

# Living with endometriosis: Comorbid pain disorders, characteristics of pain and relevance for daily life

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## Funding information

This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors.

## Abstract

**Background:** Pain plays a central role in endometriosis. The complex relationship among pain characteristics, comorbid pain disorders and daily life represents a challenge for medical support. This multicentre cross-sectional case-control study analysed the association between endometriosis-related chronic pain and functions of daily life in 510 women with endometriosis, 265 (52%) who experienced chronic pain, either from endometriosis alone ( $N = 134$ , 26.3%) or in association with additional pain disorders ( $N = 131$ , 25.7%).

**Methods:** Self-administered questionnaires from the Brief Pain Inventory and the Pain Disability Index were used to investigate associations between pain characteristics (frequency, duration, intensity) and daily life. Also, associations between different endometriosis characteristics (rASRM stage, presence of adhesions, localisation of lesions) and pain were evaluated.

**Results:** Chronic pain is negatively associated with almost all (12/14) aspects of daily life investigated, including standing, walking, sitting, defaecation, sleep, sports activities, family and domestic responsibilities, sexuality, social functioning, professional life, mood, and joy of life. Altogether, 33.7% of women with chronic pain reported moderate and 27.5% severe limitations. Comorbid pain disorders resulted in significantly more limitations. The length of pain episodes showed a particularly important influence, especially for family/domestic responsibilities (OR 22.94,  $p < 0.001$ ), professional life (OR 16.56,  $p < 0.001$ ) and social functioning (OR 41.03,  $p < 0.001$ ).

**Conclusions:** Our data confirm that despite treatment, about 50% of women experience pain. Pain was associated with at least moderate negative effects on almost all areas of daily life; additional pain comorbidities increased limitations. Improving pain management is essential for improving quality of life in women with endometriosis.

**Significance:** The study provides an accurate overview of the impact of endometriosis-associated pain on daily life. This is important because pain plays

a central role in women living with endometriosis, and despite modern therapies, many women continue to suffer from chronic pain. The detailed analysis of its impact with a comprehensive survey of all aspects of daily life in a very large study population is unique. We expect an improved understanding of consequences of pain to significantly advance medical support in these patients.

## 1 | INTRODUCTION

Endometriosis is one of the most common benign gynecological conditions that occur in women's reproductive years, affecting about 10% of the female population (Bernuit et al., 2011). It is an estrogen-dependent chronic disorder characterised by the development of ectopic endometrial tissue, most frequently in the small pelvis (Parasar et al., 2017; Vercellini et al., 2014). Altogether, 30% of women with endometriosis are asymptomatic, about 50% suffer from chronic endometriosis-related pain and the remaining 20% suffer from occasional endometriosis-related pain (Adamson, 2004), ranging from chronic pelvic pain, dysmenorrhoea, dyspareunia and dysuria to dyschezia (Schliep et al., 2015). The pathophysiology of pain in endometriosis is still unclear; a complex interaction between physical and psychosocial factors is suggested (van Aken et al., 2017; Leeners & Imthurn, 2007; Moore & Kennedy, 2005). Other important disease symptoms are fatigue, infertility and bleeding disorders (Bernuit et al., 2011; Maggiore et al., 2017; Ramin-Wright et al., 2018; Vercellini et al., 2014).

Surgical and medical treatments reduce endometriosis-related pain, but pain often recurs (Seracchioli et al., 2010). Medical pain management includes pain killers, progestins, combined oral contraceptives and GnRH agonists (Becker et al., 2017; Vercellini et al., 2014). The lack of long-term efficacy of medical treatment (Adamson, 2004; Becker et al., 2017) and the major side effects of currently available painkillers often lead women to forgo treatment and remain symptomatic (Bhala et al., 2013; Califf et al., 2016).

Furthermore, other chronic pain disorders are associated with endometriosis; this makes treatment more challenging (Schliep et al., 2015; Surrey et al., 2018). These pain disorders include migraine headache, irritable bowel syndrome, painful bladder syndrome and rheumatic diseases (e.g. fibromyalgia, rheumatoid arthritis) (Mirkin et al., 2007; Sinaii et al., 2002; Surrey et al., 2018).

Pain is considered to represent the leading negative factor in health-related quality of life (HRQoL). (Different definitions of QoL are used in current studies Fonseca et al., 2018; De Graaff et al., 2013; Facchin et al., 2015; Jones et al., 2004; Moradi et al., 2014.) In many clinical

studies, information about endometriosis pain is limited to general presence, aetiology and pathophysiology (Coxon et al., 2018). In our study, pain was analysed in great detail. The duration, intensity and frequency were recorded, and their effects on a very differentiated series of aspects of daily life were evaluated. Such detailed analysis is unique. Most studies on HRQoL include only a small number of study participants, who are recruited primarily through tertiary care centres and are therefore not representative. In addition, most studies examine only individual aspects of daily life and therefore do not provide an overall view of the impact on all major aspects of daily life (Fonseca et al., 2018; De Graaff et al., 2013; Facchin et al., 2015; Nnoaham et al., 2011; Schliep et al., 2015; Sperschneider et al., 2019) and the only comparable study lacks a control group (Fourquet et al., 2010) (Table 1). Consequently, there are currently very few data on the extent of limitations in daily life caused by specific pain characteristics and pain comorbidities. This makes it difficult not only for medical support, but also for the understanding of the condition itself and for determining the right support from the social and professional environment. As many women continue to complain about a lack of understanding of their daily lives by various professionals, our goal was to provide reliable data that increase awareness of the impact of endometriosis in their daily lives, thereby leading to better support.

Therefore, this study investigates the association between endometriosis-related chronic pain and different aspects of daily life. Pain characteristics (frequency, intensity, duration), endometriosis characteristics (e.g., rASRM stage, localisation of lesions) and comorbid pain disorders were evaluated to determine their role in influencing endometriosis-related pain.

## 2 | MATERIAL AND METHODS

### 2.1 | Study design

The study was designed as a multicentre cross-sectional study analysing the impact of pain on daily life in women with endometriosis (ClinicalTrials.gov NCT 02511626). The analysis included only women

**TABLE 1** Overview of previous studies ( $n > 100$ ) investigating the impact of endometriosis or endometriosis-related pain on daily life

