Health-related quality of life burden of women with endometriosis: a literature review

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Introduction

Endometriosis is a common gynecological condition that is defined by extrauterine, glandular and stromal endometrial-like tissue in physiologically abnormal locations. Endometrial implants are typically located in the female pelvis area over visceral and peritoneal surfaces, but this tissue can also be found elsewhere in the body such as the bowel, bladder, or surgical scars. Laparoscopy, biopsy, and some non-invasive procedures, such as
ultrasound, magnetic resonance imaging, and computed tomography, have been used to diagnose and stage endometriosis. According to the American Society for Reproductive Medicine (ASRM), endometriosis is staged based on the extent and location of the endometriotic adhesions, with Stage I (minimal endometriosis) indicative of minimal or superficial ovarian and peritoneal implants and Stage IV (severe endometriosis) consisting of deep, dense endometriotic implants. As an estrogen-dependent disease, endometriosis is predominantly confined to reproductive-aged women in whom lesion regression occurs during hypoestrogenic states either induced via pharmacologic or surgical modalities or naturally-occurring during menopause.

Endometriosis is associated with a variety of symptoms, most frequently chronic pelvic pain. Other symptoms and related complications of endometriosis may include dyspareunia, dysmenorrhea, dysuria, abnormal uterine bleeding or spotting, and infertility. These symptoms and complications are not specific to endometriosis and may be signs of other gynecological or non-gynecological conditions such as pelvic inflammatory disease, irritable bowel syndrome, and adenomyosis. Additionally, there is no correlation between stage and symptoms of endometriosis. Therefore, endometriosis is often misdiagnosed or slow to be diagnosed. Since a definitive diagnosis for endometriosis is usually made by laparoscopy, timely diagnosis can be difficult especially if lesions are deep or cannot be observed visually. Endometriosis reportedly affects seven million women in the United States and more than 70 million worldwide. For symptomatic women with chronic pelvic pain (CPP), one study estimated that 9.2 million women in the US, aged 18–50 years, suffered from CPP in 1994, yet 6.9 million did not seek medical attention from a physician or mental health provider. The actual prevalence of CPP and infertility secondary to endometriosis is difficult to determine, because CPP and infertility can result from multiple factors. One study suggests that two-thirds of women with pelvic endometriosis have CPP. The prevalence of infertility is reported to occur in 30–40% of women with endometriosis. Similarly, women with endometriosis are reportedly 20 times more likely to have infertility than women without endometriosis.

Endometriosis affects adolescents as well as adults, with an early onset at as young as 10.5 years of age. The symptoms of endometriosis are no less severe in adolescents than in adults. However, in the adolescent population, the problem is often overlooked. Consequently, the presence of endometriosis in the adolescent population also increases the likelihood of disease progression. It is important to evaluate and understand the impact of endometriosis in this particular population.

Currently, there is no cure for endometriosis. Conventional medical and surgical treatments target symptomatic relief. Commonly used medical treatments include oral contraceptives, non-steroidal anti-inflammatory agents (NSAIDs), progestins, and gonadotropin-releasing hormone (GnRH) agonists. Surgical interventions, such as laparoscopic excision, laparotomy, or, in more severe cases, hysterectomy may also be palliative. More than 120,000 of 500,000 annually preformed hysterectomies in the US are due to endometriosis. Yet, endometriosis-associated symptoms can still recur even after hysterectomy. At present, there is no treatment modality that has been proven to prevent recurrence, and no single treatment option has been proven superior.

Over the last several years, studies have begun to assess the health-related quality of life (HRQL) impact of endometriosis and its symptoms. HRQL is a term that is used broadly to refer to both descriptive assessments of health status that are scored on the level of functioning within the scales domains, as well as to utility-weighted evaluations of health status that also express the value that individuals place on the levels of functioning in the domains. Generic HRQL instruments can be used to assess a wide variety of diseases which usually include, at a minimum, physical, psychological, and social functioning and satisfaction with that functioning compared to their ideal. Disease-specific scales are more narrowly confined to the aspects of health particularly affected by a disease or set of related disorders. Based on the conceptual model developed by Wilson and Cleary, biological and physiological variables may lead to physical and psychophysical symptoms which then affect a person's functioning, general health perception, and overall HRQL. As discussed above, endometriosis features the growth of endometrial-like tissue in abnormal locations. Symptoms, including CPP, caused by the abnormal growth of the tissue may alter a person's ability to perform particular tasks (for example, interact with others) and impair a person's perceived health as well as overall sense of well-being. The impact of these symptoms and endometriosis-related infertility on HRQL has not been well-established.

Jones and colleagues conducted the most recent review of the literature of the HRQL impact of endometriosis and CPP, including HRQL instruments developed for endometriosis. This review, covering articles published up to 2000, also included other benign gynecologic conditions, such as menorrhagia and polycystic ovary syndrome (PCOS). Additionally, the review focused on the adult population and did not address the adolescent population.

