronic pelvic pain, and dysuria. The VAS is considered the gold standard and consists of a 10 cm long horizontal line with the ends marked "no pain" and "worst imaginable pain."<sup>22</sup> Numerical Rating Scale (NRS) is a segmented numerical version of the VAS in which patients select, on a

horizontal line or a bar, an integer from 0 to 10 and NRS better reflects the intensity of pain. Another scale used to evaluate different types of pain is the Verbal Rating Scale (VRS): with this type of scale, patients evaluate their pain intensity from absent (0) to severe (3) or from none (0) to very severe (5).<sup>23</sup>

Dyspareunia is the symptom that most of all affects the quality of the sexual life of women with endometriosis: the DYSPI diary evaluates it in the last 24 hours. The response options vary from absent =0 (no discomfort during sexual intercourse), mild =1 (discomfort during sexual intercourse was tolerated), moderate =2 (intercourse was interrupted due to pain) to severe =3 (sexual intercourse was avoided because of pain).<sup>24</sup> To assess the quality of the sexual life of the patients, various questionnaires were used including the Female Sexual Function Index (FSFI) widely used in various studies. It is made up of 19 items encompassing six domains: desire, arousal, lubrication, orgasm, satisfaction, and pain. Sexual dysfunction was defined as a FSFI score <26.55, based on published validation studies.<sup>25</sup>

Female sexual dysfunction can be also evaluated with Female Sexual Distress Scale Revised (FSDSR) consisting of 13 elements to measure anxiety related to sex. The fixed choice response format offers five increments: never, rarely, occasionally, often, and always. Sexual distress was defined as an FSDSR score >11 based on published validation studies. The higher the score, the greater the distress.<sup>26</sup> Questionnaire on Sexual Health Outcomes in Women (SHOWQ) is another complete questionnaire on women's sexual function that assesses satisfaction, orgasm, desire of women, and the interference of disease with the sex.<sup>27</sup>

A disease specific QoL measure is the Endometriosis Health Profile 30 (EHP 30), a validated and reliable questionnaire that measures the patient's perspective about her experiences with the impacts of endometriosis. The EHP 30 is composed of a core questionnaire of 30 items, in addition to 6 modular parts containing 23 items. One of the 6 modular parts specifically addresses sexual intercourse, which includes questions about pain, guilt, worry, frustration, and avoid-



ance associated with sexual intercourse. The reliability and validity of the EHP 30 have been assessed and affirmed.<sup>28</sup> A shorter version of EHP30, more practical and suitable for clinical practice and also for research, was the Endometriosis Health Profile 5 (EHP 5). The EHP 5 is built in two parts: a 5-item core questionnaire about pain, control and powerlessness, emotions, social support, self image, and a 6-item modular questionnaire about work life, relation with children, sexual intercourse, medical profession, treatment and infertility. The response system consists of five levels ranged in order of severity: never, rarely, sometimes, often and always.<sup>29</sup>

All these questionnaires are used to evaluate how endometriosis affects the various aspects of patients' life; however, it is not yet clear which one is the best. A recent review by Bourdel *et al.* shows that the two scales most frequently used are the SF 36 and EHP 30 and that the most validated scales were SF 36 and EQ 5D for general questionnaires and EHP30 and its abbreviated form EHP 5 for specific ones.<sup>17</sup>

## Endometriosis and psychosocial impact

### Quality of Life

World Health Organization (WHO) defines Quality of Life as an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. Due to the chronicity of this condition, endometriosis may be associated with considerable physical and emotional morbidity and the reduction of QoL in this population can be explained by the complexity of disease etiology and manifestations, as well as by the interference in women's reproductive capacity.<sup>30</sup> Chronic pain, occurring with typical cyclicity and severity, may significantly reduce the QoL of women with endometriosis. The QoL indices include the ability to play previous life roles, adaptability, psychological well-being and functioning within social groups.<sup>31</sup>

The review conducted by Culley *et al.* regarding the social and psychological impact of endometriosis on women's lives showed that endometriosis leads to significant disability in

physical and mental health components affecting daily activities, intimate relationships, planning and having children, education and work and emotional well-being.<sup>4</sup> Endometriosis symptoms, and specifically pain, have a detrimental impact on daily life and physical functioning (*e.g.* sleeping, eating, moving): between 16% and 61% of women experience difficulties with mobility, daily activities and/or self-care.<sup>4</sup> In addition to losing health, the disease leads to loss of security, self-confidence and often hope. Pain comes unexpectedly, hampering daily functioning. Physical symptoms of pain and psychological distress associated with difficulty regulating emotions can adversely affect HRQoL in women with endometriosis. Poor QoL (SF-36) scores for vitality, low energy levels with a negative impact of pain on sport and exercise has also been demonstrated.<sup>4</sup>

In the cross-sectional study conducted by Pessoa de Farias Rodrigues *et al.*, 106 women with endometriosis and infertility, divided in two endometriosis groups based on the stage of disease, responded to the Short Form (SF) Health Survey-36.<sup>30</sup> The authors found QoL levels below the cutoff values in the following domains: vitality, general health, pain, and mental health. Women tended to feel tired most of the time; evaluated their personal health as precarious; experienced pain that was severe and limiting; and felt the presence of a constant feeling of nervousness, anxiety, stress, and depression.<sup>30</sup> However, this study pointed out that it is not the stage of endometriosis that interferes in the QoL of women with endometriosis and infertility but rather the clinical manifestations, such as dyspareunia and pain. These findings indicate that the participants' perception of endometriosis and infertility are aspects that should be considered in health care, since the loss of QoL would not depend directly on the staging of the disease but on how the participants perceive it.<sup>30</sup>

### Diagnostic delay

Women with endometriosis frequently experience significant delays from symptom onset to diagnosis ranging from 5 to 8.9 years.<sup>32</sup>

Women do not seek medical assistance due to the difficulty in distinguishing between normal

and pathological symptoms; they consider themselves “unfortunate” as opposed to “sick” and they fear that reporting the illness would involve embarrassment and perceive them as weak, thus leading to an average delay of 3.8 years between onset of symptoms and help-seeking behavior. The perception of menstrual irregularities as “normal” and the perception of menstrual pain as something to be endured also contribute to delay in seeking help particularly for adolescents.<sup>4</sup> Prior to diagnosis, women commonly experience repeated doctor visits where symptoms are normalized, dismissed or trivialized, resulting in women feeling ignored and disbelieving. Women are often initially referred to inadequate secondary care or misdiagnosed (often with irritable bowel syndrome or pelvic inflammatory disease), and general practitioners have been reported as lacking knowledge and awareness of endometriosis. On receiving a diagnosis, symptomatic women frequently reported that they felt a sense of relief, legitimation, liberation and empowerment, replacing feelings of fear and self-doubt. Delay of diagnosis and worsening and recurrence of pain, exacerbate dyspareunia and dysfunctional behavior, prolonging the distress.<sup>8</sup> Furthermore, a longer delay in diagnosis was also associated with low work ability. A smaller proportion of women categorized as having poor work ability, as measured by the Work Ability Index, were diagnosed with endometriosis within 2 years of symptom onset compared with women categorized as having excellent work ability (16.2% and 48.2%, respectively). In contrast, a delay in diagnosis of 7 to 8 years was more common among women with poor vs. excellent work ability (24.2% and 5.4%, respectively).<sup>33</sup>

Consequently, all these aspects have been shown that diagnostic delay is associated with reduced health-related QoL.<sup>4</sup>

### Education, employment and career

Pain appears to have a significant negative impact on women’s education, employment and career. Women consider endometriosis as a reason for missing opportunities related to their education and career and a good percentage of them stated that they had not pursued further education because of endometriosis.<sup>1</sup> A cross-sectional study

within a longitudinal study of women’s health from 2 tertiary care centers enrolled adolescents ( $\leq 18$  years; N.=295) and adults ( $>18$  years; N.=107) with surgically confirmed endometriosis; a high percentage of women (61% and 60%, respectively) reported moderate to extreme interference with work or school due to pain associated with endometriosis.<sup>34</sup> Furthermore, a web-based questionnaire with questions on menstrual symptoms distributed to adolescent girls residing in the city of Stockholm (N.=3998) showed that dysmenorrhea, regardless of the diagnosis of endometriosis, was linked to school absences.<sup>35</sup> Although this could indicate that dysmenorrhea and perhaps pain in general, rather than endometriosis per se, causes greater school absences, it is expected that a large percentage of the study participants had undiagnosed endometriosis. Moreover, it has been shown that deep endometriosis is associated with greater school absenteeism during menstruation than other forms of endometriosis (37.7% [N.=98] vs. 25.2% [N.=131]), respectively) in French adolescents undergoing surgical treatment.<sup>36</sup>

