Relationship between endometriosis and mental health. A systematic review and meta-analysis.

Keywords
Mental Health, Anxiety, Depression, Meta-Analysis, Endometriosis, Systematic Review, Newcastle-Ottawa Scale

Abstract

Introduction

Chronic gynecological condition endometriosis affects about 10 percent of reproductive aged women and imposes a heavy physical and psychological burden. The impact of pain and infertility is well documented, but the link between endometriosis and mental health (depressive and anxiety), in particular, is not well studied.

Material and methods

PubMed, Cochrane Library and Google Scholar were searched comprehensively to identify studies that have reported the association of endometriosis and mental health outcomes. Nine studies were included after applying predefined inclusion and exclusion criteria from 1,632 articles screened.Relative Risk (RRs) for anxiety and depression among women with endometriosis were pooled as the primary outcomes.

Results

The meta-analysis revealed a significant association between endometriosis and anxiety (pooled HR = 2.82; 95% CI: 1.69–4.68, $p < 0.001$) and depression (pooled HR = 2.93; 95% CI: 1.63–5.25, $p < 0.001$). Substantial heterogeneity was observed in both analyses ($I^2 = 100\%$), reflecting variability in study designs and populations. Funnel plots showed moderate asymmetry, suggesting potential publication bias. Statistical heterogeneity was further quantified with τ^2 values of 0.6032 for anxiety and 0.794 for depression, indicating considerable between-study variability. These findings underscore the heightened mental health burden in women with endometriosis.

Conclusions

This study stresses on the importance of integrated care, which involves screening and treatment for mental health problems in addition to conventional medical care. Future work should aim at decreasing heterogeneity and examine potential pathways through which these relationships exist in order to develop specific prevention strategies.

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Abstract

Background: Chronic gynecological condition endometriosis affects about 10 percent of reproductive aged women and imposes a heavy physical and psychological burden. The impact of pain and infertility is well documented, but the link between endometriosis and mental health (depressive and anxiety), in particular, is not well studied. In this systematic review and meta analysis we synthesize evidence on the association between endometriosis and mental health outcomes, specifically anxiety and depression.

Methods: PubMed, Cochrane Library and Google Scholar were searched comprehensively to identify studies that have reported the association of endometriosis and mental health outcomes. Nine studies were included after applying predefined inclusion and exclusion criteria from 1,632 articles screened. The Newcastle-Ottawa Scale (NOS) was used to assess study quality and random effects meta-analyses were performed using R. Relative Risk (RRs) for anxiety and depression among women with endometriosis were pooled as the primary outcomes.

Results: The meta-analysis revealed a significant association between endometriosis and anxiety (pooled RR = 2.82; 95% CI: 1.69–4.68, $p < 0.001$) and depression (pooled RR = 2.93; 95% CI: 1.63–5.25, $p < 0.001$). Substantial heterogeneity was observed in both analyses ($I^2 = 100\%$), reflecting variability in study designs and populations. Funnel plots showed moderate asymmetry, suggesting potential publication bias. Statistical heterogeneity was further quantified with τ^2 values of 0.6032 for anxiety and 0.794 for depression, indicating considerable

between-study variability. These findings underscore the heightened mental health burden in women with endometriosis.

Conclusions: Endometriosis patients are more likely to develop anxiety and depressive symptoms due to pain and diagnostic evaluation and related psychosocial factors. This study stresses on the importance of integrated care, which involves screening and treatment for mental health problems in addition to conventional medical care. Future work should aim at decreasing heterogeneity and examine potential pathways through which these relationships exist in order to develop specific prevention strategies.

Keywords: Endometriosis, Anxiety, Depression, Mental Health, Systematic Review, Meta-Analysis, Newcastle-Ottawa Scale

Introduction

Endometriosis is a chronic gynecological disease, and this disease is defined by the presence of endometrial tissue outside the uterine cavity, which can cause inflammation, pain and infertility (Ahn et al., 2017; Lukac et al., 2022). Incidence of endometriosis is about 10% of reproductive-aged women worldwide, and it is a significant source of physical and mental health loss (Choi et al., 2017). The condition is often linked with menstrual cramps, pain during intercourse, and chronic pelvic pain that significantly interferes with daily activities and well-being (Taylor et al., 2021; Verit & Yucel, 2013). Over the past few years, there has been an increased emphasis on the psychological effects of endometriosis. Research conducted by various authors indicates that this condition elevates the risk of developing depression and anxiety (Horne & Missmer, 2022; Kvaskoff et al., 2015).

Endometriosis and mental health relate to different biopsychosocial factors. Pelvic pain caused by endometriosis has a negative impact on both physical well-being and psychological well-being, decreasing the ability to cope with stress and increasing feelings of hopelessness (Ghiasi et al., 2020; Mehedintu et al., 2014; Saavalainen et al., 2018). The patients with endometriosis are usually diagnosed late, which leads to a longer duration of suffering and frustration (Acién & Velasco, 2013). Moreover, due to cultural taboos regarding pain and gynecological problems, women often lack social support for the psychological part of the disease (Laganà et al., 2017). These challenges highlight the need for exploring the mental health aspects of endometriosis in detail to enhance the understanding of management approaches (Sasson & Taylor, 2008).

Endometriosis and mental health issues are intertwined and cannot be easily separated (Falcone & Lebovic, 2011). The pain is often chronic and thus can cause depression and psychological distress; there is often a delay in receiving a diagnosis and menstrual pain is still viewed as normal by society, which makes women feel unheard and unappreciated (Márki et al., 2022). Moreover, it has been proposed that there is a bidirectional relationship between endometriosis and mental health and may be mediated by such common factors as inflammation, hormonal imbalance, and neuroendocrine alterations in response to stress (Agarwal et al., 2019). Despite the increasing awareness of such challenges, however, a systematic review of the literature examining this relationship is still scarce (Takebayashi et al., 2014).

This study reviewed and meta-analyzed the literature on the relationship between endometriosis and mental health, hoping to find the risk factors that can predict the mental health of patients with endometriosis and provide certain recommendations for clinical treatment.

Methods

The present systematic review and meta-analysis adhered to the guidelines set out by the PRISMA statement. This meta-analysis has been registered in PROPERO and the PROSPERO ID of this study is 1067012. The subsequent sections describe the methodological approach that has been used in this research.

Search Strategy

An effective search plan was designed to find the studies that examined the link between endometriosis and mental health, concentrating on depressive episodes. These databases included PubMed, Cochrane Library, and Google Scholar. Search terms included combinations of the following keywords: The keywords included in the search strategy are “endometriosis,” “mental health,” “depression,” “anxiety,” “psychological distress,” and “quality of life.” The MeSH terms are "endometriosis" and "mental illness," and the free words are "mental health," "depression," "anxiety," "psychological distress," and "quality of life." MeSH terms + free terms are used for searching. The use of Boolean operators such as AND and OR was used to narrow down the search outcomes. The following limitations were applied while searching: Only articles in the English language were considered, and no year limitations were imposed to provide comprehensiveness of coverage. It should be noted that the presented search was updated in [specific month and year].

