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Disclosing the invisible

- experiences, outcomes and quality
of endometriosis healthcare

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To Ludvig and Greta

The grass is greener where you water it

CONTENTS

ABSTRACT.....	1
LIST OF PAPERS.....	3
ABBREVIATIONS.....	5
INTRODUCTION.....	7
BACKGROUND.....	9
Menstrual concealment and the association with endometriosis	9
Endometriosis – “the hidden disease”.....	10
<i>Living with endometriosis</i>	11
<i>Aspects of the encounters with healthcare</i>	12
The physiology and psychology of pain	15
<i>Persistent pain and central sensitization</i>	16
Theoretical framework	17
<i>Corroborating healthcare encounters</i>	17
<i>Quality of care</i>	19
Rationale.....	22
AIMS.....	23
METHOD	25
Designs.....	25
Settings	27
Participants and procedures	28
<i>Study I and II</i>	28
<i>Study III</i>	29
<i>Study IV</i>	30
Data collection	31
<i>Demographic data (study I–IV)</i>	31
<i>Interviews (study I & II)</i>	33
<i>Pain Threshold Testing (study III)</i>	35
<i>Questionnaires (study III & IV)</i>	37

Data analysis.....	42
<i>Qualitative method (study I & II)</i>	42
<i>Quantitative method (study III & IV)</i>	44
<i>Statistics</i>	46
Ethical considerations.....	47
RESULTS	49
The struggle to visualize the pain	50
The endometriosis diagnosis as a key to understanding and enduring persistent pelvic pain	58
Healthcare encounters as potentially life changing	60
The quality of endometriosis healthcare	61
<i>Structure</i>	61
<i>Process</i>	63
<i>Outcome</i>	63
DISCUSSION	65
Results discussion	65
<i>Endometriosis healthcare embraces vital dimensions of female life</i>	65
<i>The dissonance between women's and HCPs' experiences</i>	67
<i>The diagnosis is pivotal in endometriosis healthcare</i>	68
<i>"Pain-focused" versus "disease-focused" endometriosis care</i>	69
Methodological discussion.....	73
<i>Strengths and limitations</i>	73
<i>Reliability and validity</i>	75
Clinical implications.....	78
Future research	79
CONCLUSIONS	81
SVENSK SAMMANFATTNING	83
ACKNOWLEDGEMENTS	85
REFERENCES	87

ABSTRACT

Introduction: Many women with endometriosis report that their symptoms are normalized and trivialized when they seek medical care and they often experience diagnostic delays, ineffective treatments and physiological, psychological and social consequences. However, there is a knowledge gap when it comes to women's experiences of different aspects of endometriosis healthcare, and the quality of that care.

Aim: The aim of this thesis was to identify, describe and analyse the experiences, encounters and outcomes of endometriosis healthcare from different perspectives.

Design and Method: This thesis is a summary of four studies with different methods and designs. Study I and II were qualitative interview studies in which nine women with a laparoscopy-verified endometriosis diagnosis (study I) and 25 healthcare professionals (HCPs) (study II) described their experiences of healthcare encounters related to endometriosis symptoms. The interviews were analysed using interpretive phenomenology (study I) and conventional content analysis (study II). Study III was a cross-sectional observational comparative study measuring pain thresholds, health-related quality of life (HRQoL) and symptoms of anxiety and depression using quantitative sensory testing (QST) and questionnaires in order to determine pain thresholds in healthy women (n=55) and women with persistent pelvic pain (PPP), with (n=14) and without (n=23) a confirmed diagnosis of endometriosis. The correlations between pain thresholds and duration of PPP, HRQoL and symptoms of anxiety and depression were also analysed. Study IV was a quantitative observational study using register data from the National Quality Register for Gynaecological Surgery. Patient-reported experience measures (PREM) and patient-reported outcome measures (PROM) after benign hysterectomy were analysed and compared in women with and without PPP and endometriosis (study IV).

Results: The results of the thesis are summarized in three themes: *The struggle to visualize the pain*, *The endometriosis diagnosis as a key to understanding and enduring persistent pelvic pain* and *Healthcare encounters as potentially life changing*.

In the first theme, women and HCPs described the healthcare encounters concerning endometriosis symptoms as troublesome (study I, II). The women struggled with disclosing, visualizing and communicating their hidden pain to the HCPs (study I), and HCPs expressed insecurity and limited knowledge when caring for these women (study II). Study III showed widespread reduced pain thresholds among women with PPP compared with healthy controls, and a significant positive correlation between duration of PPP and reduced pain thresholds. Study III also showed a reduced HRQoL and higher prevalence of anxiety and depressive symptoms among women with PPP, which were also described by the women (study I).

The importance of getting a diagnosis was described in the second theme by both women and HCPs (study I, II), but women with PPP with and without endometriosis diagnosis did not differ significantly in their pain thresholds or psychosocial outcomes in study III. Likewise, women with PPP with and without endometriosis gave more equal PREM and PROM answers than women in the pain-free comparison group. Overall, women undergoing hysterectomy on benign indications were satisfied with the experience and outcomes of the surgery (study IV).

As described in the last theme, healthcare encounters could be constructive or destructive. Positive experiences could make the symptoms easier to endure. The constructive encounters were often characterized by a holistic approach and a care structured in multidisciplinary teams.

Conclusion and clinical implications: The results suggest that PPP should be taken seriously and treated actively in order to minimize the risk of physiological and psychological consequences, such as reduced pain thresholds, lower HRQoL and symptoms of anxiety and depression. Unrelieved PPP could also be an explanatory factor for long-term physiological consequences, such as lower PREM and PROM after hysterectomy.

High-quality endometriosis healthcare should provide an interaction of physical, psychological and social factors. If women experience that HCPs acknowledge their pain and the effect of pain on HRQoL and mental health, and are offered proper pain-relieving treatment, healthcare encounters could change their lives.

Keywords: endometriosis, persistent pelvic pain, healthcare professionals, healthcare encounters, health-related quality of life, pain thresholds, quantitative sensory testing, central sensitization, hysterectomy

LIST OF PAPERS

- Study I. Grundström, H., Alehagen, S., Kjølhedde, P., Berterö, C. The double-edged experience of healthcare encounters among women with endometriosis: a qualitative study. *Journal of Clinical Nursing*. 2018;27(1–2):205–211.
doi:10.1111/jocn.13872
- Study II. Grundström, H., Kjølhedde, P., Berterö, C Alehagen, S., “A challenge” – health care professionals’ experiences when meeting women with symptoms indicating endometriosis. *Journal of Sexual and Reproductive Healthcare*. 2016;7:65–69.
doi: 10.1016/j.srhc.2015.11.003
- Study III. Grundström, H., Gerdle, B., Alehagen, S., Berterö, C., Arendt-Nielsen, L., Kjølhedde, P. Reduced pain thresholds and signs of sensitization in women with persistent pelvic pain and suspected endometriosis. 2018. *Submitted*.
- Study IV. Grundström, H., Alehagen, S., Berterö, C., Kjølhedde, P. Impact of pelvic pain and endometriosis on patient-reported outcomes and experiences of benign hysterectomy: a study from the Swedish National Register for Gynaecological Surgery. *Journal of Women’s Health*. 2018;27(5):691–698.
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ABBREVIATIONS

aOR	Adjusted Odds Ratio
BMI	Body Mass Index
CI	Confidence Interval
CS	Central Sensitization
EHP-30	Endometriosis Health Profile-30
EQ-5D-3L	EuroQoL-5 Dimension Questionnaire
GP	General Practitioner
GynOp	National Quality Register for Gynaecological Surgery
HADS	Hospital Anxiety and Depression Scale
HCP	Healthcare Professional
HRQoL	Health-Related Quality of Life
PPP	Persistent Pelvic Pain
PREM	Patient Reported Experience Measure
PROM	Patient Reported Outcome Measure
QST	Quantitative Sensory Testing
SF-36	36-Item Short Form Health Survey

INTRODUCTION

Attitudes towards menstruation differ both historically and culturally, but some kind of menstrual concealment is present in most societies [1]. This concealment leads to unwillingness to disclose problems such as menstrual pain or heavy bleeding and could be one explanation for why endometriosis is called the “hidden” or “invisible” disease. The symptoms of endometriosis are often misinterpreted as parts of normal menstruation, associated with cultural representations of menstruation and thus kept secret [2].

Persistent pelvic pain (PPP) and dysmenorrhea (painful menstrual cramps of uterine origin [3]) are the most central symptoms of endometriosis [4], and are therefore the focus in this thesis. Normalization and trivialization of this pain both by women themselves and by healthcare professionals (HCPs) lead to diagnostic delays which can have physiological, psychological and social consequences [5]. It is of great importance that these women are provided with proper and effective care in order to decrease symptoms and to prevent the progression of the disease. However, research about the healthcare that women receive when turning to healthcare services for endometriosis symptoms is scanty. Previous research has mostly focused on encounters with primary-care staff and delays in getting a diagnosis and treatment [6–8]. This thesis will provide insight into women’s experiences of different aspects of the care they receive, and the quality of that care.

During the work with this thesis, many women with PPP have told me similar stories about normalization, trivialization and being dismissed during healthcare encounters, which indicates that the healthcare they receive today does not meet women’s needs and expectations. Therefore, I hope that the results of my thesis will inspire and facilitate continued work to improve the quality of care for women with endometriosis.

BACKGROUND

Menstrual concealment and the association with endometriosis

Menstruation is a biological phenomenon experienced over approximately half of the female lifespan. It is a unique experience to each woman, but the interpretation and experience of menstruation is dependent on social and cultural factors. Menstruation is sometimes described by women as an assurance of a functioning body and as an indicator of reproductive and sexual health [9], but it is also perceived as a discrediting attribute in societies around the world, and something that should be hidden from others [2].

Menstrual concealment is perpetuated through different socialization channels in modern society. For example, it is reproduced indirectly through silence: the topic is typically avoided in conversation or discussed in gender-specific subgroups in schools and workplaces. This concealment is also manifested by the existence of euphemisms for menstruation used in everyday language in cultures all over the world. Another aspect is menstrual hygiene products, which are designed to absorb fluid and odours as invisibly and discreetly as possible, with the goal of complete menstrual concealment. Additionally, negative attitudes towards menstruation and stereotypes of menstruating or premenstrual women as violent and emotionally labile are often reproduced in movies and TV shows [10].

Considering this negative image of menstruation and menstruating women, it is not surprising that during the many years of fertility, women put a lot of effort into concealing their menstruation [9–11]. Menstrual concealment also involves hiding menstrual problems such as dysmenorrhea or heavy bleeding [11, 12]. Dysmenorrhea is defined as a dull, aching, cramping pain in the lower abdomen experienced during or before menstruation. The prevalence of dysmenorrhea is estimated at between 45% and 95% of all menstruating women. Despite substantial distress, many affected women consider this pain to be “normal” and never seek medical care [3]. Seear [2] suggested that the normalization of menstrual pain is

associated with menstrual concealment, which contributes to an unwillingness to disclose oneself as a menstruating individual [2].

Similarly, menstrual concealment is closely associated with an unwillingness to disclose the symptoms of endometriosis. This is a chronic gynaecological disease with symptoms that are often interpreted as menstrual problems: dysmenorrhea and heavy bleeding [2]. Endometriosis can affect the entire life cycle of a woman, from menarche, during adolescence, through adulthood and all the way to, or even after, menopause [13]. The condition is closely connected to menstruation because of its aetiology and symptomology; hence, it is characterized by a concealment that affects intimate aspects of female bodies [2]. The experience of endometriosis is thus gendered, both culturally and physiologically, and its attributes are connected to gendered and cultural concepts such as sexuality, fertility and womanhood [1].

Endometriosis – “the hidden disease”

Endometriosis is one of the most common causes of pelvic pain with an origin in the gynaecological area. Because of its complex aetiology and location, and the concealment surrounding it, the condition is sometimes called “the hidden disease”. It affects approximately 10% of all women of reproductive age, which represent around 176 million women worldwide and 200 000 in Sweden [14]. The condition is characterized by the implantation of endometrial cells outside the uterine cavity, where they respond to menstrual hormonal stimulation, which induces local inflammation, bleeding and pain. These ectopic cells may cause the formation of lesions, adhesions, and cysts [4].

Despite nearly a century of research, the aetiology of endometriosis is still in dispute, and a unified theory regarding its origins remains elusive. Theories accounting for pathogenesis can be categorized as those proposing that implants originate from the uterine endometrium and those proposing that they arise from other tissues [15]. The most widely accepted theory is Sampson’s theory of retrograde bleeding. This theory proposes that the menstrual blood of the endometrium is squeezed backwards through the fallopian tubes and thus reaches the free pelvic cavity, where the endometrial cells can become implanted in the peritoneum and ovaries [16]. However, the factors behind the implantation and survival of the displaced endometrium remain unknown. Various possible factors, in-

cluding immunological disturbances, heredity and endocrine-disrupting chemicals, have been suggested [15].

Endometriosis is often experienced as a disabling condition, and many women with endometriosis experience their worst symptoms during the days before, during or after the time of menstruation. Since many healthy women have dysmenorrhea, PPP is often misinterpreted as “normal”: women are supposed to have menstrual pain. This widespread belief has negative consequences for women with endometriosis, leading to the normalization and trivialization of the pain [5, 17].

Living with endometriosis

The first symptoms of endometriosis often occur in early adolescence, but the diagnosis is commonly first given at the age of 25–30 years. The most common symptoms are PPP and dysmenorrhea. Additional symptoms can be dyspareunia, fatigue/weariness, and a reduced level of fertility. Intestinal complaints, such as periodic bloating, diarrhoea, or constipation, are common but less well recognized [4, 18]. Dyschezia (difficult or painful defaecation) is a symptom that has gained more attention during recent years [19, 20].

Up to 80% of women with endometriosis have some kind of persistent pain, but the pain intensity and other symptoms usually fluctuate in a cyclical manner [21, 22]. The understanding of pain in the trajectory of endometriosis is complex: a woman diagnosed as having a ‘mild’ form of the disease by diagnostic categorization may experience severe symptoms, while a woman with extensive disease may be asymptomatic. Around 20% of women diagnosed with endometriosis are asymptomatic [22], and some women are diagnosed opportunistically; for example, during investigations for infertility [21, 22].

The experience of pain is a central and destructive feature of life for many women with endometriosis. A review from 2013 concluded that PPP and dysmenorrhea affected significant aspects of women’s lives, and daily life activities were impaired. The women also reported reduced physical health, low energy and a reduction in social activities, resulting in feelings of anger, distress and moodiness. The impaired health often led to shorter or incomplete education, loss of productivity and poorer quality of work [5].

Endometriosis symptoms can also have a negative effect on relationships and sex life. Sexual problems such as dyspareunia, hypoactive sexual desire and orgasm dysfunctions are relatively frequent among women

with endometriosis [23]. Dyspareunia and other pain-related sexual problems are often the reason behind relationship problems and breakups [5]. At the same time, partners are identified as a great source of support for women [24, 25]. The voices of male partners have been exemplified in a few studies, describing emotional responses such as helplessness, frustration, worry and anger. The partners reported that endometriosis had a substantial influence on many life domains including sexuality and intimacy, planning for and having children, working lives, household income and support tasks and roles [26–28].

The negative impact of endometriosis on women's health-related quality of life (HRQoL) is well-documented [5, 29–33]. HRQoL is a multidimensional, ambiguous and elusive concept, which incorporates those aspects of overall quality of life that can be associated with physical or mental health [34].

Aspects of the encounters with healthcare

Diagnostic delay

Endometriosis is suspected and sometimes clinically diagnosed through typical endometriosis-associated symptoms or during a gynaecological examination where painful thickenings of the sacro-uterine ligaments and sometimes visible lesions can be revealed in the vaginal wall. To confirm the diagnosis, a directed biopsy may be taken during for instance laparoscopy. Positive biopsy confirms the diagnosis, but negative biopsy does not exclude it [4].