A considerable deleterious influence of endometriosis on work productivity and capacity as well as career and salary growth were also reported. Statistically significant associations were detected between symptom severity and absenteeism, presenteeism, work productivity loss, poor performance, failure to be promoted, not receiving bonuses, missed professional seminars, and lost clients.<sup>32, 37</sup>

Women with endometriosis have more sick days than women without disease (41% vs. 25%) and have more frequent work-day disturbances due to symptoms and lower working capacity than women without endometriosis. Fatigue, frequent pain, more severe pain, increased sickness days, and depression at work have been associated with reduced ability to work.<sup>33</sup>

In a survey conducted by Fouquet *et al.*, women (N.=193) reported an average of 7.41 hours per week of missed work when symptoms were at their worst, and work-related losses of 13% due to absenteeism, 65% due to presenteeism, and 64% from decreased work productivity, as measured on the Work Productivity and Activity Impairment Questionnaire.<sup>38</sup> Endometriosis neg-



actively impacts women's careers, forcing them to take a break from work, opt for a part-time job, miss promotion opportunities, give up a favorite job, or choose a less stressful job.<sup>39,40</sup> Women in the youngest age more frequently report having given up or dropped out of education or job due to their endometriosis compared with the older age groups.<sup>14</sup>

Facchin *et al.* compared the employment status (having vs. not having a job) and the association between pelvic pain and employment status in 298 consecutive endometriosis patients and in 332 women without a history of endometriosis (control group). Women with symptomatic endometriosis were significantly less likely to be employed compared with women without endometriosis (OR=0.35 [95% CI: 0.18-0.65]) or women with asymptomatic endometriosis (OR=0.36 [95% CI: 0.17-0.79]) No significant differences emerged between asymptomatic endometriosis and the control group. Unemployed women with endometriosis had a greater severity of dysmenorrhea, dyspareunia, chronic pelvic pain, and dyschezia compared with employed women with endometriosis.<sup>41</sup>

Notably, women often do not inform employers of their diagnosis or symptoms for a range of reasons including the potential implications of this and because they find it difficult to discuss a private and gender specific condition.<sup>42</sup> The disruptive impact of endometriosis has negative consequences not only for the psychological and physical well-being of women, but also for the economic costs of the disease for patients, employers and society.<sup>41</sup> Women with endometriosis not only have significantly higher direct health costs (hospital and outpatient costs, drug treatments and other health services), as well as indirect costs due to decreased work productivity, sick leave and free time to attend medical appointments, or even job loss due to short- or long-term absenteeism and disability.<sup>11</sup>

As pointed out by Hummelshoj,<sup>43</sup> the costs of treatment represent only one third of the total annual economic burden of endometriosis because two thirds of this cost is caused by the loss of productivity due to pain symptoms. Additionally, as most women may begin to experience endometriosis-related pain during adolescence,

the cumulative impact of endometriosis on employment and career may be greater resulting in a greater economic burden.

### Social life

The diagnosis of endometriosis controls and limits women's lives and the effects on women's social life were one of the most well-known impacts of the disease among age groups.<sup>39</sup> A high proportion of women with endometriosis experience detrimental impact on social functioning as a result of their condition. Women with chronic pelvic pain experienced a reduction in social activities due to pain, bleeding, fatigue and the need for toilet access, or worry about the onset of pain while they were out, leaving them feeling depressed, moody and angry. Women also described feeling less able to socialize when they are out (due to being preoccupied with worry about their condition), resulting in reduced confidence.<sup>4</sup> Approximately half of women with self-reported, surgically diagnosed endometriosis (N.=107) who were enrolled in a long-standing registry expressed perceived physical limitations to social activities. The presence of incapacitating pain or dyspareunia was associated with social impairments in this cohort.<sup>32</sup> Between 23% and 71% of women with endometriosis reported that household and housekeeping activities were affected by their disease, and 45% of women reported a negative effect on childcare.<sup>32</sup> Decreased social interaction and withdrawal from social activities may be a reaction to depression, feelings of isolation, dissatisfaction with body appearance, low self-esteem, or lack of self-confidence.<sup>44</sup> Pain in young adults can lead to loneliness and hopelessness if met with distrust from health care, thus influencing the development of identity.<sup>45</sup> The role of pain in social withdrawal is underscored by results from a web-based questionnaire of Swedish adolescents in which 59% of participants reported avoiding social activities because of dysmenorrhea.<sup>35</sup> In addition, in a cross-sectional web-based survey study, fatigue/weariness/anemia has been shown to correlate with impaired perceived quality of social support as well as self-rated emotional well-being.<sup>46</sup> Women are reluctant to discuss their experienc-



es with others, as they feel their accounts are not always believed leading to feelings of loneliness and isolation.<sup>42</sup>

### Endometriosis and mental health: depression and anxiety

Endometriosis with or without chronic pelvic pain may have a significant association with mental health in women, as exemplified by changes in temperament (mood swings, easily angered) to feelings of distress, depression, anxiety, and negative perceptions of self (low self-esteem, self-consciousness).<sup>39, 47, 48</sup> Women with endometriosis articulate feelings of worthlessness, guilt, and frustration connected with disease-related limitations on participation in daily activities, social functioning, independence, and interpersonal relationships.<sup>44, 47</sup> Frustration may also stem from a woman's inability to manage or predict her pain and the feeling that endometriosis/endometriosis-associated pain controls her life.<sup>49</sup> Negative emotions may be reinforced by the perception that others (even healthcare professionals) consider what they are experiencing to be "all in their heads."<sup>50</sup> These feelings may also be stronger in women with a higher endometriosis symptom burden.<sup>51</sup> In an analysis of comorbidity among women with and without endometriosis, women with the disease were at increased risk of developing depression and anxiety compared with women without disease (Hazard Ratio [HR]=1.5, 95% confidence interval [CI]: 1.4-1.6).<sup>48</sup> According to these data, Chen *et al.* found that endometriosis increased the risk of developing major depression (HR=1.56, 95% CI: 1.24-1.97) and any depressive disorder (HR=1.44, 95% CI: 1.25-1.65) and anxiety disorders (HR=1.44, 95% CI: 1.22-1.70) compared to healthy women.<sup>52</sup> Results from a cross-sectional Italian study evaluating the presence of psychiatric comorbidities among women with endometriosis with and without pelvic pain revealed mental health disorders in 59% of women surveyed (N.=134); some of these issues included somatoform disorder, panic and other anxiety disorders, major and other depressive disorders, and eating disorders.<sup>51</sup> Women positive for a psychiatric disorder were significantly more

likely to report severe endometriosis-associated pain than were women with a negative screening result (53% vs. 22%; P=0.003). The presence of mental health disorders was not significantly associated with the need for surgery, number of interventions, or infertility.<sup>51</sup> Similar results were reported in a case-control study in which women with surgically diagnosed endometriosis and healthy controls were evaluated for the presence of psychiatric disorders. Cavaggioni *et al.* reported that women with endometriosis had a higher prevalence of any depressive (18.9 versus 9.3%) and anxiety disorders (29.7 versus 7.0%) than controls.<sup>53</sup>

There is still no agreement on the origin of this evident correlation. Some authors showed that depression and anxiety may be the result of the experience of pelvic pain itself rather than of endometriosis since the rate of these psychological disorders was not different between women with endometriosis-related pelvic pain and those with pelvic pain of another nature.<sup>54, 55</sup> However, even when rates of depression and anxiety appeared to be higher for women with endometriosis-related pain, the causal direction could not be identified. Anyway, a mutual relationship between pelvic pain and emotional function has been highlighted; anxiety and depression increase pain perception, and pain can compromise the psychological state in a vicious circle.<sup>2, 53</sup> Depression negatively affects different aspects of QoL such as relationships, sex, work, and even sleep quality. Poor sleep quality (reduction of total sleep time, frequent awakenings, and difficulty falling asleep) can in turn negatively affect the ability to perform daily functional activities in women with endometriosis. Moreover, poorer and poorer sleep can lead to an exacerbation of pelvic pain, and this negatively affects the QoL.<sup>56</sup> The association between sleep quality and depression is probably two-way, with poor sleep quality worsening mood and depression which in turn affects sleep.<sup>57</sup>