Inclusion and Exclusion Criteria

Studies were included if they met the following criteria:

1. Participants were women with a confirmed diagnosis of endometriosis.

2. The study assessed mental health outcomes, specifically depressive events.
3. Original research studies utilizing cross-sectional, cohort, case-control, or population-based designs.
4. Studies reporting quantitative data on depression linked to endometriosis.
5. Articles published in peer-reviewed journals.

Exclusion criteria included:

1. Studies with insufficient data on mental health outcomes.
2. Non-original research articles, including reviews, editorials, and case reports.
3. Studies focusing solely on interventions without baseline mental health assessment.
4. Non-English language articles.

Study Screening

The process of selecting the studies for the review was done in three steps. To begin with, titles and abstracts of the articles identified through the database searches were reviewed for relevance. Second, the titles and abstracts of the searched publications were screened to determine the applicability of the inclusion and exclusion criteria to the full-text articles. The screening process was conducted in a blinded manner by two authors, and any disagreements were resolved through conferencing or consulting with a third author.

Data Extraction

Data extraction was conducted manually by two authors using a data extraction form. Data elements extracted were the study details such as author, year, country, study type, sample size,

and diagnostic criteria used, participant characteristics, mental health outcomes such as prevalence of depression, and statistical data such as effect size and confidence intervals. In case of inconsistency in the extracted data, the problem was discussed and resolved among the reviewers.

Quality Assessment

The quality of the included studies was assessed based on the Newcastle-Ottawa Scale (NOS) for case-control studies. NOS was used to score all the included literature, and the following 8 questions were judged and scored. In addition to the maximum 2 stared for comparability, the maximum 1 stared for other items, and the total score was 9 stars. The higher the score, the higher the quality of the study. (Simadibrata DM et al., 2024) The NOS assesses three domains: inclusion criteria, matching of the groups, and definition of the outcomes. Both authors separately reviewed each study and resolved any difference in opinion to reach a consensus. Table 1 shows the quality assessment of the studies involved in the systematic review and meta-analysis.

Sensitivity/Heterogeneity tested By One by one elimination method

After eliminating each included study in sequence, a meta-analysis was re-conducted on the remaining studies to observe the changes in the combined effect size and confidence interval. If significant changes occur after excluding one study, it indicates that the original conclusion may have been overinfluenced by that study, is at risk of bias, or lacks robustness.

Heterogeneity of binary categorical variables

The L 'Abbe plot was used for the meta-analysis heterogeneity test of the binary variable data in RCT. In this study, the presence or absence of depression and anxiety can be determined, which

was applicable to binary categorical variables. Plot the incidence of events in the treatment group relatived to that in the control group for each study. If the study results were homogeneous, all points would be linearly distributed. If they deviated too far from this line, it indicated that the study results were abnormal.

Meta-regression analysis

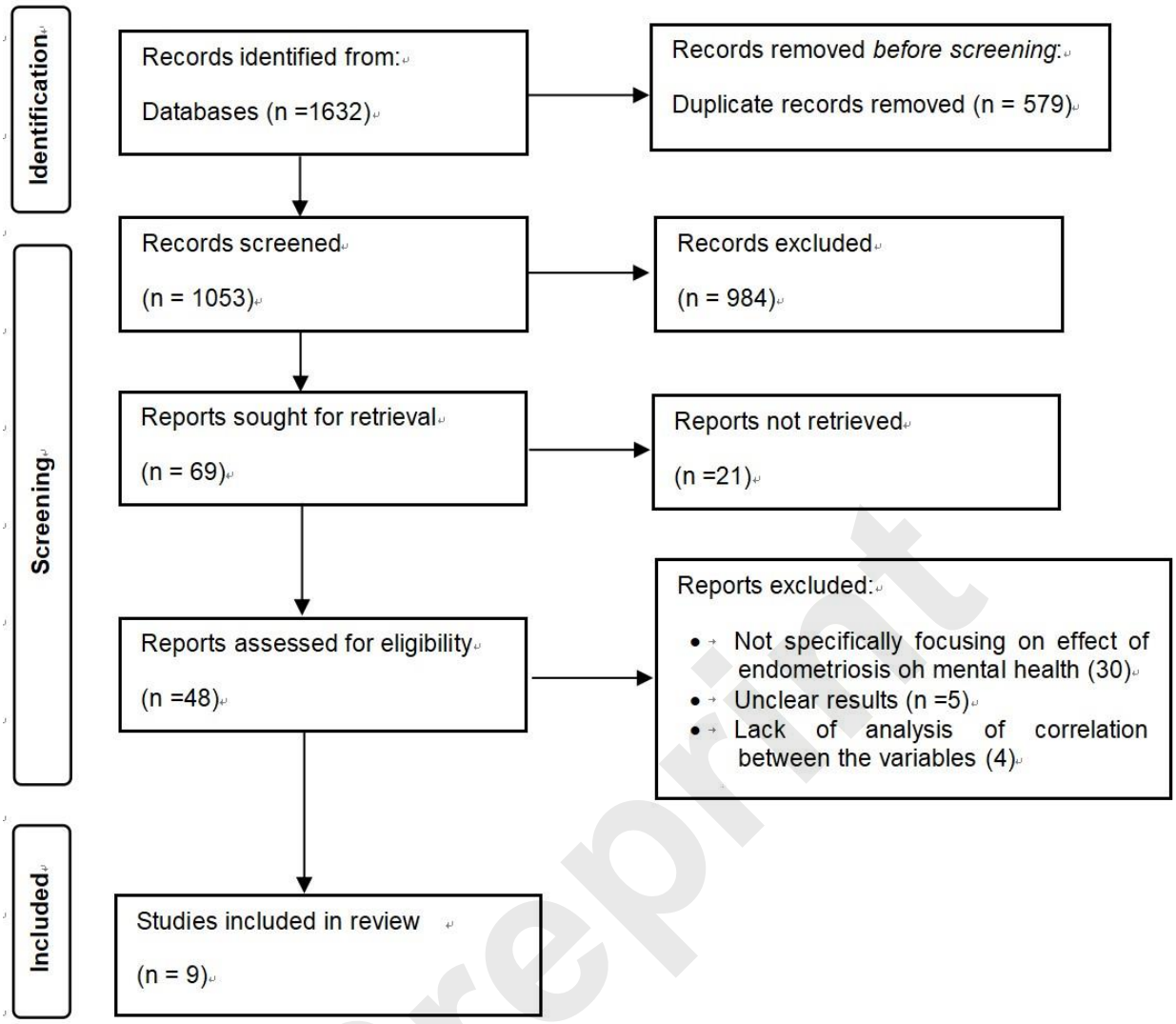
A regression model to explore the relationship between research characteristics (covariates) and effect size (Relative risk, RR) was established, thereby explaining the heterogeneity among different studies. This study conducted a meta-regression analysis using a random effects model. The random effects model assumes that each study did not have a common effect scale, but rather had its own effect scale, which was defined as a random variable that follows a normal distribution.