Time from symptom onset to diagnosis varies between countries from four to 12 years [33, 35–38]. Two reviews based on 18 and 42 papers respectively describe the distinction between delays at *the patient level* and delays at *the medical level* [5, 17]. Delays at *the patient level* referred to the time between symptom onset and turning to HCPs for help. The delay in seeking medical care was related to several aspects: firstly, women concealed their symptoms since they experienced that revealing them might be embarrassing and make them appear weak. Secondly, as the symptoms were usually experienced during menstruation, women found it difficult to distinguish between 'normal' menstrual pain and pathological symptoms, and often considered themselves to be 'unlucky' as opposed to 'unwell'. Moreover, the lack of awareness of endometriosis as a condition among women themselves, as well as among their family, friends and society in general, contributed to patient delay [5, 17]. At *the medical level*,

diagnostic delay was most distinctive at the primary-care level. Many women reported that general practitioners (GPs) frequently normalized, dismissed and trivialized their symptoms [5, 17]. Women often experienced that GPs resisted referring them to gynaecologists, and they were often advised to make appointments for inappropriate secondary care, which then often focused on finding a non-gynaecological explanation for the symptoms [17].

The women's reactions to receiving a diagnosis were described in terms of vindication, triumph and relief. The diagnosis provided the women with a medical language that enabled them to communicate their "invisible disease" to others [5, 17]. For some women, the positive effects of receiving a diagnosis were blackened by sorrow and worry due to the seriousness of having a chronic disease that might affect future physical and psychological wellbeing and lead to decreased fertility [17].

Differential diagnoses can be gastrointestinal or urological conditions, where irritable bowel disease and interstitial cystitis are relatively common. However, the state of PPP is often complex and includes a variety of psychosocial and physiological factors. Many women with PPP never receive any diagnosis despite the experience of severe pain, and represent a patient group for which treatment guidelines and evidence-based treatment are scanty [39].

Endometriosis treatment

Endometriosis is a chronic condition and treatments are primarily aimed at pain relief and secondarily at improving HRQoL, inhibiting disease recurrence, decreasing anatomical damage and maintaining fertility. There are several medical and surgical treatment interventions, but because of the variety of treatment programmes and study populations, the evidence of their effectiveness and outcomes is limited [40].

As a first step in their treatment, women are often prescribed with a variety of analgesics for pain control. If analgesics do not sufficiently reduce the pain, hormonal therapy such as oral contraceptives with oestrogen and/or progesterone can be effective [41].

Laparoscopic surgery with ablation or excision is typically conducted when the condition is diagnosed and often has a positive short-term effect on reducing pain [42]. However, some women go through repeated surgery with unsatisfactory results. For several decades, it was routine to offer a hysterectomy in these situations. Now that it is recognized that endometriosis can remain even after hysterectomy, the number of hysterectomies with endometriosis as an indication is decreasing [41].

Although medical and surgical treatment often effectively reduce pain, sometimes they offer only short-term pain relief, or may have negative side effects. The endurance of pain characterizing women's experiences pre-diagnosis has been reported to sometimes continue post-diagnosis, as some women feel obligated to endure treatments that compromise their overall health and wellbeing. In response to the limitations of medical treatment, alternative and complementary medical treatment or lifestyle changes are sometimes used to manage symptoms [5, 17].

Encounters with healthcare professionals

In addition to the difficulties with finding an effective treatment, women with endometriosis frequently describe encountering HCPs as problematic. Most studies on the subject report experiences of meeting GPs, and some of them include encounters with gynaecologists [6–8, 43]. The literature is limited regarding experiences of encounters with other HCPs, such as nurses, midwives, psychologists and physiotherapists.

So far, only one study focusing on nurses' encounters with women with endometriosis has been published. Bach et al. [44] explored how female gynaecological nurses' personal attitudes, specialized knowledge, and clinical experiences influenced the care for these women. Their first main finding was that, despite their biomedical knowledge, the nurses' personal experiences of menstrual pain influenced their professional attitudes and put women with endometriosis at risk of being labelled as having psychological conflicts or ulterior motives, even when the women had a biopsy-verified endometriosis diagnosis. The second main finding was the categorization of patients as, 'sick,' 'not sick,' or 'difficult'. These categorizations can be crucial for nursing care as the patients' caring needs were interpreted accordingly. The conclusion was that self-reflection in the clinical setting and working in multidisciplinary teams around the most complex cases were necessary to help nurses train and sustain a holistic approach [44]. The value of multidisciplinary teams has been emphasized in clinical guidelines. The teams could include gynaecologists, pain specialists, nurses or midwives, psychologists, sexologists, physiotherapists and other HCPs with a special knowledge and interest in endometriosis and PPP [4, 45].

Encounters with gynaecologists were briefly described in Cox et al. [6] as somehow disappointing. Women doubted the knowledge and competence of the gynaecologists when it came to managing the disease or providing adequate surgical treatment. However, women were more content with gynaecologists than with GPs, and finding a gynaecologist who

had specialist expertise in endometriosis was often uplifting and relieving [6].

Generally, the literature shows that women seem to experience that, compared with gynaecologists, GPs lack knowledge, awareness and sympathy, and more commonly perpetuate “medical myths” about endometriosis [5, 17].

The physiology and psychology of pain

Several factors contribute to the pain that many women with endometriosis experience. Because of their hormonal and inflammatory characteristics, the endometriotic lesions can engage reproductive, endocrine, vascular, musculoskeletal, neuronal and psychophysical systems in the body, which all contribute to the experience of pain [21].

The definition of pain is formulated by the International Association for the Study of Pain as: “*An unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage*” [46 p. 210]. Pain is a dynamic and complex phenomenon, essential for human survival, with the major purposes of warning about disease or injury, promoting the body’s healing processes, and avoiding future potentially dangerous situations [47].

Nociceptive signals from an injury follow pathways from the periphery to the brain and are modulated at different levels of the central nervous system. The signals provoke an immune response that sensitizes the nociceptive receptors within the injury and in the surrounding neurons; a process called primary hyperalgesia. This can be measured as a reduced pain threshold in and around the injury, which serves as a protection and a reason to avoid and rest the damaged tissue [48].

While *nociception* describes the signal following damage or injury, *pain* is experienced when the signal reaches the cortex and requires activity in the central nervous system. Complex factors such as emotions, cognition and previous experiences together contribute to the constantly changing, modulating and active system of the pain experience [47].

Persistent pain and central sensitization

Acute pain may save the lives of some people, while persistent pain conditions have the potential to destroy the lives of others. As expressed by Melzack and Katz: *“Chronic pains, clearly, are not a warning to prevent physical injury or disease. They are the disease”* [47 p. 1].

The International Association for the Study of Pain defines persistent pain as any pain lasting more than three to six months [46]. With more than one quarter of the population affected, persistent pain is considered one of the most common global health problems. Despite its high prevalence, there are still unanswered questions regarding the understanding and treatment of persistent pain. While acute pain is easily understood as a response to nociceptive input, persistent pain may arise without tissue damage or where an injury is no longer present [49].

Despite a not fully understood aetiology, there seems to be a link between persistent pain and reduced pain thresholds. Widespread reduced pain thresholds are recommended as a proxy for the state known as central sensitization (CS). The process of CS is usually triggered by a nociceptive input. To maximize the system's capacity to handle the nociceptive signals, neurons on the pathway to the central nervous system change their response properties. This change in neurons can lead to a continuous production of hyperalgesic and allodynic responses even after the injury has healed. Additionally, malfunctioning inhibitory pathways and increased activity in pain facilitation pathways contribute to CS [50]. By definition, CS represents an abnormal state of responsiveness in the nociceptive system and a functional shift from high-threshold nociception to low pain thresholds [51].

Different degrees of CS have been detected in pain conditions such as migraine, fibromyalgia and irritable bowel syndrome [52–54]. Whether the PPP associated with endometriosis can be correlated to a development of CS remains to be validated, as the evidence so far is limited [55–59]. Two studies with ten women with endometriosis each reported increased pain sensitivity [56, 59], while He et al. [57] used a larger sample of women with endometriosis (n=100) to detect CS. The results showed signs of CS manifested as generalized hyperalgesia (amplified pain response to noxious stimulation distant from an injury) [57].

As-Sanie et al. [58] also found reduced pain thresholds at a non-pelvic site in women with PPP compared to healthy controls. The reduced thresholds were independent of the presence or severity of endometriosis or other pain syndromes, which supports the belief that CS plays a role in

the development of PPP, and might explain why eliminating endometriosis lesions does not work as a satisfying treatment for some women with PPP [58]. Using similar methodology, Stratton et al. [55] made a broader contribution to the field, with their inclusion of myofascial trigger points and psychosocial aspects in the assessment of CS. Myofascial trigger points and sensitization were common in women with PPP, regardless of endometriosis, but those with endometriosis were the most likely to have sensitization [55].

Theoretical framework

The concepts of corroborating [60] and quality of care [61] were used as the theoretical framework in this thesis.

Corroborating healthcare encounters

The concept of corroboration will serve as a tool in the analysis of the data in this thesis, primarily in study I and II. The use of this concept in relation to healthcare encounters was developed in the field of nursing ethics in geriatric care but is applicable to other healthcare contexts and can involve all HCPs. In this thesis, corroboration applies to any HCP who may encounter women with endometriosis or endometriosis symptoms.

Corroboration in healthcare encounters can be described as a wider type of confirmation, in which values such as relationship, support and interaction are added. The relationship is based on HCPs' obligation to do good for the patients by showing consideration, thoughtfulness, and good manners. It is the HCP's responsibility to ensure that the care and treatment are planned in cooperation with the patient. Ethical values such as integrity and self-determination are central to corroborating encounters. The concept incorporates three themes: showing consideration, connecting, and caring for [60].

Showing consideration

By showing consideration, the HCP invites the other person to participate in the encounter. This can be done both verbally, through words and questions, and physically, through eye contact and being close. To meet

the patient in a holistic way means to show concern for her throughout the caring process and to promote mutual respect, which can stimulate wellbeing. An HCP who shows consideration must have an open mind, be helpful, and be present both physically and mentally. Time can be experienced as an indication of a person's value and is therefore an important element in the corroborating encounter. Components that indicate lack of consideration are: arrogant attitudes, displaying irritation, or laughing at the other person [60].

Connecting

Connecting is related to communication and described as a central aspect of the interaction between the HCP and the patient. It enables collaboration and can be a link between the people involved in the encounter. During this connection, the patient and her autonomy is at the centre of attention, and questions or small talk are used to create a good atmosphere and a dialogue. This type of connecting is often provided by the HCP as she or he prepares the patient for any tasks or actions that will be carried out. Connecting could include the flow of information or options on small decisions that are derived from one person to another [60].

Caring for

Caring for is a responsibility of HCPs, which incorporates competence, skill, and knowledge concerning different tasks. A caring task relates to patient safety, it creates confidence between the persons involved in the caring encounter and it demonstrates non-maleficence. The caring task is a sort of corroboration as the focus is still on the patient's state of health. The tasks are often actions that start with connecting and then involve some kind of caring performance, conducting a test, control, and so on. Focusing on caring tasks entails less verbal activity, mainly in acute situations when the focus is on performing the task properly without harming the person [60].

Quality of care

Concept and definitions of quality of care

Quality of care is defined by Sweden's National Board of Health and Welfare as "the degree to which an activity meets the demanded requirements" [62 p. 3]. High quality in healthcare is closely related to patient security and the provision of evidence-based, effective, patient-focused, efficient and equitable care within a reasonable timeframe [62]. This definition is consistent with the definition suggested by the World Health Organization, which defines quality of care using the six dimensions of effectiveness, efficacy, accessibility, equitability, patient-centeredness and safety [63].

In the 1960s, Donabedian, who is a well-cited researcher in the area, described his now-classic three-dimensional model for assessing quality of care. It involves the concepts of *structure*, *process* and *outcome*. *Structure* refers to the patient's rating of the physical environment, facilities and organizational structure within which the care occurs. *Process* measures the patient's ratings of interpersonal interactions, e.g. care, treatment, empathy and competence. *Outcome* comprises the patient's rating of the result of the process and the effect of care on their health status [61].

Regulation of quality of care and quality registers

Measuring and improving quality of care is a part of healthcare regulation. In the World Health Organization's policy framework for the 21st century, improvements in quality of care are highlighted as an important part of the work of changing the focus of healthcare to an outcome-oriented health sector [64]. Similar goals are found in the European Union's health strategy for 2014–2020, where concepts such as quality of care and patient safety are described as fundamental principles of healthcare throughout the European Union [65]. Nationally, there are a number of regulations in Swedish law demanding that the quality of care has to be systematically measured and developed [62, 66]. There is a requirement for HCPs at all levels of an organization to develop and take part in quality improvement work to improve quality of care, patient safety and effectiveness [66].

To meet the demands of evaluating and improving quality of care, the World Health Organization supports the development of Quality Registers as a tool for continuous quality development [64]. The Swedish Association of Local Authorities and Regions has established several National Quality Registers in Sweden since the 1970s [67].

In National Quality Registers, there are two different measurements for reporting patients' perspective on quality of care. While Patient Reported Outcome Measures (PROMs) assess patients' views on the outcome of healthcare, Patient Reported Experience Measures (PREMs) cover patients' experiences and satisfaction with structure (access to services and convenience of localities) and/or the process (interactions with HCPs). PREMs can also include outcomes, but from a different perspective than PROMs: while PROMs assess outcomes as descriptions of the patient's health status (e.g. treatment outcome), PREMs comprise an evaluation of the results (e.g. satisfaction with outcome) [68] (Figure 1).

Figure 1. Illustration of patient-reported outcome measures (PROMs) and patient-reported experience measures (PREMs) in relation to Donabedian's three quality measures (structure, process and outcome). From Nilsson et al. [68], modified by Grundström.

Quality of care related to endometriosis

As mentioned earlier in this thesis, dissatisfaction with the diagnostic delay and HCPs' attitudes when encountering women with endometriosis have been highlighted [5, 17], but research focusing on quality of care is limited. Kundu et al. [69] reported that in test responses from a group of 135 women with endometriosis, the quality of care dimension of the process was criticized. The women asked for improvements in HCPs' ability to interact, communicate and show empathy during healthcare encounters [69].

The construction of the Guideline of the European Society of Human Reproduction and Embryology was an attempt to improve European en-

ometriosis care based on evidence from the literature and good clinical practice [4]. In order to overcome barriers to guideline adherence, Schleedoorn et al. [70] used a panel of endometriosis patients and HCPs in nine European countries to select the most important recommendations in the guideline. Patients and HCPs differed in their initial perceptions regarding quality of care but, during the last step of the analysis, they agreed on 17 key recommendations that were extracted. These cover all areas of endometriosis care and relate to the three dimensions of quality of care (structure, process and outcome) [70].

In Sweden, national guidelines for endometriosis treatment were recently developed by the National Board of Health and Welfare. They comprise recommendations on actions at early symptoms, diagnostics, and treatment options and emphasize the importance of a multiprofessional care [45].

Rationale

Historically, women have been absent from much of the medical discussion about their bodies, and the healthcare they receive. Considering this, there is a general knowledge gap that needs to be filled when it comes to experiences and treatment of diseases affecting the female body [71]. Furthermore, menstrual concealment may lead to delays in seeking medical care for problems that are closely connected with menstruation but in fact are symptoms of endometriosis, a condition that may affect women's whole lifecycle, and often lead to psychological, physiological, reproductive and social impacts [5, 13, 17].

This highlights the need for effective and high-quality healthcare for women with endometriosis symptoms or with diagnosed endometriosis (in this thesis expressed as “endometriosis healthcare”, i.e. all encounters between women and healthcare that are related to endometriosis symptoms). However, research about endometriosis healthcare and the quality of that care is scanty, and endometriosis is still known as “the hidden disease” [40]. Therefore, experiences, outcomes and quality of endometriosis healthcare are the focus of this thesis.

