

# Evaluation of the SF-36 questionnaire for assessment of the quality of life of endometriosis patients undergoing treatment: A systematic review and meta-analysis

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**Abstract.** Endometriosis has a negative influence on the physical, psychological, and social aspects of a patient's life; therefore, it affects the health-related quality of life (HRQoL). The current review aimed to investigate the efficiency of a 36-item generic questionnaire survey (SF-36) for patients with endometriosis who were undergoing medical or surgical treatment. A search strategy including the key words 'endometriosis', 'quality of life' (QOL), and 'questionnaire SF-36' was applied using the PubMed/MEDLINE, EMBASE, and Cochrane databases in order to include articles that evaluated the QOL among women with endometriosis using the SF-36. Only articles that included interviews of patients both before and after surgical or medical endometriosis treatment or those articles that compared study groups were considered. The qualitative analysis was based on 37 articles, whereas the quantitative analysis utilized 14 articles.

The research participants included 11,101 women, among whom 6,888 patients were diagnosed with endometriosis. The analysis recorded 17 studies dealing with all types of endometriosis, 9 studies dealing with deep infiltrative endometriosis (DIE), and 9 studies dealing with bowel endometriosis or DIE with bowel involvement. QOL was evaluated using only SF-36 in 12 studies that collectively included 1,912 women and using SF-36 in association with other questionnaires in 25 studies that collectively included 8,022 women. For patients with endometriosis, physical functioning [odds ratio (OR), 78.87; 95% confidence interval (CI), 68.97-88.77;  $I^2=98.77\%$ ;  $P\leq 0.001$ ] was the most affected life parameter. This parameter showed the highest improvement after surgical intervention (OR, 63.39; 95% CI, 48.71-78.07;  $I^2=97.65\%$ ;  $P\leq 0.001$ ) or hormonal treatment (OR, 38.65; 95% CI, 14.39-62.91;  $I^2=38.65\%$ ;  $P\leq 0.001$ ). The 36-item survey generic questionnaire seems to be an efficient tool for assessment of the QOL of life of women with endometriosis who are undergoing surgical or medical treatment. It can be applied before and after the procedure, and it can also be used for comparing study groups.

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**Key words:** endometriosis, quality of life, SF-36, endometriosis therapy, laparoscopy

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## 1. Introduction

Endometriosis is a condition resulting from ectopic endometrial cell implants that grow progressively and determine an inflammatory response (1). The ovaries are the most common locations for endometriotic lesion formation, followed by the anterior and posterior cul-de-sac, the posterior surface of the broad ligaments, the uterosacral ligaments, the serosa of the uterus, the fallopian tubes, the sigmoid colon, the appendix, and the round ligament (2). The therapeutic options are based on clinical presentation, including infertility, pain, or mass; they are individualized according to disease severity, patient age, and reproductive desires while considering the medication side effects, costs and morbidity of the surgical procedures (3,4).

Endometriosis negatively affects the physical, psychological, and social aspects of women's lives (5), and therefore has a great impact on the health-related quality of life (HRQoL). It is difficult to characterize the quality of life (QOL) among specific patient groups because it is a broad concept that includes life satisfaction, good health, education, personal and family safety, adequate housing, employment, interrelationships, and leisure pursuits (6). Globally, in the scientific literature, QOL is evaluated using a multitude of validated and non-validated questionnaires, such as the 36-item survey generic questionnaire (SF-36). It includes eight conceptual health domains: General Health (GH), Physical Functioning (PF), Bodily Pain (BP), Role Physical (RP), Vitality (VT), Social Functioning (SF), Mental Health (MH), and Role Emotional (RE); these are summarized in the physical (PCS) and mental (MCS) component scores (7).

Recently, a number of original studies and systematic reviews have evaluated the impact of endometriosis on patient QOL (8-10). Studies have also reported the impact of different therapeutic approaches on the QOL of patients with endometriosis (11). A systematic review detailed the quality of sexual life after endometriosis-targeted laparoscopic surgery (12). Another recent meta-analysis showed that endometriosis-targeted surgical resection can improve the major domains of QOL (13). However, systematic reviews that evaluate the impact of surgical and non-surgical treatments on the QOL of patients with endometriosis are scarce.

The main objective of the present review was to investigate the efficiency of questionnaire SF-36 in assessing the QOL of patients with endometriosis who were undergoing medical or surgical treatment.

## 2. Research methods

We utilized the 'Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)' guideline to conduct this study' (14).

*Data sources and search strategies.* A combination of key word terms including 'endometriosis', 'quality of life' and 'questionnaire SF-36' were utilized for the literature research conducted in October 2018. The utilized databases included PubMed/Medline, Embase, and Cochrane; some other additional sources and references of the identified articles were also utilized. The search strategy that was utilized for PubMed/MEDLINE is outlined as follows.

*Study selection.* Articles that evaluated the quality of life (QOL) and used the SF-36 to assess women with endometriosis were evaluated. Articles that interviewed patients both before and after endometriosis-related surgical or medical treatment were included in our analysis. We also utilized the reports of women with endometriosis that were compared with a control group. Studies that focused on any type of endometriosis and were published in English, German, or French were considered in our analysis. There were no restrictions based on publishing year, journal, author, or institution.