Author, year	Sample Size	Objective, Characteristics assessed	Main findings
Barbara et al. (2017)	210 women with endometriosis	Mental health in women with endometriosis.	Not only pelvic pain, but also individual characteristics (i.e. self-esteem, body esteem and emotional self-efficacy), time since diagnosis and intimate relationship status influence psychological health in women with endometriosis.
Bernays et al. (2020)	565 women with endometriosis, 565 control women	Sexual activity, dysmenorrhoea, dyspareunia, chronic pain and infertility were evaluated for their associations with different sexual activities.	Women with endometriosis report lower frequencies of petting, foreplay and vaginal intercourse. Dyspareunia is negatively associated with sexual activity.
Chen et al. (2016)	10,439 women with endometriosis, 10,439 control women	Endometriosis as a risk factor for depression and anxiety disorders.	Endometriosis was associated with an increased risk for depression and anxiety disorders.
De Graaff et al. (2013)	931 women with endometriosis	Effect of endometriosis on education, work and social wellbeing. Impact of endometriosis-associated symptoms on health-related quality of life.	Endometriosis affected work, relationships and quality of life. Comorbidities, chronic pain and dyspareunia negatively influenced physical and mental health.
De Graaff et al. (2016)	83 women with endometriosis with 74 partners, 40 control women with 26 partners	Association between endometriosis and its related physical and mental symptoms with sexual functioning in women and male partners.	Dyspareunia and depressive symptoms are associated with impaired sexual functioning in women with endometriosis, whereas sexual functioning in their male partners is not affected.
Facchin et al. (2015)	78 women with endometriosis with pelvic pain, 32 women with endometriosis without pelvic pain, 61 control women	Impact of endometriosis and pelvic pain on mental/physical quality of life, anxiety and depression.	Pelvic pain led to poorer quality of life and mental health. No difference between asymptomatic endometriosis and control group. Dysmenorrhoea had significant effects only on physical activity of life, non-menstrual pelvic pain affected all variables, no significant effects were found for dyspareunia and dyschezia.
Fourquet et al. (2010)	108 women with symptomatic endometriosis	Impact of endometriosis-related pain and/or co-existing symptoms on daily life activities (household chores, child care, sexual relationships, studies, appetite, exercise, sleeping, work and social life)	Symptoms disrupted all aspects of daily life. Menstrual pain, incapacitating pain, abdominal pain and depression were identified as predictors of poor performance at work and home. Incapacitating pain and dyspareunia predict impairments in social and sexual aspects of life.
Lorenatto et al. (2006)	100 women with endometriosis (44 of which have chronic pelvic pain)	Prevalence of depression in women with endometriosis with and without pelvic pain.	Depression is highly prevalent in women with endometriosis, especially those with pelvic pain.
Nnoaham et al. (2011)	745 women with endometriosis (587 of which were symptomatic), 673 control women	Impact of endometriosis on health-related quality of life (HRQoL) and work productivity.	Physical HRQoL was significantly reduced in affected women compared with women with similar symptoms but no endometriosis. Women with endometriosis showed greater work productivity loss compared with symptomatic control women. Pelvic pain and disease severity are major drivers for work productivity loss in endometriosis.

(Continues)

**TABLE 1** (Continued)

Author, year	Sample Size	Objective, Characteristics assessed	Main findings
Schliep et al. (2015)	190 women with endometriosis, 147 women with other gynecologic pathology, 136 control women	Description of pain characteristics in women with endometriosis compared with other or no pelvic pathology in women receiving laparoscopy	More cyclic pelvic pain, chronic pain, dyspareunia, dysmenorrhoea and dyschezia was reported in women with endometriosis compared with women with other or no gynaecological pathology.
Sperschneider et al. (2019)	505 women with endometriosis, 505 control women	Association between endometriosis/disease symptoms and professional life.	Endometriosis is associated with impairment of professional life. Chronic pain was significantly associated with increased sick leave and loss of productivity.
Vercellini et al. (2012)	100 women with rectovaginal endometriosis, 100 women with peritoneal and/or ovarian endometriosis, 100 control women	Impact of rectovaginal endometriosis on dyspareunia and sexual functioning.	Women with endometriosis experience more frequent and more severe deep dyspareunia as well as worse sexual functioning. Differences between diverse endometriosis forms were marginal.

with endometriosis confirmed in surgical reports, as this is the only reliable way to confirm the presence of endometriosis. The manuscript was drafted according to the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) recommendations (von Elm et al., 2014).

## 2.2 | Data collection

Study participants were recruited between January 2010 and December 2016. In different university departments, district hospitals and associated private practices in Switzerland, Germany and Austria, medical staff other than their treating physicians approached women afflicted with endometriosis, giving them information about the study and asking them to participate. Women who came for regular monitoring of the course of the disease were invited to participate whether or not there were any acute disease symptoms or past surgery.

After verbal consent to participate, all documents, including additional information about the study, a declaration of written consent for study participation and for confirmation of their diagnosis, and a questionnaire with a return envelope (see below) were provided to the participants by post or in person.

The majority of the data were collected from the University Hospital Zurich, Triemli Hospital Zurich, district hospitals in Winterthur, Schaffhausen, St. Gallen, Baden, Solothurn, and Walenstadt, Charité University Hospital Berlin, University Hospital Aachen, Albertinen-Hospital Hamburg, Vivantes Humboldt-Klinikum Berlin, and University Hospital Graz. A subgroup of women was

recruited through a cooperation arrangement with endometriosis self-help groups in Germany.

## 2.3 | Inclusion and exclusion criteria

All study participants were between 18 and 50 years old and had the required mental, psychological and language abilities to understand and complete the German-language questionnaire. Pregnancy at the time of recruitment was an exclusion criterion. Women were included if the diagnosis of endometriosis was surgically and histologically confirmed, regardless of their disease symptoms, disease stage, location and number of lesions, current or previous treatment, or length of time since the initial diagnosis. The reason women underwent surgical intervention in the first place was because of either pain symptoms (dysmenorrhoea, dyspareunia, chronic pelvic pain) and/or endometriosis-suspicious lesions (detected by rectovaginal palpation or ultrasound examination).

Women experiencing endometriosis-related chronic pain (a confirmed diagnosis of endometriosis with chronic pelvic pain, dysmenorrhoea, deep dyspareunia, dysuria and/or dyschezia) were eligible for the case group. Eligible women were asked to report other types of chronic pain, i.e., migraine headache, inflammatory bowel disease, back pain, stomach pain, rheumatic disorders and arthrosis.

All surgical reports were reviewed to identify endometriotic lesions at the following locations: endometrioma (ovary), uterosacral ligaments, vaginal fornix, involvement of the rectovaginal septum/Douglas, lesion of the

pelvic wall, Douglas obliteration (frozen pelvis) and intra-abdominal adhesions. Endometriosis was staged using the rASRM classification (American Society for Reproductive Medicine, 1997).

Data were reviewed if at least 80% of the questionnaire were completed and all relevant information required for the study was available. Out of the 847 women invited to participate, 748 (88.3%) agreed to participate, and 654 (77.2%) returned a completed questionnaire. In total, 568 (86%) questionnaires were sufficiently complete (>80%), 14 questionnaires had to be excluded due to lack of consent to collect information from the medical charts and 19 were excluded because of unavailability of surgical reports. Another 25 women reporting chronic pain due to a cause other than endometriosis were excluded. Of the 510 women with endometriosis eligible for our study, 265 women had experienced endometriosis-related chronic pain (cases), and 245 had not (control women). Of the women with chronic pain, 134 suffered from endometriosis-related chronic pain only, whereas 131 indicated other types of chronic pain in addition (migraine headache, inflammatory bowel disease, back pain, stomach pain, rheumatic disorders or arthrosis).

