



Review

Health-related quality of life in individuals with endometriosis and mental health symptoms: A scoping review



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ABSTRACT

Individuals with endometriosis present a high prevalence of mental health symptoms, including depressive and anxiety symptoms, which may contribute to lower health-related quality of life (HRQoL). Therefore, we conducted a scoping review to determine the association between mental health symptoms and HRQoL in individuals with endometriosis. Seven databases were queried with the search strategy. Studies were eligible for inclusion if the population examined included people with endometriosis and mental health symptoms. All studies were screened and data synthesized by a minimum of two reviewers. The findings are reported narratively.

Of the 10,847 records identified, five were included in this scoping review. A cross-sectional study found a moderate correlation between worse HRQoL and both depressive symptoms ($r = -0.54$, $p < 0.001$) and anxiety symptoms ($r = -0.60$, $p < 0.001$). Similarly, two small cross-sectional studies found a correlation between depressive symptoms and worse HRQoL ($r = 0.701$, $p < 0.01$; $r = 0.515$, $p < 0.01$), and between anxiety symptoms and worse HRQoL ($r = 0.546$, $p < 0.01$; $r = 0.295$, $p < 0.01$); these correlation coefficients are positive as this study utilized a scale in which a higher value indicated worse HRQoL. A larger cross-sectional study found that both depressive and anxiety symptoms were associated with a greater number of endometriosis symptoms. A recent cross-sectional study found that the HRQoL score was significantly higher (indicating worse HRQoL) in individuals with endometriosis with any of the six types of mental health symptoms considered than in those without mental health symptoms, $96.47(\pm 28.37)$ and $72.41(\pm 29.43)$ respectively ($p < 0.001$).

The results of this scoping review suggest that depressive and anxiety symptoms negatively impact HRQoL in people with endometriosis. Further research in this field is required, and future studies should aim to report standardized outcomes that can be statistically assessed.

Introduction

Endometriosis is characterized by endometrial-like tissue found outside the uterus [1] and can present with dysmenorrhea, dyspareunia, and noncyclic chronic pelvic pain [2] or with no symptoms at all. There is no cure for this chronic disease; at present, it is managed with various

complementary treatments, medications including hormonal suppression, and surgery [4]. Although the etiology of endometriosis is still unknown, it is estimated to affect 10% of individuals assigned female at birth (AFAB) of reproductive age and up to 50% of individuals AFAB with infertility [3]. Chronic pain and infertility can have direct impacts on psychological well-being and quality of life [14].

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Individuals with endometriosis have an increased likelihood of developing comorbid diseases, including autoimmune disease [5], gastrointestinal disorders [6], certain cancer types, hypothyroidism, and fibromyalgia [7,8]. Each of these chronic diseases, with their own set of symptoms and prognoses, only serve to further impact both the physical and mental well-being of these individuals.

In addition to physical comorbidities, individuals with endometriosis also have a high prevalence of psychiatric symptoms [9] and a high degree of comorbidity with mental health disorders, particularly generalized anxiety disorder (GAD) and major depressive disorder (MDD) [10,11]. Furthermore, chronic pelvic pain appears to exacerbate mental health disorders, with higher levels of GAD and MDD linked to people with endometriosis who experience pelvic pain compared to control groups of healthy individuals and people with asymptomatic endometriosis [12,13].

Individuals with endometriosis report a lower health-related quality of life compared to those without the condition [15,16]. Health-related quality of life (HRQoL) is defined as the attributes valued by patients including comfort, physical, emotional, and intellectual functioning as well as the degree to which individuals are able to participate in valued activities within the family, workplace, and community [16].

The primary aim of this scoping review is to assess the multidirectional relationship between endometriosis, mental health symptoms, and HRQoL. We hypothesize that having both endometriosis and comorbid mental health symptoms will subsequently lead to a lower HRQoL. Understanding comorbid conditions of endometriosis and their impact on overall HRQoL is essential to achieving refined and individualized diagnostic and treatment pathways and to ultimately improve treatment outcomes.