*Data extraction.* All the selected studies were independently evaluated by two reviewers. Any disagreements regarding the articles were solved by the third more experienced author and the senior authors. The data were extracted in tables that consisted of first author's name, publication year, study type, number of initial participants, treatment type, presence of a control group or lack thereof, endometriosis type, treatment, follow-up, and the final number of participants.

*Quality assessment.* To evaluate the quality of the included studies, the modified Newcastle-Ottawa Scale (NOS) was applied (15). This scale helped to assess the risk of bias in the remaining studies. The studies were classified as 'good' when they fulfilled at least 70% of the 12 criteria, 'fair' when they fulfilled at least 50%, and 'poor' when they fulfilled less than 50%.

*Statistical analysis.* Since we observed between-study heterogeneity, we applied random-effects meta-analyses, using odds ratios (OR) and 95% confidence intervals (95% CI). The results were presented as pooled prevalence values. Studies that reported data by comparing various endometriosis types were included in the data for the most severe, whereas studies that dealt with different types of surgical treatment were considered the most difficult interventions. Statistical analysis was performed using the Open-Meta analyst [CEBM Brown, open-source, OpenMetaAnalyst for Windows 10 (64-bit)].

In our study, statistical results were calculated as follows. The first report was based on a comparison between patients with endometriosis and a control group (healthy women); the second considered surgical treatment, and the third group considered hormonal treatment.

## 3. Results of the study research

*Study research.* In accordance with our research plan, we initially identified the records of 657 articles that corresponded to our search strategy. Furthermore, 25 articles were sourced generated from additional sources (cross references). Any duplicates were removed, and the final database consisted of 345 articles. Excluding some articles due to language issues, we obtained reviews, case reports, or abstracts from 127 records for screening. Among these, 55 studies were excluded based on the inclusion criteria. Finally, full-text evaluation was conducted for 72 studies. The qualitative analysis was based on 37 articles, whereas the quantitative analysis utilized 14 articles.

Regarding the study types, our qualitative analyses included 21 prospective studies, 3 retrospective studies,

and 7 randomized clinical trials. A total of 25 studies that associated other questionnaires with the SF-36 to evaluate the QOL of patients with endometriosis were identified.

Based on our study protocol, we observed that 13 studies did not apply the SF-36 questionnaire before and after treatment. The results were specified only in the graphics and not in the text. Some studies reported the results as a total number; thus, it was impossible to include them in the statistics. Only studies that had all the reported numerical data from the questionnaires were selected for the meta-analyses.

**Quality and the risk of bias.** Based on the inclusion criteria, we obtained 37 studies; among these, 16 articles were considered as being of 'good' quality (between 6 and 8 points), and 11 articles were considered as being of 'fair' quality (between 3 and 5 points). Table I includes evaluations for each study.

**Study characteristics.** The characteristics for each study are recorded in Table II. The research included 1,1101 women, among whom 6,888 patients were diagnosed with endometriosis. Based on the endometriosis type, 17 studies dealt with all types of endometriosis, 9 studies focused on deep infiltrative endometriosis, and another 9 studies identified bowel endometriosis or deep infiltrative endometriosis with bowel involvement. QOL was evaluated by using only the SF-36 in 12 studies including 1,912 women and by using SF-36 associated with various other questionnaires in 25 studies that had a collective total of 8,022 women.

As part of the SF-36 questionnaire's general evaluation, it was applied for studies that presented the QOL of the patients with endometriosis in comparison to that of healthy women or patients with endometriosis that were interviewed using SF-36 just once (without any follow-up period). Based on this classification, the review included 15 studies with a general overview on endometriosis. Among them, 6 studies evaluated the QOL of patients with endometriosis compared with that of healthy women, and 9 studies compared different types of treatment among patients with endometriosis. On this topic, 6,810 women were evaluated, and 6,393 had endometriosis. The classification based on endometriosis subtypes confirmed that 5,410 patients had all the endometriosis types, 416 had deep infiltrative endometriosis (DIE), and 198 had minimal endometriosis.

For this group of the review, the quantitative analysis could be performed in 6 studies. Our study revealed that patients with endometriosis had an altered QOL compared to the control healthy women group. The pooled prevalence showed that the selected parameters were influenced as follows: Physical Functioning (PF): OR, 78.87 (95% CI, 68.97-88.77;  $I^2=98.77\%$ ;  $P\leq 0.001$ ); Bodily Pain (BP): OR, 51.63 (95% CI, 45.23-58.03;  $I^2=92.62\%$ ;  $P\leq 0.001$ ); Role Physical (RP): OR, 56.12 (95% CI, 45.08-67.12;  $I^2=95.40\%$ ;  $P\leq 0.001$ ); Vitality (VT): OR, 43.09 (95% CI, 32.23-53.95;  $I^2=98.67\%$ ;  $P\leq 0.001$ ); Social Functioning (SF): OR, 58.10 (95% CI, 47.28-68.91;  $I^2=97.67\%$ ;  $P\leq 0.001$ ); Mental Health (MH): OR, 55.65 (95% CI, 45.58-65.72;  $I^2=98.41\%$ ;  $P\leq 0.001$ ); and Role Emotional (RE): OR, 57.84 (95% CI, 47.21-68.48;  $I^2=95.19\%$ ;  $P\leq 0.001$ ). Based on pooled prevalence, for patients with endometriosis, the most affected parameter was Physical Functioning (PF): OR, 78.87 (95% CI, 68.97-88.77;  $I^2=98.77\%$ ;  $P\leq 0.001$ ).