## 2.4 | Questionnaire

Specialists in endometriosis and gynaeco-psychosomatics from the universities of Zurich and Berlin developed a self-administered questionnaire with support from the governing body of endometriosis self-help groups in Germany. The questionnaire was divided into sections covering socio-economic background, personal and family history, medical and psychological history, chronic pain, well-being, menstruation, pregnancy, partnership and sexuality (Hämmerli et al., 2018, 2020; Kohl Schwartz et al., 2017; Liebermann et al., 2018; Ramin-Wright et al., 2018; Sperschneider et al., 2019).

Women were asked whether or not they suffered from chronic pain (pain duration >6 months) and if this pain was endometriosis related. Women with chronic pain were asked to complete an additional section addressing different pain characteristics and the effect of chronic pain on different activities of daily life. The Brief Pain Inventory (Cleeland & Ryan, 1994; Tan et al., 2004) and the Pain Disability Index (Gronblad et al., 1993; Tait et al., 1990) were used to evaluate endometriosis-related pain and its consequences. The following questions from the Brief Pain Inventory regarding pain characteristics were included: localisation of the most severe pain felt (pelvis/lower abdomen, anus, vagina, other location) and average pain intensity in the previous 24 h (11-point scale from 'no pain' (0) to 'strongest pain' (10)). We added questions

on average pain intensity in the previous month (11-point scale from 'no pain' (0) to 'strongest pain' (10)), pain frequency (constant, several times a day, once a day, several times per week, a few times per month, a few times per year), and total length of pain episodes per day (<1 h, 2–3 h, 4–9 h, 10–18 h, 18–24 h).

The effect of pain on different aspects of daily life was evaluated using an 11-point scale from 'no effect' (0) to 'strongest effect' (10). The influence of pain on walking, professional life, sleep, mood and joy of life was investigated using questions from the Brief Pain Inventory. Information on family and domestic responsibilities, social functioning, sexuality and eating was collected using questions from the Pain Disability Index. Additionally, standing, sports activities, sitting, defaecation and urination were assessed.

The following pain characteristics were evaluated: pain frequency, total length of pain episodes per day, pain intensity (average pain intensity in the previous 24 h and in the previous month) and pain location. The endometriosis characteristics included rASRM stage; the presence of adhesions; endometrioma; involvement of the uterosacral ligaments, pelvic wall; lesions in the vaginal fornix and in the Douglas/rectovaginal septum; Douglas obliteration (frozen pelvis); and the number of surgical interventions due to endometriosis.

For the assessment of additional chronic pain disorders, study participants had to report the diagnosis of different pain-inducing diseases from a preselected list, including the possibility to report further diseases as well as to categorise the frequency of pain symptoms into five different levels (1 = never to 5 = very frequently), based on their experiences in the previous 6 months. Any rating above 3 was considered to indicate chronic pain and a relevant additional chronic pain disorder. In the control group, we could not divide the women into the two groups (with and without non-endometriosis-related chronic pain), because the number of women with pain co-morbidities was too small to allow reliable statistical evaluation (Table 2).

## 2.5 | Confounders

The association between endometriosis-related chronic pain and different aspects of daily life was controlled for the confounding effects of different chronic pain disorders (migraine/ headache, inflammatory bowel disease, back pain, stomach pain, rheumatic diseases, arthrosis), BMI, fatigue, and depression. Based on their experiences in the previous 6 months, study participants categorised the extent of fatigue into five different levels (1 = never to 5 = very frequently) (Ramin-Wright et al., 2018). A score  $\geq 10$  in the Patient Health Questionnaire (PHQ-9) indicated depression (Kroenke & Spitzer, 2002). A BMI

between 18.5 and 24.9 was considered normal weight, a BMI below 18.5 underweight, and a BMI greater than 30 overweight, with a pre-obesity category from 25 to 29.9 (World Health Organization, 2019).

## 2.6 | Statistical analysis

To test for differences in socio-epidemiologic factors, the Kruskal–Wallis test was used for continuous variables, and Fisher's exact test was used for categorical variables. To examine differences in pain characteristics, impairment of various aspects of daily living, and number of impaired aspects in the absence or presence of additional chronic pain disorders, Fisher's exact test was used for categorical variables and the independent t-test to calculate the difference between means. Pearson chi-square test was used for categorical variables, and the Kruskal–Wallis test was used for ordinal variables, both to evaluate differences in endometriosis characteristics in women with and without chronic pain. The difference between the means was evaluated using the independent t-test. When assessing a possible association between pain characteristics or pain location and endometriosis characteristics in women experiencing chronic pain, Fisher's exact test was used for categorical variables and Spearman's rank correlation for ordinal variables. Women with multiple lesions were assessed for every association in which the respective lesion was present.

The association between endometriosis-related chronic pain and different aspects of daily life was quantified using odds ratios. As the association between chronic pain and daily life had to be evaluated in the context of other disease-related symptoms, we conducted a multifactorial regression analysis taking the following factors into account: significant variables in the socio-epidemiologic overview (marital status and BMI), significant variables in endometriosis lesions (intra-abdominal adhesions, endometrioma, involvement of the vaginal fornix, involvement of the rectovaginal septum, complete Douglas obliteration (frozen pelvis), and number of surgical interventions), different chronic pain disorders (migraine/headache, inflammatory bowel disease, back pain, stomach pain, rheumatic diseases, arthrosis), fatigue and depression.

Data analysis was conducted using *R: A language and environment for statistical computing*, R Foundation for Statistical Computing, Vienna, Austria.

## 2.7 | Ethical approval

Ethical approval was obtained from local ethical review committees in Switzerland, Austria and Germany. Study

participants each signed an informed consent form. The study was conducted according to the guidelines of the [World Medical Association Declaration of Helsinki 1964](#), updated in October 2013.

## 3 | RESULTS

When calculating the reliability of the questionnaire section on endometriosis-related pain, the Brief Pain Inventory evaluation showed a Cronbach's alpha of 0.85 for intensity factors and 0.88 for the interference factors; the *r*-value was 0.40 for intensity and 0.57 for interference. Cronbach's alpha for the Pain Disability Index was 0.86 and the *r*-value for disability was 0.74.

Of the 510 women with endometriosis, 265 (52%) experienced endometriosis-related chronic pain. About half of the women experiencing chronic pain also suffered from additional chronic pain disorders. [Table 2](#) provides an overview of different socio-epidemiologic characteristics in the study participants. In comparing women with endometriosis-related chronic pain with and without other chronic pain disorders and those without chronic pain, no significant differences were found regarding age, nationality, education, family income, smoking behaviour or motherhood, whereas marital status, BMI, time since initial diagnosis of endometriosis, time since last surgery, fatigue and depression differed significantly. [Table S1](#) provides data on women recruited in hospitals/private practices and through self-help groups.