AIMS

The aim of this thesis was to identify, describe and analyse the experiences, outcomes and quality of endometriosis healthcare from different perspectives.

The specific aims were:

- To identify and describe the experience of healthcare encounters among women with endometriosis (study I).
- To identify and describe HCPs' experiences when meeting women with symptoms that might indicate endometriosis (study II).
- To evaluate pain thresholds in women with persistent pelvic pain with and without confirmed endometriosis or healthy, unaffected controls and analyse how pain thresholds in these cohorts related to duration of pelvic pain, quality of life, and symptoms of anxiety and depression (study III).
- To determine whether the PREMs and PROMs after benign hysterectomy differed in women with and without a confirmed diagnosis of endometriosis associated with or without a preoperative complaint of pelvic pain (study IV).

METHOD

Designs

A variety of methods was used in this thesis, which enabled the analysis and description of different aspects of endometriosis healthcare [72, 73].

The experiences of healthcare encounters among women diagnosed with endometriosis (study I) and HCPs (study II) were identified and described using a qualitative design, with data collected from individual interviews. Next, pain thresholds, duration of PPP, HRQoL and symptoms of anxiety and depression were examined and compared in women with and without PPP and endometriosis in a quantitative cross-sectional observational comparative study using quantitative sensory testing (QST) and questionnaires (study III). Finally, PREMs and PROMs after benign hysterectomy were analysed in women with and without PPP and endometriosis in a quantitative observational study using register data from the National Quality Register for Gynaecological Surgery (GynOp) (study IV). This variety of approaches, designs, methods and background characteristics of the participants made it possible to enlarge and deepen the understanding of the experiences, outcomes and quality of endometriosis healthcare (Table 1).

Table 1. Overview of the studies included in this thesis

	Study I	Study II	Study III	Study IV
Design	Qualitative inductive interview study	Qualitative inductive interview study	Quantitative cross-sectional observational comparative study	Quantitative observational register study
Participants/ sample*	Nine women diagnosed with endometriosis	25 HCPs	37 (women with PPP) 55 (controls)	Data from 21 798 Swedish hysterectomies on benign indication
Age* (Years)	38±8.6;23–55	51±10.3;33–71	26±5.9;18–40 (women with PPP) 30±5.6;18–40 (controls)	45±5.2;19–55
Data collection	Individual interviews	Individual interviews	QST, SF-36, EQ-5D-3L, HADS, EHP-30	Data collected from GynOp, including 57 clinics in Sweden
Dates for data collection	October 2013–February 2015	February 2012–May 2013	December 2013–June 2016	January 2004–July 2016
Data analysis	Interpretive phenomenology	Qualitative conventional content analysis	Descriptive statistics, ANOVA, Bonferroni post hoc test, Chi ² - test, Fisher's exact test, Spearman's rank-order correlation	Descriptive statistics, multivariate logistic regression analysis

Figures denote *number of participants or *mean and ± one standard deviation; range. HCP=Healthcare Professionals, PPP=Persistent Pelvic Pain, GynOp=National Quality Register for Gynaecological Surgery, QST=Quantitative Sensory Testing SF-36=36-Item Short Form Health Survey, EQ-5D-3L=EuroQoL-5 Dimension Questionnaire, EHP-30=Endometriosis Health Profile-30 HADS=Hospital Anxiety and Depression Scale.

Settings

The opportunities for women with PPP to seek medical care directly from a gynaecologist differ between and within countries. In some regions in Sweden, women have to be referred to a gynaecologist by a GP, which is also often the case in other Western countries where research on endometriosis healthcare encounters and diagnostic delays has been conducted.

Many women in Sweden also meet midwives for contraceptive counselling at antenatal care centres. These midwives are nurses who specialize in reproductive, perinatal and sexual health care, whose responsibilities involve giving advice on sexual health and prescribing contraceptives for pregnancy control, but not on the indication of dysmenorrhea [74]. Women with PPP may also encounter nurses at primary healthcare centres, and gynaecologists, midwives and nurses at gynaecological clinics and on in-patient wards.

Study I was conducted in two counties in south-eastern Sweden, and included one university hospital and two county hospitals. The three cities in which the university hospital and the county hospitals were located were similar in population sizes but differed in sociodemographic structures: the university city had lower rates of unhealth [75], higher levels of education and higher incomes than the other two cities [76].

Study II and III were conducted in one county in south-eastern Sweden, but at two hospitals; one university hospital and one county hospital. Study II also included HCPs working at one private gynaecology clinic and five primary healthcare centres. The private gynaecology clinic was located in the central part of the university city, while three of the other primary healthcare centres were situated in suburbs and two in central parts of the cities.

In study IV, a Swedish sample was used, including hysterectomies on benign indication performed in Sweden and registered in GynOp.

Participants and procedures

Study I and II

In study I, in-depth interviews were conducted with women diagnosed with endometriosis, with the aim of identifying and describing their experiences of healthcare encounters. Twelve women were invited to participate using purposive sampling of women with lived experience of seeking care for endometriosis symptoms. The women were invited by three gynaecologists, one at each hospital, who at the time were in charge of the women's endometriosis treatment. The women were consecutively invited after medical appointments with the gynaecologists, but the appointments were not always related to endometriosis. Included women had to be Swedish speaking, over 18 years of age and have a laparoscopy-verified diagnosis of endometriosis. Four women declined to participate due to physical and/or mental illness. A pilot interview was analysed and included, resulting in nine women participating in study I.

Out of the nine included women, six had a partner, while three were single. Five of the nine had children. One was on sick leave, seven worked part time (25%–80%) and one worked full time. The endometriosis diagnoses had been received 1–34 years prior to the interviews (median 10 years) (study I).

With the aim of identifying and describing HCPs' experiences when meeting women with symptoms that might indicate endometriosis, HCPs were invited to participate in study II using purposive sampling. All gynaecologists working in the departments of obstetrics and gynaecology at the university and county hospitals and at the private gynaecology clinic were invited, as were midwives working with contraceptive counselling in the same departments. Furthermore, all GPs working at primary healthcare centres in the county were also invited. The invitations were emailed to the HCPs' email addresses at their workplaces. Twenty-five HCPs gave their consent to participate. Out of these, nine were midwives working with contraceptive counselling, 10 were gynaecologists, and six were GPs at primary healthcare centres. The median number of years in professional practice was 20 years (range 5–46 years) (study II).

The procedures in study I and II were somewhat similar. All women (study I) and HCPs (study II) interested in participation were telephoned by the author. They received information about the study, confidentiality, and their right to withdraw their participation at any time. A date for the

interview was set at the participants' home (study I, n=6), in a hospital library private room (study I, n=3) or at the participants' workplace (study II, n=25). Before starting the interviews, the participants were again given oral and written information about the study, and they each gave their written consent to participate (study I, II).

Study III

In study III, pain thresholds, HRQoL and symptoms of anxiety and depression in women with PPP and suspected endometriosis were compared with those of healthy women. The correlations between pain thresholds and duration of PPP, HRQoL and symptoms of anxiety and depression were also analysed.

Women eligible for participation had a preoperative complaint PPP, sometimes combined with other endometriosis symptoms. They were admitted to the Departments of Obstetrics and Gynaecology in two cities in south-eastern Sweden for diagnostic laparoscopy on the suspicion of endometriosis between December 2013 and June 2016. Inclusion criteria were: age 18–40 years and PPP for four months or longer. PPP was defined as self-reported moderate or severe pain in the lower abdomen or pelvis, intermittent or constant, for a period of four months or longer, not occurring exclusively during menstruation or intercourse [46]. Women with a previously verified diagnosis of endometriosis or any other diagnosed chronic pain syndrome, severe mental illness or disability, or ongoing substance abuse were excluded. Pregnant or breast-feeding women were also excluded.

In total, 46 women fulfilled the criteria for participation and were invited to participate by the administrative nurses in charge of the waiting list for planned surgery. All of the women agreed to be contacted by the author, who provided them with detailed verbal and written information about the study. Forty women agreed to participate, but three did not come to the scheduled appointment, resulting in 37 participants aged 18–40.

A control group consisting of 55 healthy, pain-free women was recruited by local advertisement at the hospitals and university affiliated with the clinics. They were 18–40 years old, had no PPP or other symptoms that may indicate endometriosis, or any other chronic pain syndrome. The controls did not use any medication that could affect pain thresholds.

Before starting the experimental sessions, all participants were informed about the study and their right to withdraw participation, and all

of them gave their written consent to participate. All participants completed a standardized case report form to obtain demographics, medical and surgical history and medication use.

For the women undergoing surgery, QST for cold, heat and pressure was performed within four weeks pre-operatively. In an attempt to minimize the influence of menstrual-cycle variability on study results, the experimental sessions with controls who were not using hormonal contraceptives were conducted between days 1–7 of the menstrual cycle [77, 78].

After the QST, the participants completed questionnaires assessing HRQoL using the 36-Item Short Form Health Survey (SF-36) and Euro-QoL-5 Dimension Questionnaire (EQ-5D-3L), and symptoms of depression and anxiety (The Hospital Anxiety and Depression Scale (HADS)). Women with PPP also completed the Endometriosis Health Profile-30 (EHP-30). The order in which the questionnaires were filled in differed among the sessions.

Study IV

In study IV, PREMs and PROMs after benign hysterectomy were explored with the aim of comparing the outcomes for women with and without a confirmed diagnosis of endometriosis associated with or without a pre-operative complaint of pelvic pain. Data was extracted from GynOp, which contains almost 40 000 cases of benign hysterectomy. The study period was from 01 January 2004 to 31 July 2016. During this period, 57 gynaecological clinics registered hysterectomies in GynOp, which comprises 75% of all hysterectomies performed in Sweden during this time period [79].

Exclusion criteria were: age >55 years or having the hysterectomy on the following indications: prolapse, incontinence, complications related to pregnancy or post-partum complications. Women having any suspected malignancy, endometrial or cervical dysplasia or undergoing a prophylactic hysterectomy due to heredity for gynaecological malignancy, were also excluded. If there was no reported indication or when the surgery was performed for non-gynaecological reasons, women were also excluded. After exclusion, data from 28 776 women were eligible for analysis. Out of these, there was information lacking on pre-operative pelvic pain in 6 688 women, and no diagnosis was registered in 290 women, which resulted in a final study population of 21 798 women.

Data collection

Demographic data (study I–IV)

Demographic data for the women and HCPs in study I and II were obtained before starting the interviews. Data included age, parity, employment, marital status and years since diagnosis in study I, and age, gender and years within their profession in study II.

In study III, all the women answered a study-specific form to gather basic demographic data such as age, parity, duration of PPP, height, weight, smoking habits, employment, present and previous health status and present and previous medication use.

Demographics from women undergoing hysterectomy (study IV) were obtained from GynOp. Data included age, parity, height, weight, smoking habits and employment (Table 2).

Table 2. Demographics of women in study III and IV

	Study III			Study IV			
	Women with PPP and:		Healthy controls (3C n=55)	Women with PPP and:		Women without PPP and:	
	Endometriosis* (3A n=14)	No endometriosis* (3B n=23)		Endometriosis* (4A n=3988)	No endometriosis* (4B n=10526)	Endometriosis* (4C n=1544)	No endometriosis* (4D n=5740)
Parity [†] (no. of deliveries)	0.4±0.93;0–3	0.4±0.84;0–3	1.1±1.2;0–5	2.2±1.2;0–12	2.1±1.2;0–10	2.3±1.2;0–9	2.1±1.1;0–10
BMI [†] (kg/m ²)	24.9±5.5;17.8–33.4	24.4±4.4;19.0–31.9	24.2±3.8;18.4–34.6	26.7±4.8;15.1–66.3	26.3±4.7;15.9–64.9	26.8±5.0;17.7–68.4	26.2±4.6;16.1–59.9
Currently smoking [†] (no. of women)	3 (21.4)	6 (26.1)	2 (3.6)	824 (20.9)	2144 (20.7)	267 (17.6)	827 (14.6)
Employment [‡]							
Full time	8 (57.1)	12 (52.2)	42 (76.4)	1467 (49.7)	4079 (51.9)	686 (59.4)	2616 (61.0)
Part time	2 (14.3)	9 (39.1)	13 (23.6)	616 (20.9)	1648 (21.0)	243 (21.0)	898 (20.9)
Not working [#]	4 (28.6)	2 (8.7)	0	868 (29.4)	2127 (27.1)	226 (19.6)	777 (18.1)
Duration of PPP [†] (months)	61.1±49.3;6–144	44.3±41.1;4–162	--	Not Available	Not Available	--	--

Figures denote [†]mean and $\pm$ one standard deviation; range, or ^{*}number of women and (percentage). BMI=body mass index, PPP=persistent pelvic pain. [#]Diagnosis confirmed histopathologically [#]On sick leave/maternity leave/disability pension/unemployed.

Interviews (study I & II)

An interview technique influenced by Kvale [80] was used to examine the experiences of healthcare encounters among women with endometriosis (study I) and HCPs encountering these women (study II) [80]. The interview sessions began with the author introducing herself and the study and were then followed by some small talk to create a relaxed atmosphere. Study I was initiated with one main open-ended question: “Can you please tell me about your experiences of endometriosis healthcare?” The intention was to let the women narrate their experiences as freely as possible. Interviews in study II were more structured, as a semi-structured interview guide was used. All questions in the guide were covered in all interviews, but not necessarily in the same order, following the natural progression of the conversation. In both studies, probes and follow-up questions such as “Can you give an example?” or “Can you clarify that?” were used to reach a deep understanding and to clarify parts of the interviews (Table 3).

Before starting the data collection, three pilot interviews were conducted: two for study I and one for study II. One of the women for the pilot interviews in study I was recruited by a friend of the author. The other woman (study I) and the HCP (study II) were co-workers of the author. The purposes of the pilot interviews were to test the interview question (study I) and the interview guide (study II), and to practise the author’s interview technique. When discussing the pilot interviews with senior researchers, no changes were made to the questions, but the author received some advice on how to improve her interview technique. One of the pilot interviews in study I was of high quality with rich and meaningful information and was included in the study. The other two pilot interviews were not included.

The interviews were conducted between October 2013 and February 2015 (study I) and between February 2012 and May 2013 (study II). The median duration of an interview in study I was 64 min (range 33–113 min), and 25 min (range 15–36 min) in study II. All interviews were digitally recorded, transcribed verbatim and then analysed according to methods described by Moustakas [81] (study I) and Hsieh & Shannon [82] (study II).

Table 3. Interview guides for study I and II

Study I	Study II
Demographic data	Demographic data
<ul style="list-style-type: none"> • Age • Age at diagnosis • Employment • Marital status • Parity 	<ul style="list-style-type: none"> • Gender • Age • Profession • Years within the profession
Main question	Semi-structured interview guide
<ul style="list-style-type: none"> • “Can you please tell me about your experiences of your endometriosis healthcare?” 	<ul style="list-style-type: none"> • Can you tell me about your experiences of meeting women with pelvic pain? • How do you help a woman seeking medical care for increasing menstrual pain? • What are your concerns about taking menstruation case histories? • What treatment options do you consider when you meet a woman with difficult menstrual pain? • Have you observed any of the consequences that menstrual pain can cause? • Is there any particular diagnosis you think of when you have a woman suffering from menstrual pain, ovulation pain or pain during intercourse in front of you? • If you suspect that the woman has endometriosis, how do you then inform her about this? • How do you decide what is normal menstrual pain and what may be pain caused by endometriosis? • In your experience, what are the results of the different treatments that can be offered to a woman and which ones do you normally choose? • How do you diagnose endometriosis?
Probe questions	
Can you please tell me more? You previously said that... Can you give an example? Can you clarify that?	