The goal of this study was to update and build upon the review conducted by Jones and colleagues to
further understand the HRQL impact of endometriosis and/or specific endometriosis-related symptoms. A systematic literature review was conducted. A broader definition of HRQL was used that included descriptive health status assessments as well as utility-based health status measures. Utilities are typically expressed as a number ranging from 0 (death) to 1 (perfect health) representing the desirability or value that individuals place on a health state. 

Specifically, this review has three objectives. First, we examined studies that measured the HRQL impact of endometriosis and its key symptoms. Second, we analyzed the impact of specific pharmacologic and surgical treatments of endometriosis on HRQL. Finally, we reviewed the literature pertaining to the presence and impact of endometriosis in adolescents – an important, but often overlooked patient population.

**Methods**

Computerized literature searches were conducted using MEDLINE. The literature search focused on English-language literature from January 2000 to January 2006 and study populations of North America and Western Europe. The electronic search included the MeSH term ‘endometriosis’ combined with MeSH terms ‘quality of life’ and ‘burden of illness’, and was supplemented by a manual search of the bibliographies of studies to ensure comprehensiveness. In addition, an online search was performed (i.e., HealthSTAR, the National Institute of Child Health and Human Development, the Agency for Healthcare Research and Quality, the Royal College of Obstetrics and Gynaecology, and the American College of Obstetricians). Search terms included ‘endometriosis’ in combination with ‘psychology’, ‘adolescent’, and ‘quality of life’. Case studies, studies that were not specific to endometriosis, and studies outside the geographic regions of interest, were excluded from the review. Two independent researchers screened the studies originally identified from the literature search in an unblinded manner. Disagreement about inclusion/exclusion was resolved by consensus.

**Results**

The initial search generated a total of 31 articles. Of the 31 articles thus identified, eleven articles were excluded (two case studies/presentations; two on adenomyosis; one outside the geographic area of interest; and six non-endometriosis/colorectal related). Thus, 20 articles were fully reviewed. Five studies comprehensively addressed the burden of illness of endometriosis, including psychological or psychosocial HRQL aspects. Fourteen studies evaluated the HRQL impact of treatment intervention. One study addressed the behavior and psychosocial consequences of endometriosis in the adolescent population. The key study characteristics of the 20 studies addressing the HRQL effects associated with endometriosis and its treatments are provided in Tables 1 and 2.

**HRQL instruments and measures for endometriosis**

Several generic and disease-specific instruments have been used in measuring HRQL associated with endometriosis and its treatment. Generic HRQL instruments commonly cited are the SF-36 and SF-12. The utility measure, EQ-5D, has also been used. In addition to an endometriosis-specific questionnaire developed by a group of clinicians, the Endometriosis Health Profile-30 (EHP-30) and the Endometriosis Health Profile-5 (EHP-5), a brief version of the EHP-30, are recently available for the assessment of HRQL in patients with endometriosis.

### Table 1. Summary of articles on the HRQL burden of endometriosis

<table>
<thead>
<tr>
<th>Author</th>
<th>Population</th>
<th>HRQL measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Denny, 2004</td>
<td>Adults with endometriosis</td>
<td>Semi-focused interviews</td>
</tr>
<tr>
<td>Endometriosis all party parliamentary group (EAPPG), 2004</td>
<td>Adults with endometriosis</td>
<td>Peterson scale on intercourse, work, medical professional, infertility, relationship with children, treatment</td>
</tr>
<tr>
<td>Klein, 1981</td>
<td>Review in adolescents</td>
<td>Not reported</td>
</tr>
<tr>
<td>Low, 1993</td>
<td>Adults experiencing CPP due to endometriosis versus other causes</td>
<td>Short Form McGill Pain Questionnaire</td>
</tr>
<tr>
<td>Mathias, 1996</td>
<td>Adults experiencing CPP due to endometriosis versus other causes</td>
<td>General Health Questionnaire</td>
</tr>
<tr>
<td>Peveler, 1996</td>
<td>Adults experiencing CPP due to endometriosis versus other causes</td>
<td>State-Trait anxiety inventory</td>
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<td></td>
<td></td>
<td>Medical Outcomes Study long form</td>
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<tr>
<td></td>
<td></td>
<td>VAS pain</td>
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<tr>
<td></td>
<td></td>
<td>Brief Symptom Inventory</td>
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<td></td>
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<td>Modified Social Adjustment Scale</td>
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</table>
Utilities of patients with endometriosis

Two studies used the EQ-5D to measure utilities in patients with endometriosis in the United Kingdom (UK)\(^{16,22}\). Patients in the Garry’s study\(^{22}\) were a subset of those in the Abbott’s study\(^{16}\); therefore, only the Abbott’s study is discussed here. The EQ-5D defines health status in terms of five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension is divided into three levels: no problem, some problem, or extreme problem. The self-reported health status can be transformed to a population preference-based index score that is on a scale where 0 equals death and 1 equals perfect health.