Methods

This scoping review was reported according to the Scoping Review Extension of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA-ScR) checklist [17].

Data sources and searches

A systematic search was conducted in seven databases from inception until 7th August 2022: PubMed, Medline, EMBASE, PsycINFO, CINAHL, Web of Science, and the Cochrane Library. The full search strategy can be visualized in the Supplementary Appendix. No restrictions were placed on publication date, publication type, or journal; however, only studies completed in English were included. Reference lists of all selected studies were manually reviewed to identify sources that the electronic search may have missed. Duplicate records were removed, and study screening was performed independently by two members of the research team (SV and JS), initially by title and abstract, then by full-text review. Where disagreement occurred, the study was discussed, and consensus was reached with input from a third team member.

Inclusion and exclusion criteria

Peer-reviewed case-control, cohort, and cross-sectional studies were eligible for inclusion in this review if the outcome measured HRQoL by a validated HRQoL scale. Animal studies, case reports and series, conference abstracts, review articles, editorials, and commentaries were excluded.

The population examined included people with endometriosis and mental health symptoms. No limitations were placed on the stage of endometriosis, the location of endometriosis, or the type of endometriosis. The primary mental health symptoms considered were those of major depressive disorder or generalized anxiety disorder; however, symptoms of all other mental health disorders were considered among secondary outcomes. Endometriosis can be diagnosed via several

methods, including clinical (history or physical examination), ultrasonography, magnetic resonance imaging (MRI), laparoscopy, and histopathology [4]. In this review, symptoms of mental health symptoms were identified by a mental health screening questionnaire.

Data charting

Data was synthesized and interpreted by two research team members (ZB and MG) and collated to minimize errors. Categories of data charted (when reported) included author name(s), year of publication, time period of the study, study design, method of diagnosis of endometriosis, stage of endometriosis, location of endometriosis, therapy for endometriosis, type of mental health symptoms, psychiatric treatment, mental health questionnaire utilized, domains of HRQoL scale, adjustment for confounding factors (e.g. body mass index, hormonal therapy), and overall result. The overarching trends in each outcome were identified and reported narratively. Where studies calculated the Pearson product-moment correlation coefficient, a value between 0.1 and 0.39 or -0.1 and -0.39 was considered a weak correlation, between 0.4 to 0.69 or -0.4 to -0.69 a moderate correlation, between 0.7 to 0.99 or -0.7 to -0.99 a strong correlation, and a perfect correlation if the value was 1 or -1 [18].