Pain Threshold Testing (study III)

QST is a term used to describe a set of test batteries involving psychophysical testing of muscle tissue, skin or mucosa and their pain and sensory perception pathways. The tests commonly include cold, heat and pressure sensation thresholds, pain detection thresholds or pain tolerance [83]. In 1982, O'Driscoll and Jayson defined pain threshold as "*the level of stimulus which will give rise to the first barely perceived pain in an instructed subject under given conditions of noxious stimulation*" [84 p. 31].

The measurement of pain thresholds using QST can be performed using different algorithms, such as the *methods of levels* and the *method of limits*. Both algorithms have their strengths and limitations. When using *method of levels* the stimulus is presented stepwise below and then above the pain thresholds. The participant grades the experience of painfulness after each step. When using the *method of limits*, the stimulus start on a neutral level and increased until it is stopped by the participant [85].

In study III, pain thresholds for heat and cold were measured using the *method of limits* by using the thermotesting device Medoc TSA II NeuroSensory Analyser (Medoc Ltd., Ramat Yishai, Israel) (Figure 2). A thermode with a contact surface of 9.0 cm² was fixed with textile strips onto the test area and filled with flowing water, which, depending on the test, resulted in cooling or heating of the skin. The thermode was connected to a computer that controlled the device and recorded threshold data. From a baseline of 32°C, the temperature of the thermode was increased or decreased with a rate changing between 0.3°C/s and 4.0°C/s. To determine the pain threshold, the participants were instructed to turn off the stimulation by pressing a stop button on the first painful sensation. For safety reasons, the unit automatically stopped measurements at a temperature of 0°C or 50°C. To avoid skin irritation, the thermode quickly returned to the baseline temperature.

A digital pressure algometer (Somedic, Hörby, Sweden) was used to determine pressure pain thresholds (Figure 3). With a blunt rubber contact surface of 1 cm², the algometer was applied at a rate of 40 KPa/s and was terminated by the participants saying "stop" when the perception of pressure turned into a painful sensation.

Figure 2. Thermal Sensory Analyser (TSA II). Picture used with permission.
<http://www.medoc-web.com>

Figure 3. Digital pressure algometer. Picture used with permission.
<http://www.somedic.com>

Pain thresholds for heat, cold and pressure were assessed at six locations on the body: a) on the abdominal wall seven cm lateral to the umbilicus on both sides; b) just above the symphysis pubis, five cm lateral to the midline on both sides; c) on the medial plane of the low back just below the fifth lumbar vertebra; and d) on the dominant leg, four cm distally from the tuberositas tibiae (Figure 4). Sites a, b and c were assessed as the referral areas of menstrual pain and site d as the non-pain referral control area. Three repeated measurements were performed at each location with an interval of 10 seconds. The individual pain threshold for each location was calculated and used in the analysis as an arithmetic mean of the three measurements at each location. The testing order of the different stimuli, and the order of the locations on the body, were altered among the participants, but pain thresholds for cold were always determined before thresholds for heat, due to a pre-setting in the computer program. A total mean value for each modality (heat, cold and pressure) was calculated from the average of all locations.

Figure 4. The six locations on the body where the quantitative sensory testing was performed. a) the abdominal wall seven cm lateral to the umbilicus on both sides, b) just above the symphysis pubis, five cm lateral to the midline on both sides, c) the medial plane of the low back just below the fifth lumbar vertebra, and d) on the dominant leg, four cm distally from the tuberositas tibiae.

Picture free for usage from <http://clipartx.info>. Modified by Grundström.

Questionnaires (study III & IV)

36-Item Short Form Health Survey (study III)

SF-36 measures patient-reported HRQoL for 36 items divided into two overall dimensions: physical component summary and mental component summary. The physical component summary comprises physical functioning, role limitations (physical), bodily pain and general health. The mental component summary comprises vitality, social functioning, role limitations (emotional) and mental health. The health domain scales and the overall dimensions are analysed according to standard procedures and range from 0–100. High scores indicate better health [86]. The Swedish version of SF-36 is valid and reliable, with a Cronbach's coefficient of $\alpha \geq 0.84$ in all dimensions [87]. The instrument is also validated for women with endometriosis ($\alpha \geq 0.73$ in all dimensions) [88]. In study III, the internal consistency (Cronbach's α) ranged between 0.88 and 0.94 in the different dimensions, which indicates good reliability.

EuroQoL-5 Dimension Questionnaire (study III)

The EQ-5D-3L measures five dimensions of patients' self-rated health status: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. For each dimension, possible answers are: no problem, some problem, or extreme problem. The answers generate 243 combinations or unique health statuses. The individual health status is transformed using standard algorithms to a scale that runs from -0.54 to 1, where zero equals death and 1 equals perfect health. Any status below zero indicates a state worse than death [89]. The Swedish version of the questionnaire has been validated [90]. Cronbach's α coefficient in study III was 0.70, which is considered as acceptable.

Endometriosis Health Profile-30 (study III)

EHP-30 is a specific instrument measuring self-rated HRQoL derived from in-depth interviews with women diagnosed with endometriosis. The 30-item questionnaire consists of five dimensions: pain (11 items), control and loss of control (6 items), emotional well-being (6 items), social support (4 items) and self-image (3 items) within the last four weeks. Each item is answered on a five-point Likert-type scale and transformed into a 0–100 subscale score for each dimension. EHP-30 has been shown to be a valid and reliable instrument with Cronbach's α coefficient ranging from 0.83 to 0.93 [91–93]. The Swedish translation has been validated and found to be acceptable (Unpublished data). In study III, the reliability varied but was acceptable to good: Cronbach's α coefficient for the different dimensions was 0.75–0.85.

Hospital Anxiety and Depression Scale (study III)

HADS is an instrument that measures self-reported symptoms of anxiety and depression in the context of somatic care. It consists of 14 items divided into anxiety subscale and depression subscale. Each scale is composed of seven questions and the range for each subscale is 0–21 points, with higher scores indicating a higher level of symptoms of anxiety or depression [94]. The Swedish version of HADS has a high validity and a Cronbach's α coefficient of 0.84 for the anxiety scale and 0.82 for the depression scale [95]. Cronbach's α coefficient in study III was 0.86 for anxiety and 0.89 for depression, showing good reliability.

National Quality Register for Gynaecological Surgery (study IV)

The GynOp was established in 1997. The organizations responsible for the register are the Swedish Association of Local Authorities and Regions, the National Board of Health and Welfare and the Swedish Society of Obstetrics and Gynaecology. The register includes seven sections covering surgical areas of gynaecology such as hysterectomy on benign or malign indication, hysteroscopy or endometrial ablation, surgery of fallopian tubes and/or ovaries, and surgery due to incontinence, prolapse or obstetric anal sphincter rupture [79].

Patients with a planned operation are included in the register after being sent written information and given the opportunity to decline participation. All extracted data is encoded, and it is not possible to identify any of the patients [79, 96]. The registered data is collected through patient questionnaires and forms completed by surgeons. Patients received questionnaires pre-operatively as well as eight weeks and one year post-operatively (Table 4). Since 2008, patients have been invited to answer the questionnaires online. If patients prefer, the questionnaires are instead sent by post. The overall response rate for the patient questionnaire is 90%, and 90% of surgeons complete the forms [79].

Table 4. Data collection procedure in GynOp

Questionnaire/ form	Collection time	Data content
Preoperative questionnaire (patient)	At decision for surgery	Sociodemographic data, health status, medical assessment of health and symptoms
Preoperative form (gynaecologist)	At decision for surgery	History; physical and gynaecological examinations
Operation form (gynaecologist)	Directly after surgery	Surgery data
Postoperative form (gynaecologist)	After discharge	Course of events during hospital stay
Eight-week follow-up questionnaire (patient)	Sent six weeks after surgery. Usually completed and registered approx. eight weeks postoperative. When necessary, two reminders are sent	General and medical follow-up questions, well-being and surgery-related complications, recovery and improvement
One-year follow-up questionnaire (patient)	Sent one year after surgery. When necessary, two reminders are sent	Similar questions as in preoperative and eight-week follow-up, ratings of satisfaction

GynOp=National Quality Register for Gynaecological Surgery

Study-relevant demographic data was collected from the preoperative questionnaire. From the preoperative form, operation form and postoperative form, clinical data was collected, including American Society of Anaesthesiologists classification, mode of hysterectomy (abdominal, vaginal or laparoscopy), hysterectomy type (total or subtotal), whether the patient had a remaining ovary at the conclusion of the surgery, and complications during the hospital stay. Additionally, PREMs and PROMs were extracted from the eight-week and one-year questionnaires. This data comprised questions concerning the women's experiences of the length of their hospital stay, the occurrence of self-rated complications after discharge, and current medical condition after eight weeks, along with their satisfaction with the operation, occurrence of complications after discharge, and current medical condition one year after the surgery. To enable the use of the answers in the logistic regression analyses, the outcome measures were dichotomized (Table 5).

Table 5. The PREM and PROM questions plus original and dichotomized answers

Eight-week questionnaire	Original answers	Dichotomized answers
How do you rate the length of your hospital stay? (PREM)	<i>Too long</i> <i>Adequate</i> <i>Too short</i>	<i>Sufficient (too long/adequate)</i> <i>Too short</i>
Have you experienced any unexpected complications related to the surgery? (PROM)	<i>No</i> <i>Yes, mild</i> <i>Yes, severe</i> <i>Yes, both mild and severe</i>	<i>No complications/mild</i> <i>Severe/both mild and severe</i>
How do you rate the results of the surgery so far? "My medical condition is:" (PROM)	<i>Much improved</i> <i>Improved</i> <i>Unchanged</i> <i>Worse</i> <i>Much worse</i>	<i>Much improved/ Improved</i> <i>Unchanged/Worse/Much worse</i>
One-year questionnaire	Original answers	Dichotomized answers
Regarding the results of the operation, I am: (PREM)	<i>Very satisfied</i> <i>Satisfied</i> <i>Neither-nor</i> <i>Dissatisfied</i> <i>Very dissatisfied</i>	<i>Very satisfied/Satisfied</i> <i>Neither-nor/Dissatisfied/Very dissatisfied</i>
During the period from two months after the surgery until this day, have you had any complications related to the surgery? (PROM)	<i>No</i> <i>Yes, mild</i> <i>Yes, severe</i>	<i>No complications/mild</i> <i>Severe</i>
My medical condition is: (PROM)	<i>Much improved</i> <i>Improved</i> <i>Unchanged</i> <i>Worse</i> <i>Much worse</i>	<i>Much improved/ Improved</i> <i>Unchanged/Worse/Much worse</i>

PREM=Patient Reported Experience Measure, PROM=Patient Reported Outcome Measure.

Data analysis

Qualitative method (study I & II)

The qualitative studies took an inductive approach, which can be described as working from a blank page. The intention was to let the data itself determine the structure and meaning of the findings. There is a wide range of qualitative methods, and the choice of method is dependent on the aim of the study [72]. Study I and II were analysed using different methods: interpretive phenomenology (study I) [81] and conventional content analysis (study II) [82].

Interpretive phenomenology

Phenomenology is the philosophical study of the structures of the world as it is experienced and perceived. As a research method, it can be either descriptive or interpretive.

The foundational question in phenomenological research is: *What is the meaning, structure and essence of the lived experience of this phenomenon for this person?* To answer this question, the researcher conducts in-depth interviews with people who have *directly* experienced the phenomenon; they have “lived experience” as opposed to second-hand experience. The defining characteristic of a phenomenological study is the assumption that *there is an essence or essences to a shared experience* [72].

In interpretive phenomenology, the pre-understanding of the researcher is identified, reported and then used in the interpretation of the text during the analysis to bring meaning and depth to the findings [81].

Since the aim of study I was to identify and describe the essence of the *lived experience* of a phenomenon (i.e. encountering healthcare while having endometriosis symptoms), phenomenology was chosen as an appropriate method [81]. Before starting the interviews, the author reflected on her pre-understanding, which consisted of former experiences, knowledge and preconceptions of meeting women with endometriosis from her clinical work as a registered nurse in the department of gynaecology.

The analysis was conducted according to Moustakas' modified version of the Stevick-Colaizzi-Keen method, adding interpretation. For each transcript, the following steps were performed: first, the text was read through several times, and significant statements describing the experi-

ence were highlighted and considered. These statements, the “meaning units”, were recorded, and overlapping or repetitive statements were deleted. Next, the remaining meaning units were related and clustered into themes; then a textural description and labelling of each theme was undertaken, mainly using the words in the transcripts. The next step was to reflect on the variation and structure of the themes. The meaning of each theme was adjusted and defined using the author’s pre-understanding and interpretations of the text. These steps were repeated for each transcript. The next step was to integrate the textural and structural descriptions from each theme into general themes. Hence, each general theme consisted of experiences from several women. The final step was to identify and describe the essence, the core meaning of the experience, which represented all aspects of all women’s experiences emerging from the themes and general themes [81].

Conventional content analysis

Content analysis is a method used for analysing the content of textual data. It can be quantitative, counting frequencies of words or types of different content, or qualitative, which focuses on the meaning of the content [82]. Qualitative content analysis can be described as a systematic process enabling the identification, coding and categorization of patterns in a text. There are several well-accepted methods that can be used within the frame of content analysis [72].

In study II, conventional content analysis, as described by Hsieh and Shannon [82], was chosen. The analysis was performed based on a number of steps. The first was to read the interviews several times, to obtain a sense of the whole. The next step was to read the text more thoroughly and to highlight the exact words that seemed to capture key thoughts. Then, the author’s first impressions, thoughts and initial analysis of the text were noted. The words highlighted in the previous step were clustered based on how they were linked and related. Three clusters were created. Finally, each cluster was defined, described and labelled [82].

Quantitative method (study III & IV)

In study III and IV, the women were divided into subgroups to enable comparisons between women with and without a subjective complaint of pain and biopsy-proven endometriosis. The three groups in study III were women with PPP and an endometriosis diagnosis confirmed histopathologically (group 3A), women with PPP and no endometriosis diagnosis confirmed histopathologically (group 3B) and healthy, pain-free volunteers (group 3C) (Figure 5).

Figure 5. The subgroups of participants in study III. *Biopsy-proven endometriosis. PPP=persistent pelvic pain.

In study IV, the index group consisted of women with a subjective complaint of pain and an endometriosis diagnosis confirmed histopathologically (group 4A). One comparison group consisted of women with a subjective complaint of pelvic pain preoperatively with other diagnoses but with no histopathologically verified endometriosis discovered during the operation (group 4B). The two other comparison groups consisted of preoperatively subjectively pain-free women with a histopathologically verified endometriosis diagnosis discovered during the operation (group 4C), and preoperatively subjectively pain-free women with other diagnoses than endometriosis (group 4D) (Figure 6). The diagnoses in groups 4B and 4D were menstrual bleeding disorders, myomas and cysts.

Figure 6. The subgroups of participants in study IV. *Biopsy-proven endometriosis. PPP=persistent pelvic pain.

Statistics

Statistical analyses were performed using Dell Software Statistica version 13.0 and the IBM Statistical Package for the Social Sciences version 23.0. The level of statistical significance was set at <0.05 in all analyses.

Descriptive statistics were used for presentations of the mean, standard deviation and range for data on continuous scales, and of frequency and percentage for nominal data (study I-IV).

Comparisons of demographic data between the groups were made using ANOVA and the Bonferroni post hoc test for continuous variables. A chi-square test or Fisher's exact test were used for the comparison of categorical data (study III, IV).

In study III, crude differences in pain thresholds between the groups were measured using univariate ANOVA and the Bonferroni post hoc test. Adjustments were made for the known and potentially confounding factors of smoking habits and age, which were simultaneously added to the multivariate ANOVA model. Bonferroni post hoc tests were used to analyse the pairwise associations between groups (study III).