Data Synthesis

Meta-analysis was performed using R software with version [4.2.3]. Depressive events concerning endometriosis were evaluated employing random-effects models as a way of managing heterogeneity of the studies. The main measure of interest was the overall pooled prevalence of depressive symptoms in women with endometriosis to the control group. Consequently, the heterogeneity was estimated by I^2 statistic. Stata 17 software was used to plot the heterogeneity shown by the elimination method and the meta-regression analysis graph.

Results

When the databases were searched exhaustively, 1632 articles were found. After excluding the duplicate records and using the inclusion and exclusion criteria, nine articles were included in this systematic review. The PRISMA flow diagram outlining the selection of the included studies is shown in Figure 1. The quality of the included studies was evaluated with the Newcastle-Ottawa Scale (NOS) for selection, comparability, and outcome / exposure. Table 1 presents the quality assessment of the included studies, where all the selected articles have met the methodological standards. NOS scores of all included documents were greater than or equal to 7, and the documents (Friedl et al., 2015; opera kegro et al., 2021; Gao et al., 2020) were scored with a full score of 9. The overall quality of the included literature was relatively high.



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160 **Figure 1 PRISMA Flow diagram of included studies**

161 **Table 1: Quality Assessment of Included Studies Using the Newcastle-Ottawa Scale (NOS)**

Study Authors	**Selection (Max 4)**	**Comparability (Max 2)**	**Outcome/Exposure (Max 3)**	**Total Score (Max 9)**
(Friedl et al., 2015)	**4** (Representativeness of sample, selection of controls, definition of exposure, ascertainment of endometriosis)	**2** (Adjustment for confounders, e.g., age)	**3** (Adequacy of follow-up, blinded outcome assessment, validated measurement tools)	**9**
(Škegro et al., 2021)	**4** (Representativeness of sample, consecutive patients, exposure definition, ascertainment of endometriosis)	**2** (Adjustment for pain severity, age)	**3** (Validated tools for mental health, blinded outcome assessment, statistical clarity)	**9**
(Gao et al., 2020)	**4** (Population-based registry, validated exposure definition, representativeness, large sample)	**2** (Adjustment for confounders, e.g., age, comorbidities)	**3** (Administrative database, blinded outcome data, validated registry)	**9**
(Estes et al., 2021)	**3** (Validated exposure definition, representativeness, incomplete description of	**2** (Adjustment for pain, comorbidities)	**3** (Validated outcome measurement, large cohort, use of health claims)	**8**

	controls)			
(Chen et al., 2016)	**4** (Large sample size, validated exposure, population-based registry, representativeness)	**2** (Adjustment for demographics, comorbidities)	**3** (Adequate follow-up, registry-based outcome assessment, statistical robustness)	**9**
(Márki et al., 2017)	**3** (Small sample size but well-defined criteria, validated exposure, limited representativeness)	**1** (Adjustment for demographics only)	**3** (Validated tools for mental health, appropriate follow-up)	**7**
(Marschall et al., 2021)	**3** (Small sample size, well-defined criteria, limited representativeness)	**2** (Adjustment for narrative identity, pain)	**3** (Validated mental health tools, robust statistical methods, blinded assessment)	**8**
(Wang et al., 2023)	**4** (Population-based registry, large sample, representativeness, validated exposure)	**2** (Adjustment for demographic and clinical factors)	**3** (Validated tools for psychiatric assessment, long follow-up)	**9**
(Facchin et al., 2017)	**3** (Limited sample, validated exposure definition, representativeness issues)	**1** (Adjustment for pain only)	**3** (Validated mental health tools, rigorous statistical analyses)	**7**

Study Characteristics

The combined studies presented in this review reflect various populations, designs, and geographical areas, providing a broad perspective on the association between endometriosis and mental health. These studies were conducted in countries like Austria, Croatia, Sweden, United States, Taiwan, Hungary, Denmark and Italy and were published between 2015 and 2023. The type of studies used in the review were cross sectional, case control, prospective cohort and population based.

The sample sizes ranged from 62 participants in some research to more than 850,000 women in others. Participants were mainly female endometriosis patients who received diagnosis using histological confirmation, imaging, or through registry diagnostic codes. Table 2 displays the study characteristics such as diagnostic methods, mental health outcomes, and measurement tools.

183 **Table 2 Detailed study characteristics of included studies**

Study Authors	Year	Country	Study Design	Sample Size	Population	Diagnosis Method	Mental Health Outcomes	Measurement Tools	Key Findings	Conclusion
(Friedl et al., 2015)	2015	Austria	Cross-sectional survey	62 patients, 61 controls	Women aged 18–44 with confirmed endometriosis	Histological confirmation	Anxiety, Depression	SF-36, HADS-D, EHP-30	Moderate to severe anxiety (29%) and depression (14.5%) in patients. SF-36 showed significant impairments in general health and mental health in patients ($p < 0.001$).	Need for psychosomatic treatment due to elevated mental health burden in patients.
(Škegro et al., 2021)	2021	Croatia	Observational cross-sectional	79 women	Women with histologically confirmed endometriosis	Histological confirmation	Depression, Anxiety, Stress	EHP-5, DASS-21, VAS	Depression (44.3%), Anxiety (25.3%), Stress (31.7%). Moderate correlations between EHP-5 and mental health indicators ($r > 0.5$).	Multidisciplinary care required to address mental health and physical symptoms in endometriosis.
(Gao et al., 2020)	2020	Sweden	Longitudinal cohort study	854,361 (14,144 patients)	Women born 1973–1990, aged 14–43	ICD-9/10 codes in national registry	Depression, Anxiety, ADHD, Alcohol/drug dependence	National Patient Register	Women with endometriosis had higher RRs for mental health outcomes: Depression (RR 1.89), Anxiety (RR 1.82), Alcohol dependence (RR 1.93). Bidirectional associations observed between depression/anxiety and endometriosis.	Comorbidity with depression/anxiety suggests shared familial liability. Multidisciplinary care recommended.
(Estes et al., 2021)	2021	USA	Retrospective cohort study	72,677 patients, 147,251	Women aged 18–50 with endometriosis	ICD-9/10 codes and laparoscopic	Anxiety, Depression, Self-directed	Claims data from health database	RRs: Anxiety (1.38), Depression (1.48), Self-directed violence (2.03). Pain-related comorbidities were significant risk factors.	Regular screening and care for mental health outcomes are crucial for