[Table 3](#) summarises information on different pain characteristics, pain location and specific pain types in women suffering from endometriosis-related pain, with and without additional chronic pain disorders. Women with additional chronic pain disorders indicated significantly higher pain frequencies, longer episodes of pain and greater pain intensities. In addition, current dysmenorrhoea was significantly more often reported by women suffering from additional chronic pain disorders. No difference in distribution was found regarding dyspareunia and the localisation of the most severe pain. Both groups reported the most severe pain in the pelvis/lower abdomen.

For both women with and women without additional chronic pain disorders, endometriosis-related chronic pain was associated with at least moderate negative effects ( $\geq 4$  on an 11-point scale) on most aspects of daily life investigated, i.e., standing, family and domestic responsibilities, sports activities, walking, sitting, social functioning, professional life, sleep, mood, defaecation, joy of life and sexuality, with the exceptions of urination and eating ([Table 4](#)). Overall, 33.7% of the women reported moderate limitations and 27.5% reported severe limitations. Women

**TABLE 2** Socio-epidemiologic characteristics of study participants

	<b>Women with endometriosis-related chronic pain n = 265 (52%)</b>		<b>Women without endometriosis-related chronic pain n = 245 (48%)</b>	<b>p-value<sup>a</sup></b>
	<b>No other pain disorders n = 134 (26.3%)</b>	<b>+ Other pain disorders<sup>c</sup> n = 131 (25.7%)</b>		
Age in years	n = 134	n = 131	n = 245	
Mean in years (Median, IQR)	38.3 (39, 11)	37.4 (37, 11.5)	38.0 (38, 9)	0.688
Nationality	n = 133	n = 131	n = 244	
German, Swiss, Austrian	120 (90.2%)	116 (88.5%)	218 (89.3%)	0.895
Other	13 (9.8%)	15 (11.5%)	26 (10.7%)	
Marital status	n = 133	n = 131	n = 243	
Solid partnership	120 (90.2%)	111 (84.7%)	192 (79%)	0.017
Single	13 (9.8%)	20 (15.3%)	51 (21%)	
School Education	n = 128	n = 130	n = 242	
Primary	4 (3.1%)	8 (6.2%)	12 (5.0%)	0.811
Lower secondary education	13 (10.2%)	17 (13.1%)	18 (7.4%)	
Upper secondary education	19 (14.8%)	20 (15.4%)	41 (16.9%)	
Apprenticeship	42 (32.8%)	38 (29.2%)	79 (32.6%)	
Tertiary education	47 (36.7%)	43 (33.1%)	88 (36.4%)	
Others/no school grade	3 (2.3%)	4 (3.1%)	4 (1.7%)	
Monthly Family net income in EUR	n = 117	n = 110	n = 200	
No income	2 (1.7%)	6 (5.5%)	13 (6.5%)	0.271
≤2500	37 (31.6%)	41 (37.3%)	64 (32%)	
>2500	78 (66.7%)	63 (57.3%)	123 (61.5%)	
Smoking behaviour	n = 126	n = 119	n = 230	
Never smoked	64 (50.8%)	60 (50.4%)	128 (55.7%)	0.069
Former smoker	34 (27%)	22 (18.5%)	60 (26.1%)	
Current smoker	28 (22.2%)	37 (31.1%)	42 (18.3%)	
Motherhood	n = 134	n = 131	n = 245	
Yes	98 (73.1%)	94 (71.8%)	167 (68.2%)	0.563
BMI >24.9 <sup>b</sup>	n = 134	n = 131	n = 243	
Yes	42 (31.8%)	42 (32.3%)	52 (21.4%)	0.024
Time since initial endometriosis diagnosis	n = 115	n = 103	n = 199	
Mean ± SD in months (Median, IQR)	56 ± 54.6 (39, 77.5)	64 ± 53.8 (42, 80)	58.8 ± 137 (36, 55.5)	0.034
Time since last surgery	n = 127	n = 122	n = 222	
≤1 month	28 (22%)	28 (23%)	30 (13.5%)	0.039
>1 month	99 (78%)	94 (77%)	192 (86.5%)	
Fatigue	n = 133	n = 129	n = 243	
(Very) frequently	68 (51.1%)	97 (75.2%)	79 (32.5%)	<0.001
Depression	n = 126	n = 123	n = 224	
Yes	34 (27%)	60 (48.8%)	28 (12.5%)	<0.001
Other Pain disorders				
Migraine/headache (Very) frequently	n = 261 0 (0%)		n = 242 38 (15.7%)	<0.001

(Continues)

TABLE 2 (Continued)

	Women with endometriosis-related chronic pain <i>n</i> = 265 (52%)		Women without endometriosis-related chronic pain <i>n</i> = 245 (48%)	<i>p</i> -value <sup>a</sup>
	No other pain disorders <i>n</i> = 134 (26.3%)	+ Other pain disorders <sup>c</sup> <i>n</i> = 131 (25.7%)		
Back pain	<i>n</i> = 262		<i>n</i> = 243	
(Very) frequently	0 (0%)	115 (43.9%)	41 (16.9%)	<0.001
Stomach pain	<i>n</i> = 261		<i>n</i> = 240	
(Very) frequently	0 (0%)	68 (26.1%)	20 (8.3%)	<0.001
Inflammatory bowel disease (IBD)	<i>n</i> = 245		<i>n</i> = 224	
(Very) frequently	0 (0%)	15 (6.1%)	1 (0.4%)	<0.001
Rheumatic diseases	<i>n</i> = 263		<i>n</i> = 242	
(Very) frequently	0 (0%)	2 (0.8%)	0 (0%)	0.5
Arthrosis	<i>n</i> = 263		<i>n</i> = 241	
(Very) frequently	0 (0%)	2 (0.8%)	0 (0%)	0.5

IQR, interquartile range.

<sup>a</sup>Kruskal–Wallis test for age and time since initial endometriosis diagnosis, Fisher's exact test for categorical variables.

<sup>b</sup>BMI 24.9–29.9 = Pre-obesity, BMI >30 = Obesity (World Health Organization, 2019).

<sup>c</sup>Other (chronic) pain disorders = migraine/headache, inflammatory bowel disease, back pain, stomach pain, rheumatic disorders and arthrosis.

with additional chronic pain disorders experienced more severe limitations in sleep and in joy of life as well as a tendency towards greater impairment of professional life. Table 5 provides an overview of the number of daily life activities affected moderately and severely. On average, only 17.7% of the women reported no impairment, while 61.1% of women reported up to nine impaired aspects, and 18.9% reported more than nine impaired aspects. For women with additional chronic pain disorders, the numbers with regard to both moderate restricted activities (2.7 vs. 1.4,  $p < 0.001$ ) and severe restricted activities (3.9 vs. 1.9,  $p < 0.001$ ) were higher.

Table 6 shows that at least one of the pain characteristics could significantly predict effects in standing, walking, sleep, defaecation, urination, family and domestic responsibilities, sports activities, professional life, social functioning, mood, and joy of life. No association was found between different pain characteristics and sitting, eating and sexuality. Not included in Table 6 are the impacts of the pain characteristics 'pain frequency  $\leq 1$  per week vs. daily' and 'total length of pain episodes 2–9 h vs. <1 h', as no significant impact on daily life activities was found. When included as one of several potential confounders, additional chronic pain disorders showed no significant effect on restricting daily life activities (therefore not shown in table).