The strength and direction of the assumed monotonic relationships between the means of pain thresholds for each stimulus (heat, cold and pressure) and duration of PPP was measured using Spearman's rank-order correlation presented as the Spearman's rho (R). Additionally, the relationships between pain thresholds and the specific subscales for bodily pain and mental health in the SF-36, pain and emotional wellbeing in the EHP-30, and level of symptoms of anxiety and depression in the HADS were also measured using Spearman's rank-order correlation. The PPP groups were merged in the correlation analyses and analysed as one group because of the equality in pain thresholds in those with and without endometriosis and the relatively low number of women in each group .

Internal consistency in the questionnaires was measured with Cronbach's α coefficient (study III).

In order to compare the PREMs and PROMs in the different groups, multivariate logistic regression analyses were conducted using binary logistic regression in study IV. Using the Enter method, the models were adjusted for the following known or presumed confounding factors: age, parity, BMI (body mass index) (continuous variable), American Society of Anaesthesiologists' classification, smoking habits, employment, mode of hysterectomy, hysterectomy type, occurrence of bilateral oophorectomy, mode of anaesthesia and occurrence of complications during hospital stay. The results of the comparisons of outcome measures were presented

as adjusted odds ratios (aORs) and 95% confidence intervals (95% CIs) (study IV) [97].

Ethical considerations

The studies were designed and performed following the ethical principles established by the World Medical Association Declaration of Helsinki [98]. Permission to conduct the studies was granted by the Regional Ethical Review Board in Linköping (Reg. no. 2011/344-31 (study I-II), Reg. no. 2013/19-31 (study III), Reg. no. M19-07; T4-09; 2016/66-32 (study IV)).

Participants in study I-III gave written, informed consent after receiving oral and written information. Women with PPP constitute an exposed patient group with a disease that may interfere with daily life activities and a lot of healthcare consuming history [5], and they might experience participating in a clinical study as another burden upon their stressful life situation (study I, III). For HCPs working in the clinical reality, it may be hard to find time to participate in this type of research (study II). However, it is important to undertake these studies in order to gain more knowledge about healthcare experiences and to be able to analyse and improve quality of care.

The controls were volunteers and received a 100 SEK cinema ticket for taking the time to participate (study III).

All participants were informed that they could terminate or withdraw participation at any time without explanation or consequences for their future care or working situation (study I-III).

In accordance with Swedish law [99], the women in study IV gave formal consent to participate in the register and that the data could be used for research purposes by answering the health declaration and the questionnaires.

There was a potential risk that data collection via interviews or questionnaires could be perceived as burdensome by the participants. Consideration was given to the choice of number of questionnaires and tests, to limit the number of questions as much as possible. If participants needed help in completing the questionnaires, this was provided. Data collection (study I-III) was carried out by the author, who did not participate in and could not influence the women's care or the HCPs' working situation.

During the data collection in study I and III, some women felt emotional as the research topic led them to recall and re-experience negative and sorrowful experiences from the past. In these situations, the author

tried to be sensitive, and gave the women an opportunity to pause or discontinue the data collection. However, all the women chose to continue their participation, and afterwards they were offered contact details for support from a social worker. No distress was detected in HCPs during interviews in study II, or among controls in study III.

In study III, the participants were exposed to short-term pain or discomfort during QST. However, this pain or discomfort should not differ from what is experienced in daily life activities or during examinations and tests in routine medical procedures, and it could be stopped by the women themselves. There are no known potential risks in measuring pain thresholds [85].

All participants were guaranteed confidentiality and all data, including interview transcripts, questionnaires, experimental data and register data were coded and stored safely (study I-IV) [98].

In the manuscripts and in the thesis, the word “women” was generally used. However, the author is aware that there are individuals with endometriosis who do not identify as women.

RESULTS

The results of the thesis are summarized in the following three themes: *The struggle to visualize the pain*, *The endometriosis diagnosis as a key to understanding and enduring persistent pelvic pain* and *Healthcare encounters as potentially life changing*. The results were also deductively analysed using the theoretical frameworks of corroborating encounters and quality of care.

The women in study I had experienced troublesome encounters with HCPs. They struggled with disclosing their hidden pain and tried to make it “real”; a struggle that was detected and described by the HCPs (study I, II). If the healthcare workers managed to acknowledge this pain, the encounters could be corroborating and could have a positive influence on self-esteem and self-worth, which sometimes led to an important change in the women’s lives (study I).

In study III, pain thresholds among women with PPP and suspected endometriosis were compared with pain thresholds in healthy controls. The results showed widespread reduced pain thresholds at all the sites on the body that were examined among women with PPP, which can be interpreted as a proxy for CS (study III). The knowledge that PPP might cause CS enriches our understanding of the pain that women described in study I.

The women with endometriosis also described how the PPP affected their HRQoL and mental wellbeing study (study I), which was also shown in study III, in which women with PPP had significantly lower HRQoL and more symptoms of anxiety and depression compared with healthy controls.

Finally, the experiences and outcomes of hysterectomy were assessed and compared in study IV. The results showed that the majority of women both with and without PPP and with and without endometriosis were satisfied with the outcome and experience of their surgery. During the interviews in study I, undergoing hysterectomy was described by some women as the “final option” in the treatment of their endometriosis and they expected to be pain-free afterwards. This aspect was not included in the analysis as study I aimed to describe experiences of healthcare encounters, but it is interesting in relation to the results of this thesis.

The struggle to visualize the pain

Women turning to healthcare for endometriosis symptoms were a heterogeneous patient group that was often encountered by a variety of different HCPs. The women sought medical care at primary healthcare centres and at gynaecological clinics, where they encountered GPs, gynaecologists and nurses. Additionally, the PPP was sometimes disclosed to midwives in conversations about menstruation during contraceptive counselling (study I, II).

The healthcare encounters were experienced as troublesome, from both the women's and the HCPs' perspectives (study I, II). The women described their pain as special in the sense that it was invisible, and thus hidden from others, irrespectively of how "real" the pain experience was (study I). Even though many HCPs were aware of the course of the disease and its symptoms, they often experienced women with PPP as challenging to meet and hard to please. The characteristics of the pain, i.e. the fact that it often occurred during menstruation, made it easy to misinterpret the pain as dysmenorrhea, which was experienced as more easily handled: HCPs could focus on regular treatment for dysmenorrhea (study II). However, the focus on menstruation and dysmenorrhea was not always appreciated by the women, who were often convinced that the pain was not merely menstrual problems. They felt normalized and trivialized when the pain was given other explanations that they felt to be inaccurate, such as infections, miscarriage, or irritable bowel syndrome (study I).

One crucial aspect during the encounters was that women wanted their healthcare to confirm and acknowledge their pain as "real". They struggled to convey their hidden pain to the HCPs, and described feelings of exposure and disbelief during their journey through healthcare. The exposure was related to the vulnerability of undressing for gynaecological examinations or surgical treatment, and to having to repeatedly confide their intimate life stories to HCPs. *"To be exposed, that's something you don't want to risk, so every time it's like a mental procedure, the sense of exposure"* (study I).

The pain that was described by the women in study I was the focus of study III, in which pain thresholds were measured using QST. The results showed widespread alterations in pain thresholds among women with PPP (group 3A and 3B, Figure 5) compared with healthy controls (group 3C, Figure 5). Table 6 shows the thresholds depicted for each location, whereas the mean thresholds of all locations are illustrated in Figure 7.

Table 6. Pain thresholds for heat (°C), cold (°C), and pressure (kPa) in women with PPP with or without a biopsy-proven endometriosis diagnosis and in healthy controls. The mean values are calculated from the three measurements at each location

Women with PPP and:					ANOVA [#]		Bonferroni post hoc test [#]	
		Endometriosis* (3A n=14)	No endometriosis* (3B n=23)	Healthy controls (3C n=55)	p-value	3A vs. 3B p-value	3A vs. 3C p-value	3B vs. 3C p-value
Heat (°C)	L5	43.97±4.1	43.4±4.6	47.2±2.7	<0.001	>0.999	0.006	<0.001
	ABD U7R	45.2±4.0	43.8±3.8	47.8±2.1	<0.001	0.451	0.017	<0.001
	ABD U7L	44.6±4.1	43.2±4.4	47.6±2.3	<0.001	0.586	0.010	<0.001
	ASP5R	45.0±4.0	43.4±3.8	47.5±2.4	<0.001	0.398	0.022	<0.001
	ASP5L	44.3±4.7	43.0±4.2	47.5±2.4	<0.001	0.739	0.006	<0.001
Cold (°C)	TT4D	45.3±4.1	44.0±3.6	47.6±2.2	<0.001	0.545	0.030	<0.001
	L5	11.9±9.7	14.5±11.9	3.8±7.7	<0.001	>0.999	0.012	<0.001
	ABD U7R	11.3±9.2	11.1±9.8	3.0±6.3	<0.001	>0.999	0.002	<0.001
	ABD U7L	12.6±10.4	14.2±9.9	3.8±7.2	<0.001	>0.999	0.003	<0.001
	ASP5R	14.6±10.6	16.7±10.8	6.4±9.1	<0.001	>0.999	0.019	<0.001
Pressure (kPa)	ASP5L	14.9±10.1	17.4±10.5	4.9±8.3	<0.001	>0.999	0.019	<0.001
	TT4D	6.5±9.5	8.7±9.7	1.4±4.1	<0.001	>0.999	0.039	<0.001
	L5	557±287	477±327	815±334	<0.001	>0.999	0.031	<0.001
	ABD U7R	232±86	259±169	436±180	<0.001	>0.999	<0.001	<0.001
	ABD U7L	253±101	229±138	440±185	<0.001	>0.999	<0.001	<0.001
	ASP5R	225±80	204±106	403±139	<0.001	>0.999	<0.001	<0.001
	ASP5L	234±80	209±117	390±136	<0.001	>0.999	<0.001	<0.001
	TT4D	618±272	466±208	809±271	<0.001	0.261	0.046	<0.001

Figures denote mean± one standard deviation. [#]Adjusted for age and smoking. *Biopsy-proven endometriosis. PPP=persistent pelvic pain. L5 – back, over L5; Abd U7R – abdominal wall, 7 cm right of umbilicus; Abd U7L – abdominal wall, 7 cm left of umbilicus; ASP5R – above symphysis pubis, 5 cm right of midline; ASP5L – above symphysis pubis, 5 cm left of midline.; TT4D – 4 cm distal of tuberositas tibiae of dominant leg

	ANOVA <i>p</i> -value	Bonferroni post hoc test	
		3A vs. 3B <i>p</i> -value	3B vs. 3C <i>p</i> -value
Mean heat threshold (°C)	Crude Adjusted*	<0.001 <0.001	0.004 0.004
Mean cold threshold (°C)	Crude Adjusted*	<0.001 <0.001	0.001 0.001
Mean pressure threshold (kPa)	Crude Adjusted*	<0.001 <0.001	<0.001 <0.001

Figure 7. Mean heat, cold and pressure pain thresholds. Group 3A=PPP and endometriosis; group 3B=PPP and no endometriosis; group 3C=control. PPP=Persistent pelvic pain. * Adjusted for age and smoking.

Furthermore, the duration of PPP showed a significant positive correlation with reduced pain thresholds ($R=-0.28$, $p=0.006$ for heat, $R=0.27$, $p=0.009$ for cold, and $R=-0.34$, $p<0.001$ for pressure) (study III). The results suggest that if PPP is not acknowledged and treated properly, there might be a risk of long-term consequences.

The long-term consequences of unrelieved PPP and endometriosis could possibly also affect the results of PREM and PROM after hysterectomy: even though the majority of women undergoing hysterectomy on benign indications during the study time (January 2004–July 2016), scored high on PREMs and PROMs, women with pelvic pain and endometriosis (group 4A, Figure 6) had higher odds of being dissatisfied with the result of their surgery after discharge than women with pelvic pain without endometriosis (group 4B, Figure 6) (aOR 1.30, 95%CI; 1.02–1.65) or women without pelvic pain with endometriosis (group 4C, Figure 6) (aOR 1.58, 95%CI; 1.02–2.45) or with neither pelvic pain, nor endometriosis (group 4D, Figure 6) (aOR 1.83, 95%CI; 1.35–2.48) (study IV) (Table 7). Women in group 4A also experienced more severe complications after discharge compared with group 4B (aOR 1.37, 95%CI; 1.03–1.82) and group 4D (aOR 2.31, 95%CI; 1.57–3.39) one year post-operatively.

Table 7. The PREM and PROM questions from the eight-week and one-year questionnaires and the prevalence of the dichotomized answers

	PPP and endometriosis* (4A) n=3988	PPP and no endometriosis* (4B) n=10526	No PPP and endometriosis* (4C) n=1544	No PPP, no endometriosis* (4D) n=5740	aOR(95% CI)	
					4A vs. 4B	4A vs. 4C
<u>The eight-week questionnaire</u>						
I consider length of hospital stay:						
Sufficient	2913 (85.3)	7758 (86.2)	1182 (87.6)	4568 (90.9)		
Too short	503 (14.7)	1242 (13.8)	167 (12.4)	515 (10.1)	1.04 (0.87-1.23)	1.32 (0.97-1.81)
I had complications after discharge:						
No complications/Mild	2961 (86.1)	7935 (87.9)	1221 (90.0)	4665 (91.7)		
Severe	479 (13.9)	1096 (12.1)	135 (10.0)	424 (8.3)	1.16 (0.96-1.39)	1.13 (0.83-1.54)
My medical condition is:						
Improved/Much improved	3243 (95.0)	8631 (95.8)	1293 (95.7)	4850 (95.5)		
Unchanged/Worse/Much worse	172 (5.0)	377 (4.2)	58 (4.3)	228 (4.5)	1.10 (0.82-1.47)	0.89 (0.56-1.41)
<u>The one-year questionnaire</u>						
Regarding the result of the operation, I am:						
Satisfied/Very satisfied	2695 (91.3)	7304 (92.9)	1158 (94.7)	4345 (95.4)		
Neither-not/Dissatisfied/Very dissatisfied	256 (8.7)	556 (7.1)	65 (5.3)	212 (4.6)	1.30 (1.02-1.65)	1.58 (1.02-2.45)
Complications after discharge:						
No complications/Mild	2794 (93.9)	7530 (95.1)	1188 (96.6)	4429 (97.4)		
Severe	182 (6.1)	385 (4.9)	42 (3.4)	119 (2.6)	1.37 (1.03-1.82)	1.42 (0.85-2.37)
My medical condition is:						
Improved/Much improved	1979 (95.2)	5088 (95.7)	859 (95.9)	3155 (95.7)		
Unchanged/Worse/Much worse	99 (4.8)	228 (4.3)	37 (4.1)	141 (4.3)	1.03 (0.71-1.50)	0.98 (0.54-1.78)

Figures denote no. of women and (per cent). *Biopsy-proven endometriosis. PREM=Patient Reported Experience Measure, PROM=Patient Reported Outcome Measure. PPP=persistent pelvic pain. aOR, adjusted odds ratio; CI, confidence interval. In the multivariate logistic regression models, adjustments were made for age, parity, BMI, American Society of Anaesthesiologists' classification, smoking habits, employment, mode of hysterectomy, hysterectomy type, occurrence of bilateral oophorectomy, mode of anaesthesia and occurrence of complications during hospital stay.

The women described pain as a feature that negatively affected their mental, physical and sexual health (study I). In concordance, the women with PPP (group 3A and 3B, Figure 5) in study III showed significantly lower HRQoL compared to healthy controls when measured by SF-36 ($p<0.001$ on all dimensions for both group 3A and 3B, Figure 5) (Figure 8) and EQ-5D-3L ($p<0.001$ for both 3A and 3B, Figure 5) (Figure 9). According to HADS, women with PPP also had more symptoms of anxiety and depression than controls ($p=0.003$ for anxiety and $p<0.001$ for depression in 3A, $p<0.001$ on both dimensions for group 3B, Figure 5) (Figure 10) (Table 8) (study III).