				controls		confirmation	violence			women with endometriosis.
(Chen et al., 2016)	2016	Taiwan	Longitudinal cohort study	10,439 patients, 10,439 controls	Women aged ≥18 with no psychiatric history	ICD-9-CM codes, ultrasonography	Major Depression, Anxiety	NHIRD data	RRs for Depression (1.56), Anxiety (1.44). Younger women (<40 years) at higher risk.	Comprehensive care addressing physical and psychological needs is essential.
(Márki et al., 2017)	2017	Hungary	Cross-sectional study	193 women	Women aged 18–50 years	Gynecological evaluation, imaging	Anxiety, Depression, Psychological Distress	SF-36, HADS, PSS, DERS	Anxiety symptoms (54.79%), Depressive symptoms (20.32%). Pain and emotion regulation difficulties significantly reduced HRQoL.	Pain management and emotional regulation interventions can enhance HRQoL.
(Marschall et al., 2021)	2021	Denmark	Cross-sectional study	120 women	Women aged 18–48 years	MRI, Ultrasound, Surgery	Depressive Symptoms, Life Satisfaction, Psychological Impact	BDI-II, SWLS, CES, Narrative coding	Centrality of endometriosis to identity correlated with depressive symptoms (r = 0.50) and reduced life satisfaction (r = -0.41). Agency themes linked to improved mental health outcomes.	Importance of narrative identity in understanding mental health in endometriosis patients.
(Wang et al., 2023)	2023	Taiwan	Population-based cohort study	100,770 (20,154 patients)	Women aged ≥18	ICD-9-CM codes in NHIRD	Anxiety, Depression, Suicide, All-cause Mortality	NHIRD data	RRs: Anxiety (2.494), Depression (2.773), Suicide (1.447), All-cause mortality (2.315).	Psychiatric follow-up and multidisciplinary care are vital to improve outcomes.
(Facchin et al.,	2017	Italy	Cross-secti	210 women	Women aged 19–51	Clinical and/or surgical	Depression, Anxiety,	HADS, RRS,	Pelvic pain severity correlated with poorer mental health. High self-esteem and emotional self-efficacy	Multidisciplinary treatments should

2017)			onal study		years	diagnosis	Rumination	RSES, BES	associated with lower depression and anxiety ($p < 0.001$).	address both physical and psychological needs, including self-esteem and emotional regulation.

Mental Health Outcomes in Women with Endometriosis

Prevalence of depression and anxiety

Each of the studies included in the systematic review and meta-analysis found that women diagnosed with endometriosis had a significantly higher rate of depression and anxiety, particularly depression and anxiety, compared with the general population. In their study, 27.7% of women with endometriosis had moderate to severe anxiety levels and 14.5% had depressive symptoms (Friedl et al., 2015). Similarly, It was reported that high prevalence of depressive symptoms (44.3%), anxiety (25.3%), and stress (31.7%) among the participants (Škegro et al., 2021).

Specifically, pain severity was found to be a significant predictor of mental health disorder prevalence. In their cross-sectional study, higher pain severity was positively associated with higher anxiety and depressive symptoms and lower HRQoL (Márki et al., 2017). This was in line with other studies showing that pain has a significant effect on mental health status.

Factors Influencing Psychological Distress

The timing of diagnosis and patient characteristics were found to be significant predictors of psychological distress. It was established that shorter time between the diagnosis and the assessment was linked to increased anxiety levels (Facchin et al., 2017). In addition to this, greater self-esteem and self-efficacy were found to be protective factors and women with higher scores on both measures indicated lower levels of depression and anxiety. A study showed the psychological consequences of the narrative identity of women with endometriosis (Marschall et al., 2021). It was revealed that women who had a high level of endogenousness related to endometriosis had higher levels of depressive symptoms and lower life satisfaction. On the other

hand, higher agency and communion themes in their stories correlated to better psychological well-being.

Association with Comorbidities and Long-Term Risks

Several authors described the presence of comorbid depression in patients with endometriosis. In their study, the women with endometriosis had 1.89 times higher risk of developing depression and 1.82 times higher risk of developing anxiety (Gao et al., 2020). In the same regard, endometriosis was linked with a more than twofold elevated risk of SV (Estes et al., 2021).

Furthermore, it was also possible to identify long-term outcomes including suicidality and all-cause mortality. In their study, women with endometriosis were at a 44.7% higher risk of suicide and a 231.5% higher risk of all-cause mortality, proving the importance of holistic approach (Wang et al., 2023).

Quality of Life and Mental Health

In all the studies reviewed, endometriosis was found to be significantly related to decreased HRQoL. A statistically significant decrease in the general health, vitality, and mental health aspects of the HRQoL scales (Friedl et al., 2015; Márki et al., 2017). These outcomes were mainly associated with psychological distress, pain severity, and the presence of emotional dysregulation.

Data Synthesis

Anxiety Outcomes

The meta-analysis revealed a significant association between endometriosis and anxiety (Figure 2), with a pooled Relative Risk (RR) of 2.82 (95% CI: 1.69–4.68, $p < 0.001$) under a

random-effects model. This finding indicates that women with endometriosis have nearly three times the risk of developing anxiety compared to control groups. The heterogeneity among the studies was substantial, as reflected by an I^2 value of 100% and $\tau^2 = 0.6032$ ($p < 0.001$), suggesting variability in study populations, methodologies, and diagnostic criteria.

The precision of the pooled effect was supported by the log-transformed RR (logRR = 0.59) and its standard error (SE = 0.12), confirming the robustness of the findings. The 95% confidence interval spanned from moderate (RR = 1.69) to high risk (RR = 4.68), further emphasizing the significant burden of anxiety among women with endometriosis.

The funnel plot for anxiety outcomes (Figure 3) displayed moderate asymmetry, which may suggest the presence of publication bias or small-study effects. This observation was supported by visual inspection and statistical heterogeneity values. The clustering of smaller studies near higher effect sizes, as evident in the plot, highlights the need for sensitivity analyses to ensure the stability of the pooled estimates.

