



# Psychological interventions for endometriosis-related symptoms: a systematic review with narrative data synthesis

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## Abstract

Endometriosis impacts the physical, psychological and quality of life domains of women. Despite the medical and/or surgical management of endometriosis, the presence of persistent pelvic pain and psychological distress often continues, suggesting a role for psychological interventions in treatment planning. The present study aimed to conduct the first systematic review, with narrative data synthesis, on psychological interventions for endometriosis-related symptoms. The study also aimed to determine the effectiveness of current interventions in resolving psychological and pain-related loss of function associated with endometriosis and to identify gaps in the literature requiring further research. A total of 15,816 studies were retrieved through database searching and handsearching, with two researchers identifying 11 full-text studies that met inclusion criteria. Three studies of ‘moderate’ quality were identified, although the overall quality of studies was found to be ‘weak’, with a ‘high’ risk of bias. The findings regarding the effectiveness of psychological interventions for endometriosis-related symptoms remain inconclusive. Further research into psychological interventions for women with endometriosis that employ evidence-based protocols with high intervention integrity is recommended.

**Keywords** Endometriosis · Psychological intervention · Persistent pelvic pain · Quality of life

## Introduction

Endometriosis is a common and incapacitating gynaecological disease involving the development of endometrial-like cells outside the uterus, most frequently within the abdominal cavity (Prentice 2001). The unusually placed endometrial-like tissue responds in a physiologically similar manner to the endometrium and is described as an oestrogen-dependent chronic inflammatory response (Leyland et al. 2010). Currently, the pathogenesis of the disease is unknown (Young et al. 2015). The prevalence rates of endometriosis vary but epidemiological research suggests that approximately 10% of women are affected by the disease during their reproductive years (Vigano et al. 2004). The impacts of endometriosis are far reaching, affecting numerous interrelated aspects of women’s lives. Although it is possible to consider these impacts individually, it is difficult to separate effects, as they often exist in overlapping domains

including psychological, physical, reproductive, relational and quality of life (Chaman-Ara et al. 2017).

The physical symptoms of endometriosis vary across individuals. Symptomology may include dysmenorrhea, dyspareunia, dyschezia, gastrointestinal issues, fatigue, headaches, cyclic and acyclic pelvic pain, lower abdominal pain and back pain, infertility, as well as a variety of symptoms that are unspecific (Chiantera et al. 2017; Tripoli et al. 2011). The experience of endometriosis pain has been described by women as intense, overwhelming, sharp, crippling and horrific (e.g. Denny 2004; Huntington and Gilmour 2005; Jones et al. 2004). The level of physical disability associated with endometriosis is primarily related to the impact of persistent pain that limits occupational, social and activities of daily living (e.g. Culley et al. 2013; Nnoaham et al. 2011).

Diagnostic delays reported by many women often result in adverse psychological consequences, with considerable uncertainty and distress reported (Culley et al. 2013; Young et al. 2015). A recent review of psychological symptoms experienced by women with endometriosis indicated prevalence rates of 86% for depression, 29% for moderate to severe anxiety and 68% for mood disturbances, which is significantly higher than the prevalence of these disorders within the normal population

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(Chaman-Ara et al. 2017). A greater prevalence of depression among women with endometriosis has been reported for women who experience persistent pelvic pain relative to women without pain (Lorençatto et al. 2006). Qualitative studies have identified a broad range of feelings experienced by women with endometriosis including: emotional distress, hopelessness, worthlessness and depression, isolation, and suicidality (Cox et al. 2003). Similar psychological consequences are also reported in relation to infertility due to endometriosis, including feelings of worry, inadequacy, depression and relationship breakdown (Jones et al. 2004), although research in this area is disappointingly limited.

The impact of endometriosis-related symptoms on quality of life (QoL) of women with the disease has been the subject of a large volume of research, and numerous reviews have published the findings (e.g. Chiantera et al. 2017; Jia et al. 2012; Petrelluzzi et al. 2008; Nnoaham et al. 2011; Young et al. 2015). One well-documented finding is the negative impact of endometriosis symptoms on role function, including activities of daily living, occupational engagement and advancement and parenting (e.g. Daniels and Khan 2010; Gilmour et al. 2008; Jones et al. 2004).

Current treatment approaches predominantly fit within a biomedical model of illness with treatment aiming to restore health by attenuating or removing the disease (Wade 2004). There are varying rates of success for surgical or pharmacological management (e.g. Culley et al. 2013; Wee-Stekly et al. 2015), and the relief provided may only be short-term (Denny 2009). Based on the finding of a higher prevalence of psychological consequences associated with endometriosis compared to the normal population, recent research has explicitly highlighted a role for psychological interventions in the treatment of endometriosis-related symptoms and distress (e.g. Chaman-Ara et al. 2017; Chiantera et al. 2017).