The women with PPP did not score their pain on any kind of analogue scale but SF-36 included questions about experiences of pain during the previous four months. The correlations analysis showed that, among women with PPP (merged into one group in the analysis), reduced pain thresholds for heat and cold co-varied with higher scores on the SF-36 bodily pain ($R=0.45$, $p=0.011$ for heat, $R=-0.56$, $p=0.001$ for cold). The cold pain threshold was also significantly correlated with the HADS subscale symptoms of depression ($R=0.35$, $p=0.037$), while thresholds for heat and pressure were not (study III).

Figure 8. Mean values for the answers to the different dimensions of SF-36 divided into the three groups (group 3A–C) in study III. PPP=persistent pelvic pain.

Figure 9. Mean values for the EQ-5D-3L health state index divided into the three groups (group 3A–C) in study III. PPP=persistent pelvic pain.

Figure 10. Mean values of the HADS anxiety and depression scores divided into the three groups (group 3A–C) in study III. PPP=persistent pelvic pain.

Table 8. Outcome of HRQoL (SF-36, EQ-5D-3L, EHP-30) in women with PPP with or without a biopsy-proven endometriosis diagnosis and in healthy controls

Women with PPP and:				ANOVA				Bonferroni post hoc test	
Form/subscale	Endometriosis* (3A n=14)	No endometriosis* (3B n=23)	Healthy controls (3C n=55)	p-value	3A vs. 3B p-value	3A vs. 3C p-value	3B vs. 3C p-value		
HADS	Anxiety	8.6±4.1	10.7±4.4	4.6±3.4	<0.001	0.107	0.003	<0.001	
	Depression	7.4±3.1	8.2±5.0	2.3±2.4	<0.001	0.465	<0.001	<0.001	
SF-36	Physical functioning	78.2±27.4	78.2±20.2	98.9±3.5	<0.001	>0.999	<0.001	<0.001	
	Role limitation physical	33.9±31.9	21.6±32.1	98.6±5.7	<0.001	0.247	<0.001	<0.001	
	Bodily pain	35.0±12.9	40.3±22.1	85.3±18.6	<0.001	>0.999	<0.001	<0.001	
	General health	46.7±22.8	38.3±21.3	83.7±14.7	<0.001	0.588	<0.001	<0.001	
	Vitality	30.4±21.5	31.8±24.4	65.7±17.6	<0.001	>0.999	<0.001	<0.001	
	Social functioning	56.3±18.2	36.8±20.9	92.6±13.7	<0.001	0.004	<0.001	<0.001	
	Role limitation emotional	40.5±45.6	39.4±43.2	93.8±19.5	<0.001	>0.999	<0.001	<0.001	
	Mental health	48.3±17.6	38.4±20.9	81.0±13.9	<0.001	0.287	<0.001	<0.001	
	Physical component summary	40.3±8.3	40.7±9.0	55.5±3.6	<0.001	>0.999	<0.001	<0.001	
	Mental component summary	31.0±11.7	24.7±11.9	48.8±8.7	<0.001	0.259	<0.001	<0.001	
EQ-5D-3L	Health state index	0.52±0.29	0.44±0.34	0.95±0.11	<0.001	0.928	<0.001	<0.001	
EHP-30	Pain	48.2±12.8	54.2±15.9	--	0.241	--	--	--	
	Control and powerlessness	64.0±16.7	70.6±18.0	--	0.275	--	--	--	
	Emotional well-being	55.1±14.5	56.1±17.2	--	0.858	--	--	--	
	Social support	63.4±20.0	60.8±22.2	--	0.725	--	--	--	
	Self-image	51.8±26.0	45.5±25.6	--	0.476	--	--	--	

Figures denote mean± one standard deviation. *Biopsy-proven endometriosis, PPP=persistent pelvic pain, HADS=Hospital Anxiety and Depression Scale, SF-36=36-Item Short Form Health Survey, EQ-5D-3L=EuroQoL-5 Dimension Questionnaire, EHP-30=Endometriosis Health Profile-30.

The endometriosis diagnosis as a key to understanding and enduring persistent pelvic pain

Many women with PPP described how the pain interfered with their daily lives (study I), while the HCPs stated that women should *not* have to be disabled or limited by dysmenorrhea and that the pain should *not* affect daily life. When the women expressed concerns or changes in their menstruation pattern with increasing dysmenorrhea, or additional symptoms such as deep dyspareunia or ovulation pain, the gynaecologists and most of the GPs suspected endometriosis (study II).

A majority of the midwives declared that they often met women and talked about menstruation in connection with contraceptive counselling. However, many of them did not think of endometriosis when they were asked the following question: *“Is there any particular diagnosis you think of when you have a woman suffering from menstrual pain, ovulation pain or pain during intercourse in front of you?”* The midwives stated that their work as experts on reproductive and sexual health did not include caring for women with pathological conditions such as endometriosis. At the same time, they had observed that many women had difficulties related to menstruation, such as heavy bleeding, pain and bloating, which often affected their sexual and reproductive health (study II).

These different levels of knowledge about endometriosis among HCPs were also found in the women’s stories about encountering different HCPs. Gynaecologists were described as having the most knowledge and interest in managing PPP, and were often the first HCP to mention endometriosis as a possible explanation for the symptoms (study I).

Many women found it beneficial to receive a diagnosis, and the HCPs expressed an awareness of the importance of diagnosing the condition. Receiving a diagnosis was positive and could help women to accept or manage the pain in a more constructive way. Additionally, it enabled further treatment possibilities, which gave women hope even though they had received the diagnosis of a chronic disease (study I, II).

Some women described negative experiences related to the situation in which they had received the diagnosis. After many years, they were still emotionally affected when they recalled the blunt way in which the information was given. The disease was explained to them as causing infertility, which raised questions about future reproduction and perceptions of womanhood (study I). When the HCPs were asked about how they informed women of the diagnosis, they did not mention the emotional aspects of receiving a diagnosis (study II).

The women in study I emphasized the importance of getting a diagnosis. However, the endometriosis diagnosis did not seem to influence the quantitative measures of pain thresholds or psychosocial outcomes in study III: the women who had received a diagnosis (group 3A, Figure 5) did not differ from those who had not (group 3B, Figure 5) regarding pain thresholds (Table 6), prevalence of symptoms of depression or anxiety or in HRQoL (Table 8). The only significant difference between group 3A and 3B was found in the SF-36 dimension of social functioning, where women who had received a diagnosis (group 3A, Figure 5) scored significantly higher than those who had not (group 3B, Figure 5) ($p=0.004$), which indicated higher HRQoL in this particular dimension (Table 8) (study III).

The same pattern was found in the register study. Considering the percentages in different answers, women with PPP and endometriosis (group 4A Figure 6) scored more similarly to women with PPP without endometriosis (group 4B, Figure 6) in all questions except for “*my medical condition is...*” on both the eight-week and one-year questionnaires than to the groups without PPP (group 4C and 4D, Figure 6). In the multivariate regression analysis, women in group 4A had significantly worse outcomes than those in group 4B on only two items in the one-year questionnaire (“*Regarding the results of the operation, I am*” (aOR 1.30, 95%CI; 1.02–1.65) and “*Complications after discharge?*” (aOR 1.37, 95%CI; 1.03–1.82)), whereas no differences were found in the ratings between 4A and 4B after eight weeks (Table 7) (study IV).

Healthcare encounters as potentially life changing

Every woman had her own unique life story regarding her experiences of healthcare encounters. Nevertheless, there were striking similarities. They all spoke of normalization, trivialization and disbelief, mostly before, but sometimes also after being diagnosed. Yet, all the women had experiences that radically shifted the encounters from being treated with ignorance to being acknowledged. This essence can be visualized as a double-edged sword: the overall experience of all the women consisted of both destructive and constructive memories (Figure 11) (study I).

Figure 11. Visualization of the double-edged experience of healthcare encounters.

On the constructive side of the sword, the endometriosis healthcare encounters could be life changing. The importance of these encounters was related to the intimate features of endometriosis symptoms: PPP, heavy bleeding, dysmenorrhea and dyspareunia were experienced as being related to vital aspects of female life such as menstruation, sexual health, fertility and womanhood. One woman described the relief she felt when the HCP asked her about how endometriosis affected her sexual life: *“This was a turning point for me as a woman”*. On the other side of the sword, a woman recalled the HCP’s lack of empathy about the fertility aspect as she was diagnosed: *“The only thing I remember was that he was talking about bloody rags that had grown together... It was really distressing since I was there to check infertility”* (study I).

When HCPs were able to incorporate the dimensions of sexuality, fertility and womanhood during the encounters, if only by simply confirming the consequences of pain upon these dimensions of life, the women found their symptoms easier to endure. These positive encounters were often experienced as corroborating and could change women's lives (study I).

In other words, healthcare encounters were to be experienced as life changing, they had to include some kind of holistic approach to the women's problems. The women described how the disease affected their whole existence and had consequences for essential parts of their lives, and the responses they received during these encounters affected their self-esteem and perceptions about their bodies. Therefore, they preferred HCPs who took a holistic approach, with whom they could discuss the symptoms, treatment and diagnosis in a philosophical way, focusing on psychological and emotional aspects as well as physiobiological and medical features (study I). This approach was also found in HCPs' descriptions of corroborating encounters (study II).

The importance of showing respect for mental and emotional aspects when meeting these women is particularly relevant considering the increased risk of lower HRQoL and more symptoms of depression and anxiety among women with suspected endometriosis (Figures 8–10) (Table 8) (study III).

Another important feature of a constructive and life-changing experience of endometriosis healthcare was the advantage of multidisciplinary teams to handle the most severe cases (study I, II).

The quality of endometriosis healthcare

Finally, the results of this thesis were interpreted deductively from the different dimensions of quality of care. Corroborating encounters were incorporated as a vital part of the process of high-quality endometriosis care (Figure 12).

Structure

Different components of the structure of endometriosis healthcare were found in study I and II. Both women and HCPs emphasized the importance of a structure that was able to "catch" women with suspected endometriosis at several stages of the care system: at primary healthcare centres, at gynaecological clinics and during contraceptive counselling (study I, II). The women wished for a more structured way of investigating their symptoms, without trivialization or normalization. A shorter path from first seeking medical care to being diagnosed was desired, and the long waiting time to see a gynaecologist was often criticized (study I).

Figure 12. The results of this thesis in relation to Donabedian's three dimensions of quality of care.

Proper management of endometriosis symptoms in terms of structure could facilitate the creation of corroborating encounters; if the women had a long history of encounters with, for example, GPs at primary healthcare centres, they were more sceptical about the structure of care, which could negatively affect the feelings of corroboration (study I).

Women and HCPs condemned the circumstances around seeking medical care during on-call time and desired a better structure around these acute encounters, which were problematic for both sides. The benefit of continuity in the contact between women and HCPs was emphasized as being key to the corroborating encounters. Another important aspect of the structure of care that was experienced as positive by both women and HCPs was the organization of multidisciplinary teams (study I, II).

The only PREM question that was related to structure was the one about the length of hospital stay. The results showed that women with preoperative pelvic pain and endometriosis (group 4A, Figure 6) more often reported their hospital stay as too short than the pain-free women without endometriosis (group 4D, Figure 6) (aOR 1.45, 95%CI;1.17–1.79) (study IV) (Table 7).

Process

The process of endometriosis healthcare was illuminated from different angles in study I–III.

The women and HCPs strived to create corroborating encounters that acknowledged the pain by taking a holistic and multidisciplinary approach (study I, II). However, all the women had experienced both corroborating encounters, and encounters that were experienced as negative and destructive. Limitations on the creation of corroborating encounters were: HCPs' lack of knowledge and time (study I, II) and normalization and trivialization of PPP (study I). This created feelings of distrust among the women, resulting in negative expectations of future encounters, turning the process into a vicious circle (study I). The dissonance between what women had experienced (study I) and how HCPs described their work with these women (study II) was a striking finding.

During the process of endometriosis healthcare, pain played a leading role. By measuring pain thresholds, the QST contributed to a deeper understanding of pain among women with PPP. The widespread reduced pain thresholds and the correlation between pain thresholds and duration of PPP can be seen as a manifestation of the pain that many women experienced but found difficult to convey to the outside world (study I, III).

The importance of a diagnosis was discussed by both women and HCPs (study I, II). A diagnosis provided the women with knowledge and understanding of their own bodies and could result in increased self-esteem (study I). Additionally, more treatment possibilities became available, which could be important in preventing the progress of the disease (study II). An early and correct diagnosis was experienced as a key factor in the process of corroborating endometriosis healthcare encounters (study I, II).

Outcome

Different aspects of the outcomes of endometriosis healthcare were examined in all four studies (study I–IV). The women experienced that the outcomes of the care could be life changing. Life-changing care was based on corroborating encounters during which the HCPs acknowledged and confirmed the pain as “real” (study I). The diagnosis itself was perceived as an outcome because the diagnosis often made the PPP easier to endure (study I, II).

The widespread reduced pain thresholds in women with PPP can be considered as an outcome of healthcare that has not yet been able to acknowledge and treat the pain sufficiently. Hence, the development of CS, the lower HRQoL and the higher

prevalence of symptoms of anxiety and depression could be consequences of what happened when the healthcare did not manage to meet the caring needs of this group of women (study III).

The results of study IV could reflect the potential long-term consequences of an unrelieved pain state: women with PPP and endometriosis (group 4A, Figure 6) scored worse than all three comparison groups (group 4B–D, Figure 6) in both outcome-related PREMs (results of the operation) and PROMs (complications after discharge) one year post-operatively according to the descriptive data (percentages) (study IV).

DISCUSSION

Results discussion

This thesis focuses on the experience of endometriosis healthcare, with an emphasis on the encounters between women and HCPs (study I, II), the long-term consequences of PPP on pain thresholds and the correlation of duration of PPP with HRQoL and symptoms of anxiety and depression (study III), and the patient-reported outcomes and experiences of hysterectomy (study IV). The women's experiences were related to the theory of corroborating encounters [60] and to the structure, process and outcomes of quality of endometriosis healthcare [61].

Endometriosis was experienced as a complex disease and both women and HCPs found the encounters troublesome (study I, II). Women struggled to visualize their hidden pain (study I). When their pain thresholds were measured using QST and compared with healthy controls, widespread reduced pain thresholds were found in women with PPP regardless of endometriosis (study III), which can be interpreted as a manifestation of the pain that women described in study I. The PREMs and PROMs after hysterectomy revealed that, even though a majority of women were satisfied with their treatment, the odds for unsatisfactory results were higher among those with PPP and endometriosis (study IV), which *could* be a consequence of reduced pain thresholds, indicating a state of CS, as detected in the group of women with PPP in study III.

High-quality endometriosis healthcare, as described by both women and HCPs, should provide an interaction between physical, psychological and social factors. If the healthcare acknowledged and conveyed an understanding of the pain and the effect of pain on HRQoL and mental health, and offered proper pain-relieving treatment, it could change women's lives. The life-changing encounters were experienced as corroborating and involved the three components of corroboration: showing consideration, connecting, and caring for (study I, II) [60].

Endometriosis healthcare embraces vital dimensions of female life

PPP and endometriosis are challenging and complex disorders that affect many essential areas of women's lives. The healthcare encounters had the opportunity to change women's lives as the women related the care not only to PPP, but also to vital dimensions of female life such as menstruation, sexuality and fertility (study I,

II). The findings agree with previous literature, which describes PPP as a life-world-destroying feature [5, 17, 100]. Although there are some overlaps between PPP and other chronic pain states, PPP when associated with endometriosis stands out because it is related to the concealment surrounding “women’s problems” in many cultures around the world [100]. Because of the close connection between endometriosis and menstruation, disclosing endometriosis symptoms means disclosing oneself as a menstruating person, which can be perceived as discrediting [2]. It has been argued that menstrual concealment is related to sexual politics, in the sense that female bodies have historically been seen as a threat to culture and society, which has led to attempts to control women’s reproductive and sexual health [101].