Qualitative analysis regarding QOL for patients that underwent surgical treatment for endometriosis was evaluated with a SF-36 tool, and it included 21 studies with a collective population of 3,368 patients (Table III). In all the selected studies, the questionnaire was completed before and after surgery. The various studies' follow-up periods ranged between 7 weeks and 3 years. The types of endometriosis were all types of endometriosis (3 studies), DIE (14 studies), or intestinal endometriosis (3 studies). Statistical analyses were performed for 5 studies that included mean values for each result. The studies confirmed that the parameters evaluated with SF-36 improved after surgical treatment. Pooled prevalence revealed that each parameter improved as follows: Physical Functioning (PF): OR, 63.39 (95% CI, 48.71-78.07;  $I^2=97.65\%$ ;  $P\leq 0.001$ ); General Health (GH): OR, -0.71 (95% CI, -1.20--0.23;  $I^2=90.04\%$ ;  $P\leq 0.001$ ); Bodily Pain (BP): OR, 41.25 (95% CI, 38.95-43.55;  $I^2=97.33\%$ ;  $P\leq 0.001$ ), Role Physical (RP): OR, 43.16 (95% CI, 32.74-53.58;  $I^2=91.83\%$ ;  $P\leq 0.001$ ); Vitality (VT): OR, 37.99 (95% CI, 30.54-45.44;  $I^2=93.45\%$ ;  $P\leq 0.001$ ); Social Functioning (SF): OR, 48.09 (95% CI, 30.67-63.50;  $I^2=98.69\%$ ;  $P\leq 0.001$ ); Mental Health (MH): OR, 51.78 (95% CI, 44.70-58.87;  $I^2=92.73\%$ ;  $P\leq 0.001$ ); and Role Emotional (RE): OR, 50.65 (95% CI, 41.37-59.93;  $I^2=88.39\%$ ;  $P\leq 0.001$ ). In the case of patients who had their endometriosis surgically treated, among the parameters evaluated by SF-36, the highest rate of improvement was observed in Physical Functioning (PF): OR, 63.39 (95% CI, 48.71-78.07;  $I^2=97.65\%$ ;  $P\leq 0.001$ ).

Quantitative analysis was conducted for 7 studies on patients who underwent hormone treatments, which were evaluated with SF-36, whereas the statistic forest plots were based on 3 studies. The patients with endometriosis (392 in number) were compared with a control group that did not receive the same treatment (placebo or control). The studies showed that parameters evaluated with SF-36 improved after hormonal treatment. Pooled prevalence revealed that each parameter improved as follows: Physical Functioning (PF): OR, 38.65 (95% CI, 14.39 -62.91;  $I^2=38.65\%$ ;  $P\leq 0.001$ ); General Health (GH): OR, -0.60 (95% CI, -1.78-0.57;  $I^2=94.13\%$ ;  $P\leq 0.001$ ); Bodily Pain (BP): OR, 28.51 (95% CI, 10.05-41.96;  $I^2=97.33\%$ ;  $P\leq 0.001$ ); Role Physical (RP): OR, 32.42 (95% CI, 0.62-64.49;  $I^2=98.62\%$ ;  $P\leq 0.001$ ); Vitality (VT): OR, 31.49 (95% CI, 6.58-56.39;  $I^2=98.58\%$ ;  $P\leq 0.001$ ); Social Functioning (SF): OR, 35.86 (95% CI, 12.01-59.7;  $I^2=97.92\%$ ;  $P\leq 0.001$ ); Mental Health (MH): OR, 35.11 (95% CI, 5.72-64.50;  $I^2=98.85\%$ ;  $P\leq 0.001$ ); and Role Emotional (RE): OR, -0.39 (95% CI, -0.90-0.20;  $I^2=74.57\%$ ;  $P\leq 0.001$ ). After the hormonal treatment, the parameter that showed the most improvement was Physical Functioning (PF): OR, 38.65 (95% CI, 14.39 -62.91;  $I^2=38.65\%$ ;  $P\leq 0.001$ ).

#### 4. Discussion

Our meta-analyses revealed that the SF-36 questionnaire had a heterogenous applicability in all the studies. Recently, Chauvet *et al* performed a recent systematic review, which proved that the SF-36 was the most frequently used scale, followed by the EHP-30, for evaluating quality of life (QOL) of patients with endometriosis (16). The design of our study was different from previous meta-analyses as we included articles

Table I. Quality assessment of the studies.