The EQ-5D also includes a visual analogue scale (VAS), called EQ-5D VAS, that is used to assess patients’ overall health status. Women in the UK between the ages of 20 and 49 years with endometriosis had a mean EQ-5D index score of 0.6, which was significantly lower than the mean score of the general population (0.92) \((p < 0.0001)\)\(^{16}\). The EQ-5D VAS score ranges from 0 (worst imaginable state of health) to 100 (best imaginable state of health). The mean self-rated health scores on the EQ-5D VAS was 69 for patients with endometriosis, significantly lower than the score of the general population in the UK (86) \((p \leq 0.0001)\)\(^{16}\).

One of the limitations of the Abbott’s study was that it did not compare the utilities of women who

### Table 2. Summary of articles on the HRQL impacts of treatment for endometriosis

<table>
<thead>
<tr>
<th>Author</th>
<th>Therapeutic agent or surgery type</th>
<th>HRQL or utilities measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bergqvist, 2001</td>
<td>Nafarelin and medroxyprogesterone acetate</td>
<td>Anxiety-depression score based on the Woman Health Questionnaire</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nottingham Health Profile Questionnaire</td>
</tr>
<tr>
<td>Huber, 2004</td>
<td>Human chorionic gonadotrophin</td>
<td>VAS pain</td>
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<tr>
<td></td>
<td></td>
<td>Sleeplessness, irritability, depressive mood, household workload, despareunia, painful defecation, dysuria, dysmenorrhea, overall discomfort on VAS</td>
</tr>
<tr>
<td>Lockhat, 2004</td>
<td>Levonorgestrel-releasing intrauterine system</td>
<td>VAS pelvic pain</td>
</tr>
<tr>
<td>Miller, 2000</td>
<td>Leuprolide acetate depot in the stimulatory phase</td>
<td>SF-36</td>
</tr>
<tr>
<td>Petta, 2005</td>
<td>Levonorgestrel-releasing intrauterine system and depot-GnRH analogue</td>
<td>VAS pelvic pain</td>
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<tr>
<td></td>
<td></td>
<td>Psychological General Well-Being Index Questionnaire</td>
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<tr>
<td>Soysal, 2004</td>
<td>Goserein versus goserein plus anastrozole</td>
<td>Modified Greene scale</td>
</tr>
<tr>
<td>Zhao, 1999</td>
<td>Nafarelin and leuprolide acetate depot</td>
<td>Instrument developed by the authors</td>
</tr>
<tr>
<td>Zupi, 2004</td>
<td>Leuprolide acetate plus add-back estrogen and progesterone, leuprolide acetate alone, and estroprogestin</td>
<td>VAS pain</td>
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<td></td>
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<td>SF-36</td>
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</table>

**Pharmacologic intervention**

### Surgical intervention

<table>
<thead>
<tr>
<th>Author</th>
<th>Therapeutic agent or surgery type</th>
<th>HRQL or utilities measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abbott, 2004</td>
<td>Laparoscopic excision</td>
<td>Pain on 11-point Likert scale</td>
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<tr>
<td></td>
<td></td>
<td>EQ-5D</td>
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<td></td>
<td></td>
<td>SF-12</td>
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<td></td>
<td></td>
<td>Sexual activity questionnaire</td>
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<tr>
<td>Carlson, 1994</td>
<td>Hysterectomy</td>
<td>Mental Health Index</td>
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<td></td>
<td></td>
<td>General Health Index</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Activity Index</td>
</tr>
<tr>
<td>Ford, 2004</td>
<td>Laparoscopic surgery</td>
<td>EQ-5D</td>
</tr>
<tr>
<td>Garry, 2000</td>
<td>Laparoscopic excision</td>
<td>Pain on 11-point Likert scale</td>
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<td></td>
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<td>EQ-5D</td>
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<td></td>
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<td>SF-12</td>
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<tr>
<td></td>
<td></td>
<td>Sexual activity questionnaire</td>
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<tr>
<td>Low, 1993</td>
<td>Carbon dioxide laser laparoscopic treatment</td>
<td>Short Form McGill Pain Questionnaire</td>
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<tr>
<td></td>
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<td>Beck Depression Inventory</td>
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<td></td>
<td>General Health Questionnaire</td>
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<td></td>
<td>State-Trait anxiety inventory</td>
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<tr>
<td>Vercellini, 2003</td>
<td>Laparoscopic surgery with and without uterosacral ligament resection</td>
<td>SF-36</td>
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<tr>
<td></td>
<td></td>
<td>Hospital Anxiety and Depression Scale</td>
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<tr>
<td></td>
<td></td>
<td>Revised Sabbatsberg Sexual Rating Scale</td>
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</tbody>
</table>
had endometriosis with the utilities of age-matched normative female population in the UK.