HRQoL scales

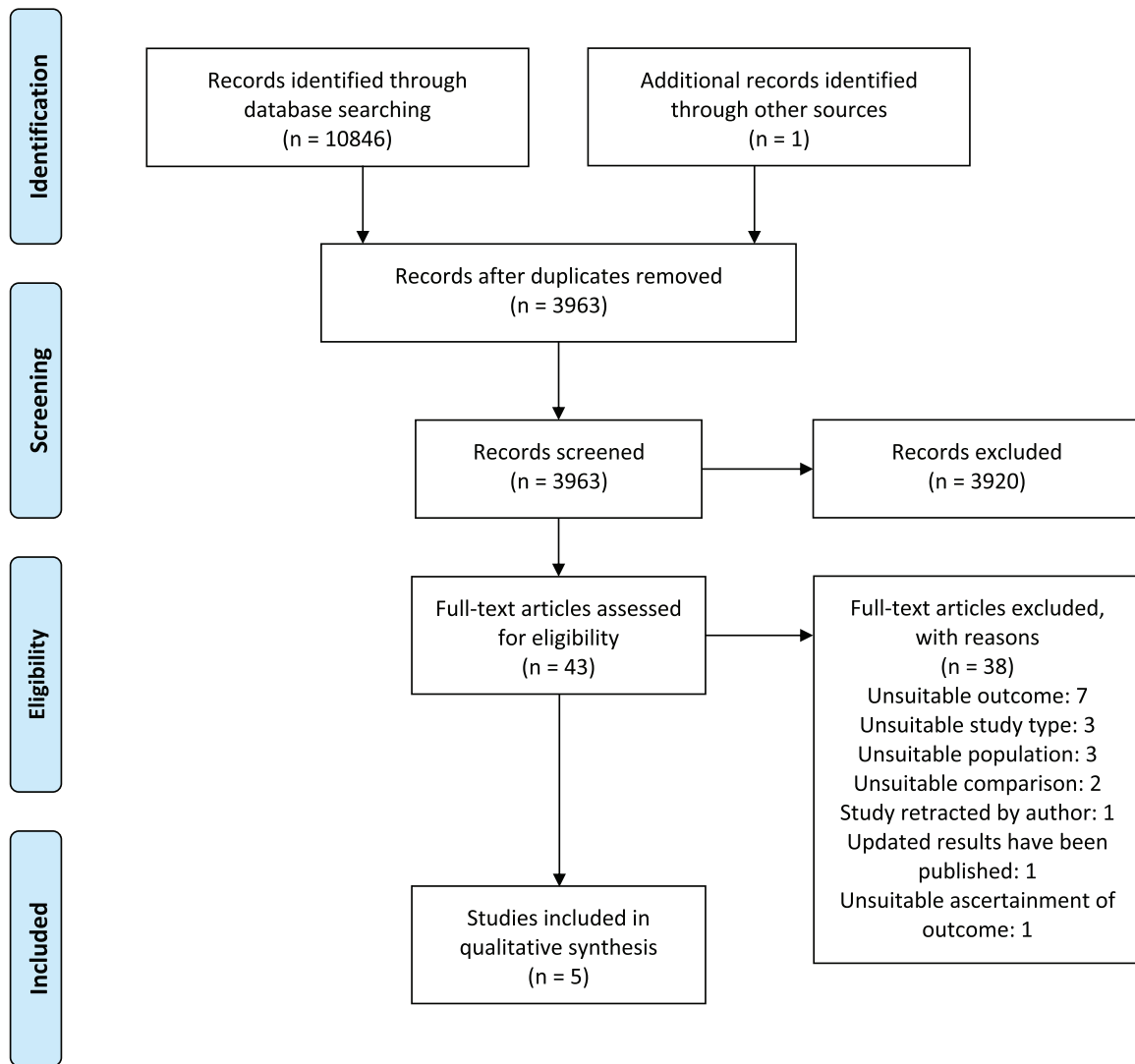
The principal HRQoL scales utilized in the studies included in this review were the SF-36 and EHP-30 and variations thereof [19,20,22,23,25]. The SF-36 is a generic questionnaire for assessing HRQoL that has been validated for use in individuals with endometriosis [40]. The breadth of the questionnaire allows it to be utilized across a variety of medical conditions, adding to its validity, and permitting a comparison between a variety of pathologies. However, certain key aspects that should be taken into consideration when evaluating HRQoL in endometriosis patients, such as dyspareunia, are missing in this questionnaire [41]. The EHP-30 provides a solution, as it is a comprehensive scale designed specifically for endometriosis and is recommended by the American Society for Reproductive Medicine (ASRM) and the European Society for Human Reproduction and Embryology (ESHRE) for research in the endometriosis population [24,42]. This HRQoL questionnaire contains thirty core items and a modular questionnaire assessing categories that may not be relevant to all individuals completing the questionnaire, such as infertility. The five overall domains of this scale include: pain, control and powerlessness, emotional well-being, social support, and self-image [24]. A disadvantage of this scale is its length, and by extension the time necessary to complete this questionnaire. The EHP-5 was developed to address this shortfall, and includes five core items and a shortened version of the modular questionnaire, providing a condensed and verified alternative to the EHP-30 [21]. In the SF-36, a lower score indicated a worse quality of life, whereas the EHP-30 considered a higher score to indicate a worse quality of life. The heterogeneity in the measures of the scales, while useful with respect to evaluating a variety of interpretations of HRQoL, provided a challenge in the interpretation of results.