Table 7 summarises different endometriosis characteristics (rASRM stage, localisation and number of different endometriotic lesions, and number of surgical

interventions). Intra-abdominal adhesions, involvement of the vaginal fornix or the rectovaginal septum and a frozen pelvis were significantly associated with chronic pain. Endometrioma were observed more frequently in women without chronic pain. Women with chronic pain had more than one endometriosis-related surgery significantly more often than women without chronic pain.

When analysing the association between rASRM stage, adhesions, the localisation of the endometriotic lesions and different pain characteristics (pain frequency, duration of pain episodes per day, pain intensity) and locations, a significant association was found only between frequency of pain episodes and the presence of endometrioma ( $p = 0.005$ , Table S2). Altogether, higher frequencies of pain were found more often in women with endometriotic lesions than in women with endometrioma.

## 4 | DISCUSSION AND CONCLUSION

Pain has a central role in the daily life of women with endometriosis. Despite treatment and access to excellent health care systems, more than half of the study participants suffered from endometriosis-related chronic pain, nearly 80% reported dysmenorrhoea, 77% at least sometimes, and 28% almost always. This is in agreement with other research (De Graaff et al., 2013; Fourquet et al., 2010; Schliep et al., 2015).



**TABLE 3** Pain in women diagnosed with endometriosis experiencing chronic pain

	Women with endometriosis-related chronic pain		p-value <sup>b</sup>
	No other pain disorders n (%)	+ Other pain disorders n (%) <sup>a</sup>	
Pain frequency	n = 133	n = 131	
Daily	37 (27.8%)	58 (44.3%)	<0.001
>1 per week	33 (24.8%)	41 (31.3%)	
≤1 per week	63 (47.4%)	32 (24.4%)	
Total length of pain episodes per day	n = 130	n = 130	
<1 h	23 (17.7%)	8 (6.2%)	0.010
2–9 h	63 (48.5%)	79 (60.8%)	
10–24 h	44 (33.8%)	43 (33.1%)	
Average pain intensity in last 24 h	n = 122	n = 120	
<4	87 (71.3%)	55 (45.8%)	<0.001
≥4	35 (28.7%)	65 (54.2%)	
Average pain intensity in last 4 weeks	n = 124	n = 119	
<4	47 (37.9%)	27 (22.7%)	0.012
≥4	77 (62.1%)	92 (77.3%)	
Localization of most severe pain	n = 131	n = 128	
Pelvis/Lower abdomen	115 (87.8%)	105 (82.0%)	0.444
Anus	6 (4.6%)	8 (6.2%)	
Vagina	3 (2.3%)	2 (1.6%)	
Other localisation	7 (5.3%)	13 (10.2%)	
Dyspareunia	n = 130	n = 117	
Never, very rarely	36 (27.7%)	20 (17.1%)	0.141
Rarely, sometimes	60 (46.2%)	62 (53.0%)	
Normally, almost always	34 (26.2%)	35 (29.9%)	
Dysmenorrhoea	n = 128	n = 128	
Never	2 (1.6%)	3 (2.3%)	0.001
Yes, but only in the past	36 (28.1%)	14 (10.9%)	
Yes, currently	90 (70.3%)	111 (86.7%)	

<sup>a</sup>Fisher's exact test for categorial variables.

<sup>b</sup>Other (chronic) pain disorders = migraine/headache, inflammatory bowel disease, back pain, stomach pain, rheumatic disorders and arthrosis.

Table 1 presents an overview on studies with at least 100 study participants examining various aspects of the association of endometriosis or endometriosis-associated pain on daily life. These studies confirm a severe impact of endometriosis on quality of life. However, most studies address only isolated factors such as mental diseases, sexuality or professional activity. Only one small study, which unfortunately did not compare women diagnosed with endometriosis to control women and included only symptomatic women with endometriosis, presented data on unavoidable basic daily life functions as in our study. Therefore, we consider our overview on the association between endometriosis on a broad specter of daily life experiences, controlled for pain experiences as helpful to

refine strategies how to improve quality of life in the context of endometriosis.

To gain full insights into the daily lives of women, we investigated 14 different aspects of daily life (Jones et al., 2004; Moradi et al., 2014). Chronic pain led to at least moderate effects on these aspects in up to 84.7% of women and severe effects in up to 82.4%. Restricted activity occurred in *basic functions* such as standing, walking, sitting, sleep and defaecation. Although associations were not so pronounced as for other consequences of endometriosis, the clinical relevance is all the greater as these are unavoidable activities with only limited adaptability. Our results show that longer pain episodes prevent women from falling asleep or from *sleeping* without

**TABLE 4** Chronic pain and associated impairment of different aspects of daily life

Aspects of daily life <i>n</i> = 265 <sup>b</sup>	Endometriosis-related pain No other pain disorders			Endometriosis-related pain + Other pain disorders <sup>a</sup>					
	Moderate <i>n</i> (%) <sup>c</sup>	Severe <i>n</i> (%) <sup>d</sup>	Mean ± SD	Median <sup>e</sup>	Moderate <i>n</i> (%) <sup>c</sup>	Severe <i>n</i> (%) <sup>d</sup>	Mean ± SD <sup>e</sup>	Median <sup>e</sup>	<i>p</i> -value <sup>f</sup>
Standing	48 (37.21%)	28 (21.71%)	4.5 ± 3.1	5	52 (40.94%)	30 (23.62%)	5.0 ± 3.0	5	0.651
Sitting	49 (37.98%)	23 (17.83%)	4.2 ± 3.0	4	41 (32.54%)	30 (23.81%)	4.6 ± 3.1	4	0.449
Walking	50 (39.06%)	21 (16.41%)	4.2 ± 3.1	4	42 (33.33%)	21 (16.67%)	4.2 ± 3.0	3.5	0.605
Urination	28 (22.22%)	14 (11.11%)	2.8 ± 3.1	2	37 (29.6%)	20 (16%)	3.5 ± 3.3	3	0.134
Defaecation	38 (29.46%)	36 (27.91%)	4.7 ± 3.4	5	48 (38.4%)	33 (26.4%)	5.0 ± 3.3	5	0.286
Eating	33 (26.19%)	9 (7.14%)	2.7 ± 2.8	2	25 (20.16%)	17 (13.71%)	3.1 ± 3.0	2	0.168
Family and domestic responsibilities	43 (34.13%)	28 (22.22%)	4.4 ± 3.1	4	52 (41.27%)	33 (26.19%)	5.1 ± 2.9	5	0.193
Sports activities	47 (36.72%)	48 (37.5%)	5.7 ± 3.2	7	47 (37.01%)	47 (37.01%)	5.8 ± 3.1	6	1.000
Social functioning	42 (32.31%)	42 (32.31%)	5.1 ± 3.3	5.5	48 (37.8%)	39 (30.71%)	5.6 ± 3.1	5	0.639
Professional life	44 (34.38%)	35 (27.34%)	5.0 ± 3.1	5	45 (36.29%)	47 (37.9%)	5.9 ± 3.1	6.5	0.073
Sleeping	41 (31.54%)	24 (18.46%)	4.1 ± 3.0	3.5	48 (37.5%)	36 (28.12%)	5.1 ± 3.0	5	0.030
Mood	42 (32.56%)	48 (37.21%)	5.6 ± 3.1	6	46 (36.22%)	57 (44.88%)	6.4 ± 2.8	7	0.103
Joy of life	45 (34.35%)	37 (28.24%)	4.8 ± 3.3	5	39 (30.71%)	54 (42.52%)	6.0 ± 3.2	6	0.045
Sexuality	41 (31.78%)	59 (45.74%)	6.2 ± 3.2	7	38 (31.4%)	62 (51.24%)	6.8 ± 3.0	8	0.553
Mean over all aspects	42.2 (32.8%)	32.3 (25.1%)	4.6 ± 3.3	5	43.4 (34.5%)	37.6 (29.9%)	5.2 ± 3.2	5	0.518