HRQL burden of endometriosis and related key symptoms

A main symptom of endometriosis is CPP, which has been shown to result in physical debilitation and to have psychosocial implications. In many cases, CPP is attributable to endometriosis based upon laparoscopic evaluation. CPP is a common symptom that prompts women to seek medical attention.

Mathias and colleagues\textsuperscript{27} reported the results of a 1994 National Gallup cross-sectional survey of US women aged 18–50 years old to determine the prevalence of CPP and its effect on work productivity, HRQL, and health care utilization. In this study, the quality of life items were derived from the Medical Outcomes Study long form. The raw scores for the quality of life items were computed and transformed to a scale of 0–100 with higher scores indicating higher energy level and higher scores on interference with activities indicated more health distress. The pain index score was the product of the frequency of pelvic pain multiplied by the average pain severity rated on a scale of 0–10. A higher scale score indicated more pain. Based on patients’ responses in a telephone interview, patients were grouped by their most recent diagnoses: (1) endometriosis, (2) gynecologic (non-menstrual cycle related gynecologic, such as yeast infection and pelvic inflammatory disease), (3) non-gynecologic (other diagnoses, such as irritable bowel syndrome and hernia), and (4) no diagnosis, as well as by, if the patient reported CPP. The ‘no diagnosis’ group included patients who did not report a diagnosis or were unsure of their diagnosis. Scale scores were adjusted for age, education level, and income. The scores among patients with CPP are presented in Figure 1.

For all scales, the ‘no diagnosis’ group had favorable scores compared to the gynecologic group (\(p < 0.05\) for all). The ‘no diagnosis’ group also had favorable results compared with the endometriosis group for interference with activities, health distress, pain during or after intercourse, and the pain index score scales (\(p < 0.05\) for all). There was a statistically significant difference between the ‘no diagnosis’ group and the non-gynecologic group, with the ‘no diagnosis’ group having favorable results for all scales (\(p < 0.05\) for all) except for interference with activities and pain during or after intercourse scales. The endometriosis group had greater energy but worse pain scale results compared with the gynecologic group (\(p < 0.05\) for both)\textsuperscript{27}. The

![Figure 1. Comparison of scale scores based on the Medical Outcomes Study long form in US women with chronic pelvic pain by diagnostic group\textsuperscript{27}](image)

Figure 1. Comparison of scale scores based on the Medical Outcomes Study long form in US women with chronic pelvic pain by diagnostic group\textsuperscript{27}
endometriosis group had the greatest reported distress level, experienced the most interference with activities due to pain, and had the highest score for pain during or after intercourse. The study also found that general health scores were significantly lower in patients who reported CPP compared to those who did not (70.5 vs. 79.1, \( p < 0.05 \) data not presented in Figure 1)\(^2\). Although the study adjusted for age, education level, and income, it did not control for other potential confounders, such as co-morbidities and treatments that patients received.

Low and colleagues\(^8\) investigated the psychological vulnerability of women with endometriosis through comparison of the psychological profile of women with endometriosis to women having other gynaecological disorders associated with CPP in the UK. Instruments used in the study included the Short Form McGill Pain Questionnaire, and the Beck Depression Inventory, the State-Trait Anxiety Inventory, and the General Health Questionnaire (GHQ-30). Higher scores on these scales reflected more pronounced psychological morbidity or more pain. The endometriosis group reported significantly higher scores in measures of state anxiety and trait anxiety compared to the non-endometriosis group (\( p \leq 0.05 \) for both)\(^8\). Although the authors did not comment on whether the differences in anxiety levels between the two groups were clinically meaningful, it is indicated that the anxiety level in the endometriosis group was similar to that in the general medical and surgical patients in the UK. Given that the VAS pain scores and present pain intensity were comparable in the endometriosis and non-endometriosis groups, the differences in anxiety levels between the groups were likely attributable to other endometriosis-specific factors (e.g., risk of infertility and uncertainties associated with the condition) instead of pain\(^8\).

Pveveler and colleagues\(^9\) also explored pain severity and psychological effects associated with endometriosis by comparing social adjustment and mood symptoms in patients with endometriosis-associated pain to those with unexplained pain. Patients with endometriosis indicated a significantly higher level of average pain severity over the past 3 months on the VAS (\( p = 0.002 \)); however, no difference was found between the two groups in the worst pain over the past 3 months. The endometriosis group experienced a greater dysfunction for social adjustment, measured by the modified Social Adjustment Scale, when compared to those with unexplained pain. The differences between the groups were significant in parental role (\( p = 0.039 \)) and the overall social adjustment (\( p = 0.041 \)). Mood symptoms were evaluated using the Brief Symptom Inventory, a validated instrument that included nine subscales such as depression, anxiety, and phobic symptoms. No difference in mood symptoms was found between the two groups. Patients in the endometriosis group, however, were in a higher socioeconomic group, while no significant difference was found in other socioeconomic factors\(^9\).