The range of psychological interventions that have been recommended include improved pain coping and minimization of pain catastrophising (Chiantera et al. 2017), psychological assessment and consultation for both patients and their families, psychiatric treatment where warranted and increased social and occupational supports (Chaman-Ara et al. 2017). Current treatment guidelines indicate that women diagnosed with endometriosis may require a broad range of treatments given the complexity of adverse psychological, physical, relational and quality of life impacts (Dunselman et al. 2014). Despite the common findings that endometriosis is linked to a reduction in psychological health and quality of life, the efficacy and effectiveness of psychological interventions in the treatment of endometriosis-specific symptomology have not been established to date.

The present study aimed to conduct the first systematic review, with narrative data synthesis, on psychological interventions for endometriosis-related symptoms. The effectiveness of current interventions in resolving the psychological and pain-related loss of function associated with endometriosis was

examined, with identification of gaps in the literature requiring further research. A final aim of the study was to develop practice recommendations for psychological interventions for endometriosis-related symptoms.

## Methods

A systematic review of the literature was conducted according to PRISMA-P guidelines (Shamseer et al. 2015) and the Cochrane Handbook for Systematic Reviews of Interventions (Higgins and Green 2011). The systematic review was registered and updated with the International Prospective Register of Systematic Reviews (PROSPERO) (28 July 2017 and 7 May 2018; CRD42017072793). Although the reviewed literature reported quantitative data, the study designs and intervention types were heterogeneous overall. For this reason, a meta-analysis was considered inappropriate for this study.

## Information sources and search strategy

Systematic searches were conducted within four scientific databases (PsycINFO (OVID), EMBASE, MedLINE and CINAHL) dating from their inception to September 2017 and May 2018. A search of the Cochrane Central Register of Controlled Trials and conference abstracts was also completed. Search terms included: ('endometriosis') AND ('psycholog\*' OR psychology\* intervention' OR 'psycholog\* treat\*') OR 'CBT' OR 'Cognit\* Behavio\*r Therapy' OR 'self-efficacy' OR 'cop\*' OR 'pain' OR 'educat\*' OR 'psychoeducat\*' OR 'educat\* seminar\*' OR 'mindfulness' OR 'ACT' OR 'Acceptance Commitment Therap\*' OR 'non-pharmacological' OR 'non-medical'. Medical subject headings (MeSH) were used for Medline searches; Keywords were used for Cochrane Library; and Subject headings were used for CINAHL, EMBASE and PsycINFO. Reference lists of full-text articles were hand-searched for any additional publications that may have been overlooked by the online searches.

## Eligibility, inclusion and exclusion criteria

Peer-reviewed, English-language, quantitative studies that assessed psychological interventions for women diagnosed with endometriosis were included. Included studies were further restricted to those that reported pre- and post-intervention outcomes (e.g. psychological symptoms, persistent pain, quality of life, functional capacity). Intervention delivery modalities were specified as individual or group based. Studies were excluded if they (a) did not separately report outcomes for women with endometriosis; (b) were reviews, theses, dissertations, abstracts and opinions only; (c) animal studies or (d) focused on endometrial cancer.

## Screening, data collection and analysis

Following the initial search, the title and/or abstract of all documents were screened independently by two researchers (BWP, LVN). The full-text articles of these included articles were screened again, independently, by two researchers (BWP, LVN). Where consensus was not reached between the first two researchers, a third researcher determined suitability for further inclusion (MM). Only one article required resolution by the third reviewer because consensus could not be reached on including a single-case study design. This article was included for further review.

## Assessment of quality and risk of bias

Assessment of quality and risk of bias was completed using the Quality Assessment Tool for Quantitative Studies (Cochrane Public Health n.d.). This assessment focused on nine criteria: Selection Bias, Allocation Bias, Confounding, Blinding Bias, Data Collection Methods, Withdrawals, Statistical Analysis, Intervention Integrity (adherence, exposure, quality of delivery) and Contamination Bias. The methodological quality of a study was established a priori in consensus between two researchers (BWP, LVN). A study was assessed as 'strong' overall if seven or more criteria were met, 'moderate' if five or six criteria were met and 'weak' when four or fewer criteria were met. Full consensus was reached between the two researchers and therefore a third assessment of quality and risk of bias by researcher MM was not required.

Narrative data synthesis was carried out in consensus between two researchers (BWP and LVN) according to the Guidance on the conduct of narrative synthesis in systematic reviews (Popay et al. 2006).