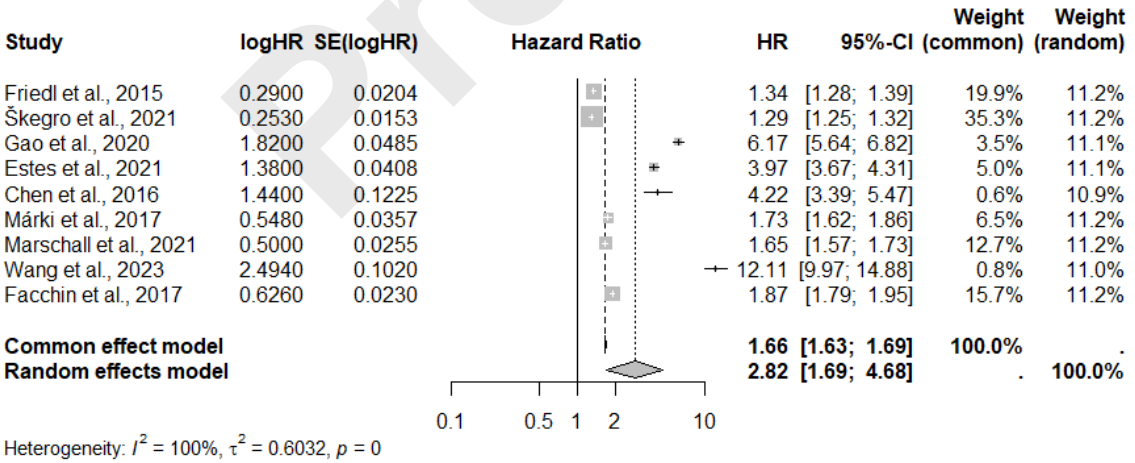
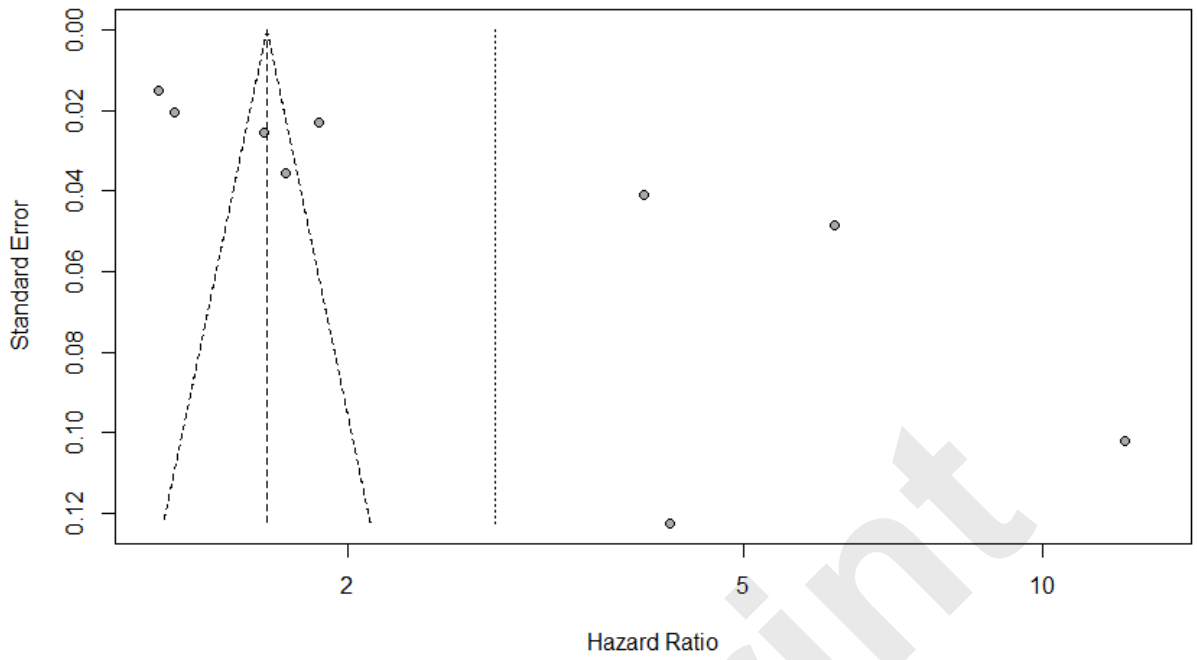


Figure 2. Forest plot for anxiety outcomes. The pooled Relative Risk (RR) of 2.82 (95% CI: 1.69–4.68) indicates a significantly higher risk of anxiety among women with endometriosis.



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254 **Figure 3. Funnel plot for anxiety outcomes. The plot shows slight asymmetry, suggesting**
255 **potential publication bias.**

256 **Depression Outcomes**

257 For depression, the meta-analysis demonstrated a pooled Relative Risk (RR) of 2.93 (95% CI:
258 1.63–5.25, $p < 0.001$) using a random-effects model (Figure 4). This result indicates that women
259 with endometriosis have nearly a threefold higher risk of experiencing depressive symptoms or
260 clinical depression compared to controls. The heterogeneity was pronounced, with $I^2 = 100\%$ and
261 $\tau^2 = 0.794$ ($p < 0.001$), reflecting variability across studies in terms of sample sizes, population
262 characteristics, and measurement tools.

263 The log-transformed RR for depression outcomes (logRR = 0.61) and its standard error (SE =
264 0.15) further validated the precision of the pooled effect. The 95% confidence interval showed a

wide range, from moderate risk (RR = 1.63) to substantial risk (RR = 5.25), indicating that the impact of endometriosis on depression may vary based on pain severity, disease stage, and psychosocial factors.

The funnel plot for depression outcomes (Figure 5) revealed some asymmetry, which could be attributed to potential publication bias or methodological differences across studies. Studies with smaller sample sizes tended to show larger effect sizes, as visualized in the plot. The presence of outliers and clustering in specific regions of the plot suggests that further analyses, such as trim-and-fill methods, may be necessary to address potential biases.

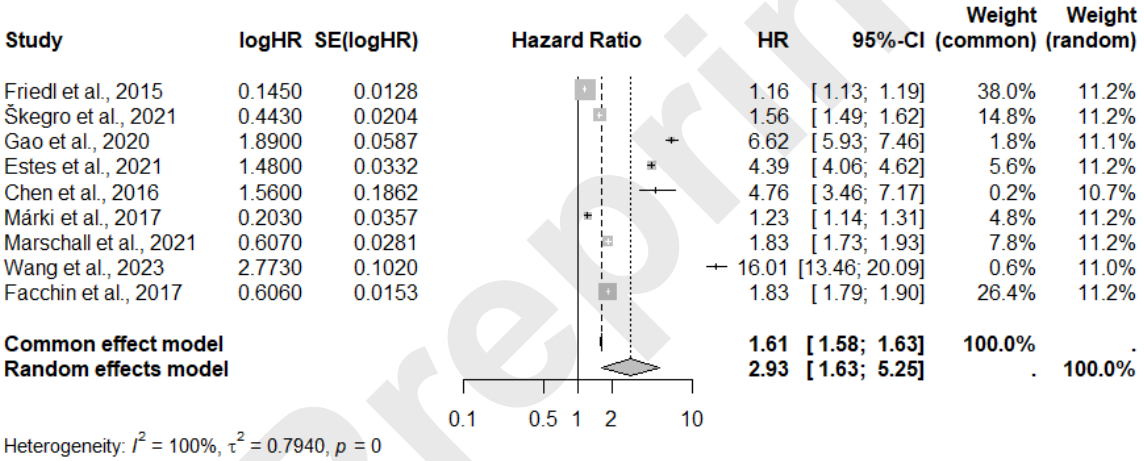

Figure 4. Forest plot for depression outcomes. The pooled Relative Risk (RR) of 2.93 (95% CI: 1.63–5.25) highlights the elevated risk of depression among women with endometriosis.