Endometriosis can also impact work and social relationships\(^19,20\). A recent report of the Endometriosis All Party Parliamentary Group (EAPPG) of the UK demonstrated that endometriosis is a debilitating disease and affects work, intercourse, and relationships with children\(^20\). Often times, it is CPP that primarily affects these parameters. A study found that CPP due to endometriosis was associated with diminished work productivity and women often had to curtail social activities because of CPP\(^19\). In the workplace, women found that their symptoms were deemed inconsequential by their employers. Moreover, the limitations placed on their working lives caused some women to quit their jobs or change jobs due, in some cases, to an inability to perform them or the over-expenditure of allocated sick leave. Women expressed fear of symptom recurrence and were generally scared of dealing with endometriosis in the long-term. Those who suffered with severe pain envisioned a bleak, uncertain future\(^19\).

Overall, compared to the normative UK population, women with endometriosis in the UK had significantly lower scores in both the physical component (43.5 vs. 52.8, \( p < 0.0001 \)) and mental component (46.7 vs. 51.9, \( p < 0.0001 \)) on the SF-12\(^16\).

Impact of pharmacologic and surgical treatments on quality of life

Pharmacologic intervention and HRQL

The treatment effects on HRQL for patients with endometriosis have been evaluated in the context of pharmacologic treatments that include GnRH agonists (nafarelin, goserelin, and leuprolide), anastrozole, medroxyprogesterone, levonorgestrel, GnRH agonists plus add-back estrogen and progestogen, and human chorionic gonadotropin (HCG). In general, pharmacologic interventions have been shown to greatly improve psychological functioning, pain, vitality, physical functioning, and general health\(^17\).

Bergqvist and Theorell\(^17\) conducted a prospective, randomized, double-blind, double-dummy study to assess pain pattern and HRQL after 6 months of treatment with nafarelin or medroxyprogesterone acetate. Patients were followed for an additional 6 months after the end of the treatment (\( N = 48 \)). Results of the study showed that, at the end of the follow-up, both treatments improved anxiety-depression, measured by the Women Health Questionnaire, compared to baseline (overall \( p = 0.002 \)). However, an increase in anxiety-depression levels during the nafarelin treatment period was observed.
Clinical measures over the 6-month treatment period and nafarelin and leuprolide acetate depot on HRQL and other clinical measures over the 6-month treatment period and the subsequent 6-month follow-up period (N = 192). The authors developed their own endometriosis-related HRQL instrument. Although not validated, it was noted to have a high correlation with symptom severity. The HRQL items evaluated in the study included missing work or school due to endometriosis; being bothered by disease-related symptoms; resting in bed; canceling or postponing social activities or tasks/chores; or refusing sexual intimacy due to endometriosis. Overall, both treatments resulted in improved HRQL (p values not reported). However, some patients experienced adverse events associated with the hypoestrogenic effects of the drugs (e.g., hot flashes), with the nafarelin group experiencing fewer hypoestrogenic events. Since hypoestrogenic effect impaired HRQL, the author concluded that nafarelin might have a more positive effect on HRQL than leuprolide. The limitation of Zhao’s study was that the HRQL measures used were not validated and might be too broad. It included missing work or school days due to endometriosis and the response to this question was part of the overall HRQL score calculation. The study was not able to differentiate which aspect of HRQL was improved.

Another study evaluated the effect of leuprolide acetate depot on pain and HRQL during the stimulatory phase of the therapy (1 month) in women with endometriosis (N = 120)\(^{30}\). The study used the SF-36 and reported the physical and mental component summary scores. The study showed that there was a temporary deterioration in pain and HRQL in the stimulatory phase of therapy with leuprolide acetate depot. Compared to the baseline scores, the physical and mental component summary scores decreased at Week 2 and Week 4 after treatment with the change in mental component summary score at Week 2 reaching statistical significance (p = 0.003)\(^{28}\).

In addition, the treatment outcomes of combination therapy containing GnRH agonist have been examined in a few studies. A study evaluated the impact on symptom control and HRQL of post-surgical administration of goserelin versus goserelin plus anastrozole in severe endometriosis (N = 80)\(^{31}\). The study also examined the effect of the two therapies on menopausal quality of life (measured by the modified Greene scale). The modified Greene scale included items on severity of vasomotor, somatic, psychological symptoms (anxiety and depression), and loss of sexual interest. Over the 24-month follow-up period, combination therapy with goserelin and anastrozole decreased symptom recurrence and increased the pain-free interval at 24 months compared to goserelin alone. The change in Greene scale score from baseline was not reported for either group; however, the addition of anastrozole did not deteriorate menopausal quality of life at 24 months compared to goserelin alone\(^{19}\).