Authors, year	Selection				Outcome				Total Score (Refs.)
	Representativeness of exposed cohort	Selection of non-exposed cohort	Ascertainment of exposure	Outcome not present at baseline	Compatibility of cohort (matched for)	Assessment of outcome	Sufficient follow-up duration	Adequate follow-up	
Van Aken <i>et al</i> , 2017	+	+	+		+	+	+		Fair (18)
Angioni <i>et al</i> , 2015	+		+	+	+	+		+	Good (31)
Silveira da Cunha Araújo <i>et al</i> , 2014	+		+		+		+		Fair (26)
Bassi <i>et al</i> , 2011	+		+	+		+		+	Good (27)
Caruso <i>et al</i> , 2015	+	+	+	+	+	+		+	Good (28)
Chauvet <i>et al</i> , 2018	+		+	+	+				Fair (16)
Comptour <i>et al</i> , 2020	+	+	+	+	+	+		+	Good (13)
Darai <i>et al</i> , 2010	+	+	+	+	+	+		+	Good (40)
Darai <i>et al</i> , 2017	+		+	+	+	+			Fair (37)
Dubernard <i>et al</i> , 2008	+		+	+	+	+		+	Good (29)
Friedl <i>et al</i> , 2015	+		+	+	+			+	Good (24)
Garavaglia <i>et al</i> , 2018	+		+	+	+	+		+	Good (38)
De Graaff <i>et al</i> , 2013	+		+	+	+	+			Fair (39)
Grandi <i>et al</i> , 2015	+	+	+	+	+			+	Good (54)
Jones <i>et al</i> , 2004	+		+	+	+	+		+	Good (56)
Laursen <i>et al</i> , 2005	+	+	+	+	+	+			Good (19)
Ledu <i>et al</i> , 2018	+	+	+	+	+	+			Good (33)
Lovkvist <i>et al</i> , 2016	+	+	+		+	+			Fair (55)
Mabrouk <i>et al</i> , 2011	+	+	+	+	+				Fair (43)
Mabrouk <i>et al</i> , 2012	+	+	+	+	+	+			Good (36)
Melis <i>et al</i> , 2015	+	+	+	+	+				Fair (47)
Miller, 2000	+		+	+	+	+		+	Good (44)
Marki <i>et al</i> , 2017	+		+	+	+				Fair (45)
Nnoaham <i>et al</i> , 2011	+		+	+	+			+	Good (51)
Nunes <i>et al</i> , 2014	+	+	+	+	+	+			Good (48)
Petrelluzzi <i>et al</i> , 2008	+	+	+	+	+	+			Good (52)
Ribeiro <i>et al</i> , 2014	+		+	+	+	+		+	Good (30)
Riiskjær <i>et al</i> , 2018	+		+	+	+	+		+	Good (34)



Table I. Continued.

Authors, year	Selection			Outcome				Total Score (Refs.)	
	Representativeness of exposed cohort	Selection of nonexposed cohort	Ascertainment of exposure	Outcome not present at baseline	Compatibility of cohort (matched for)	Assessment of outcome	Sufficient follow-up duration		Adequate follow-up
Roman <i>et al.</i> , 2012	+	+	+	+	+	+		+	Good (21)
Roman <i>et al.</i> , 2018	+	+	+	+	+	+		+	Good (32)
Roman <i>et al.</i> , 2018	+	+	+	+	+			+	Fair (32)
Teixeira <i>et al.</i> , 2017	+	+	+	+	+			+	Good (49)
Touboul <i>et al.</i> , 2015	+	+	+	+	+	+	+		Good (41)
Valentin <i>et al.</i> , 2017	+		+	+	+	+			Fair (25)
Verket <i>et al.</i> , 2018	+	+	+	+	+	+			Good (20)
Bi and Xie, 2018	+	+	+	+	+			+	Good (22)
Zhao <i>et al.</i> , 2012	+	+	+	+	+	+		+	Good (46)

that evaluated patients with endometriosis using the SF-36 questionnaire before and after surgical or medical treatment or as a comparison tool between groups. The literature did not reveal a similar approach. For example, Arcoverde *et al* performed another meta-analysis utilizing generic questionnaires and revealed that surgery improved the quality of life for patients with all types of endometriosis (17). We excluded cases with hormonal approach and cases that were evaluated using different questionnaires (18). There was no meta-analyses that evaluated the efficiency of SF-36 for patients with endometriosis treated with hormonal therapy or as a comparison method between study groups.

Regarding the first issue of our classification, we identified 6,393 women who received treatment for endometriosis and answered the SF-36 questionnaire. Based on this approach, we observed that, for women with endometriosis, compared with the control groups, physical functioning was the main parameter that received the most alteration. Two peculiar studies were included within this group of studies. Laursen *et al* (19) compared patients with fibromyalgia/whiplash, endometriosis, lower back pain, or rheumatoid arthritis and healthy women. We included this study because of its data accuracy; furthermore, there was no other pathological influence on the women with endometriosis. The second study was the Verket *et al* study (20), which evaluated women from the general population, women with endometriosis, and women with rheumatoid arthritis. We incorporated it into the analyses of this study because it did not have a control group of healthy women for comparison to women with endometriosis, and the arthritis had no impact. For both of these studies, we considered only the data for the endometriosis patients.

Van Aken *et al* demonstrated that, for endometriosis patients, pain cognition and QOL are independently associated (18). Verket *et al* highlighted that patients with moderate to severe endometriosis had overall impaired QOL compared to women from the general population (20). Women with DIE reported constipation, defecation pain, appetite disorders, longer evacuation time, and increased stool consistency without laxatives (21). Neuromuscular electro-stimulation was found to be an efficient method for alleviating endometriosis-related pain (22).