Facchin *et al.* reported several correlations between endometriosis-related factors and mental health in 210 Italian women with clinical or surgical diagnosis of endometriosis, showing that lower self-esteem, body esteem and emotional self-efficacy were associated with poorer mental

health.<sup>9</sup> These collective findings on the psychological well-being of women with endometriosis are consistent with other conditions involving chronic pain, such as chronic back pain or migraines.<sup>1, 58</sup>

### Endometriosis and sexual function

The sexual response is a psychophysiological experience. It is a sequence of physiological events, including sexual desire, arousal and genital responses.<sup>8</sup> 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.<sup>59</sup> Therefore, a global approach has been proposed in the Diagnostic and Statistical Manual of Mental Disorders (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 genitopelvic 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.<sup>60</sup> 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. 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.<sup>8, 60</sup>

Female sexuality can be negatively influenced by numerous factors, such as psychiatric and psychological dysfunctions, chronic diseases, endocrine disorders, drug use, and operative vaginal delivery. Moreover, women who are affected by chronic inflammatory gynecological diseases such as endometriosis may report sexual dysfunctions.<sup>7</sup> Endometriosis is also associated with a 9-fold increased risk of deep dyspareunia: the presence of endometriotic lesions infiltrating the posterior vaginal fornix, the pouch of Douglas, the uterosacral ligaments, and the rectum – known as deep infiltrating endometriosis (DIE) – causes pain at intercourse due to mechanical pressure on lesions occurring during coitus or due to traction of scarred and inelastic endometriotic tissue.<sup>61</sup> Because the disease afflicts about 5% to 10% of reproductive-age women,<sup>62</sup> it is reasonable to suppose that at least 2% to 4% of all sexually active women may experience painful intercourses due to endometriosis. As demonstrated by several studies pain during intercourse is frequently associated with a wide range of different sexual dysfunctions, such as hypoactive sexual desire, lubrication, arousal, and orgasm disorders.<sup>7, 63, 64</sup> Moreover, fear and anticipation of pain, resulting from repeated painful sexual experiences, represent powerful inhibitors of the sexual response cycle.<sup>65</sup> Endometriosis-related dyspareunia may negatively affect women's lives to the point that some participants were completely avoiding sexual activity, with decreased self-esteem and quality of couple relationships.<sup>8</sup>

### Studies on sexual dysfunctions in women with endometriosis

Studies comparing sexual outcomes in women with endometriosis *versus* healthy women or women without endometriosis, showed a significantly worse sexual functioning in the endometriosis population.<sup>7</sup> Tripoli *et al.* investigated sexual satisfaction in 84 women having chronic



pelvic pain (CPP) with or without endometriosis versus 50 healthy controls.<sup>54</sup> Sexual functioning was assessed using the GRISS questionnaire, a psychometric instrument focused on frequency of relations, sexual communication, sexual satisfaction, sexual aversion, lack of expression of sensuality, vaginismus, and anorgasmia. Of the 84 participants with CPP, 40% were sexually unsatisfied and reported decreased frequency of sexual intercourses, reduced expression of sensuality, and higher rates of sexual aversion. No significant differences were found between the 2 CPP conditions (with and without endometriosis).<sup>54</sup> As regards the prevalence of sexual dysfunctions in women with endometriosis, in a multicenter cohort study on 125 women with endometriosis and dyspareunia lasting for at least 6 months, sexual dysfunction and sexual distress were found in 32% and 78% of participants, respectively.<sup>66</sup> Interestingly, 30% of patients referred that the primary motivation for sexual intercourse was just to try to conceive, whereas 46% of women reported that they were willing to tolerate pain at intercourse in order to satisfy their partner and avoid conflicts. There were significant correlations between female sexual dysfunctions and pain intensity during or after intercourse, sense of guilt toward the partner, and fewer feelings of femininity, whereas no significant associations were found with DIE.<sup>66</sup> Women with endometriosis perceived the frequency of sexual contacts significantly more often as “too low” than the control women (42.3 vs. 30.5% respectively;  $P < 0.001$ ). There was also a significantly lower frequency in preliminary performance (“never” 31.3%, vs. 26.6% respectively;  $P = 0.003$ ).<sup>10</sup> Other studies showed significantly decreased sexual functioning in women with endometriosis relative to the control/comparison group.<sup>54, 64, 65, 67</sup>

Jia *et al.* investigated the factors associated with the presence of sexual dysfunctions in women with endometriosis.<sup>68</sup> In their study on 111 women with endometriosis, the prevalence of sexual dysfunction was 73%, and 3 potential predictors of dysfunctions were identified: pelvic pain intensity, presence of DIE, and advanced American Society for Reproductive Medicine classification stages.<sup>69</sup>

Vercellini *et al.* evaluated sexual functioning and deep dyspareunia in 100 women with rectovaginal endometriosis, 100 women affected by peritoneal and/or ovarian endometriosis, and 100 women without endometriosis.<sup>64</sup> Items of the self-assessment questionnaire of sexual functioning (SRS) measured sexual interest, sexual activity, sexual satisfaction, experience of sexual pleasure, orgasm capacity, and sexual relevancy. Women with endometriosis (either rectovaginal or peritoneal/ovarian endometriosis) reported worse sexual functioning relative to women without endometriosis, although with marginal differences. The majority of participants with endometriosis experienced deep dyspareunia (67% in the rectovaginal group, 53% in the peritoneal/ovarian group vs. 26% in women without endometriosis), but no statistically significant differences were observed between women with different localization of endometriosis (rectovaginal or peritoneal/ovarian).<sup>64</sup> Surprisingly, the severity of dyspareunia did not affect overall sexual functioning in women with endometriosis. A possible explanation of this unexpected finding was that because female sexuality is a multidimensional phenomenon and includes psychological processes, the effect of dyspareunia could have been diluted by other factors, such as degree of couple intimacy, coping capacity, personality traits, marital adjustment, and partner support.

In contrast to previous data Mabrouk *et al.*, in a more recent observational study, founded that women with DIE experienced deep dyspareunia more frequently (85.2%) than women with isolated ovarian endometriosis (70.9%).<sup>70</sup> In addition, previous studies have correlated the presence of dyspareunia with the presence of DIE, specifically of the uterosacral ligaments resulting in a significant reduction in QoL and sexual function. Indeed, Ferrero *et al.* demonstrated that among subjects with deep dyspareunia, those with DIE of the uterosacral ligaments have the most severe impairment of sexual function. The authors investigated the quality of sexual life in 309 women having deep dyspareunia by comparing 3 conditions: DIE of the uterosacral ligaments, endometriosis without deep infiltrating lesions of the uterosacral ligaments, and a con-



control group composed of women without endometriosis.<sup>71</sup> The prevalence of deep dyspareunia was significantly higher in the 2 endometriosis groups (60.6%) compared with controls (34.9%). Women with DIE of the uterosacral ligaments exhibited the most severely impaired sexual functioning, with higher pain scores, reduced number of intercourses per week, and a less satisfying orgasm and felt less relaxed and fulfilled after sex than the other 2 groups. The presence of bilateral uterosacral ligament lesions did not affect symptom severity.<sup>71</sup> A cross-sectional study by Montanari *et al.*, investigating the specific sexual impact of different endometriosis symptoms and types of lesions in women with DIE, revealed that dyspareunia and vaginal nodules were significantly associated with poorer sexual functioning.<sup>63</sup>

The authors have assessed sexual function with SHOWQ scores and health related QoL through SF36 in particular in women with DIE. They founded a significant correlation between the SF36 scores and the SHOWQ scores ( $P < 0.0001$ ). Overall, women showed impaired sexual functioning and satisfaction was the most affected dimension, followed by orgasm; 61.5% of patients with DIE indicated a low frequency of sexual intercourse, whereas 71.4% reported remarkable interference of their pelvic problems with sexual activity.<sup>63</sup>

Evangelista *et al.* reported high prevalence of dyspareunia in 75% of women with DIE *versus* 34% in healthy controls.<sup>72</sup> Patients with DIE reported greater pain at intercourse (*i.e.*, the pain domain of the FSFI questionnaire), although with no effects on the overall sexual functioning (*i.e.*, the FSFI global score). Di Donato *et al.* used the SHOW-Q to evaluate sexual functioning in 182 women with DIE *versus* 182 healthy women.<sup>65</sup> Women with DIE exhibited greater sexual impairment in all sexual functioning domains (satisfaction, desire, orgasm, and pelvic problem interference with sex) relative to healthy controls; 58% of participants in the DIE group (*vs.* only 1% in the control condition) reported that pelvic pain severely affected their sexual functioning. Sexual desire was absent or experienced less than 1 or 2 times per month in 45% of patients with DIE relative to 14% of

healthy controls.<sup>65</sup> These data show that DIE is the type of endometriosis most associated with dyspareunia and so with impaired sexual function.<sup>73</sup> Furthermore, deep dyspareunia was associated with worse sexual QoL in women with endometriosis independently of other confounders.<sup>74</sup>