Results

The search strategy identified 10,847 records. After duplicates were removed, 3963 studies remained, of which 43 were eligible for full-text review. Following the full-text review, five studies met the criteria for inclusion in this review, comprising a total of 1,040 individuals. A flow chart of the search and selection process is presented in Fig. 1.

Study characteristics

The baseline characteristics of the studies included in this scoping review are reported in Table 1. All included studies were cross-sectional



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Fig. 1. Flowchart of study selection.

studies conducted between 2014–2020 in Puerto Rico, Hungary, Australia, Indonesia, and Croatia. HRQoL was assessed with varying scales in each study: González-Echevarría et al. 2018 [19] and Škegro et al. 2021 [20] used the short-form version of the Endometriosis Health Profile (EHP-5) [21], while Sullivan-Myers et al. 2021 [22] and Muharam et al. 2022 [23] used the long-form version of the Endometriosis Health Profile (EHP-30) [24]. On the EHP scale, the scores range from 0 to 100, with a higher score indicating a poorer HRQoL. Conversely, Márki et al. 2017 [25] used the Short Form Survey (SF-36) [26], in which a higher score indicates better HRQoL. Sullivan-Myers et al. 2021 [22] used the Short Form Survey Version 2 (SF-36v2) [27] in addition to the EHP-30.

All studies included in this review identified mental health symptoms via self-administered questionnaires. González-Echevarría et al. 2018 [19] used the Beck Anxiety Inventory (BAI) [28] and the Beck Depression Inventory-II (BDI-II) [29], Márki et al. 2017 [25] used the Hospital Anxiety and Depression Scale (HADS) [30], Sullivan-Myers et al. 2021 [22] and Škegro et al. 2021 [20] used the Depression, Anxiety, and Stress Scales (DASS-21) [31], and Muharam et al. 2022 [23] used the Mini

International Neuropsychiatric Interview International Classification of Diseases (Mini ICD-10) [32]. Based on the scores from these assessments, participants were characterized as having depressive, anxiety, other mental health symptoms, or a combination of these symptoms. In Muharam et al. 2022 [23], in addition to depressive and anxiety symptoms, other mental health symptoms assessed in the Mini ICD-10 were those of dysthymia, mania, agoraphobia, panic disorder, social phobia, obsessive-compulsive disorder, post-traumatic stress disorder, bulimia, anorexia, alcohol addiction, drug addiction, and psychosis - a total of 14 mental health symptom types. However, only six of these types of mental health symptoms were identified in the study: depressive, anxiety, panic disorder, mania, obsessive-compulsive disorder, and psychosis symptoms.

Depressive symptoms

In individuals with endometriosis, depressive symptoms were found to be related to worse HRQoL in all five studies, although the strength of

Table 1
Baseline characteristics of the included five studies examining the HRQoL in individuals with endometriosis and mental health symptoms.