The present analysis of QOL for patients with endometriosis who received surgical treatment included data from 3,368 patients. The pre- and post-surgery questionnaire in all the studies showed that physical functioning was the principal parameter that improved after the interventions. The studies proved that endometriosis symptoms such as pain showed improvement after surgical treatment (23), even though endometriosis also influenced biopsychosocial variables (24). Patients with minimal endometriosis seldom reported surgery as a good treatment for improving QOL (25). For patients with bowel endometriosis, QOL improved significantly after laparoscopic treatment (26,27), with long-term results (28-30). The study by Angioni *et al* (31), a randomized clinical trial, included a surgery group as well as a hormonal treatment group. For this group, we considered the arm A results, with a complete resection of DIE. The study by Roman *et al* (2018) (32) was analyzed with regard to the segmental resection of the rectum, and the study by Ledu *et al* (33) was utilized for the group consisting of patients with stoma; this was because of the

Table II. Characteristics of the studies.

Authors, year	Type of study	Number of included patients/lost to follow-up	Selection			Type of endometriosis	Outcome		
			Additional questionnaires used with SF-36	Comparison and control groups			Treatment	Follow-up	Final no. of patients (Refs.)
Van Aken <i>et al.</i> , 2017	Cross-sectional questionnaire-based survey	92/9	EHP-30, PCS, PVAQ, PASS and NRS	Patients with endometriosis compared with healthy women		Women with variety in their disease severity. The majority of patients (74%) presented a moderate-to-severe stage of endometriosis	Therapeutic surgical interventions	/	83 (18)
Angioni <i>et al.</i> , 2015	Randomized clinical trial	159/0	/	Complete laparoscopic excision of DIE (Arm A) and incomplete excision of DIE (Arm B).		DIE	GnRHa after laparoscopic excision of DIE (Arm 2A) or incomplete excision of DIE (Arm 2B).	3, 6 and 12 months	159 (31)
Silveira da Cunha Araújo <i>et al.</i> , 2014	Observational prospective cohort	45/0	/	/		DIE with colorectal involvement	Laparoscopy with colorectal resection	12 and 48 months	45 (26)
Bassi <i>et al.</i> , 2011	Prospective	151/0	/	/		DIE with colorectal involvement	Resection of a segment of the rectosigmoid	12 months	151 (27)
Caruso <i>et al.</i> , 2015	Prospective	92/0	VAS, FSFI, FSDS	Study group and control group		All types	Study group (DNG) and control group (AINS)	3 and 6 months	92 (28)
Chauvet <i>et al.</i> , 2018	Cross-sectional	1,156/243	EHP-30	/		All types	Confirmed surgical diagnosis of endometriosis	/	913 (16)
Comptour <i>et al.</i> , 2020	Prospective, multicenter cohort	1237/256	VAS	/		All types	Laparoscopic treatment	3 years	981 (13)
Darai <i>et al.</i> , 2010	Single-center, retrospective	29/0	IPSS, BFLUTS	Laparoscopy group and laparotomy group		Extensive pelvic endometriosis	Radical en bloc hysterectomy and colorectal resection (REHCR)	16 months and 11 months	29 (40)

Table II. Continued.

Authors, year	Type of study	Selection			Comparison and control groups	Type of endometriosis	Outcome		
		Number of included patients/lost to follow-up	Additional questionnaires used with SF-36				Treatment	Follow-up	Final no. of patients (Refs.)
Darai <i>et al</i> , 2017	Prospective	46/26	/	/	/	DIE and colorectal involvement	Osteopathic manipulative therapy	/	20 (37)
Dubernard <i>et al</i> , 2008	Prospective	93/35	/	/	/	Colorectal endometriosis	Laparoscopic segmental colorectal resection	22.5 months	58 (29)
Friedl <i>et al</i> , 2015	Prospective	61/0	HADS-D	/	/	All types	Previous operations	/	61 (24)
Garavaglia <i>et al</i> , 2018	Prospective observational	20/0	/	/	/	Bowel endometriosis	Laparoscopic colorectal resection	12 months	20 (38)
De Graaff <i>et al</i> , 2013	Cross-sectional questionnaire-based survey	1450/519	GSWH instrument	/	/	All types	Laparoscopic and/or histological diagnosis of endometriosis, who had at least one contact related to endometriosis-associated symptoms	/	931 (39)
Grandi <i>et al</i> , 2015	Prospective observational	40/6	VAS	DNG group and NSAID group	All types	All types	19 in the E2V/DNG group and 15 in the NSAID group	After 6 cycles of treatment	34 (54)
Jones <i>et al</i> , 2004	Prospective observational	66/26	EHP-30	/	/	All types	Conservative surgery	4 months	40 (56)
Laursen <i>et al</i> , 2005	Prospective observational	40/0	VAS	Fibromyalgia/whiplash group, endometriosis group, low back pain (group, or rheumatoid arthritis group and healthy women	All types	All types	Experimental pain stimulus [hyperalgesia to pressure pain threshold (PPT)]	/	40 (19)
Ledu <i>et al</i> , 2018	Retrospective	134/87	/	Stoma group vs. non-stoma group	DIE with rectal involvement	DIE with rectal involvement	Discoid resection	/	47 (33)
Lovkvist <i>et al</i> , 2016	Observational	800/369	/	/	All types	All types	Treatment	/	431 (55)
Mabrouk <i>et al</i> , 2011	Retrospective	241/135	VAS	COC users, and COC nonusers.	Uncomplicated posterior DIE	Uncomplicated posterior DIE	Laparoscopic surgery	/	106 (43)

Table II. Continued.