<sup>a</sup>*n* = women with endometriosis-associated chronic pain.

<sup>b</sup>*n* = women with moderate (≥4) impairment.

<sup>c</sup>*n* = women with severe (>7) impairment.

<sup>d</sup>Mean and median impairment on a 11-point scale from 'no pain' (0) to 'strongest pain' (10).

<sup>e</sup>Fisher's exact test for categorical variables.

<sup>f</sup>Other (chronic) pain disorders = migraine/headache, inflammatory bowel disease, back pain, stomach pain, rheumatic disorders and arthritis.

**TABLE 5** Number of moderately or severely impaired aspects in women with and without endometriosis-related pain

Number of impaired aspects of daily life	Moderate impairment ( $\geq 4$ and $< 7$ )			Severe impairment ( $\geq 7$ )		
	No other pain disorders <i>n</i> = 134	+ Other pain disorders <sup>a</sup> <i>n</i> = 131	<i>p</i> -value <sup>b</sup>	No other pain disorders <i>n</i> = 134	+ Other pain disorders <sup>a</sup> <i>n</i> = 131	<i>p</i> -value <sup>b</sup>
0	27 (20.1%)	20 (15.3%)	0.411	30 (22.4%)	23 (17.6%)	0.444
1–4	66 (49.3%)	70 (53.4%)		41 (30.6%)	43 (32.8%)	
5–9	38 (28.4%)	34 (26.0%)		42 (31.3%)	36 (27.5%)	
>9	3 (2.2%)	7 (5.3%)		21 (15.7%)	29 (22.1%)	
Mean $\pm$ SD of impaired aspects	1.4 $\pm$ 2.3	2.7 $\pm$ 2.9	<0.001	1.9 $\pm$ 3.4	3.9 $\pm$ 4.4	<0.001

<sup>a</sup>Fisher's exact test for categorial variables, independent *t*-test for difference between the means.

<sup>b</sup>Other (chronic) pain disorders = migraine/headache, inflammatory bowel disease, back pain, stomach pain, rheumatic disorders and arthrosis.

interruption, a finding supported by qualitative research (Jones et al., 2004; Moradi et al., 2014). With 80% of women reporting sexual impairment, *sexuality* was the area most impacted, and dyspareunia the main disturbing factor (Bernays et al., 2020; Bernuit et al., 2011; De Graaff et al., 2016; Hämmerli et al., 2018). However, no association was found between pain characteristics and sexuality. Dyspareunia is induced by vaginal penetration and consequently not necessarily influenced by frequency, duration and intensity of other pain. The limited association of dyspareunia with sexual functioning is confirmed by other studies (Vercellini et al., 2012); this supports the importance of additional influencing factors, including fatigue, importance of sex, desire for children and the quality of the partnership (Barbara et al., 2017; Bernays et al., 2020; Liebermann et al., 2018; Vercellini et al., 2012). Previous studies on *psychological well-being* revealed a higher prevalence of depression and anxiety in women with endometriosis attributed to chronic pain as a causal factor (Chen et al., 2016; Facchin et al., 2015; Lorençatto et al., 2006). Our data showed that psychological well-being was negatively influenced by pain duration, pain intensity and the incidence of depression. Limitations in *sports activities* increased with higher duration, intensity, as well as frequency of pain episodes. Obviously few women exercise when they feel pain (Moradi et al., 2014). Results on the influence of exercise on pain are inconclusive (Bonoche et al., 2014; Garavaglia et al., 2014), but recent studies show the beneficial effects of exercise if it is not too vigorous (Armour et al., 2019; Awad et al., 2017). In addition, chronic pain causes limitations in *professional life* (De Graaff et al., 2013; Fourquet et al., 2010; Nnoaham et al., 2011; Sperschneider et al., 2019), *family and domestic responsibilities* as well as *social functioning* (Denny, 2004; Gilmour et al., 2008; Jones et al., 2004; Moradi et al., 2014). The degree of limitations was significantly greater the longer the length of pain episodes per day. In addition,

social functioning showed a strong relationship with pain frequency. When in pain, women not only feel tired and weak, but they also worry about pain symptoms occurring in public (Jones et al., 2004). High frequency of pain episodes might increase anxiety towards reoccurring pain events. Although pain-associated nausea or appetite loss might prevent women from *eating* (Jones et al., 2004), we found no association between pain characteristics and eating; women experiencing endometriosis-related pain were significantly more often obese. This could be due to either pain-related reduced physical activity or reduced psychological well-being.

Very frequently, women reported being severely impaired in at least four different areas of daily life; about one-third reported being severely impaired in up to nine different areas of daily life. Our results confirm the great clinical need for further improvement in pain management and support a multimodal approach that incorporates daily-life functioning and quality of life in pain management, as recommended by the International Association for the Study of Pain (IASP) (Aziz et al., 2019). Medical support should include optimised interdisciplinary pain treatment and strategies to manage remaining pain. Future studies on treatment outcomes should address endometriosis-related limitations in daily life in greater detail.

The total length of pain episodes per day appears to be a major factor in predicting the impairment of daily life activities. Pain lasting longer than 1 hour per day was a better predictor of limitations than pain frequency or intensity. These findings are important, since research often assesses only the presence and intensity of pain; this should be corrected in future studies to include the length of pain episodes (Salamon et al., 2014).