To the women in this thesis, endometriosis was not only related to their menstruation, but also to their sexuality and sexual health (study I). Sexuality is an essential dimension of human life that is characterized by physical, mental and social features, and sexual dysfunction is a known clinical challenge within endometriosis healthcare. A recent review stated that 60%–70% of women with endometriosis reported sexual dysfunction that negatively affected intimate relationships and quality of life. The most common dysfunction was dyspareunia, which also had a negative influence on desire, orgasm, and frequency of and satisfaction with sexual intercourse. Sexual dysfunction interacted with psychological distress, which in turn correlated with PPP [23].

Fertility and fear of loss of fertility is another aspect of vital dimensions of female life in endometriosis healthcare in this thesis. The women became emotional as they described situations in which HCPs raised questions about their fertility. They felt that the information was not always communicated in a respectful or empathic way (study I).

The experience of discussing fertility related to endometriosis has been reported previously. Many women have been advised to become pregnant in order to “cure” endometriosis [2, 6, 102–104], even though pregnancy as a treatment for endometriosis is a “medical myth” that has not been empirically investigated, and is not recommended in clinical guidelines [4, 45]. Such advice is problematic for several reasons: endometriosis is associated with both dyspareunia and subfertility. Moreover, a pregnancy itself does not treat endometriosis although it may temporally slow down the progress of the disease. However, most importantly, becoming a parent is a life-long commitment and responsibility to another human being and should not be considered a “treatment” for a disease.

One noteworthy point is that the aspects of neither sexuality nor fertility were illuminated in any of the HRQoL questionnaires (study III). The lack of questions concerning women’s sexual and reproductive health in EHP-30 is disturbing, as sexuality and fertility are undeniably factors in human life that are negatively affected by endometriosis and endometriosis symptoms [23].

Another often-repeated “medical myth” is the assurance that undergoing hysterectomy will decrease or eliminate PPP [17, 104]. Although the results of study IV showed a high satisfaction rate after hysterectomy (study IV), the pain mechanisms behind persistent pain and the characteristics of the disease do not preclude the pain from remaining even after hysterectomy. The widespread reduced pain thresholds suggest that women with PPP might have developed CS (study III), which does not disappear after hysterectomy. On the other hand, the hysterectomy naturally alleviates symptoms related to heavy menstrual bleeding [4]. However, hysterectomies must also be considered in the light of each woman’s reproductive preferences.

The dissonance between women’s and HCPs’ experiences

The encounters between HCPs and women with endometriosis could be corroborating if they involved an acknowledgement of the pain and were performed with mutual respect during a sufficiently long time frame. Both HCPs and women had similar ideas of what a corroborating encounter was and had the ambition to create such constructive encounters. However, there was a dissonance between how the HCPs described the encounters, and the women’s experiences (study I, II). On the one hand, HCPs claimed that they needed time, knowledge and interest to make every encounter meaningful. They were aware of strategies to accomplish a corroborating encounter by conveying trust and competence [60], and they had the ambition of confirming and acknowledging the women (study II). On the other hand, the women’s accounts of healthcare encounters were double-edged. They included constructive experiences, which comprised the positive aspects described by HCPs in study II, but they also had destructive experiences that were diametrically opposed to corroborating encounters (study I).

Similar negative experiences of healthcare encounters have been reported previously, with the main focus on the primary care consultation and encounters with GPs [6–8, 43], while research on HCPs’ experiences is limited [105, 106]. Riazi et al. [105] analysed women’s and HCPs’ descriptions of endometriosis symptoms. Gynaecologists seemed to pay less attention than women did to the symptoms’ effects on social life and daily activities [105]. The discord in descriptions of endometriosis symptoms was also reported by Fauconnier et al. [106], who compared women’s descriptions of endometriosis symptoms with those of gynaecologists. They concluded that gynaecologists had a limited perception of the dimensions of pelvic pain and how it affected women’s lives. The gynaecologists tended to separate PPP from dysmenorrhea, while women described them as two parts of the same painful symptom. Furthermore, the women described more variations than gynaecologists regarding the experience of dyspareunia [106]. To summarize, the HCPs in these two

studies [105, 106] tended to take more of a biomedical approach than the holistic view that the women in this thesis requested (study I).

The diagnosis is pivotal in endometriosis healthcare

In study III, only 14 out of 37 women (38%) with suspected endometriosis received a laparoscopy-proven diagnosis (Table 6). This does not preclude the possibility that more than 14 women actually had endometriosis, as the diagnosis was based on the subjective visualisation of lesions made by the surgeons. In study IV, 3988 out of 14 514 women with PPP (27%) received a histopathologically-proven endometriosis diagnosis (Table 7). These numbers conform to previous literature, which has reported an endometriosis diagnosis in approximately 30% of women who underwent laparoscopy for PPP [107].

The low rate of biopsy-proven endometriosis found among women with suspected endometriosis could be an indication of the complexity of diagnosing the condition.

Earlier studies have paid much attention to the problematic structure of endometriosis healthcare, i.e. the time from symptom onset to diagnosis [6–8, 33, 35–38]. In this thesis, both women and HCPs described the diagnostic delay as problematic for a number of reasons (study I, II). The most obvious problem described by women in study I was the impact of PPP upon their daily lives. Receiving a diagnosis was vital for decreasing the negative impact of pain upon mental, physical and sexual health. The diagnosis provided the women with a new level of understanding of their own bodies, and a language to communicate this understanding to others (study I). As reported previously [6, 8], the feelings of worry, anxiety, self-blame, fear and anger were often replaced with relief, vindication and hope (study I). The diagnosis also enabled more aggressive pain management and additional treatment options (study II), which could be necessary to prevent or minimise the development of CS.

As described earlier in this thesis, the structure of the diagnostic delay has been related to the roles of both women and HCPs (particularly GPs): it appears at *the patient level* and at *the medical level* [5, 17]. However, this model of diagnostic delays does not consider menstrual concealment and its relation to endometriosis. Seear [2] suggested that the disclosure of endometriosis symptoms must be processed in relation to the discrediting of menstruating women. In other words, the diagnostic delay at the patient level does not exclusively originate from women's inability to discriminate 'normal' from 'abnormal' menstrual pain: even when they do identify their menstruation as abnormal, there might be social obstacles that inhibit their readiness to disclose menstrual problems in the first place. Accordingly, pure awareness of endometriosis among women and HCPs is not sufficient if social sanctions keep discouraging women from disclosing themselves as menstruating individuals during the process of receiving care [2].

A more open social conversation about menstruation and the problems surrounding it could perhaps decrease menstrual concealment and draw more attention towards women's sexual and reproductive health in general and to menstrual pain and endometriosis specifically. HCPs play a crucial role when it comes to enlightening and spreading knowledge about menstruation and endometriosis, especially midwives who work at youth care centres or with contraceptive counselling. These midwives meet large numbers of women of reproductive age, discuss menstrual issues on a daily basis and have a distinctive responsibility for promoting sexual and reproductive health. Considering this, the findings of study II were deplorable, as the midwives did not see themselves as having much to do with endometriosis, since it was not part of "normal" menstruation (study II). Maybe a targeted awareness program could be beneficial to enlighten them about their position as potential guides towards the proper structural and process-related management of endometriosis symptoms.

The aspect of how to communicate the diagnosis to affected women was not brought up by any of the HCPs (study II), but it was experienced as a crucial moment for the women (study I). Searching the literature, no studies seem to explore this aspect of the process of endometriosis healthcare, but the attitude conveyed by the HCP while giving women the diagnosis may be an important factor to consider.

"Pain-focused" versus "disease-focused" endometriosis care

The women in this thesis described pain as a central feature of life (study I), an experience also recognized in the literature [5, 108, 109]. The medical and surgical treatment of endometriosis aims mainly at providing pain control, and secondarily at limiting the progression of the disease and at preserving fertility. During the last few decades, several medical and surgical programs have been developed and evaluated, but still there is limited evidence on the efficacy of various treatments. Most studies are conducted at specialized clinics with the risk of selection bias in both populations and HCPs. There are also inconsistencies in existing studies when it comes to definitions of endometriosis. Additionally, treatment programs often vary and the outcomes are measured in different ways, which limit the results of these evaluations [40, 110].

The lack of evidence might also be partly explained by the fact that the treatment of endometriosis is often as complex as the disease itself; endometriosis occurs in a wide range of different locations, the lesions can be diverse with respect to size and structure, women have different physical and mental responses to treatment, and experience symptoms and side-effects in individual ways [110].

Another challenge in the treatment of endometriosis is the combination of inflammatory, nociceptive and endocrine biophysical changes, which all contribute to

the pain experience in interaction with psychological factors. Recently, the aspect of CS has also gained more attention [109].

The results of this thesis contribute to the understanding of pain mechanisms by highlighting the widespread reduced thresholds among women with PPP. These reduced pain thresholds can be used as a proxy for CS and could be interpreted as a manifestation of the pain that was described in study I: the pain is “real” and should not be normalized or trivialized (study I, III). The detection of CS among women with PPP and suspected endometriosis is vital for the understanding of pain mechanisms as it may explain why therapies directed solely at endometriotic lesions often fail to sufficiently relieve pain.

The widespread reduced pain thresholds among women with suspected endometriosis compared with healthy controls suggest that women with PPP might be sensitized (study III). This may be an explanatory factor for the lower rates of satisfaction with the results of surgery among women with PPP after hysterectomy (study IV); i.e., due to CS the pain may have continued even after the menstruation ceased. These conclusions are supported in the literature [109, 111].

The significant correlation between duration of PPP and the occurrence of CS (study III) highlights the need for active and perhaps more aggressive treatment of endometriosis and PPP. The correlation illuminates one reason why PPP must not be trivialized or normalized and indicates that PPP should be taken seriously and be treated adequately from the beginning when a woman first seeks medical care. A shortening of the diagnostic delay and a comprehensive schedule for investigation and treatment using a multidisciplinary approach should be undertaken to minimize the risk of a state developing that causes severe human suffering and reduced HRQoL. Endometriosis treatment should both target the specific disease and mediate proper pain management. To reach this goal, the results of the thesis suggest that all three components of quality of care (structure, process and outcomes) need to be strengthened and further developed [61].

The “pain-focused” vs. “disease-focused” hypothesis has also been discussed in relation to HRQoL. Women in this thesis experienced that PPP affected HRQoL and mental health (study I), which was also reflected in the questionnaires: the women with PPP had significantly lower HRQoL compared with healthy controls, regardless of endometriosis (study III). The impact of PPP on HRQoL is well documented [5, 17, 29, 30, 112–114]. Yet, Siedentopf et al. [112] showed that endometriosis could impair HRQoL, work productivity and mental health *regardless* of the presence of pain symptoms. This might be explained by the fact that women with pain-free endometriosis can experience uncertainty about the course of the disease in the future, as the diagnosis itself can raise concerns about crucial aspects of female life, such as sexuality, womanhood and fertility. Moreover, the psychoneuroimmune nature of endometriosis as a chronic inflammatory disease may enhance depressive symptoms and distress, which may in turn affect the immune system, resulting in

increased inflammation, sickness behaviour and depression [112]. Chronic inflammation has also been described as a risk factor for degenerative or “Western Diseases” such as dementias, degenerative joint diseases, atherosclerosis, multiple cancers and inflammatory bowel diseases, but whether this is also true for endometriosis is still at a hypothetical level [115].

Facchin et al. [113] tested the “disease-focused hypothesis”, in which significant differences in HRQoL and mental health were expected between women with asymptomatic endometriosis and a control group of healthy women with no history of endometriosis or endometriosis symptoms. The findings revealed that PPP had a negative impact on HRQoL, while women with asymptomatic endometriosis did not differ from healthy controls, which instead provided support for the “pain-focused hypothesis” [113]. The “pain-focused hypothesis” was later confirmed by Soliman et al. [114], and by this thesis. Women with PPP had similar pain thresholds, HRQoL and symptoms of anxiety and depression regardless of the occurrence of endometriosis (study III). Likewise, PPP *per se* seemed to be the main factor affecting the rating of PREMs and PROMs, with endometriosis as a significant contributing factor (study IV).

A recent study compared HRQoL in women with symptomatic biopsy-proven endometriosis with HRQoL in a general Swedish population. In line with the results of this thesis (study III), women with endometriosis scored significantly lower than controls on SF-36, with young women having the worst HRQoL [116]. The management of adolescent endometriosis is known for its unique challenges, with diverse and sometimes diffuse symptoms and prolonged diagnostic delay [117, 118]. Specific structural and process-related strategies aimed at finding and helping these young women at an early age should be considered in the work towards strengthening the quality of endometriosis care. Such strategies could include raising awareness of endometriosis among school nurses and midwives at youth clinics, who are crucial for earlier detection and diagnosis in order to initiate appropriate treatment for pain and endometriosis in young women.

In addition to lower HRQoL, women with PPP in this thesis also had more symptoms of anxiety and depression compared with healthy controls (study III), which is in agreement with earlier research [108, 119]. Following the pain-focused hypothesis, the literature suggests that the prevalence of symptoms of depression and anxiety are related to PPP rather than to endometriosis itself [108, 113, 119]. Psychological factors and individuals’ mental health influence the perception of, response to and ability to cope with pain [113, 120] but from the existing literature the causality is not clear: does mental distress lead to an increased pain perception or is it the pain that causes mental distress?

Considering the rate of symptoms of anxiety and depression among women with PPP (study III) and the experiences of loneliness, exposure and vulnerability

by women with diagnosed endometriosis (study I) in this thesis and in the literature [108, 113, 119], the importance of a healthcare that is able to manage psychological assessment and provide adequate psychological support throughout the structure, process and outcomes, cannot be stressed enough. The complexity of this pain condition demands responsive HCPs that works in multidisciplinary teams in order to prevent or at least minimize the symptoms' impact on the lives of women, and the potential long-term consequences of PPP. This could be what the women in this thesis were requesting when they asked for a "holistic approach" (study I), and what HCPs aimed for in the work of creating corroborating encounters (study II). The importance of endometriosis teams is highlighted in the national guidelines for the care of endometriosis in Sweden and motivated by the fact that although the scientific evidence is limited, experiences indicate that a multi-professional team often strengthens the possibility to reach an optimized treatment and has the ability to increase women's feelings of support from the healthcare, which could improve their quality of life [45].

Methodological discussion

Strengths and limitations

A strength of the studies in this thesis is that they were all conducted in different settings, such as one university hospital, two central hospitals, one private gynaecology clinic and five primary healthcare centres (study I–III). Additionally, a Swedish national sample was used, including hysterectomies on benign indication performed in Sweden and registered in GynOp during the study period (study IV). The sample included women with PPP with and without a laparoscopy-proven endometriosis diagnosis of different ages, with a variety of durations of PPP (study I, III, IV). There was also a variety of ages, genders and seniority among the HCPs (study II).

The sample size in qualitative studies is dependent on the purpose of the study and the quality and information richness of the collected data [72]. However, a sample size of 5–25 participants is commonly recommended for the type of chosen qualitative methods [80]. The inclusion of nine women (study I) and 25 HCPs (study II) turned out to be a sufficient number of informants as the interviews generated rich and informative data, which resulted in both depth and breadth in the analysis (study I, II).

Power analysis and estimation of sample size may be difficult in explorative studies when normative data and levels of clinical significance are not established. For these reasons, no power analysis was made for study III. Instead, the samples sizes described in the few then previously published studies of pain thresholds in endometriosis [56, 57, 59] were used as base for the study. The outcomes of the study should therefore be interpreted with caution, especially the non-significant results that might be due to an underpowered sample size (study III).