Authors, year	Type of study	Selection			Type of endometriosis	Outcome		
		Number of included patients/lost to follow-up	Additional questionnaires used with SF-36	Comparison and control groups		Treatment	Follow-up	Final no. of patients (Refs.)
Mabrouk <i>et al.</i> , 2012	Prospective	47/0	VAS	/	Colorectal. endometriosis	Laparoscopic segmental resection	18 months	47 (36)
Melis <i>et al.</i> , 2015	Prospective	41/0	FSFI, BAT	Women with deep endometriosis compared with healthy women	DIE	Surgery	/	41 (47)
Miller, 2000	Prospective, randomized	120/0	VAS	/	All types	Therapy with depot leuprolide acetate	4 weeks	120 (44)
Marki <i>et al.</i> , 2017	Prospective, cross-sectional	210/17	/	/	All types	Treatment at the participating clinic	/	193 (45)
Nnoaham <i>et al.</i> , 2011	Prospective cross-sectional study	1,669/924	WPAI:GH questionnaire	i) Women with endometriosis; ii) symptomatic control women without endometriosis; and iii) sterilization control women without endometriosis	All types	Laparoscopy	/	745 (51)
Nunes <i>et al.</i> , 2014	cross-sectional	510/253	ACR criteria were used to evaluate fibromyalgia	Women with endometriosis compared with women with no history of endometriosis	All types	Laparoscopy	/	257 (48)
Petrelluzzi <i>et al.</i> , 2008	Prospective	175/82	VAS, PSQ	Women with endometriosis compared with healthy women	All types	Laparoscopy, laparotomy	/	93 (52)
Ribeiro <i>et al.</i> , 2014	Prospective observational	45/5	/	/	Intestinal deep endometriosis	Laparoscopic colorectal resections	6 and 12 months	40 (30)
Riiskjar <i>et al.</i> , 2018	Prospective, observational	185/10	NRS	/	Rectosigmoid endometriosis.	Laparoscopic bowel resection	12 months	175 (34)



Table II. Continued.

Authors, year	Type of study	Selection			Comparison and control groups	Type of endometriosis	Outcome		
		Number of included patients/lost to follow-up	Additional questionnaires used with SF-36				Treatment	Follow-up	Final no. of patients (Refs.)
Roman <i>et al</i> , 2012	Cohort prospective	116/0	GIQLI, KESS		Endometriosis involving the Douglas pouch, deep endometriosis without digestive infiltration vs. deep endometriosis infiltrating the rectum	DIE	Surgery	1 and 3 years	116 (21)
Roman <i>et al</i> , 2018	Randomized trial	60/0	VAS, KESS GIQLI, USP		Conservative surgery group vs. rectal segmental resection	DIE infiltrating the rectum	Conservative surgery or radical rectal surgery	24 months	60 (32)
Sesti <i>et al</i> , 2007	Randomized comparative trial	234/12	VAS		Placebo vs. GnRH-a vs. dietary therapy	Endometriosis stage III-IV (r-AFS)	Conservative pelvic surgery	12 months	222 (50)
Teixeira <i>et al</i> , 2017	Randomized controlled trial	41/0	VAS		Potentized estrogen vs. placebo	DIE	Potentized estrogen	24 weeks	41 (49)
Touboul <i>et al</i> , 2015	Randomized controlled trial	52/0	/		Open surgery vs. laparoscopically assisted colorectal resection	Colorectal endometriosis	Laparoscopically assisted to open surgery	13.8 months	52 (41)
Valentin <i>et al</i> , 2017	Prospective and multicenter observational	198/31	/		/	Minimal endometriosis	Laparoscopic procedure	/	167 (25)
Verket <i>et al</i> , 2018	Cross-sectional questionnaire study	1,149/992	/		Women from the general population, vs. women with endometriosis compared with women with rheumatoid arthritis (RA).	All types	Surgically confirmed diagnosis.	/	157 (20)
Xie and Bi, 2018	Retrospective study	154/0	NRS and ESSS		Treatment group vs. control group	All types	Neuromuscular electrical stimulation	After treatment	154 (22)
Zhao <i>et al</i> , 2012	Controlled, randomized study	50/0	STAI		Patients with endometriosis compared with control group	All types	Leuprolide	After treatment	50 (46)

Table III. Patient characteristics.