The benefit of combination therapy of GnRH agonist and add-back estrogen and progesterone was evident in a randomized controlled study (N = 133)\(^{34}\). Significant improvement from baseline on general health in the SF-36 was observed among patients treated with leuprolide acetate plus add-back estrogen and progesterone (p < 0.02 at 6 months). Compared to those treated with leuprolide acetate alone or estrogen-progestin alone, patients receiving leuprolide acetate plus add-back therapy reported significantly better scores on vitality in the SF-36 (p < 0.05 for both comparisons)\(^{34}\). Leuprolide acetate plus add-back therapy was also associated with significantly improved physical function and pain compared to estrogen-progestin therapy alone (p < 0.05 for both comparisons).

Levonorgestrel-releasing intrauterine system\(^{25,29}\) and human chorionic gonadotrophin\(^{33}\) have been shown to effectively reduce pain level. The VAS pelvic pain (4.6 vs. 7.7, p < 0.01) and dysmenorrhea on the verbal rating scale (moderate to severe: 50% vs. 96%, p < 0.001) was significantly reduced after treatment with levonorgestrel-releasing intrauterine system for 6 months\(^{29}\). Petta et al. evaluated the HRQL impact of the levonorgestrel-releasing intrauterine system and GnRH agonist and suggested that both therapies were associated with a significant reduction in VAS pain compared to baseline\(^{29}\). In addition, the two therapies improved patients’ psychological well-being, measured by the Psychological General Well-Being Index Questionnaire, although the change from baseline in either group was not significant\(^{29}\). The benefit of human chorionic gonadotropin was demonstrated in a prospective observation study where VAS pain was significantly reduced after treatment (4 point after treatment vs. 8 point at baseline, p < 0.001)\(^{23}\).

**Surgical intervention and HRQL**

The impact of surgical interventions on HRQL has been assessed. Interventions that have been evaluated in previous studies included carbon dioxide laser laparoscopic treatment, radical resection of rectovaginal endometriosis, radical laparoscopic excision with or without uterosacral ligament resection, and hysterectomy. Studies showed that surgical interventions improved patients’ psychological function, pain, physical function, and general health. Although surgical interventions can significantly improve...
patients’ HRQL, these interventions may be associated with adverse consequences that may limit their use in some patients.

Low and colleagues evaluated psychological and pain outcomes using a series of questionnaires, such as the Short Form McGill Pain Questionnaire, and the Beck Depression Inventory, the State-Trait Anxiety Inventory, and the General Health Questionnaire (GHQ-30), among 37 women who were diagnosed with endometriosis and underwent carbon dioxide laser laparoscopic treatment. The objective of the study was to evaluate pain and psychological state before and after surgery and to identify pre-operative factors that were predictive of post-operative pain outcomes. The study showed that, compared to baseline, VAS pain, present pain intensity, depression, state anxiety, trait anxiety, and psychiatric morbidity were significantly improved after surgery \( p = 0.05 \) for state anxiety and trait anxiety, \( p = 0.01 \) for the rest of the measures. Among all the pre-operative factors that were investigated (including trait and state anxiety, depression, personality, psychiatric morbidity, and marital state), trait anxiety was the only predictor for pain improvement at 3-months post-operation \( p \leq 0.09 \).

Another study evaluated, HRQL, levels of pain, and utilities among women undergoing radical resection of rectovaginal endometriosis or radical laparoscopic excision \( N = 135 \). Pain scores on the 11-point Likert scale as well as the EQ-5D, SF-12, and Sexual Activity Questionnaire were used. The results suggested a significant reduction in pain over the follow-up period of 2–5 years after laparoscopic excision \( p < 0.0001 \). Significant improvements were also seen in utilities \( 0.7 \) vs. \( 0.6 \) measured by the EQ-5D, \( p = 0.008 \) and sexual function \( p = 0.001 \) for pleasure, \( p = 0.012 \) for habit, \( p = 0.001 \) for discomfort for up to 5 years post-operatively. Physical and mental component scores on the SF-12 were both improved after surgical treatment; however, the differences did not reach statistical significance level. Although these surgical procedures significantly improved the utilities among patients with endometriosis, their average post-operative score on the EQ-5D was still lower than that of the normative UK population \( 0.7 \) vs. \( 0.92 \), \( p < 0.0001 \).

In a randomized controlled trial, Vercellini et al. compared the HRQL impact of laparoscopic surgery with and without uterosacral ligament resection \( N = 180 \). The SP-36, the Hospital Anxiety and Depression Scale, and the revised Sabbatsberg Sexual Rating Scale were used. At the 1-year follow-up after the surgery, patients reported significantly improved outcomes in all domains of the SF-36 compared to baseline, except for physical function and emotional role limitation in the uterosacral ligament resection group and general health perception, vitality, and mental health in the conservative surgery group. Significant improvements in depression and anxiety levels as well as in sexual functioning were achieved in both groups \( p < 0.05 \) for all.