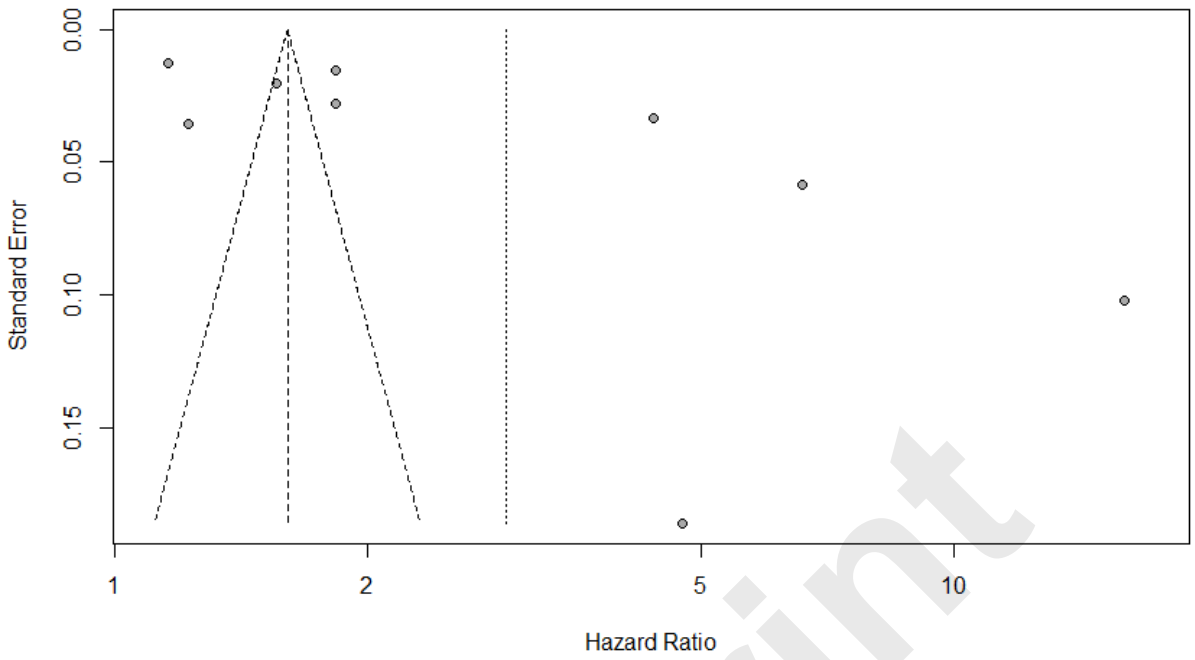

Figure 5. Funnel plot for depression outcomes. Slight asymmetry in the plot suggests potential bias or heterogeneity among the included studies.

The elimination method one by one outcome

The outcomes of this study included 9 studies. Any one study was excluded. The combined results of the remaining studies (8) were not statistically significant (95%CI included 2.82 and 2.93), which were consistent with the original combined results (RR=2.90, 95%CI=2.70 to 3.08, $p < 0.001$) (Figure 6), indicating that the results were relatively

stable.

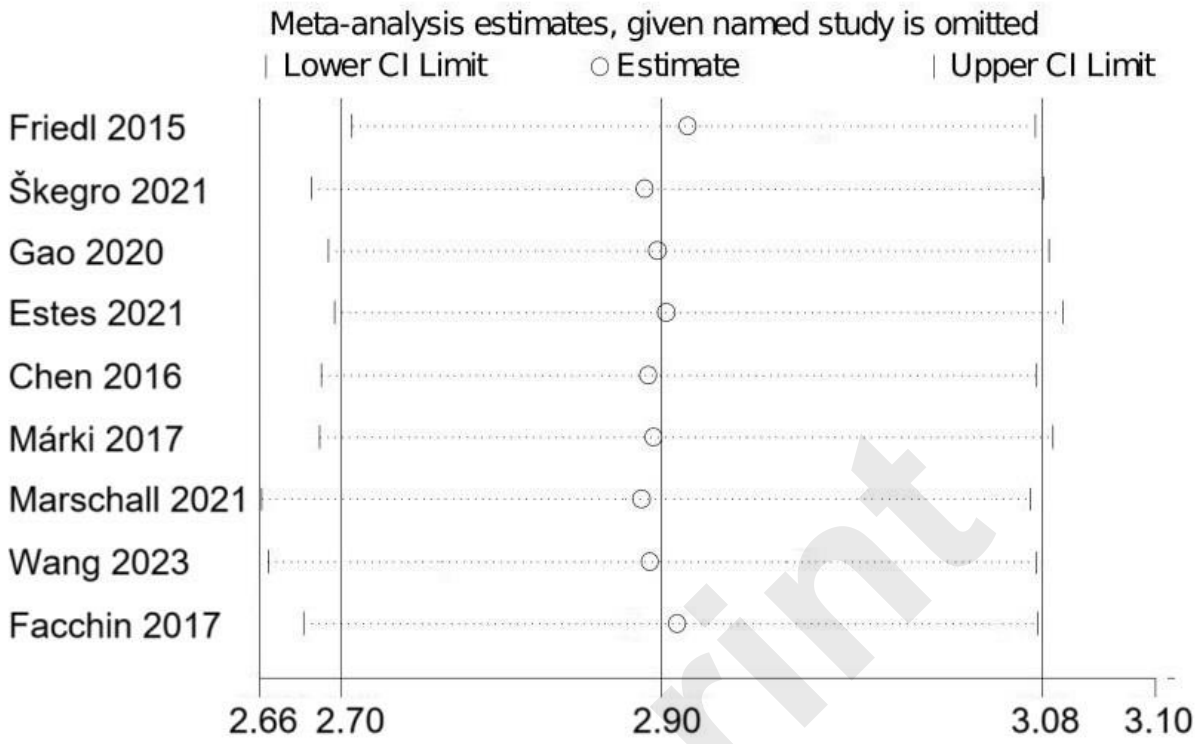

Figure 6. The elimination method one by one diagram.