Study	Study group characteristics	Control group characteristics	Type of endometriosis	Therapeutic approach	(Refs.)
Van Aken <i>et al.</i> , 2017	50 women with laparoscopically and/or magnetic resonance imaging-confirmed endometriosis	42 healthy control women	Two-thirds with DIE	Half the patients (56%) had a history of one or more therapeutic surgical interventions; 10 patients (35%) had undergone major: surgery hysterectomy, ovariectomy, bowel or bladder procedures, extended adhesiolysis, or a combination of procedures.	(18)
Angioni <i>et al.</i> , 2015	80 patients underwent complete laparoscopic excision of DIE (Arm A)	79 patients underwent incomplete surgery (Arm B)	DIE	After surgery each surgical arm was randomized in two groups: no treatment groups 1A [40 pts.] and 1B [40 pts.] and GnRHa treatment for 6 months groups 2A [40 pts.] and 2B	(31)
Caruso <i>et al.</i> , 2015	54 women with endometriosis received 2 mg/daily DNG	48 with endometriosis received non-steroidal anti-inflammatory drugs	Women affected by chronic pelvic pain with a clinical diagnosis of endometriosis	2 mg/daily DNG for 6 months	(28)
Darai <i>et al.</i> , 2010	16 women who underwent laparoscopy	13 that underwent laparotomy	Extensive pelvic endometriosis	Radical en bloc hysterectomy and colorectal resection (REHCR)	(40)
Friedl <i>et al.</i> , 2015	62 patients with a histologically confirmed diagnosis of endometriosis	61 healthy women recruited by the internet in a student community	Confirmed endometriosis	Without details about previous surgical interventions	(24)
Grandi <i>et al.</i> , 2015	19 patients with endometriosis that received E2V (quadruphasic association of E2 valerate)/DNG group	15 patients with endometriosis that received NSAID	All types (diagnosed by previous laparoscopy or laparotomy or the presence of an ovarian endometrioma diagnosed by transvaginal ultrasound)	Patients with endometriosis that were not scheduled for first or repeated surgery	(54)
Laursen <i>et al.</i> , 2005	10 patients with endometriosis	41 healthy women for control group	Chronic endometriosis	Experimental pain stimulus (hyperalgesia to pressure pain threshold (PPT)	(19)
Ledu <i>et al.</i> , 2018	33 patients who received protective stoma	14 patients without protective stoma	DIE with rectal involvement	Segmental or discoid resection of the rectum	(33)
Mabrouk <i>et al.</i> , 2011	75 patients who had received COCs during preoperative period	31 nonusers, who had not received any hormone treatment	Uncomplicated posterior DIE	Laparoscopic surgery	(43)
Melis <i>et al.</i> , 2015	41 women with deep endometriosis	40 healthy women without endometriosis	DIE	Most participants were after surgical diagnosis without any hormonal treatment, other patients entered the study before surgery	(47)

Table III. Continued.

Study	Study group characteristics	Control group characteristics	Type of endometriosis	Therapeutic approach	(Refs.)
Nnoaham <i>et al</i> , 2011	Women with endometriosis	Symptomatic control women without endometriosis; and sterilization control women without endometriosis	All types	Prospectively recruited consecutive premenopausal women, scheduled for a laparoscopy: i) to investigate endometriosis-associated pelvic pain; or ii) to be sterilized	(51)
Nunes <i>et al</i> , 2014	257 women with a laparoscopic and histopathological diagnosis of endometriosis	253 women with no signs or symptoms of endometriosis	All grades of endometriosis	Previous laparoscopy	(48)
Petrelluzzi <i>et al</i> , 2008	93 women with endometriosis	82 healthy women	All types	Laparoscopy or laparotomy for diagnosis	(52)
Roman <i>et al</i> , 2012	53 women with deep endometriosis infiltrating the rectum	21 women with endometriosis involving the Douglas pouch and 42 women with deep endometriosis without digestive infiltration	DIE	Surgically treated patients	(21)
Roman <i>et al</i> , 2018	27 patients who received conservative surgery	33 patients who received segmental resection	DIE infiltrating the rectum	Conservative surgery or radical rectal surgery	(32)
Roman <i>et al</i> , 2018	119 patients with endometriosis who received postoperative adjunctive medical or dietary therapy for 6 months	115 patients with endometriosis who received placebo for 6 months	Endometriosis stage III-IV	Laparoscopic or laparotomic diagnosis of severe endometriosis stage III-IV. Randomization was achieved at the time of postoperative control (7 days after surgery)	(32)
Teixeira <i>et al</i> , 2017	23 patients with endometriosis who received potentized estrogen	27 patients with endometriosis who received placebo	DIE	Potentized estrogen administered after diagnosis of deeply infiltrating endometriosis based on magnetic resonance imaging or transvaginal ultrasound after bowel preparation	(49)
Touboul <i>et al</i> , 2015	26 patients who underwent open surgery	26 patients who underwent laparoscopy	Colorectal endometriosis	Laparoscopically assisted or open colorectal resection for endometriosis	(41)
Verket <i>et al</i> , 2018	156 women with endometriosis	156 women from the general population, and 837 women with rheumatoid arthritis (RA)	All types	No surgical or medical treatment	(20)
Xie and Bi, 2018	83 patients with endometriosis were in the treatment group	71 patients with endometriosis represented the control group	All types	Neuromuscular electrical stimulation	(22)
Zhao <i>et al</i> , 2012	50 patients with endometriosis	50 patients with endometriosis represented the control group	All types	Patients received gonadotrophin-releasing hormone (GnRH) agonist therapy	(46)

rectal resection for DIE with rectal involvement (the study results were relevant for this group).