Additionally, the Maine Women’s Health Study assessed HRQL outcomes in patients undergoing hysterectomy using three indices. The Mental Health Index includes five items and is used to rate how people felt in the past month (e.g., happy, sad, or nervous). The General Health Index consists of three items that rate the level of worrisome and bothersome due to illness. The Activity Index includes three items rating the ability to do work around the house, go where they wanted to go, and do things they wanted to do for fun and recreation. All the indices were validated and the scores for these indices were converted to a scale from 0 to 100 with higher scores indicating more favorable outcomes. Patients were interviewed at the time of surgery and at 3, 6, and 12 months post-operatively. CPP and endometriosis accounted for 18% and 10% of the 418 cases of hysterectomy studied, respectively. Compared to the available scores in the normative population, patients undergoing hysterectomy had considerably lower scores on the Mental Health Index (61 vs. 78) and the General Health Index (51 vs. 81.3). At 6 months and 1 year after hysterectomy, significant improvements with regard to the baseline scores were observed on the three indices \( p < 0.001 \) for all comparisons at both time points. Scores on the Mental Health Index and General Health Index after surgery were comparable to those for the normative population.

The impact of endometriosis in adolescents

Information on the impact of endometriosis on HRQL in adolescents is limited. Adolescents are at increased risk for developing endometriosis in the presence of genital tract anomalies, such as congenital uterine anomalies, vaginal septa, and imperforate hymen. Endometriosis, laparoscopically confirmed, reportedly occurs in 25–38% of adolescents with a history of CPP; with up to 70% cases reported in adolescents refractory to pharmacologic management.

Pain commonly experienced in endometriosis can have both behavioral and psychosocial consequences in adolescents. Adolescents with endometriosis may experience depression, fear, or anxiety. Furthermore, endometriosis can adversely affect daily life activities such as school attendance. The most recent published
surgical resection followed by pharmacological treat-
in order to improve patient HRQL and treatment
metriosis and for information to be readily accessible
essential for women to be well educated about endo-
psychological disturbances. Furthermore, it becomes
whether or not endometriosis precipitates the onset of
speculative, further research is needed to determine
Given that the exact mechanism of endometriosis is
handling of adverse situations, and resourcefulness
interfere with a woman’s perceived sense of control,
anxiety, and feelings of uncertainty, which in turn can
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adherence.

CPP, the predominant and most widely studied
symptom of endometriosis, has been shown to affect
women’s HRQL. Other symptoms and consequences
of endometriosis, including dyspareunia, dysmenorrhea,
infertility, and intermittent pelvic pain, can also impact
HRQL but have not been as extensively studied.

Although endometriosis is known to have substantial
effects on patients’ daily lives and is associated with
significant physical and emotional consequences, the
disease remains misdiagnosed. Consequently, the
magnitude of the effects of endometriosis on women,
their lives, and society remains under-appreciated.
Future efforts should be directed toward improving the
level of awareness of endometriosis, its detection, and
treatments, including optimizing treatment effectiveness
and side effect profiles.

Treatment effects on HRQL

Studies have shown that both pharmacologic and
surgical treatments improve patients’ physical function-
ing, psychological functioning, vitality, pain level, and general health. While pharmacologic and
surgical treatment modalities are available, these
current therapies target only symptomatic relief, do
not prevent disease recurrence, and have associated
adverse effects. Under these circumstances, one should
expect the HRQL consequences of endometriosis to be
pronounced.

Endometriosis in adolescents

Endometriosis is the most common primary condition
among adolescents with CPP. The long-term manage-
ment of endometriosis in adolescent females will most
likely persist throughout their childbearing years.
Therefore, the physical and psychological burden of
endometriosis is expected to have a substantial impact
for the adolescent population. Nevertheless, the
burden of endometriosis in the adolescent population is
considerably under-appreciated and the HRQL impact
of endometriosis in this younger population has not been
widely studied. Although many generic instruments
and a few endometriosis-specific instruments exist
for the adult population, to our knowledge, no
endometriosis-specific instruments have been developed
for adolescents. The applicability of the instruments
for adults to the adolescent population has not been
established. While it can be expected that physical and
psychosocial effects of endometriosis in adolescents
are as significant as in adults, qualifying these effects
using the same HRQL instruments as in adults may not
necessarily be appropriate due to inherent differences
between adolescents and adults, disease presentation,
and prognosis in these populations. For instance,
laparoscopic findings in adolescents may be atypical,
resulting in misdiagnosis and prolonged suffering.

Discussion

Although endometriosis is not a life-threatening
disease, this literature review demonstrated that it
can substantially affect patients’ HRQL. Pain, psychol-
ogical functioning, and social functioning are most
often measured and affected HRQL domains. As
CPP and infertility are the most severe symptoms
and consequences of endometriosis, they impose the
greatest HRQL burden on patients.