In our study, depression and fatigue occurred significantly more often in women experiencing chronic pain. There is nevertheless disagreement about the causal relationship

**TABLE 6** Multivariate analysis of the association between pain characteristics and different aspects of daily life

	Standing	Walking	Sitting	Sleep	Defecation	Urination	Eating
	<b>Adjusted OR</b>						
	<b>95% CI</b>						
	<b>Adjusted <i>p</i>-value<sup>b</sup></b>						
Pain frequency	0.70	0.62	0.48	0.77	0.38	0.39	0.39
>1 per week vs. daily	0.28; 1.74	0.25; 1.50	0.20; 1.16	0.29; 2.03	0.15; 0.97	0.16; 0.95	0.14; 1.04
	0.439	0.291	0.105	0.588	0.047	0.041	0.065
Total length of pain episodes per day	3.47	4.10	2.19	12.68	0.54	3.02	1.44
>9 h vs. <1 h	1.04; 12.66	1.21; 15.95	0.69; 7.25	3.04; 70.03	0.16; 1.73	0.88; 11.77	0.36; 7.36
	0.049	0.03	0.186	0.001	0.302	0.091	0.631
Average pain in last 24h	1.13	0.76	1.26	0.71	0.62	0.45	0.84
≥4 vs. <4 <sup>c</sup>	0.46; 2.75	0.32; 1.78	0.54; 2.95	0.26; 1.81	0.24; 1.54	0.17; 1.11	0.33; 2.14
	0.786	0.528	0.593	0.478	0.312	0.09	0.717
Average pain in last month	1.69	3.09	1.81	1.17	0.79	1.81	1.22
≥4 vs. <4 <sup>c</sup>	0.71; 4.08	1.32; 7.53	0.79; 4.19	0.46; 3.01	0.32; 1.93	0.74; 4.55	0.48; 3.10
	0.234	0.011	0.163	0.734	0.6	0.196	0.678
Fatigue (Very frequently) <sup>d</sup>	1.53	1.99	1.24	1.36	1.09	2.42	0.74
	0.65; 3.63	0.87; 4.69	0.54; 2.85	0.56; 3.30	0.47; 2.50	1.03; 5.88	0.30; 1.81
	0.329	0.11	0.608	0.497	0.845	0.046	0.512
Depression Yes <sup>a</sup>	1.66	1.57	2.13	2.07	0.82	1.04	1.33
	0.73; 3.82	0.72; 3.48	0.97; 4.80	0.88; 4.96	0.36; 1.84	0.47; 2.31	0.57; 3.12
	0.229	0.256	0.063	0.096	0.634	0.92	0.511

<sup>a</sup>Adjusted for: marital status, BMI, location of endometriotic lesion (endometrioma, vaginal fornix/septum rectovaginal or Douglas), adhesions, number of surgical interventions, different pain disorders (migraine/headache, inflammatory bowel disease (IBD), back pain, stomach pain, rheumatic diseases, arthrosis), fatigue and depression.

<sup>b</sup>Average pain categorized into no-to-mild (<4) and moderate-to-severe (≥4) pain intensity (on an 11-point scale from 'no pain' (0) to 'strongest pain' (10)).

<sup>c</sup>(Very) frequently = any rating >3 (on a scale of: 1 = never to 5 = very frequently).

<sup>d</sup>Yes = score ≥10 in the Patient Health Questionnaire (PHQ-9).

and about which condition occurs first (Lorençatto et al., 2006). Our data suggest that chronic pain is more important in daily activities, whereas depression seems to be an important factor for psychological well-being.

Results on the relationship between endometriotic lesions and pain are inconsistent. However, in our study as well as in other studies (Anaf et al., 2000), deep infiltrating endometriosis was associated with pelvic pain. As anticipated, rASRM stage was not associated with pain (Gruppo Italiano per lo Studio dell'Endometriosis, 2001; Vercellini et al., 1996, 2007), but women with endometriosis-related pain had a higher number of surgical interventions.

In contrast with our expectations and results regarding dyspareunia (Fauconnier et al., 2002; Porpora et al., 1999; Vercellini et al., 1996), lesions on uterosacral ligaments and Douglas involvement were not related to chronic pain. This may be because the association was studied with chronic pain in general and not with dyspareunia alone. The mechanical origin of dyspareunia, deep penetration with tension on the uterosacral ligament, may not apply to other endometriosis-related pain, such as dysmenorrhoea

(Fauconnier et al., 2002). In addition, the lack of association could be due to the result regarding the extent of neural infiltration (Vercellini et al., 2007), a key factor in endometriosis-related pain (Anaf et al., 2000; Hsu et al., 2011). Nervous innervation and its interaction with the central nervous system seem to be more important in pain experiences than the ectopic growths themselves (Hsu et al., 2011; Stratton & Berkley, 2011). In turn, when and how innervation is sensitised can be influenced by a variety of factors, including menstruation, hormones and the type or location of the lesion (Stratton & Berkley, 2011). Deep endometriotic lesions, for example, are reported to be more neurotrophic and show high expression of nerve growth factor (Anaf et al., 2002; Vercellini et al., 2007). In contrast, endometriomas, known to lack neural infiltration (Al-Fozan et al., 2004; Anaf et al., 2000; Fauconnier et al., 2002), were not related to pain in our study and in other studies (Fauconnier et al., 2002; Porpora et al., 1999; Vercellini et al., 2007).

In our study, women with more surgeries reported significantly more chronic pain. On the one hand, persistent

Family & domestic responsibilities	Sports activities	Professional life	Social functioning	Mood	Joy of life	Sexuality
0.76	0.30	0.68	0.17	0.85	0.88	0.64
0.28; 2.05	0.10; 0.86	0.24; 1.93	0.05; 0.48	0.28; 2.56	0.32; 2.42	0.18; 2.12
0.58	0.029	0.466	0.001	0.775	0.798	0.466
22.94	6.05	16.56	41.03	4.26	3.69	1.53
4.90; 175.22	1.64; 24.35	4.22; 79.34	7.84; 349.40	1.11; 17.33	1.00; 14.57	0.38; 5.92
<0.001	0.008	<0.001	<0.001	0.037	0.054	0.541
1.37	0.86	1.30	1.19	0.71	0.74	0.71
0.52; 3.58	0.32; 2.29	0.48; 3.55	0.43; 3.27	0.25; 2.03	0.28; 1.96	0.23; 2.20
0.522	0.756	0.606	0.738	0.528	0.552	0.552
1.97	2.70	1.84	2.69	1.94	2.60	2.09
0.76; 5.17	1.05; 7.21	0.70; 4.89	0.97; 7.83	0.74; 5.26	1.03; 6.79	0.75; 6.08
0.163	0.042	0.213	0.062	0.183	0.046	0.165
1.54	1.92	0.91	1.52	2.06	1.85	1.57
0.62; 3.89	0.74; 5.17	0.35; 2.37	0.57; 4.15	0.82; 5.40	0.76; 4.59	0.59; 4.28
0.353	0.183	0.847	0.408	0.131	0.178	0.366
1.58	2.24	2.80	1.67	3.25	2.45	1.95
0.65; 3.94	0.85; 6.21	1.08; 7.68	0.62; 4.67	1.21; 9.53	1.00; 6.32	0.69; 6.05
0.314	0.11	0.039	0.315	0.024	0.055	0.224

or recurrent pain might have led to repetitive surgery; on the other hand, our results confirm once again that surgery is of limited success in improving endometriosis-related pain.