Heterogeneity of binary categorical variables

It could be seen from Figure 7 that some points were far from the reference line, which indicated that the research results were abnormal and proved the existence of heterogeneity.

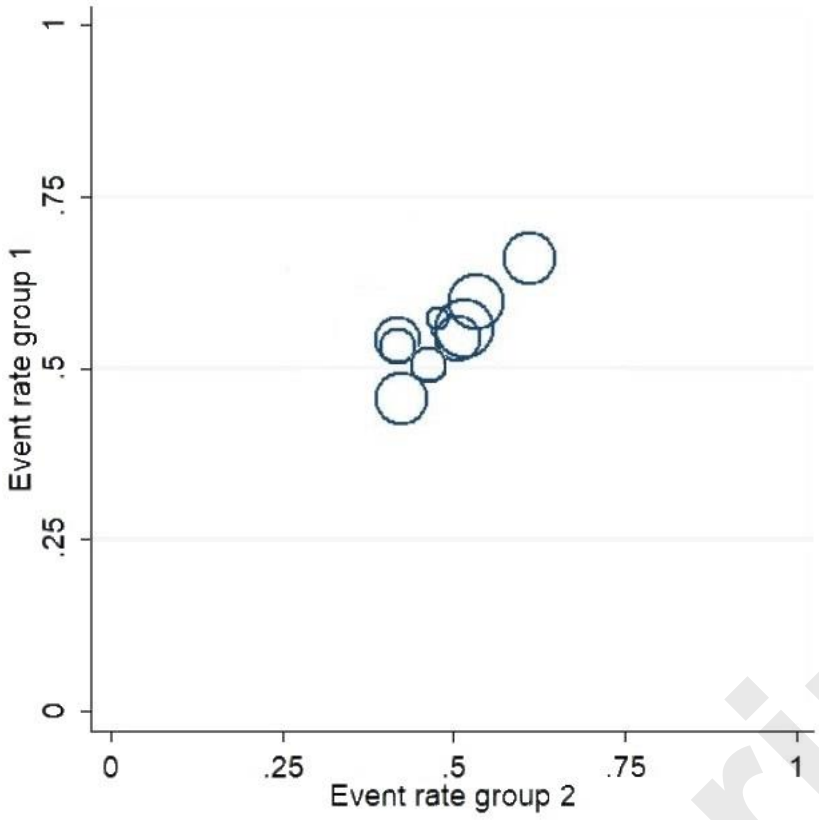

Figure 7. L 'Abbe plot.

Meta-regression analysis

Meta-regression analysis was conducted on 9 included literatures. As shown in Table 3, I2=76.37% (I2 > 50%), indicating that this meta-analysis has certain heterogeneity. However, p value > 0.05 suggests that there was no need for subgroup analysis.

Table 3. Meta-regression analysis results

Inor	Coef.	Std. Err.	t	P> | t |	[95% Conf.	Interval]
Studyperiods	**-.0359408**	**.0498238**	**-0.54**	**0.441**	**-.1391346**	**.089493**

_cons	**46.29132**	**94.07384**	**0.53**	**0.413**	**-179.2943**	**293.5463**

Discussion

This systematic review focuses on understanding the association between endometriosis and mental health, providing a detailed analysis of the interconnection between the two. The results support the hypothesis that women with endometriosis have significantly increased prevalence of depression, anxiety, and psychological distress compared to the general population. This review offers a more complex view of the contributing factors, which include pain severity, diagnostic latency, and patient-level factors like self-esteem and emotional self-efficacy, which supports a biopsychosocial model of treatment.

The Burden of Endometriosis on Mental Health

Endometriosis is defined as a chronic and severe disease that has negative impacts on the mental state of women. In line with previous research, the current review shows that women with endometriosis experience high levels of depression and anxiety, indicating that the psychological toll of the disease remains high. The high prevalence of these mental health conditions should be attributed to the pain and uncertainty the patients experienced as well as the burden of the disease on their overall functioning.

Pain was identified as an important factor that affected mental health. It was confirmed that severe pelvic pain, dysmenorrhea, and chronic pain were associated with depressive and anxious symptoms (Márki et al., 2017). Chronic pain not only impacts physical performance but also

leads to emotional fatigue, decreased ability to cope with stress, and increased risk of psychological distress. This finding supports the biopsychosocial model of pain which holds that pain is not only a physical phenomenon, but its perception and experience are influenced by factors biological, psychological and social. An observational case-control study included 344 patients with endometriosis and found that among them, 119 cases had mental disorders and 70 cases had depression. Patients with depression (EM-D) or mental state (EM-P) dyspareunia and dyschezia occurred more frequently. A total of 27,840 women from six European countries were included in the study (Becker K et al., 2021). The most common symptoms related to endometriosis are dysmenorrhea (61.8%), massive/irregular bleeding (50.8%), and pelvic pain (37.2%). Women reported that endometriosis affected their emotions; 55.6% of people felt "frustrated", depressed or desperate, and 53.2% felt defeated or disappointed with their family/friends (Arena A et al., 2021). These research results are consistent with the conclusion of this study. Endometriosis can cause pain and mental torture to patients. Medical staff and society should pay attention to the mental condition of patients with endometriosis. From January 2019 to March 2020, 104 women were included in a prospective observational study, and their anxiety levels decreased after assessment (STAI-Y6 60.0±15.0 vs 40.8±14.2). Patients with a higher baseline anxiety level (test.change-24.3;) The 95% confidence intervals were -29.2 and -19.5), and the anxiety level decreased after the physical examination (Dietrich H et al., 2023).

Diagnostic Delays and Psychological Implications

One of the significant trends identified in the reviewed research is the psychological impact of diagnostic delays. Endometriosis is often diagnosed only after years of enduring symptoms, during which time women may experience chronic pain, mistreatment, and a lack of acknowledgment from healthcare providers. This protracted diagnostic journey, characterized by

frustration and uncertainty, can exacerbate emotional distress (Facchin et al., 2017). The fact that a shorter time from the diagnosis is related to increased anxiety also points to the difficulties that women experience in dealing with the first stage of accepting an illness that is chronic and cannot be cured.

The diagnostic delay carries significant social and cultural implications. The tendency to postpone or avoid seeking care, coupled with the stigma surrounding menstrual and pelvic pain, contributes to these delays, leaving many women feeling isolated and unheard. Addressing these systemic issues requires enhanced education for both medical professionals and the public, as well as improved diagnostic practices aimed at identifying endometriosis more promptly and accurately.