Author, year, location	Design	Study period	# Participants	Endometriosis diagnostic method	Age	BMI	Endometriosis treatment	Mental Health Questionnaire	HRQoL Questionnaire	Outcome
González-Echevarría et al., 2018	Cross-sectional Puerto Rico	NR	24	Surgical diagnosis	13–19: 9 (37.5%) 20–25: 15 (62.5%)	NR	Medical treatment: 23 (95.8%)	Beck Anxiety Inventory (BAI), Beck Depression Inventory II (BDI-II)	Endometriosis Health Patient-5 (EHP-5)	Pearson's correlation coefficients: Depressive symptoms: $r = 0.701^*$ Anxiety symptoms: $r = 0.546^*$
Márki et al., 2017	Cross-sectional Hungary	Oct 2014–Oct 2015	193	Confirmed medical diagnosis	33.87 (± 5.37)	NR	Medical treatment: 51.8% Average number of surgeries: 1.85 (± 1.16)	Hospital Anxiety and Depression Scale (HADS)	Short Form Health Survey (SF-36)	Spearman's rank correlation analysis: Depressive symptoms: $r = -0.54^{**}$ Anxiety symptoms: $r = -0.60^{**}$
Sullivan-Myers et al., 2021	Cross-sectional Australia	NR	584	Self-reported surgical or clinical diagnosis	31.2 (± 7.50)	Obese (BMI 30–39.9): 26.01%	Surgery: 87.2% Hormonal medication: 67.8% Pain medication: 78.3% Allied health: 41.6%	Depression, Anxiety, and Stress Scales (DASS-21)	Endometriosis Health Profile Questionnaire (EHP-30), Short Form 36 Version 2 (SF-36v2)	HRQoL factors contributing to variance: Depressive symptoms: R^2 change: 0.279; F change: 25.19 ^{**} Anxiety symptoms: R^2 change: 0.182; F change: 14.85 ^{**}
Muharam et al., 2022	Cross-sectional Indonesia	Jun 2019–Aug 2020	160	Clinical, surgical, or histopathological diagnosis, or via US imaging	NR	Normal: 84 (52.5%) Overweight: 76 (47.5%)	Surgery: 50.6% NSAID: 45.6% Hormonal therapy: 54.4%	Mini International Neuropsychiatric Interview International Classification of Diseases (Mini-ICD)	Quality of Life with Endometriosis Health Profile (EHP-30)	EHP-30 median scores: Depressive symptoms: 50.51 (± 12.18) Anxiety symptoms: 41.59 (± 12.3); Control group: 72.41 (± 29.43)
Škegro et al., 2021	Cross-sectional Croatia	Jan 2020–Jul 2020	79	Surgical diagnosis	35.03 \pm 7.11	23.58 \pm 3.89	NR	Depression, Anxiety, and Stress Scales (DASS-21)	Endometriosis Health Patient-5 (EHP-5)	Pearson's correlation coefficient: Depressive symptoms: $r = 0.515^*$ Anxiety symptoms: $r = 0.295^*$

NR: not reported; HRQoL: health-related quality of life; NSAID: non-steroidal anti-inflammatory drugs; BMI: body mass index.

Presented as number (percentage %) or mean (\pm standard deviation).

* $p < 0.01$.

** $p < 0.001$.

this association varied. González-Echevarría et al. 2018 [19] reported a Pearson's product-moment correlation coefficient of 0.701 ($p < 0.01$), indicating a strong positive correlation between depressive symptoms and a higher EHP-5 score and, therefore, worse HRQoL. Correspondingly, Škegro et al. 2021 [20] reported a Pearson's product-moment correlation coefficient of 0.515 ($p < 0.01$), indicating a moderate positive correlation. Márki et al. 2017 [25] found that there was a moderate correlation between depressive symptoms and worse HRQoL, with a Spearman's ranked correlation coefficient of -0.54 ($p < 0.001$); the negative value indicates a lower SF-36 score and thus worse HRQoL [25].

In participants with depressive symptoms in the study by Muharam et al. 2022 [23], the mean EHP-30 score was 50.51 (standard deviation (SD) ± 12.18). In comparison, for patients where psychiatric symptoms were absent, the mean EHP-30 score was 72.41 (SD ± 29.43). The study also conducted a linear regression analysis which found that the EHP-30 score increased by 28.51 with depressive symptoms, indicating worse HRQoL (unstandardized B: 28.51; 95% confidence interval (CI): 20.06–36.05; standard error (SE): 4.07; $p < 0.001$).