When considering the relation between deep dyspareunia and sexual QoL, it is fundamental to take into account potential confounders that can affect sexual function, such as superficial dyspareunia, other types of pelvic pain, psychological comorbidities, and concurrent pain diagnoses.<sup>75</sup> Either individual factors (such as self-esteem) or relational variables (such as the quality of intimate relationships) may shape the way in which each woman experiences endometriosis and sexual activity. In addition to dyspareunia, the mental health can also compromise sexual activity. Depression has been associated with impairment of sexual QoL in terms of sexual desire, sexual arousal, sexual cognition, and orgasmic functions.<sup>2</sup> Nondistressed women were still enjoying their sexuality despite endometriosis (for instance, they had been able to find comfortable and painless sexual positions), while distressed women with clinically significant symptoms of anxiety and depression were totally avoiding any type of sexual activity due to not only pain but also overwhelming concerns about infertility and lack of support from partners.<sup>5</sup>

These findings suggest that there may be a mutual complex interaction between psychological distress, which is associated with pelvic pain (especially chronic, nonmenstrual pelvic pain), and sexual dysfunction. Thus, the high proportion of endometriosis-related sexual problems may be not only due to coital pain caused by endometriosis-related anatomical distortion or pelvic inflammation but also due to psychosocial factors, including emotional distress associated with the disease and quality of intimate relationships. Women with endometriosis may experience remarkable sexual impairment, with potential negative consequences on their psychological and physical health and QoL, especially if one considers the chronic nature of the disease and its association with infertility. Sexual health is a highly important aspect of QoL: sexual health

should be part of any clinicians' assessments and the improvement of sexual QoL should be considered as a purpose of treatment.<sup>2</sup>

### Partner's physiological and sexual perspective: relationship consequences

Endometriosis may negatively affect women's relationships,<sup>76</sup> to the point of leading to a relationship breakup in 8-10% of women.<sup>77</sup> In an international cross-sectional survey conducted by De Graaff *et al.*, 34% of 931 participants declared significant problems with their partner caused by endometriosis, and 10% of women considered endometriosis as a cause of their divorce.<sup>77</sup> 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.<sup>78</sup> Previous investigations have documented strain on social relationships, including reduced social support and various relationship difficulties. Reduced socialization due to disease and the inability of partners to tolerate chronic symptoms has been attributed to relationship breakdowns or divorces.<sup>8</sup> Women with endometriosis often identify their partners as the most important source of support, however those with symptoms of anxiety and depression perceive less support from partners than women with good psychological health.<sup>79</sup>

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.

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.<sup>64, 80</sup>

As regards the impact of endometriosis on sexuality, research has provided contradictory

findings. Sexual activity in couples living with endometriosis can be rare or even non-existent.<sup>76</sup> In the Ameratunga *et al.* study, partners who felt that their relationship had been affected by endometriosis were more likely to report that their sex life had also been affected.<sup>81</sup> In the Hammerli *et al.* study, a 33-item questionnaire (that also included selected questions from the Brief Index of Sexual Functioning and the Sexual History Form) was used to collect information regarding sexual satisfaction and desire, type and frequency of sexual activity, sexual limitations (including the role of dyspareunia), and options to overcome sexual problems in 236 male partners of women with endometriosis, compared with 236 partners of women without the condition.<sup>82</sup> Among partners of women with the disease, 75% of participants reported changes in sexuality due to endometriosis; these participants were also more likely to be unsatisfied with the sexual relationship and showed lower frequency of sexual intercourse and other types of partnered sexual activities than partners of women without endometriosis. Dyspareunia was more frequently reported as a cause of sexual impairment by the partners of women with endometriosis compared with the partners of women without the disease.<sup>82</sup>

In another study of 83 endometriosis patients and 74 partners, De Graaff *et al.* found no significant differences regarding male sexual function (assessed using a 15-item questionnaire, the International Index of Erectile Function) and overall satisfaction between partners of women with endometriosis and partners of women without the disease. However, the partners of women with endometriosis were more likely to report to have less intercourse than desired for taking into account women's wishes and pain symptoms.<sup>67</sup> On the other hand, qualitative and semi-qualitative studies revealed that partners can be hesitant to initiate sexual activity with their loved one because they are aware that sex can be painful for her.<sup>76</sup> Overall, the negative consequences of the disease on women's physical and psychological conditions (not only pain, but also fatigue, treatment effects, infertility, low mood, and poor sense of femininity) have an impact on sexuality, and partners' reactions are characterized by ac-



ceptance and understanding, along with feelings of loss and dissatisfaction.<sup>76</sup>

The consequences of endometriosis on partners including also the impact of the disease on daily life, finances, and work productivity, contribute to further understanding of the potentially devastating effect of the disease.

The importance of investigating the partners experience of people with chronic diseases is well known in the literature, as well as the fact that coping with the disease is not an individual process but of social interaction.<sup>76</sup> However, only a few studies included partners of women with endometriosis as a unit of analysis. Male partners of women with endometriosis are often reluctant to share their feelings with women and even with researchers, which may lead to isolation and lack of support.<sup>83</sup> On the one hand, disclosing feelings and emotions is not consistent with cultural expectations related to traditional ideas of masculinity, according to which men have to appear strong and stoical. On the other hand, male partners may tend to minimize their own sufferance for fear of appearing selfish, but also to protect women, who are already experiencing intense physical and psychological pain, from further emotional burden.<sup>83</sup> Anger towards doctors is common among partners. This feeling partly derives from partners' frustration for the absence of a definitive cure, for ineffective medical treatments and repeated surgical interventions.<sup>83</sup> However, partners often feel excluded by health professionals, who are not very likely to consider their emotions and to engage them in the decision-making process.<sup>81, 83</sup> Partners play an essential role for women with endometriosis, and women's perceptions of partner's support may shape their emotional reactions to the disease.<sup>76</sup> Stressed partners may not be able to provide adequate support to women, and for this reason, health professionals should give more attention to partners and engage them in the decisionmaking processes. Furthermore, partners receive little information regarding endometriosis and its consequences on the couple.<sup>81</sup> As reported by Ameratunga *et al.*, only 34% of partners felt engaged and supported by health professionals, and 80% reported that no information was provided regarding the impact of the disease on

couples. In this study study, 70% of partners reported that endometriosis had affected their daily life either moderately or severely.<sup>81</sup> Van Niekerk *et al.* performed dyadic analyses of data related to emotional intimacy, empathic concern, psychological health, and relational satisfaction in 60 women with endometriosis and their partners. The findings revealed that partner emotional intimacy and empathic concern had an impact on women's and partners' relationship satisfaction.<sup>84</sup> In this regard, there is evidence that including partners in the healthcare process, for instance by providing psychoeducational programs, may increase patients' engagement, which is associated with reduced costs and improved QoL in the context of chronic disease.<sup>76</sup> The disease, as well as treatment decisions, has an impact on partners' everyday life, because they may have to take over additional tasks when women have debilitating symptoms, or are recovering from surgery. When partners are able to take the role of caregiver, they provide different types of support (either practical or emotional) to women, which may affect family organization and work productivity. In this regard, partners are also affected by the economic burden of endometriosis (although less than women), especially when women are no longer able to work due to the disease.<sup>81, 83</sup> Despite all the difficulties related to endometriosis, the partners reported experiences of personal and relational growth, feelings of acceptance and stated that coping with endometriosis as a couple increased the sense of closeness to the spouse. In Culley *et al.* study, partners reported that living with a woman with endometriosis made them more understanding and able to listen and provide support, as well as increasing the strength of the intimate relationship.<sup>83</sup>

### **Endometriosis and infertility: the impact on sexuality and psychological well-being**

Infertility is defined as the incapacity for a couple to conceive after at least 6months for women over 35 years, or 12 months for those under the age of 35, always considering regular unprotected sexual intercourse.<sup>85</sup> A correlation between endometriosis and infertility is largely known: recent data suggest that up to 50% of women



with infertility may suffer from endometriosis, with about 16-40% of women with endometriosis experiencing difficulty conceiving.<sup>85</sup>