Individual Characteristics and Protective Factors

In addition to the physical and diagnostic approaches to endometriosis, this article explores the influence of personality traits on mental health. Higher self-esteem, enhanced emotional self-efficacy, and supportive intimate relationships are associated with improved psychological outcomes (Marschall et al., 2021; Facchin et al., 2017). These findings have significant implications for endometriosis, indicating that individual resilience and social support can prevent a significant amount of the mental health burden. Women who have a disease centrality are more likely to report depressive symptoms and lower levels of life satisfaction (Marschall et al., 2021). On the other hand, the narratives of control are related to improved mental health, implying that the interventions designed to alter the narrative might be beneficial.

Psychiatric Comorbidities and Long-Term Risks

The significant association between endometriosis and depression found in this review provokes questions regarding the common mechanisms of pathogenesis. Women with endometriosis were at a higher risk of developing depressive and anxiety than those without the disease, and that the women who already had depression and anxiety had a higher possibility of developing endometriosis (Gao et al., 2020). Some of these mechanisms include inflammation, hormonal changes, and hypothalamic-pituitary-adrenal axis abnormalities, which need to be explored in future studies.

Furthermore, the increased odds of self-harmed/suicide and all-cause mortality supported the potentially lethal consequences of untreated psychological symptoms in women with endometriosis (Estes et al., 2021; Wang et al., 2023). These results underscore the need to include mental health assessment and treatment as part of standard care for individuals with endometriosis.

Implications for Clinical Practice

The outcomes of this review also hold important implications for the medical treatment of endometriosis. First, there is a need for mental health interventions to be incorporated into the treatment of endometriosis. Depression, anxiety, and other psychological symptoms should be screened as part of routine practice, and patients should be guided on where to access psychological support. Second, the management of pain should be comprehensive, encompassing not only a physical perception of pain, but also psychological and emotional. Other methods may include cognitive behavioral therapy, mindfulness practices, and narrative therapy to support medical and surgical management.

Third, there is a systematic review on the mental health burden of endometriosis and training of healthcare providers. The nature of the disease requires that the providers acknowledge the psychosocial aspects of the illness and manage to reassure patients about their feelings. Finally, patient education and involvement should be the last of them. Women should be empowered with resources that will improve their self-esteem, emotional self-efficacy and coping mechanisms to improve their mental health.

Heterogeneity analysis

The sample size of the included literature was in line with the efficacy analysis. The results of the one-by-one elimination method to test the heterogeneity of this study showed that after all the included literatures were eliminated one by one, the confidence interval and total RR were still within the fluctuation range calculated by the forest plot, indicating that the bias of all the included literatures was controllable and stable. The L 'Abbe plot was used to conduct heterogeneity analysis on binary variables. Basically, all the included literatures showed a linear relationship, and the research results were basically homogeneous, which was of certain significance. The results of the meta-regression analysis indicated that the included literature could already yield meaningful results and there was no need for subgroup analysis. Heterogeneity analysis indicates that there was a certain degree of heterogeneity in this study, but the analysis results were still significant.

Strengths, Limitations, and Future Directions

One of the major strengths of this review is the broad coverage of the studies originating from various geographic and cultural backgrounds, which increases the external validity of the

findings. Furthermore, the application of standardized assessment instruments throughout the studies enhances the credibility of the documented results.

However, there were also some limitations that need to be considered. Many publications were horizontal, which means it was difficult to establish a causal relationship between endometriosis and mental health. More longitudinal studies were needed to conduct longitudinal investigations into this relationship, with a focus on diagnosing the consequences of delays and the outcomes of intervention measures. Furthermore, the variability of research types, participants, and measured mental health impacts complicated the analysis and comparison. Only 9 literatures were included in this study. The number was too small, which leads to certain heterogeneity in the meta-analysis and the results lacked certain persuasiveness. In future research, we will search as many databases as possible and include as many literatures as possible for meta-analysis. Additionally, we will extend our search to Embase, Scopus, and grey literature to minimise publication bias and improve the completeness of evidence.Meanwhile, we will also conduct subgroup analyses on the research design of the included literature, the family economic income of patients with endometriosis, marital status, etc., so that the obtained results are meaningful for the actual treatment. It is also necessary to consider how other aspects such as race, economic status and cultural customs affect endometriosis and its treatment. Exploring the connection between endometriosis and depression/anxiety is helpful for formulating intervention and treatment plans.

Conclusion

This systematic review focuses on the high mental health cost that has been reported among women with endometriosis with increased depression, anxiety, and psychological distress recorded. There were many factors that were associated with these outcomes, and they included

pain severity, diagnostic delay, and presence of comorbid conditions. In the same vein, self-esteem, emotional self-efficacy, and social support were revealed as moderators that could buffer the effects of the disease.

These conclusions stress the necessity for an interdisciplinary approach to the treatment of endometriosis, in which the evaluation and treatment of mental health issues should be included in addition to pain relief and pharmacological treatment. The study highlighted that early diagnosis and effective care management models for endometriosis are vital to enhancing both somatic and psychiatric recovery for affected females. Future studies should aim at identifying the long-term outcomes of these interventions and the underlying common pathways between endometriosis and depression and anxiety. As highlighted in this review, the interrelated factors that need to be addressed with a view of improving the quality of life of millions of affected women include the following:

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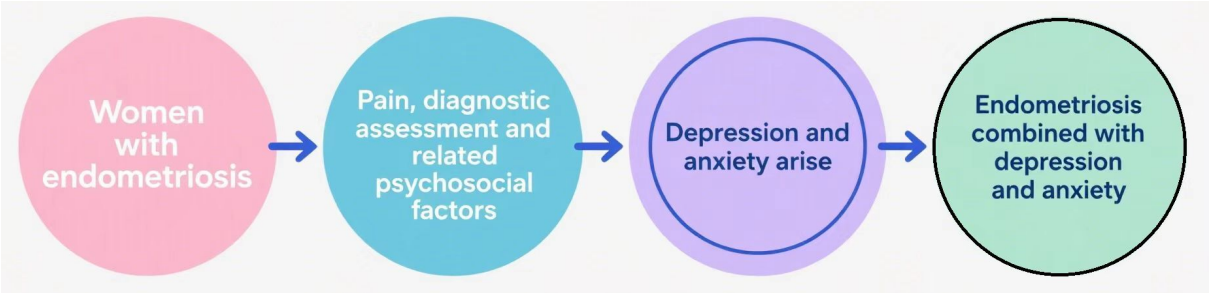
Women with endometriosis
Pain, diagnostic assessment and related psychosocial factors
Depression and anxiety arise
Endometriosis combined with depression and anxiety