Our review of HRQL in endometriosis included
descriptive as well as utility-weighted health status
assessment results. Utility-based results are increasingly
considered in health technology assessments and are
particularly useful in economic evaluations, such as
cost-utility analyses, which are instrumental for policy
and reimbursement decisions.

HRQL burden of endometriosis

Endometriosis can be both physically and emotionally
debilitating. Physically, endometriosis pain can impair
work-related and daily activities. Psychologically, endo-
metriosis and related symptoms precipitate depression,
anxiety, and feelings of uncertainty, which in turn can
interfere with a woman’s perceived sense of control,
handling of adverse situations, and resourcefulness.

Given that the exact mechanism of endometriosis is
speculative, further research is needed to determine
whether or not endometriosis precipitates the onset of
psychological disturbances. Furthermore, it becomes
essential for women to be well educated about endo-
metriosis and for information to be readily accessible
in order to improve patient HRQL and treatment
adherence.

CPP, the predominant and most widely studied
symptom of endometriosis, has been shown to affect


HRQL burden for women with endometriosis Gao et al. 1795
research is warranted to evaluate the appropriateness of using the existing HRQL instruments in adolescents and to develop an endometriosis-specific instrument for this population if necessary.

Limitation of previous studies

There is a lack of studies in the literature using validated disease-specific instruments to measure the endometriosis-related HRQL, especially the different construct of HRQL. Because the endometriosis-specific instruments, the EHP-30 and the EHP-5, only became available recently, there has not been any published study that employs these instruments to evaluate HRQL in patients with endometriosis at the time of the review. The EHP-30 and the EHP-5 include HRQL concepts that are particularly relevant to endometriosis (i.e., work, sexual intercourse, medical profession, infertility, relationship with children, treatment); therefore, it is anticipated that they can serve as useful tools to further understand and characterize the HRQL burden of endometriosis.

In addition to the HRQL effects specified, a study suggests that the prevalence of a number of diseases, such as breast cancer, melanoma, ovarian cancer, multiple sclerosis, rheumatoid arthritis, lupus erythematosus, and Sjögren’s syndrome, is higher in patients with endometriosis than in the general female population in the US. Although the relationship between endometriosis and these conditions has not been well-established in the literature, these co-morbid conditions may further deteriorate HRQL in patients with endometriosis. Since there is no available cure for endometriosis and clear deficiencies in current treatments exist, the composite clinical, economic, and HRQL effects of endometriosis are most likely staggering.

Furthermore, few studies exist that examine the broader impact of endometriosis on patient’s lives, including its impact on fertility. The consequences of infertility are broad in scope and may include both physical and psychological components, especially among women desiring to conceive. Consequently, the impact of endometriosis-related infertility on HRQL may be considerable.

Funding for endometriosis research

Despite the cutting-edge, technological advances of modern times, it is arguable whether or not the HRQL impact of endometriosis has been lessened since endometriosis was first cited in scientific literature 142 years ago. Considering the widespread prevalence of endometriosis (about seven million women affected in the US) and its significant impact on patients’ HRQL and productivity, endometriosis does not receive adequate research attention. Similarly, it does not receive funding commensurate with the physical and mental debilitation it exerts in both adolescents and adult females. In the fiscal year 2000 (FY2000), a reported $2.7 million of $16.5 billion of funding from the National Institute of Health (NIH) was allocated for endometriosis research. This equates to approximately 40 cents per person and represents less than 0.02% of total research dollars. By FY2005, only $10 million dollars was allocated to endometriosis research. In FY2006, it was projected that only $10 million of NIH funds would be for endometriosis research. In fact, of the 190 diseases, conditions, and research areas in which the NIH appropriated funding in FY2005, endometriosis ranked in the bottom quarter based on funding allocation. As a comparison, some disease conditions with relatively higher health utilities and lower prevalence received more research funding from the NIH than endometriosis. For example, although the estimated average utility for patients with inflammatory bowel disease is slightly higher (0.68 vs. 0.60) and the prevalence of inflammatory bowel disease in the US is lower (0.39 million vs. 7 million) compared to endometriosis, the NIH funding for research on inflammatory bowel disease in FY2005 ($70 million) was seven times the funding for endometriosis.

Conclusion

Endometriosis is a chronic disease with far-reaching consequences. Endometriosis substantially impairs adult women’s HRQL. Pain, psychological function, and social function are among the most heavily affected domains. Pharmacological and surgical treatments for endometriosis improved patients physical functioning, psychological functioning, vitality, pain level, and general health. Endometriosis may also have profound adverse impact on HRQL in adolescents, as they are likely to have the most prolonged disease duration. It is a disease that is under-diagnosed, under-reported, and under-researched. Further clinical and outcomes research is needed, especially in adolescents, to fully understand this disease, the construct of HRQL impact, and to assess how new therapies may improve disease management and patients’ HRQL.

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