However, it is difficult to identify a specific cause due to the multiple complex mechanisms that could be involved in the etiopathogenesis of the disease and the variety of clinical presentations. The presence of endometriotic tissue can create a pro-inflammatory environment which in turn determines a mechanical alteration of the pelvis that could affect not only the fallopian tubes, the eutopic endometrium but also the gametes and the transport of the embryo. Additionally, patients with endometriosis are more at risk of ovarian tissue damage and compromise of the ovarian reserve which can be a possible cause of infertility. This is particularly true in patients with ovarian-localized endometriosis who have undergone multiple surgical procedures.<sup>86</sup>

For these women, the experience of infertility adds to the burden of endometriosis, negatively affecting psychological health, social interactions (avoiding friends and relatives with children), and financial status (due to fertility treatment) as well as causing feelings of stigmatization and hopelessness.<sup>39, 47</sup> Additionally, some young women with endometriosis worry about finding a partner who will be accepting of possible infertility,<sup>19</sup> considering that this condition itself plays an important role in influencing psychological well-being within the couple. Indeed, studies showed that the incapacity of procreating is extremely distressing for both the individual and the couple.<sup>85, 87</sup> In several cases, this can subsequently result in loss of self-esteem, impairment of sexual function, low mood and depression, anxiety, increased levels of frustration and guilt, relational difficulties within the couple.<sup>85</sup> In addition, it is recognized that psychological factors could also affect the success rate of fertility treatments, creating a vicious cycle of worsening mental health.<sup>85</sup>

With the increased risk for infertility, family planning is of considerable concern to women with endometriosis. Women with debilitating pain may face the difficult decision between treatment for pain relief and delaying or foregoing pregnancy (for those who undergo hysterectomy).<sup>88</sup> In interviews conducted as part of the

ENDOPART study in the UK, 18 of 22 couples reported that endometriosis affected their plans to have children.<sup>88</sup> Some couples reported having children earlier than they had planned because there was potential for future infertility. Indeed, some healthcare providers counsel women to begin planning a family at a younger age because of their endometriosis and risk of infertility, which may induce anxiety associated with premature fertility choices.<sup>44</sup> Therefore, taking into account the potential negative impact of endometriosis and infertility on the mental well-being of the couple, it is crucial to offer an appropriate multidisciplinary management, including early psychological support and counseling from sexologists.

#### **Patient quality of life and sexual function after medical and surgical treatment for endometriosis**

Endometriosis treatment options include hormonal therapies in order to achieve a hypo-oesrogenic status, pain relieving agents or surgical removal of endometriotic implants. Medical therapy represents the first line of treatment, able to improve symptoms or prevent the recurrence of the post-surgical disease. This therapy does not eradicate the disease and increase fertility or resolve endometriomas or deeply infiltrating diseases, and lesions and symptoms commonly reappear upon discontinuation of therapy. The aim of the surgical approach is the excision of all visible lesions to obtain a maximum effect regarding pain relief and increase in fertility. Surgery may be associated with peri- and post-operative complications and also confers recurrence of disease even in optimally resected case. Despite all of the available treatments should be considered suppressive rather than curative. It is important to highlight the potential of medical and surgical therapy as a response to improving sexual symptoms and QoL. Among the hormonal therapies used for clinical treatment of endometriosis is Dienogest (DNG), a synthetic progestin that is currently used with a dose of 2 mg daily. The steroid also has direct antiproliferative, immunologic and antiangiogenic activities that contribute to the reduction of endome-

triosis-associated symptoms and exhibits highly selective binding to the progesterone receptor.<sup>89</sup> Caruso *et al.* evaluated the effects of DNG on QoL, and sexual function of women affected by endometriosis pain. Fifty-four women taking 2 mg/daily DNG (study group) were compared with 48 women were given non-steroidal anti-inflammatory drugs (control group). The Short Form-36 (SF-36), the Female Sexual Function Index (FSFI) and the Female Sexual Distress Scale (FSDS) were used to assess the QoL, the sexual function and the sexual distress, respectively. At the three-month follow-up, women reported QoL improvements in some functions; at the six-month follow-up, they reported improvement in all categories ( $P < 0.001$ ). The FSFI and FSDS scores both improved with respect to the baseline at the second follow-up. No change was observed in the control group.<sup>90</sup> Subsequently the same authors extended the follow-up period and confirmed the positive effects of the drug on pain; they showed a gradual and continuous improvement of QoL and sexual function and a reduction of sexual distress starting from the 6th month follow-up until the 24-month follow-up. Furthermore, the improvements are stable until 24 months.<sup>91</sup> The progressive reduction of the pain syndrome reported by women over the treatment period could contribute to improve the QoL and sexual life of women on DNG.<sup>91</sup>

Leonardo-Pinto *et al.* assessed sexual function and dyspareunia after a long-term treatment with dineogest in 30 women diagnosed with DIE (intestinal and posterior fornix). After 12-month treatment, dyspareunia showed a decrease of intensity and an improvement on FSFI Index was accomplished. Despite the improvement in sexual function after 12 months of DNG usage, it was not enough to completely restore sexual function, considering a FSFI Index cut-off of  $< 26.55$  that is usually accepted for diagnosis of female sexual dysfunction.<sup>92</sup> Although DNG is known to have antiandrogenic activity which could affect the libido of long-term users, recent studies showed that the quality of sexual life, particularly, improve during 6 months of DNG treatment of women with endometriosis.<sup>93</sup> The low antiandrogenic effect showed by DNG on sexual desire could be due to psychosexual

well-being related to the decrease in pain. DNG is believed to be a promising therapy which possibly implies in QoL enhancement. Sansone *et al.* evaluated the effects of an alternative way of delivering progestogens -the etonogestrel (ENG) implant- on pelvic pain, QoL, and sexual function in women requiring long-term reversible contraception and presenting ovarian cysts of probable endometriotic origin. After 12 months, the bodily pain, general health, vitality, social functioning, and mental health domains of the QoL score were significantly improved. The total FSFI score results increased in comparison with baseline both at 6 and 12 months. In particular, the authors highlighted a significant improvement in desire, satisfaction, and pain domains already at 6 months; the arousal domain improved only after 12 months.<sup>94</sup>

In recent years, the use of the levonorgestrel-releasing intrauterine device (IUD-LNG) in women with endometriosis has been shown to provide a significant reduction of endometriosis related pain symptoms and deep dyspareunia in patients with recto-vaginal endometriosis, comparable to the effect achieved by gonadotropin-releasing hormone (GnRH) analogues.<sup>95</sup> A randomized clinical trial of 103 women with chronic pelvic pain and dysmenorrhea due to endometriosis compared the LNG-IUD with the etonogestrel-releasing contraceptive implant over 180 days. Both contraceptives improved significantly the mean visual analogue scale endometriosis-associated pelvic pain and dysmenorrhea, without significant differences between treatment group profiles. HRQoL improved significantly in all domains of the EHP-30 questionnaire.<sup>96</sup> A recent meta-analysis concluded that the LNG-IUD was as effective in pain relief as gonadotropin-releasing hormone analogues and prevented recurrent dysmenorrhea postoperatively in women with diagnosed endometriosis.<sup>97</sup>

The review of Fritzer *et al.* evaluated the effects of surgical excision of endometriotic lesions on dyspareunia after surgery. All included studies showed a significant postoperative improvement in pain during intercourse after a follow-up period of 10 up to 60 months. A reduction in dyspareunia and an improvement in sexual activity are observed 12 months after complete



excision of endometriosis. Besides, sexual satisfaction has increased, and sexual problems have decreased significantly. QoL and mental health also improved significantly. Surgical excision of endometriosis is a feasible and good treatment option for pain relief and improvement of quality of sex life in symptomatic women with endometriosis.<sup>98</sup>