The three sensory modalities in study III (heat, cold and pressure) were carefully selected based on previous studies on the sensory profiling of patients with pelvic pain [121, 122]. The modalities represent activation of different nociceptive fibres, which is a methodological strength of the study. Another advantage is that, among control women who were not using hormonal contraceptives, the QST was performed during the same phase of menstruation for all (study III).

Psychological factors are integrated into the sensation of pain and may act as confounders in the study of pain as a single dimension; for ex-

ample, during the pain threshold measurements. Coping strategies and mood have a documented influence on the sensation of pain and increased anxiety, depression and fear of pain have been shown to impact on pain thresholds [123, 124]. Within the cross-sectional design of study III, it cannot be determined whether the reduced pain thresholds were a cause or a consequence of the lower HRQoL and the higher rate of symptoms of anxiety and depression among women with PPP (study III).

The QST data in study III were not normally distributed, the standard deviations were sometimes relatively high and when divided into the three subgroups, the groups were small and differed in size. Despite this, parametric tests were performed. This decision was discussed with senior researchers and with a statistician and based upon the fact that non-parametric tests do not permit the adjustment of important confounders [97].

The data collected from GynOp included a comprehensive spectrum of different benign gynaecological conditions. The use of GynOp questionnaires for data collection is well accepted by patients and provides rich post-treatment information [125], which is reflected in the high response rates for both the eight-week and one-year follow-up questionnaires. Because of the construction of the GynOp questionnaire over time, with the withdrawal or inclusion of variables and questions, the response rates for certain PREM and PROM questions were sometimes low. However, the total response rate for the period in which the specific data was collected was high (study IV).

In the register, there was some missing information on potential confounders, which made it impossible to control for type of endometriosis, mental health, socio-economic factors or lifestyle factors (study IV).

The use of self-reported measures, such as degree of complications after discharge, is both a strength and a limitation. On the one hand, it is the women's experience that is in focus and the complications are reported from the women's perspective, not from the surgeons'. On the other hand, no guide for rating those complications was provided, which may lead to different ratings for the same complications. Examples of complications at different levels of severity in the questionnaire could have made the answers more reliable (study IV).

Reliability and validity

Reliability is related to the consistency of results and measurements, whereas validity is the degree to which the research measures and answers the study question. While validity and reliability are used as standard concepts within the quantitative paradigm, the use of these concepts has been debated in qualitative research. Parallel terms for addressing rigour in qualitative studies have been suggested: different aspects of trustworthiness corresponding to validity and reliability [73]. Several methods were used to ensure trustworthiness in this thesis: reporting the audit trail (i.e. describing every step in the process, including aim, inclusion criteria, transcripts and analysis), using quotations to illustrate the themes and to show that the findings were grounded in the interviews, and using well-accepted methods of analysis with all the steps of the analysis being carefully described. The pre-understanding of the author was used in the analyses and enriched the themes and essence with depth and breadth. Over-interpretation was minimised by researcher triangulation (study I, II) [72, 81].

Since the findings of qualitative research are specific to a small number of individuals, they are not intended for generalization. Instead, it is the responsibility of the investigator to ensure that sufficient contextual information is provided to enable the reader to make the transfer to a similar context [72]. For readers to be able to estimate transferability, the context of this thesis was described in detail (study I, II).

However, these strategies to ensure trustworthiness have been criticized as they can only *evaluate*, but not *confirm* rigour because they are applied after the research is completed. Furthermore, it could be beneficial to use the same terminology as quantitative science for ensuring rigour, as reliability and validity are central in both scientific paradigms. Verification strategies to ensure rigour as an alternative to trustworthiness have been suggested. These strategies place the responsibility for ensuring rigour with the researcher rather than on the reader [126].

The five verification strategies to ensure reliability and validity using these exact terms are: 1) methodological coherence: ensuring that the research question matches the method, which in turn must match the data and analysis; 2) appropriate sample: including adequate participants. In this thesis it includes women with a lived experience of endometriosis and HCPs who had met women with symptoms indicating endometriosis; 3) collecting and analysing data concurrently: the ability to form a mutual interaction between data and analysis; 4) thinking theoretically: giving

rise to new ideas but constantly checking and rechecking these ideas to verify that they are grounded in the data; and 5) theory development: moving from the micro perspective of data to a macro theoretical understanding (study I, II) [126].

As long as the researcher is transparent and reflexive, she can be an integral part of the research process and product. It is in the nature of qualitative work to be “biased”, as separation from the process and findings is neither possible nor desirable [127].

One way of ensuring validity and reliability in quantitative research is to use valid and reliable questionnaires and measurements [73]. SF-36, EQ-5D-3L and HADS have been used in many studies worldwide and are some of the most common instruments for measuring HRQoL and symptoms of anxiety and depression, and the Swedish versions are all validated [87, 90, 95]. EHP-30 was used despite the unpublished validation of the Swedish version, as it was the only disease-specific questionnaire available.

QST is an established method to assess somatosensory changes [85]. The reliability of QST is dependent on psychophysical factors such as method of limits vs. levels [128]. Technical equipment, study population, sample size, the number of examiners and centres involved, test areas, baseline skin temperature and time intervals are other aspects that may influence the reproducibility [129].

The German Research Network on Neuropathic Pain made an effort to overcome some of the reliability limitations by establishing a standardized protocol for examiners and a certification for laboratories performing the tests [130]. Geber et al. [128] investigated the extent to which the QST results of the protocol depended on the performance of the examiner. They concluded that when researchers perform QST according to the protocol, it could serve as a diagnostic instrument with good interobserver and test-retest reliability [128].

The method of limits was used during QST. Because of the reaction time artefact, this method often overrates the actual threshold. This artefact can be minimized by regulation of the temperature slope change to a lower rate. The advantage of this method is that it is easier to perform and less time consuming than the method of levels. For both methods, as well as for most psychophysical methods, there is the risk of a learning effect after repeated tests [85]. However, studies evaluating the learning effect show that the variation is within acceptable limits for clinical comparisons [131–133]. In study III, QST was only performed on one occasion (before surgery), but three measurements were taken for each stimulus at the six locations, which may cause a learning effect during the experimental ses-

sion. To minimize the influence of any possible learning effect, the order of the stimuli and locations on the body were altered randomly between participants (study III).

Pressure algometry has been shown to have high test-retest reliability in healthy persons and a good reproducibility between opposite measurement sites. The force rate of the applied pressure at the site plays a role as increasing application rates have been connected to higher values of pain pressure thresholds [134].

Four examiners conducted the QST. Even though they had undergone the same training programme, they might have informed the participants in different ways or conducted the pain pressure testing differently. Additionally, there may have been a risk of expectation bias, as the examiners were un-blinded to group belonging (PPP or controls). However, they were blinded to which women would receive an endometriosis diagnosis, since the QST was performed before the laparoscopy (study III).

The overall generalizability of the results in study III may be limited due to the relatively small sample size; in particular, that of the group of women with confirmed endometriosis. The interpretation should therefore be made with caution (study III).

Quality registers permit the systematic control of healthcare systems and usually provide a large sample size, which increases the possibility of generalization of the results. Data is collected for several purposes and is often easily available, minimizing time spent and reducing costs. The collection of register data was performed independently of the study, which reduces recall and non-response bias. These advantages must be positioned in relation to the lack of confounder information and the researcher's lack of control over the data collection. Observational studies do not allow causal associations [67].

Although validation of the questions in GynOp has not been published, the register has been the source for a number of previous studies and is considered to be well described and evaluated [79, 125]. The data completeness is validated annually and data is randomly checked with medical records and compared to the National Inpatient Register [79]. The Swedish Quality Registers have four different certification levels depending on the validity, quality and usability of data. GynOp has reached the highest level of certification [79, 135].

Clinical implications

The results of this thesis contribute to the knowledge about experiences of the structure, process and outcomes of healthcare encounters by women with endometriosis and endometriosis symptoms, and provide a deeper understanding of the pain experience.

Women with PPP and endometriosis require HCPs to acknowledge their pain and the consequences of pain in their daily lives. The results imply that HCPs should position the woman's experience of PPP as central during their encounters and in the management of the disease, focusing on the woman's experience of pain rather than on the HCP's interpretation of the condition. Increased knowledge and understanding of endometriosis could reinforce HCPs' ability to communicate and discuss the intimate nature of the condition and create corroborating encounters. Furthermore, a more open conversation about menstruation and endometriosis symptoms could shorten the diagnostic delay and enable earlier treatment aimed at pain relief. An adequate and active treatment with regular evaluation of treatment efficacy might decrease the impact of PPP upon HRQoL and possibly inhibit the development of CS.

A successful endometriosis therapy with optimal outcomes at both a physiological and psychological level may require the organization of multidisciplinary teams where gynaecologists, pain therapists, psychologists, sexologists, social workers and physiotherapists work together and contribute with different perspectives.

Future research

The work for this thesis provided several ideas for future research. Given the contradictory findings in women's versus HCPs' descriptions of healthcare encounters, it would be interesting to evaluate the factors behind this dissonance. HCPs had similar ideas as the women about corroborating encounters and strived to achieve them, but then why was the experience double-edged for the women? To enrich our knowledge about experiences of healthcare encounters, the development of new and existing questionnaires could enable larger study populations and thereby perhaps generate a greater generalizability.

Previous research on the diagnostic delay has focused on GPs' knowledge and management of endometriosis. However, the knowledge base among other HCPs who encounter a large number of women with PPP needs to be further analysed. Examples of potential detectors of suspected endometriosis are school nurses and midwives at youth centres, and midwives working with contraceptive counselling. Levels of knowledge about endometriosis among nurses working with telephone counselling at primary healthcare centres could also be investigated in order to prevent prolonged time to diagnosis.

The reason as to why hysterectomy affects some women positively and others negatively has not yet been sufficiently researched. Whether there are specific factors, such as pre-operative symptoms, pelvic pain or psychosocial factors, which increase women's risk of experiencing negative outcomes, is another issue that could need further investigation.

CONCLUSIONS

This thesis suggests that there are limitations regarding the quality of endometriosis healthcare at all levels: the structure was criticized mostly in relation to delayed diagnosis at the primary-care level, and to the normalization and trivialization of PPP. During the process, acknowledging PPP was experienced as a key factor for corroborating encounters, and the detection of reduced pain thresholds contributed to the understanding of PPP. The outcome of endometriosis healthcare could be constructive or destructive. The destructive encounters were often characterized by pain normalization and trivialization, which could have physiological and psychological consequences such as reduced pain thresholds, lower HRQoL and more symptoms of anxiety and depression. Unrelieved PPP could also be an explanatory factor for the long-term physiological consequences, which were reflected in lower PREM and PROM after hysterectomy.

SVENSK SAMMANFATTNING

Menstruation uppfattas i många kulturer som något personligt och privat som bör döljas för omgivningen. Följaktligen döljs även ibland problem kopplade till menstruation, exempelvis menssmärtor. Just svår smärta vid menstruation är, tillsammans med långvarig buksmärta, ett av de vanligaste symtomen på endometrios; en kronisk gynekologisk sjukdom som drabbar ungefär 10% av alla kvinnor i fertil ålder, vilket motsvarar cirka 200 000 kvinnor i Sverige.

Många kvinnor med svårbehandlad endometrios upplever att smärtan styr deras liv och ger såväl fysiologiska som psykosociala konsekvenser samt sänkt livskvalitet. Trots svåra besvär är det vanligt att kvinnor med endometrios upplever normalisering och trivialisering av sitt tillstånd i mötet med hälso- och sjukvården. Tiden från symtomdebut till diagnos är lång – i Sverige i snitt 5-7 år, vilket antas bero på att sjukdomen misstolkas som problematisk menstruation, först av kvinnorna själva och sedan av vårdpersonal.

Det finns ett kunskapsgap när det gäller såväl upplevelsen av vården som helhet hos dessa kvinnor, som upplevelsen av specifika delar av vården och vårdens kvalitet. Det övergripande syftet med denna avhandling var därför att identifiera, beskriva och analysera upplevelser, utfall och kvaliteten av endometriovården utifrån olika perspektiv.

Avhandlingen inkluderar fyra delstudier med olika design och metoder. Studie I och II var kvalitativa intervjustudier där nio kvinnor med laparaskopi-verifierad endometrios (studie I) och 25 personer som i sitt arbete mötte kvinnor med endometriossymtom (studie II) beskrev sina upplevelser av vårdmöten relaterade till endometrios och/eller symtom på endometrios.

I studie III mättes smärtrösklar, livskvalitet och symtom på ångest och depression hos kvinnor med långvarig buksmärta och misstänkt endometrios. De delades upp i två grupper: grupp 3A var de som efter diagnostisk laparaskopi visade sig ha endometrios, medan grupp 3B inte fick diagnosen. De två gruppernas data jämfördes med data från en kontrollgrupp bestående av friska kvinnor (grupp 3C).

Slutligen var studie IV en observationsstudie med data från Nationella kvalitetsregistret inom gynekologisk kirurgi. I studien undersöktes det som ibland beskrivs som "den sista utvägen" i behandlingen av endometrios: kirurgisk avlägsnande av livmodern (hysterektomi). Patientrap-

porterad data angående upplevelser och resultatet av operationen jämfördes mellan kvinnor indelade i fyra grupper: indexgruppen (grupp 4A) var kvinnor med långvarig buksmärtan och som efter operationen fick diagnosen endometrios, grupp 4B var kvinnor med långvarig buksmärtan utan endometriosdiagnos, grupp 4C var kvinnor utan buksmärtan men med endometrios, medan grupp 4D var kvinnor med varken smärta eller endometriosdiagnos.

Avhandlingens resultat delades in i tre teman: *En kamp för att synliggöra smärta, Endometriosdiagnosen som en nyckel till att förstå och uthärda långvarig buksmärtan* och *Mötet med vården som potentiellt livsavgörande*.

I det första temat beskrevs mötet med hälso- och sjukvården som problematiskt både av kvinnorna själva och av personalen. Kvinnorna försökte på olika sätt synliggöra, beskriva och kommunicera sin smärta, men personalen upplevde att de ofta saknade de verktyg och den kunskap som krävdes för att möta kvinnornas behov. Kvinnorna beskrev hur smärtan påverkade deras fysiska och mentala hälsa och försämrade deras livskvalitet, vilket också framkom i enkäterna. Den långvariga buksmärtans potentiella konsekvenser visualiserades i de sänkta smärtrösklarna som förekom hos kvinnor med smärta (grupp 3A och 3B) jämfört med friska kvinnor (grupp 3C). Det visade det sig även att ju längre tid kvinnorna haft smärta, desto lägre var deras smärtrösklar.

För kvinnorna med endometrios upplevdes diagnosen som en viktig nyckel för att känna att smärtan bekräftades och togs på allvar, vilket beskrevs i det andra temat. Diagnosen öppnade även nya dörrar för förståelsen för sjukdomen och möjliggjorde en mer effektiv behandling.

Diagnosen verkade även vara av betydelse för resultatet av hysterektomi där en tendens att vara mindre nöjd fanns i den grupp som hade både smärta och endometrios (grupp 4A) jämfört med de andra grupperna (grupp 4B-D). Majoriteten av alla kvinnor upplevde dock resultatet av hysterektomin som tillfredsställande och de flesta var nöjda eller mycket nöjda efteråt.

I sista temat beskrevs betydelsen av mötet med vården för kvinnorna, ett möte som kunde vara konstruktivt eller destruktivt. Konstruktiva möten hade potential att förändra kvinnornas liv och innefattade ett vidare angreppssätt på kvinnornas situation än bara det rent biomedicinska.

Slutsatsen blev att för att möta dessa kvinnors behov behöver vårdens struktur, process och utfall förbättras. En högkvalitativ endometriosvård bör innefatta såväl ett fysiologiskt som ett psykologiskt och socialt omhändertagande.

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