Hierarchical linear regression was performed by Sullivan-Myers et al. 2021 [22] to assess the extent to which different variables contributed to moderate to severe depressive symptoms. Controlling for demographic and medical variables, HRQoL factors (which considered both the EHP-30 and SF-36v2) independently accounted for 27.9% of the variance in depressive symptoms (R^2 change: 0.279; F change: 25.19; $p < 0.000$). Additionally, depressive symptoms were significantly associated with higher self-rated endometriosis severity and a greater number of endometriosis symptoms.

Anxiety symptoms

There was a positive correlation between anxiety symptoms and worse HRQoL in González-Echevarría et al. 2018 [19] and Škegro et al. 2021 [20], with a Pearson's correlation coefficient of 0.546 ($p < 0.01$) and 0.295 ($p < 0.01$), respectively. The positive scores indicate a worse HRQoL as assessed by the EHP-5. Márki et al. 2017 [25] also found that there was a moderate correlation between anxiety symptoms and worse HRQoL (Spearman's ranked correlation coefficient = -0.60 ; $p < 0.001$) [25]. In Muharam et al. 2022 [23], there was no significant difference in HRQoL in individuals with anxiety symptoms compared to those without; the mean EHP-30 score for individuals with anxiety symptoms was 41.59 (SD ± 12.35), and the mean score was 38.39 (SD ± 15.2) in those without anxiety symptoms ($p = 0.213$).

In the hierarchical linear regression performed by Sullivan-Myers et al. 2021 [22], HRQoL factors (which took into account both the EHP-30 and SF-36v2) independently accounted for 18.2% of the variance in moderate to severe anxiety symptoms (R^2 change: 0.182; F change: 14.85; $p < 0.000$), controlling for demographic and medical variables. Anxiety symptoms were also associated with a greater number of endometriosis symptoms.

Other types of mental health symptoms

As reported in the study characteristics, Muharam et al. 2022 [23] assessed participants for a total of 14 types of mental health symptoms, six of which were present in the participants of the study. In individuals with any of these types mental health symptoms, the EHP-30 score was higher (96.47 SD ± 28.37) than those without mental health symptoms (72.41 SD ± 29.43) ($p < 0.001$). Multivariate analysis of the EHP-30 score found that the score increased by 9.84 with any type of mental health symptoms (unstandardized B: 9.84; 95% confidence interval: 6.07–13.60; SE: $p < 0.001$).

Discussion

Main findings

In this scoping review of the association between endometriosis, mental health symptoms, and HRQoL, five studies were identified,

comprising a total of 1,040 individuals. The findings suggest that there is likely an overall worse HRQoL in people with endometriosis and mental health symptoms compared to people diagnosed only with endometriosis. Depressive symptoms were found to contribute to a worse HRQoL in all studies, with varying strengths of association. Anxiety symptoms were correlated to a worse HRQoL in all studies but one (Muharam et al. 2022) [23]. However, this study found poorer HRQoL with any of the six types of mental health symptoms examined. These results are consistent with current literature, which has shown endometriosis to be both independently and interactively associated with depressive symptoms, anxiety symptoms, and worse HRQoL [13,33,34]. Awareness of this association should be a consideration of the individualized treatment plan for individuals with endometriosis, aiming for early identification and management of mental health symptoms in order to improve HRQoL.

Interpretation

Interestingly, while the aim of this scoping review was to examine the effect of mental health symptoms on HRQoL in individuals with endometriosis, one of the included studies, Sullivan-Myers et al. 2021 [22], investigated an opposing question by determining the effect of HRQoL in participants with endometriosis on their levels of depressive and anxiety symptoms. The hierarchical regression analysis demonstrated that factors of HRQoL independently accounted for variance in both depressive and anxiety symptoms. Another included study, Muharam et al. 2022 [23], found that high pain levels were significantly associated with mental health symptoms. Therefore, it is difficult to determine the underlying factor leading to worse HRQoL, higher levels of depressive and anxiety symptoms, and high levels of pain in the endometriosis population, as all of these elements interact and are associated with one another.