A multicenter cohort study found significant sexual pain relief and an improvement in all QoL scores as early as 6 months after laparoscopic treatment for women with endometriosis; furthermore, these improvements remained stable over a 3-year period of postoperative follow-up. This evolution was observed in patients receiving postoperative medical treatment in addition to surgery and in the surgery-only group. As regards the physical component, the most favorable postoperative results concerned the domains of role limitations due to physical problems and bodily pain, whereas improvements in the domains of social functioning and role limitations due to emotional problems for the mental component were much less. Improvement later plateaus and remains stable, allowing patients to experience the beneficial effects over a period of years.<sup>99</sup> Martinez-Zamora *et al.* demonstrated an improvement in sexual QoL and HRQL in patients with DIE undergoing complete laparoscopic endometriosis resection and these findings were comparable to those of healthy women at 6 months after surgery. Nonetheless, there was a partial decline in this improvement at 36 months of follow-up.<sup>100</sup> Vercellini *et al.* investigated which treatment – medical *versus* surgical – for severe profound dyspareunia related with endometriosis was able to achieve better results in terms of patient satisfaction, variation in coital pain and frequency of sexual intercourse.<sup>61</sup> Both strategies are effective in relieving endometriosis-associated deep dyspareunia, although with a different temporal trend, and with a greater improvement in the medical therapy group at the end of the follow-up period. Excision of lesions is followed by a rapid and substantial decrease in pain, with short- and medium-term advantage over medical treatment, but a gradual recurrence of the symptom after 6 months since surgery. The pain relief effect of the progestin

was more gradual, but progressive throughout the study period. At a 12-month follow-up, the frequency of intercourse per month (mean±SD) was 4.6±1.8 in the surgery group and 5.3±1.5 in the norethisterone acetate group (P=0.02). A total of 43% of women were satisfied in the surgery group compared with 59% in the progestin group (adjusted odds ratios [OR]=0.36; 95% CI: 0.16-0.82; P=0.015). This difference was much more marked in women without rectovaginal endometriotic lesions (33% *versus* 63%, adjusted OR=0.23; 95% CI: 0.07-0.76, P=0.02).<sup>61</sup> There are few data in the literature on the influence of medical and surgical treatments on psychiatric comorbidities associated to endometriosis. Although there are promising results on both hormone and surgical therapy in the improvement of psychiatric symptoms, further studies are needed.

## Conclusions

Endometriosis is a chronic gynecological condition affecting a large portion of the world's female population of childbearing age with a negative impact on women's quality of life and psychological health. Painful endometriosis involves remarkable limitations in everyday activities, including education and work; women suffer from dysmenorrhea as well as chronic pelvic pain and this affects work, leisure, and social and love relationships. Pain-related to endometriosis also affects the psychological aspect, compromising the quality of sleep, making women anxious and depressed. Dyspareunia is one of the cardinal symptoms of the pathology and the impact of endometriosis on sexual life is very relevant. Sexual pain in endometriosis patients induces a fear-avoidance reaction, leading to arousal/desire disorder and sexual distress in the majority of patients. Dyspareunia, female sexual dysfunction and associated infertility may disrupt the relationship with the partner and his/her sexual functioning, especially in young couples. The costs of endometriosis should not be underestimated, both in terms of treatment and loss of productivity of the woman due to the disease. In this specific long-term vision of patient-centered endometriosis care, aspects of quality of life and



sexual health play a key role and should always be evaluated with any patient as part of a multidisciplinary management.

## References

- Missmer SA, Tu FF, Agarwal SK, Chapron C, Soliman AM, Chiuye S, *et al.* Impact of endometriosis on life-course potential: A narrative review. *Int J Gen Med* 2021;14:9–25.
- Della Corte L, Di Filippo C, Gabrielli O, Reppuccia S, La Rosa VL, Ragusa R, *et al.* The burden of endometriosis on women's lifespan: A narrative overview on quality of life and psychosocial wellbeing. *Int J Environ Res Public Health* 2020;17:4683.
- Luisi S, Pizzo A, Pinzauti S, Zupi E, Centini G, Lazzeri L, *et al.* Neuroendocrine and stress-related aspects of endometriosis. *Neuroendocrinol Lett* 2015;36:15–23.
- Culley L, Law C, Hudson N, Denny E, Mitchell H, Baumgarten M, *et al.* The social and psychological impact of endometriosis on women's lives: a critical narrative review. *Hum Reprod Update* 2013;19:625–39.
- Facchin F, Saita E, Barbara G, Dridi D, Vercellini P. "Free butterflies will come out of these deep wounds": A grounded theory of how endometriosis affects women's psychological health. *J Health Psychol* 2018;23:538–49.
- Laganà AS, La Rosa VL, Rapisarda AM, Valenti G, Sapia F, Chiofalo B, *et al.* Anxiety and depression in patients with endometriosis: impact and management challenges. *Int J Womens Health* 2017;9:323–30.
- Barbara G, Facchin F, Buggio L, Somigliana E, Berlanda N, Kustermann A, *et al.* What Is Known and Unknown About the Association Between Endometriosis and Sexual Functioning: A Systematic Review of the Literature. *Reprod Sci* 2017;24:1566–76.
- Pluchino N, Wenger JM, Petignat P, Tal R, Bolmont M, Taylor HS, *et al.* Sexual function in endometriosis patients and their partners: effect of the disease and consequences of treatment. *Hum Reprod Update* 2016;22:762–74.
- Facchin F, Barbara G, Dridi D, Alberico D, Buggio L, Somigliana E, *et al.* Mental health in women with endometriosis: searching for predictors of psychological distress. *Hum Reprod* 2017;32:1855–61.
- Bernays V, Schwartz AK, Geraedts K, Rauchfuss M, Wölfler MM, Haerberlin F, *et al.* Qualitative and quantitative aspects of sex life in the context of endometriosis: a multicentre case control study. *Reprod Biomed Online* 2020;40:296–304.
- Soliman AM, Surrey E, Bonafede M, Nelson JK, Castelli-Haley J. Real-World Evaluation of Direct and Indirect Economic Burden Among Endometriosis Patients in the United States. *Adv Ther* 2018;35:408–23.
- Marinho MC, Magalhaes TF, Fernandes LF, Augusto KL, Brilhante AV, Bezerra LR. Quality of Life in Women with Endometriosis: An Integrative Review. *J Womens Health (Larchmt)* 2018;27:399–408.
- Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992;30:473–83.
- Lökvist L, Boström P, Edlund M, Olovsson M. Age-related differences in quality of life in Swedish women with endometriosis. *J Womens Health (Larchmt)* 2016;25:646–53.
- Gandek B, Ware JE, Aaronson NK, Apolone G, Bjorner JB, Brazier JE, *et al.* Cross-validation of item selection and scoring for the SF-12 Health Survey in nine countries: results from the IQOLA Project. International Quality of Life Assessment. *J Clin Epidemiol* 1998;51:1171–8.
- Harper A, Power M, Orley J, Herrman H, Schofield H, Murphy B, *et al.*; The WHOQOL Group. Development of the World Health Organization WHOQOL-BREF quality of life assessment. *Psychol Med* 1998;28:551–8.
- Bourdel N, Chauvet P, Billone V, Douridas G, Fauconier A, Gerbaud L, *et al.* Systematic review of quality of life measures in patients with endometriosis. *PLoS One* 2019;14:e0208464.
- EuroQol Group. EuroQol—a new facility for the measurement of health-related quality of life. *Health Policy* 1990;16:199–208.
- Rush G, Misajon R. Examining subjective wellbeing and health-related quality of life in women with endometriosis. *Health Care Women Int* 2018;39:303–21.
- Gilmour JA, Huntington A, Wilson HV. The impact of endometriosis on work and social participation. *Int J Nurs Pract* 2008;14:443–8.
- Soliman AM, Coyne KS, Gries KS, Castelli-Haley J, Snabes MC, Surrey ES. The effect of endometriosis symptoms on absenteeism and presenteeism in the workplace and at home. *J Manag Care Spec Pharm* 2017;23:745–54.
- Gerlinger C, Schumacher U, Wentzack R, Uhl-Hochgräber K, Solomayer EF, Schmitz H, *et al.* How can we measure endometriosis-associated pelvic pain? *J Endometr* 2012;4:109–16.
- Thong IS, Jensen MP, Miró J, Tan G. The validity of pain intensity measures: what do the NRS, VAS, VRS, and FPS-R measure? *Scand J Pain* 2018;18:99–107.
- Pokrzywinski R, Soliman AM, Chen J, Snabes MC, Taylor HS, Coyne KS. Responsiveness Evaluation and Recommendation for Responder Thresholds for Endometriosis Health Profile-30: Analysis of Two Phase III Clinical Trials. *J Womens Health (Larchmt)* 2020;29:253–61.
- ter Kuile MM, Brauer M, Laan E. The Female Sexual Function Index (FSFI) and the Female Sexual Distress Scale (FSDS): psychometric properties within a Dutch population. *J Sex Marital Ther* 2006;32:289–304.
- 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;5:357–64.
- 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.e1–8, discussion 710.e8–9.
- Jones G, Jenkinson C, Kennedy S. Evaluating the responsiveness of the endometriosis health profile questionnaire: the EHP-30. *Qual Life Res* 2004;13:705–13.
- Jones G, Jenkinson C, Kennedy S. Development of the short form endometriosis health profile questionnaire: the EHP-5. *Qual Life Res* 2004;13:695–704.
- Pessoa de Farias Rodrigues M, Lima Vilarino F, de Souza Barbeiro Munhoz A, da Silva Paiva L, de Alcântara Sousa LV, Zaia V, *et al.* Clinical aspects and the quality of life among women with endometriosis and infertility: a cross-sectional study. *BMC Womens Health* 2020;20:124.
- Chmaj-Wierzchowska K, Rzymiski P, Wojciechowska M, Parda I, Wilczak M. Health-related quality of life (Nottingham Health Profile) in patients with endometriomas: correlation with clinical variables and self-reported limitations. *Arch Med Sci* 2019;16:584–91.