Understanding the relationship between endometriosis and pain is challenging, not only because of the still unclear pathomechanism, but also because of frequent comorbid chronic pain syndromes (Mirkin et al., 2007; Schliep et al., 2015; Sinaii et al., 2002; Surrey et al., 2018; Yang et al., 2012). According to our results, additional chronic pain disorders are associated with higher frequency of pain episodes, longer pain episodes and greater intensity of endometriosis-related pain, as well as more frequent dysmenorrhoea and greater impairment in daily activities. Since nervous innervation is also discussed in comorbid diseases, neurological overlay could be another reason for the intensity of endometriosis-related pain (Stratton & Berkley, 2011). However, when comorbid pain disorders were included among other potentially relevant confounders of pain experiences, they remained no longer statistically significant, i.e., pain characteristics such

as intensity and duration of pain episodes determine the association between endometriosis-related pain and daily life. As comorbid pain syndromes are common in women with endometriosis-related chronic pain and our data show that pain may be more severe in women with endometriosis and comorbid pain syndromes, they should be considered in pain management and specific treatment options for each pain disorders should be combined (Baranowski, 2009; Schliep et al., 2015).

#### 4.1 | Strengths and limitations

This study presents data from one of the largest groups of women with endometriosis ever studied and provides a nuanced overview of the effect of chronic pain on different aspects of daily life, as well as insights into the impact of specific endometriosis lesions. Endometriosis was surgically and histologically diagnosed and categorised according to the rASRM classification. Internationally recognised and validated questionnaires were used to

**TABLE 7** Endometriosis characteristics: rASRM stage, adhesions, different locations of endometriotic lesions, and number of endometriosis-related surgeries in women with and without endometriosis-related chronic pain

	Women with endometriosis		$X^2$	p-value <sup>b</sup>
	With chronic pain n = 265	Without chronic pain n = 245		
rASRM stage				
	n = 249	n = 224		
I	45 (18.1%)	32 (14.3%)	1.084	0.298
II	47 (18.9%)	46 (20.5%)		
III	58 (23.3%)	84 (37.5%)		
IV	99 (39.8%)	62 (27.7%)		
Intra-abdominal adhesions				
	n = 249	n = 224		
Yes	202 (81.1%)	161 (71.9%)	5.146	0.023
Endometrioma				
	n = 248	n = 224		
Yes	114 (46%)	126 (56.2%)	4.576	0.032
Involvement of the uterosacral ligaments				
	n = 248	n = 224		
Yes	151 (60.9%)	137 (61.2%)	0	1.000
Involvement of pelvic wall				
	n = 248	n = 224		
Yes	206 (83.1%)	177 (79%)	1.009	0.315
Involvement of vaginal fornix				
	n = 248	n = 224		
Yes	42 (16.9%)	21 (9.4%)	5.181	0.023
Involvement of Douglas/septum rectovaginal				
	n = 249	n = 224		
Yes	187 (75.1%)	156 (69.6%)	1.499	0.221
Douglas obliteration (frozen pelvis)				
	n = 248	n = 224		
Yes	79 (31.9%)	51 (22.8%)	4.425	0.035
Number of different locations				
	n = 265	n = 245		
1	34 (12.8%)	25 (10.2%)	1.539	0.210
2	36 (13.6%)	44 (18.0%)		
3	41 (15.5%)	57 (23.3%)		
4	62 (23.4%)	47 (19.2%)		
5	79 (29.8%)	59 (24.1%)		
6	13 (4.9%)	13 (5.3%)		
Mean $\pm$ SD	3.6 $\pm$ 1.5	3.4 $\pm$ 1.4		0.291
Number of surgical interventions because of endometriosis				
	n = 250	n = 224		
1	106 (42.4%)	145 (64.7%)	25.718	<0.001
2	91 (36.4%)	55 (24.6%)		
3	22 (8.8%)	19 (8.5%)		
4	12 (4.8%)	1 (0.4%)		
$\geq 5$	19 (7.6%)	4 (1.8%)		
Mean $\pm$ SD	2.1 $\pm$ 1.5	1.5 $\pm$ 0.8		<0.001

<sup>a</sup>Pearson Chi-squared test for categorical variables, Kruskal–Wallis test for ordinal variables, independent *t*-test for difference between the means.

assess chronic pain, depression and the association of pain with daily life. With the additional recording of comorbid pain as well as controlling for it in the statistical analysis, we were able to differentiate between the impact of endometriosis and the impact of additional comorbid pain disorders. To the best of our knowledge, the differentiated assessment of different pain characteristics, pain comorbidities, together with the exploration of a broad spectrum of daily life activities, is unique.

The analysis of the impact of specific endometriotic lesions was hampered by two things: first, the surgical reports and the recording of lesion characteristics were not uniform, due to different expertise in different hospitals; second, finding a clear association between specific endometriotic lesions and associated pain was complicated by women having multiple lesions rather than isolated endometriotic lesions. Because socio-cultural factors have been shown to influence pain perception (Chen et al., 2021; Facchin et al., 2015), our predominantly Caucasian study group limits generalisability.

## 5 | CONCLUSION

Women with endometriosis reported moderate negative effects due to chronic pain in almost all aspects of daily life studied, including basic activities such as standing, walking, sitting, defaecation, sleep, sports activities, family and domestic responsibilities, sexuality, social functioning, professional life, mood, and joy of life. Comorbid pain disorders were common in women with endometriosis-related chronic pain, leading to an increased pain incidence and intensity and associated consequences on daily life. Total duration of pain episodes shows strong associations with limitations in professional life, social functioning as well as family and domestic responsibilities. The high prevalence of endometriosis-related pain, synergistic effects with comorbid pain disorders and severe limitations in daily life make pain reduction one of the most important goals to improve the quality of life in women with endometriosis.

## ACKNOWLEDGEMENTS

The authors would like to thank all the women who took part in this study. The authors thank Brigitte Alvera, Anna Dietlicher, Franka Grischott, Nicole Kuenzle, Judith Kurmann, Christina Liebermann, Karoline Stojanov, Elvira Gross, Lina Sperschneider, Sarah Schaerer, Theodosia Charpidou, Elena Lupi, and Franziska Graf for their support in data collection. Open access funding provided by Universitat Zurich.

## CONFLICT OF INTEREST

None of the authors has any conflict of interest.

## AUTHOR CONTRIBUTIONS

J.L. and B.L. were responsible for the analysis and for the preparation of the manuscript. All authors participated in finalising the manuscript. B.L. was the principal investigator and director of the study. A.S.K.S., F.H., M.E. and B.L. were investigators. Data were collected by A.S.K.S., K.G., F.H., M.E., P.I., and B.L. K.G. was responsible for the management of the database. K.G., P.I., and B.L. developed the original concept.

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**How to cite this article:** Leuenberger, J., Kohl Schwartz, A. S., Geraedts, K., Haeblerlin, F., Eberhard, M., von Orellie, S., Imesch, P., & Leeners, B. (2022). Living with endometriosis: Comorbid pain disorders, characteristics of pain and relevance for daily life. *European Journal of Pain*, 26, 1021–1038. <https://doi.org/10.1002/ejp.1926>