An alternate hypothesis may be that the higher prevalence of depressive and anxiety symptoms in individuals with endometriosis is predominantly linked to pain. This is supported by a study which observed that mental health conditions were significantly more common in individuals with endometriosis than healthy controls, but not more common in comparison to a control group with chronic pelvic pain [35]. Pain is associated with poorer psychological outcomes in people with endometriosis, as well as contributing to a worse HRQoL [12,13,36,37]. GAD and MDD have been associated with greater pain in the endometriosis population and worse HRQoL [12,34]. Neuroimaging studies in individuals with endometriosis have found changes in brain regions related to pain processing, but also emotion, cognition, self-regulation, and reward [38]. However, to counter this argument, a recent genome-wide analysis demonstrated a genetic link between endometriosis and mental health disorders [39]. Ultimately, the approach to the endometriosis patient should aim to address all these factors collectively.

Strengths and limitations

This study has several strengths, including adherence to strict inclusion criteria, broad searches of a variety of databases, and no restrictions for publication date, type, or journal. However, it has several limitations that should be considered when interpreting the results. While a systematic review and meta-analysis is higher quality evidence than a scoping review, the intricate relationship between endometriosis, mental health symptoms, and HRQoL does not lend itself to meta-analysis due to the heterogeneity of data outcomes. The nature of this study as a scoping review makes it an inappropriate format for recommendations to implement in clinical practice, and rather acts as an overview of the current literature. A further significant limitation was that the presence of mental health symptoms was determined by participants completing questionnaires themselves rather than a formal diagnosis by a clinician, which may contribute to misclassification bias. These comparisons using self-reported presence or lack of mental health symptoms may be limited,

as individuals were not entered into a formal control group at the start of the study, which may contribute to selection bias. The records included were all cross-sectional in nature, a study design not optimal for appreciating causality. Only five articles fit the rigorous inclusion criteria, resulting in a small population. Infertility is an important confounding factor on HRQoL in individuals with endometriosis [14]; although it is considered in the EHP-30 questionnaire, this factor was not fully explored in this review. Thus, conclusions should be taken with caution when generalizing to larger groups.

Conclusions

This scoping review suggests that individuals with endometriosis and mental health symptoms have a worse HRQoL compared to those with endometriosis alone. This review highlights the necessity of further research into the complex biopsychosocial interaction between these factors. In particular, future studies should aim to report standard outcomes that can be statistically assessed and consider confounding factors contributing to changes in HRQoL, such as infertility. Ultimately, if an association is confirmed it is important to introduce mental health symptom screening and thresholds to detect mental health symptoms early, aiming to improve HRQoL in individuals with endometriosis.

CRedit authorship contribution statement

GEC: conceptualization, methodology, formal analysis, investigation, data curation, writing – original draft, project administration. SVI: conceptualization, methodology, formal analysis, investigation, writing – original draft. ZB: methodology, formal analysis, investigation, data curation, writing – review & editing. MK: methodology, formal analysis, data curation, writing – review & editing. SS: methodology and writing – review & editing. SVA: methodology and writing – review & editing. JS: methodology, investigation, data curation, writing – review & editing. JT: methodology and writing – review & editing. MG: methodology, investigation, and writing – review & editing. ML: conceptualization, methodology, formal analysis, investigation, data curation, writing – original draft, supervision.

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Declaration of competing interest

A/Prof Leonardi reports consulting fees from AbbVie, Hologic, Imageno, and Chugai Pharmaceutical; personal fees from GE Healthcare, Bayer, TerSera, and AbbVie; and grants from CanSAGE, AbbVie, AIMA/SOPHIE, Hyivy/MITACS/SOPHIE, Hamilton Health Sciences, Endometriosis Australia, Medical Research Future Fund/Imageno, and Health Canada outside the submitted work. ZB's PhD was partly funded by the French National Association for Research and Technology and by Lyv Healthcare. The remaining authors report no conflict of interest.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.jeud.2024.100105>.

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