32. Fourquet J, Gao X, Zavala D, Orengo JC, Abac S, Ruiz A, *et al.* Patients' report on how endometriosis affects health, work, and daily life. *Fertil Steril* 2010;93:2424–8.
33. Hansen KE, Kesmodel US, Baldursson EB, Schultz R, Forman A. The influence of endometriosis-related symptoms on work life and work ability: a study of Danish endometriosis patients in employment. *Eur J Obstet Gynecol Reprod Biol* 2013;169:331–9.
34. DiVasta AD, Vitonis AF, Laufer MR, Missmer SA. Spectrum of symptoms in women diagnosed with endometriosis during adolescence vs adulthood. *Am J Obstet Gynecol* 2018;218:324.e1–11.
35. Söderman L, Edlund M, Marions L. Prevalence and impact of dysmenorrhea in Swedish adolescents. *Acta Obstet Gynecol Scand* 2019;98:215–21.
36. Chapron C, Lafay-Pillet MC, Monceau E, Borghese B, Ngô C, Souza C, *et al.* Questioning patients about their adolescent history can identify markers associated with deep infiltrating endometriosis. *Fertil Steril* 2011;95:877–81.
37. Nnoaham KE, Hummelshoj L, Webster P, d'Hooghe T, de Cicco Nardone F, de Cicco Nardone C, *et al.*; World Endometriosis Research Foundation Global Study of Women's Health consortium. Impact of endometriosis on quality of life and work productivity: a multicenter study across ten countries. *Fertil Steril* 2011;96:366–373.e8.
38. Fourquet J, Báez L, Figueroa M, Iriarte RI, Flores I. Quantification of the impact of endometriosis symptoms on health-related quality of life and work productivity. *Fertil Steril* 2011;96:107–12.
39. Moradi M, Parker M, Sneddon A, Lopez V, Ellwood D. Impact of endometriosis on women's lives: a qualitative study. *BMC Womens Health* 2014;14:123.
40. Sperschneider ML, Hengartner MP, Kohl-Schwartz A, Geraedts K, Rauchfuss M, Woelfler MM, *et al.* Does endometriosis affect professional life? A matched case-control study in Switzerland, Germany and Austria. *BMJ Open* 2019;9:e019570.
41. Facchin F, Buggio L, Ottolini F, Barbara G, Saita E, Vercellini P. Preliminary insights on the relation between endometriosis, pelvic pain, and employment. *Gynecol Obstet Invest* 2019;84:190–5.
42. Aerts L, Grangier L, Streuli I, Dällenbach P, Marci R, Wenger JM, *et al.* Psychosocial impact of endometriosis: from co-morbidity to intervention. *Best Pract Res Clin Obstet Gynaecol* 2018;50:2–10.
43. Hummelshoj L. Endometriosis: an old problem without a current solution. *Acta Obstet Gynecol Scand* 2017;96:779–82.
44. Hållstam A, Stålnacke BM, Svensén C, Löfgren M. Living with painful endometriosis - A struggle for coherence. A qualitative study. *Sex Reprod Healthc* 2018;17:97–102.
45. Hiort J, Lindau M, Löfgren M. Young pain patients' experience in primary care. A qualitative study. *Nordic Psychol* 2017;69:83–9.
46. Soliman AM, Coyne KS, Zaiser E, Castelli-Haley J, Fuldeore MJ. The burden of endometriosis symptoms on health-related quality of life in women in the United States: a cross-sectional study. *J Psychosom Obstet Gynaecol* 2017;38:238–48.
47. Roomaney R, Kagee A. Salient aspects of quality of life among women diagnosed with endometriosis: A qualitative study. *J Health Psychol* 2018;23:905–16.
48. Surrey ES, Soliman AM, Johnson SJ, Davis M, Castelli-Haley J, Snabes MC. Risk of Developing Comorbidities Among Women with Endometriosis: A Retrospective Matched Cohort Study. *J Womens Health (Larchmt)* 2018;27:1114–23.
49. González-Echevarría AM, Rosario E, Acevedo S, Flores I. Impact of coping strategies on quality of life of adolescents and young women with endometriosis. *J Psychosom Obstet Gynaecol* 2019;40:138–45.
50. Chauvet P, Guiguet-Auclair C, Comptour A, Denouël A, Gerbaud L, Canis M, *et al.* Feelings and expectations in endometriosis: analysis of open comments from a cohort of endometriosis patients. *J Gynecol Obstet Hum Reprod* 2018;47:281–7.
51. Vannuccini S, Lazzeri L, Orlandini C, Morgante G, Bifulco G, Fagiolini A, *et al.* Mental health, pain symptoms and systemic comorbidities in women with endometriosis: a cross-sectional study. *J Psychosom Obstet Gynaecol* 2018;39:315–20.
52. Chen LC, Hsu JW, Huang KL, Bai YM, Su TP, Li CT, *et al.* Risk of developing major depression and anxiety disorders among women with endometriosis: A longitudinal follow-up study. *J Affect Disord* 2016;190:282–5.
53. Cavaggioni G, Lia C, Resta S, Antonielli T, Benedetti Panici P, Megiorni F, *et al.* Are mood and anxiety disorders and alexithymia associated with endometriosis? A preliminary study. *BioMed Res Int* 2014;2014:786830.
54. Tripoli TM, Sato H, Sartori MG, de Araujo FF, Girão 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.
55. Roth RS, Punch M, Bachman JE. Psychological factors in chronic pelvic pain due to endometriosis: a comparative study. *Gynecol Obstet Invest* 2011;72:15–9.
56. Finan PH, Goodin BR, Smith MT. The association of sleep and pain: an update and a path forward. *J Pain* 2013;14:1539–52.
57. Roberts RE, Duong HT. The prospective association between sleep deprivation and depression among adolescents. *Sleep* 2014;37:239–44.
58. Tunks ER, Crook J, Weir R. Epidemiology of chronic pain with psychological comorbidity: prevalence, risk, course, and prognosis. *Can J Psychiatry* 2008;53:224–34.
59. Ghizzani A, Orlandini C, Bernardi MG, Cevenini G, Luisi S. Sexual pain in women: quality of sex life and marital relations. *Minerva Ginecol* 2017;69:381–9.
60. Thomtén J, Lundahl R, Stigenberg K, Linton S. Fear avoidance and pain catastrophizing among women with sexual pain. *Womens Health (Lond Engl)* 2014;10:571–81.
61. Vercellini P, Somigliana E, Consonni D, Frattaruolo MP, De Giorgi O, Fedele L. Surgical versus medical treatment for endometriosis-associated severe deep dyspareunia: I. Effect on pain during intercourse and patient satisfaction. *Hum Reprod* 2012;27:3450–9.
62. Carlyle D, Khader T, Lam D, Vadivelu N, Shiwlochan D, Yonghee C. Endometriosis Pain Management: a Review. *Curr Pain Headache Rep* 2020;24:49.
63. Montanari G, Di Donato N, Benfenati A, Giovanardi G, Zannoni L, Vicenzi C, *et al.* Women with deep infiltrating endometriosis: sexual satisfaction, desire, orgasm, and pelvic problem interference with sex. *J Sex Med* 2013;10:1559–66.
64. 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;98:1503–11.e1.
65. Di Donato N, Montanari G, Benfenati A, Monti G, Bertoldo V, Mauloni M, *et al.* Do women with endometriosis have to worry about sex? *Eur J Obstet Gynecol Reprod Biol* 2014;179:69–74.
66. Fritzer N, Haas D, Oppelt P, Renner S, Hornung D, Wölfler M, *et al.* More than just bad sex: sexual dysfunction and



distress in patients with endometriosis. *Eur J Obstet Gynecol Reprod Biol* 2013;169:392–6.