Some authors have recommended surgery for rectosigmoid endometriosis in cases where the disease is unresponsive to conservative treatments (34-36). Daraï *et al* supported the finding that osteopathic manipulative therapy has a good impact on endometriosis symptoms in women with colorectal involvement (37). However, although the radical surgical approach can have a major positive impact on QOL, it does not improve all symptoms, as reported by Garavaglia *et al* (38). De Graaff *et al* concluded that many patients with endometriosis experienced better QOL and continued to have endometriosis-associated symptoms even when they were treated in tertiary care centers (39). Roman *et al* reported that conservative surgery should be reserved for patients with large deep rectal endometriosis (32). Daraï *et al* recommended laparoscopy for patients that required radical en bloc hysterectomy and colorectal resection (40). Laparoscopic colorectal resection was also indicated for cases of lower intraoperative and postoperative complications for patients with rectal endometriosis due to higher spontaneous post-surgery pregnancy rates (41). Araujo *et al* reported that gonadotropin-releasing hormone agonist (GnRHa) administration was followed by a temporary improvement in pain among patients with incomplete resection of deep infiltrative endometriosis (DIE), but it did not affect postsurgical pain when DIE implants were completely excised (42).

The study by Angioni *et al* (31) was considered for the medical treatment group because it applied postoperative randomization (of initial groups with complete or incomplete resection of endometriosis) to receivers or non-receivers of GnRHa. It selected a group with complete resection of endometriosis, which received GnRH, and compared it with complete resection of endometriosis without medical treatment. Regarding statistics, the Caruso group (28) was not considered because it compared GnRH receivers with AINS receivers.

Mabrouk *et al* confirmed the role of combined oral contraceptive therapy in curbing the progression of dysmenorrhea and dyspareunia and the growth of deep endometriotic nodules (43). Meanwhile, Miller concluded that the stimulatory phase of the GnRHa therapy could be correlated with an increase in pain and a decrease in the QOL (44). Márki *et al* emphasized that pain management and emotion regulation strategies can be utilized for improving the QOL of patients with endometriosis. The authors suggest that it could be obtained through simultaneous application with physical treatment and psychological care (45).

Zhao *et al* conducted the first study to explore only the effects of psychosomatic therapy on the QOL of endometriosis patients and demonstrated that progressive muscular relaxing (PMR) training could serve as a reference for future psychosomatic interventions regarding endometriosis. PRM works efficiently for anxiety and depression related to endometriosis (46). Melis *et al* further suggested that a patient-centered approach that is integrated with various medical, psychological, and sexual issues should be applied in the treatment of patients with endometriosis (47).

Nunes *et al* compared the QOL of patients with fibromyalgia and women with and without endometriosis. The QOL of women with endometriosis showed the highest impairment (48).

Teixeira *et al* demonstrated that potentated estrogens significantly reduced endometriosis-associated pain compared to a placebo (49). Sesti *et al* demonstrated that, for endometriosis stage III-IV, QOL can be improved through postoperative hormonal suppression treatment or dietary therapy compared to surgery as well as a placebo for relieving pain (50).

Regardless of the differences across country- and ethnicity-level contexts, endometriosis was found to impair QOL and work productivity for women who continued to experience diagnostic delays in primary care (51). Even if hypocortisolism could be sometimes considered a consequence of the aversive symptoms of endometriosis, the etiopathology remains unelucidated (52,53). The relationship between endometriosis and ovarian cancer was studied by Grandi *et al* and the preventive effect of inhibiting ovulation and menstruation was highlighted (54).

EHP-30 and SF-36 questionnaires are sensitive to changes related to endometriosis, especially correlations between increased pressure pain sensitivity and hyperalgesia and the impairment of QOL parameters, as reported by Laursen *et al* (19). Thus, healthcare resource allocators should focus on women with endometriosis as the disease may have a different impact for each woman (55). The SF-36 seems to be a valid instrument for evaluating QOL in women with endometriosis (56,57).

In conclusion, the 36-item survey generic questionnaire, SF-36, seems to represent an efficient/valid method for assessing the QOL of patients with endometriosis who are undergoing surgical or hormonal treatments. It can be applied before and after procedures or in order to compare study groups.

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## Availability of data and materials

The information and data contained in this review and meta-analysis are documented by relevant references. Any other details can be obtained upon request.

## Authors' contributions

LP and JCR performed the conceptualization of the study and had major contributions in writing the manuscript. BHH contributed to the methodology. MCTD and CC analyzed and interpreted the patient data. PS, III, MPR, IJB and EFS provided the formal analysis and visualization. IN, ADS and BS conducted the literature investigation and data curation. RMS provided resources and contributed to writing the manuscript (review and editing). MCTD, BS, and DS searched the literature for similar work and articles and contributed to writing the manuscript. LP and JCR supervised the study and provided project administration. All authors read and approved the final manuscript for publication.



## Ethics approval and consent to participate

Not applicable.

## Patient consent for publication

Not applicable.

## Competing interests

The authors declare no conflict or competing interests.

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