67. De Graaff AA, Van Lankveld J, Smits LJ, Van Beek JJ, Dunselman GA. Dyspareunia and depressive symptoms are associated with impaired sexual functioning in women with endometriosis, whereas sexual functioning in their male partners is not affected. *Hum Reprod* 2016;31:2577–86.

68. Jia SZ, Leng JH, Sun PR, Lang JH. Prevalence and associated factors of female sexual dysfunction in women with endometriosis. *Obstet Gynecol* 2013;121:601–6.

69. Canis M, Donnez JG, Guzik DS, Halme JK, Rock JA, Schenken RS, *et al*. Revised American Society for Reproductive Medicine classification of endometriosis: 1996. *Fertil Steril* 1997;67:817–21.

70. Mabrouk M, Del Forno S, Spezzano A, Raimondo D, Arena A, Zanello M, *et al*. Painful Love: Superficial Dyspareunia and Three Dimensional Transperineal Ultrasound Evaluation of Pelvic Floor Muscle in Women with Endometriosis. *J Sex Marital Ther* 2020;46:187–96.

71. 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;83:573–9.

72. Evangelista A, Dantas T, Zendron C, Soares T, Vaz G, Oliveira MA. Sexual function in patients with deep infiltrating endometriosis. *J Sex Med* 2014;11:140–5.

73. Vitale SG, La Rosa VL, Vitagliano A, Noventa M, Laganà FM, Ardizzone A, *et al*. Sexual function and quality of life in patients affected by deep infiltrating endometriosis: current evidence and future perspectives. *J Endometr Pelvic Pain Disord* 2017;9:270–4.

74. Shum LK, Bedaiwy MA, Allaire C, Williams C, Noga H, Albert A, *et al*. Deep Dyspareunia and Sexual Quality of Life in Women With Endometriosis. *Sex Med* 2018;6:224–33.

75. La Rosa VL, De Francis P, Barra F, Schiattarella A, Tropea A, Tesarik J, *et al*. Sexuality in women with endometriosis: a critical narrative review. *Minerva Med* 2020;111:79–89.

76. Facchin F, Buggio L, Saita E. Partners' perspective in endometriosis research and treatment: A systematic review of qualitative and quantitative evidence. *J Psychosom Res* 2020;137:110213.

77. De Graaff AA, D'Hooghe TM, Dunselman GA, Dirksen CD, Hummelshoj L, Simoens S; WERF EndoCost Consortium. The significant effect of endometriosis on physical, mental and social wellbeing: results from an international cross-sectional survey. *Hum Reprod* 2013;28:2677–85.

78. 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;88:914–9.

79. Denny E. Women's experience of endometriosis. In: Denny E, editor. *Routledge International Handbook of Women's Sexual and Reproductive Health*. London: Routledge; 2019.

80. 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;11:1283–93.

81. Ameratunga D, Flemming T, Angstetra D, Ng SK, Sneddon A. Exploring the impact of endometriosis on partners. *J Obstet Gynaecol Res* 2017;43:1048–53.

82. Hämmerli S, Kohl Schwartz AS, Geraedts K, Imesch P, Rauchfuss M, Wölfler MM, *et al*. Does Endometriosis Affect Sexual Activity and Satisfaction of the Man Partner? A Comparison of Partners From Women Diagnosed With Endometriosis and Controls. *J Sex Med* 2018;15:853–65.

83. Culley L, Law C, Hudson N, Mitchell H, Denny E, Raine-Fenning N. A qualitative study of the impact of endometriosis on male partners. *Hum Reprod* 2017;32:1667–73.

84. Van Niekerk LM, Schubert E, Matthewson M. Emotional intimacy, empathic concern, and relationship satisfaction in women with endometriosis and their partners. *J Psychosom Obstet Gynaecol* 2021;42:81–7.

85. La Rosa VL, Barra F, Chiofalo B, Platania A, Di Guardo F, Conway F, *et al*. An overview on the relationship between endometriosis and infertility: the impact on sexuality and psychological well-being. *J Psychosom Obstet Gynaecol* 2020;41:93–7.

86. Carrillo L, Seidman DS, Cittadini E, Meirou D. The role of fertility preservation in patients with endometriosis. *J Assist Reprod Genet* 2016;33:17–23.

87. Vitale SG, La Rosa VL, Rapisarda AM, Laganà AS. Psychology of infertility and assisted reproductive treatment: the Italian situation. *J Psychosom Obstet Gynaecol* 2017;38:1–3.

88. Hudson N, Culley L, Law C, Mitchell H, Denny E, Raine-Fenning N. 'We needed to change the mission statement of the marriage': biographical disruptions, appraisals and revisions among couples living with endometriosis. *Sociol Health Illn* 2016;38:721–35.

89. Harada T, Taniguchi F. Dienogest: a new therapeutic agent for the treatment of endometriosis. *Womens Health (Lond Engl)* 2010;6:27–35.

90. Caruso S, Iraci M, Cianci S, Casella E, Fava V, Cianci A. Quality of life and sexual function of women affected by endometriosis-associated pelvic pain when treated with dienogest. *J Endocrinol Invest* 2015;38:1211–8.

91. Caruso S, Iraci M, Cianci S, Vitale SG, Fava V, Cianci A. Effects of long-term treatment with Dienogest on the quality of life and sexual function of women affected by endometriosis-associated pelvic pain. *J Pain Res* 2019;12:2371–8.

92. Paulo Leonardo-Pinto J, Laguna Benetti-Pinto C, Angerame Yela D. When Solving Dyspareunia Is Not Enough to Restore Sexual Function in Women With Deep Infiltrating Endometriosis Treated With Dienogest. *J Sex Marital Ther* 2019;45:44–9.

93. 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* 2014;183:188–92.

94. Sansone A, De Rosa N, Giampaolino P, Guida M, Laganà AS, Di Carlo C. Effects of etonogestrel implant on quality of life, sexual function, and pelvic pain in women suffering from endometriosis: results from a multicenter, prospective, observational study. *Arch Gynecol Obstet* 2018;298:731–6.

95. Yucl N, Baskent E, Karamustafaoglu Balci B, Goynumer G. The levonorgestrel-releasing intrauterine system is associated with a reduction in dysmenorrhoea and dyspareunia, a decrease in CA 125 levels, and an increase in quality of life in women with suspected endometriosis. *Aust N Z J Obstet Gynaecol* 2018;58:560–3.

96. Carvalho N, Margatho D, Cursino K, Benetti-Pinto CL, Bahamondes L. Control of endometriosis-associated pain with etonogestrel-releasing contraceptive implant and 52-mg levonorgestrel-releasing intrauterine system: randomized clinical trial. *Fertil Steril* 2018;110:1129–36.

97. Song SY, Park M, Lee GW, Lee KH, Chang HK, Kwak SM, *et al*. Efficacy of levonorgestrel releasing intrauterine system as a postoperative maintenance therapy of endometriosis: A meta-analysis. *Eur J Obstet Gynecol Reprod Biol* 2018;231:85–92.

98. Fritzer N, Hudelist G. Love is a pain? Quality of sex life after surgical resection of endometriosis: a review. *Eur J Obstet Gynecol Reprod Biol* 2017;209:72–6.

99. Comptour A, Chauvet P, Canis M, Grémeau AS, Pouly

JL, Rabischong B, *et al.* Patient Quality of Life and Symptoms after Surgical Treatment for Endometriosis. *J Minim Invasive Gynecol* 2019;26:717–26.

**100.** Martínez-Zamora MA, Coloma JL, Gracia M, Rius M,

Castelo-Branco C, Carmona F. Long-term Follow-up of Sexual Quality of Life after Laparoscopic Surgery in Patients with Deep Infiltrating Endometriosis. *J Minim Invasive Gynecol* 2021;28:1912–9.

---

*Conflicts of interest.*—The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

*Authors' contributions.*—Stefano Luisi and Libera Troia have given substantial contributions to study conception and design, data acquisition and interpretation, manuscript writing and critical revision. Both authors read and approved the final version of the manuscript.

*History.*—Article first published online: April 14, 2022. - Manuscript accepted: April 8, 2022. - Manuscript revised: March 14, 2022. - Manuscript received: December 1, 2021.