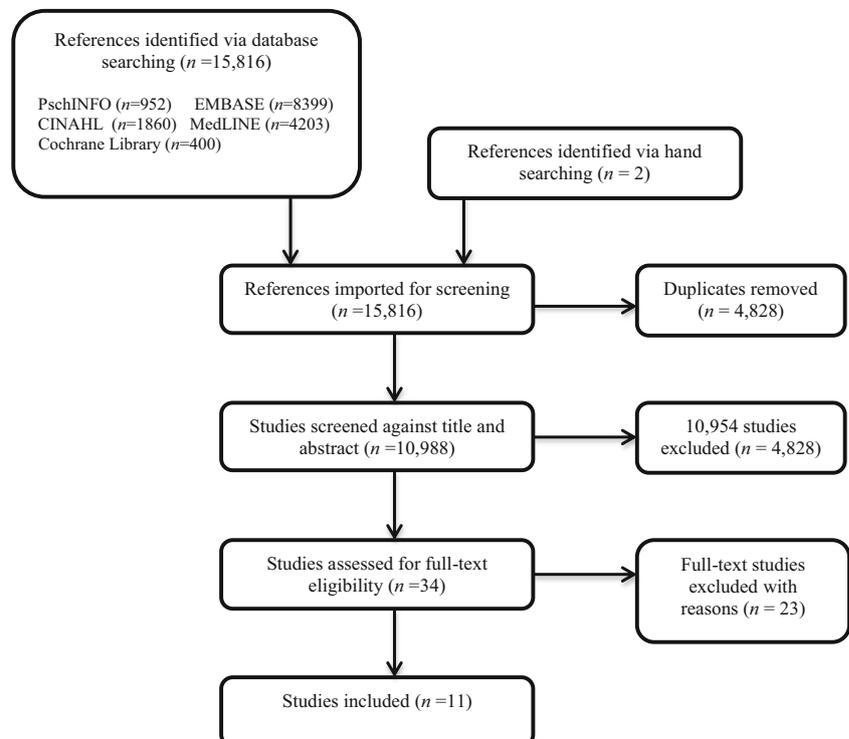
## Results

The first search yielded a total of 13,899 articles. A total of 3936 duplicates were removed using the Covidence software. The remaining 9963 studies were screened by title and abstract resulting in 9931 exclusions. A total of 32 full-text publications were retrieved and a 97% inter-rater agreement reached. Of the full-text publications, 21 were excluded due to: study design (e.g. lack of psychological intervention, 11 papers), participant population (e.g. failure to report endometriosis-specific results, 7 papers) or abstract only publications (2 papers). Eleven remaining studies met inclusion criteria and were included in the present review.

The second search (May 2018) yielded an additional 1915 studies, with 892 duplicates removed via Covidence. The remaining 1023 titles and abstracts were screened for relevance as per the first search, and 2 full-text articles were retrieved. Of these, both studies were excluded due to having study designs incongruent with the inclusion criteria. A PRISMA-P flow diagram summarising the final search results is presented in Fig. 1.

Of the 11 studies selected for full-text review, publication dates ranged from 1997 to 2017. These studies revealed heterogeneity across intervention tested and research design.

**Fig. 1** PRISMA-P flowchart of study selection from database inception to May 2018



Interventions implemented included progressive muscle relaxation, mindfulness, biofeedback, psychotherapy with somatosensory stimulation, hypnotherapy with traditional Chinese medicine, music therapy, yoga with breathing and relaxation techniques, cognitive behaviour therapy with physiotherapy and psychological pain management. The interventions were delivered in group- or individual format.

The study designs included unblinded randomised controlled trials, two-arm quasi-experimental studies, single-arm studies, long-term follow-up of single- and multiple-arm studies and multiple- and single-case study designs. An overview of the study characteristics is provided in Tables 1 and 2.

Considerable variability existed in relation to primary and secondary outcomes and domains measured across the 11 studies. Outcomes included quality of life; pain intensity, duration and coping and psychological symptoms. The outcomes and domains for each study can be seen in Fig. 2.

The quality and risk of bias assessment failed to find a study that received an overall rating of ‘strong’ quality and ‘low’ risk of bias for seven or more criteria. Three studies achieved a ‘moderate’ overall rating as they were assessed as ‘strong’ for five criteria (Hansen et al. 2016; Kold et al. 2012; Zhao et al. 2012). Six of the included studies were assessed as ‘weak’ overall, with ratings equal to or less than four ‘strong’ criteria met (Colwell 1997; Hawkins and Hart 2003; Lorençatto et al. 2007; Meissner et al. 2010; Meissner et al. 2016).

Areas of lowest quality and highest risk of bias included Confounding Variables and Integrity of the Intervention, with only one study rated as ‘strong’ for each of these criteria

(Hansen et al. 2016). The most stringent risk of bias criteria revealed was the Data Collection Method criterion, although only 6 of the 11 papers were rated as ‘strong’ on this criterion (Gonçalves et al. 2017; Hansen et al. 2016; Kold et al. 2012; Meissner et al. 2016; Petrelluzzi et al. 2012; Zhao et al. 2012). The quality and risk of bias assessment for the 11 studies is presented in Fig. 3.

As seen in Table 3, the magnitude of treatment effects was found to vary considerably across the 11 studies. Interventions found to be effective in improving psychological outcomes were also effective in regard to a reduction in reported pain intensity and increased pain-related coping. Effective interventions included progressive muscle relaxation (Zhao et al. 2012), group mindfulness combined with individual psychotherapy (Kold et al. 2012), combined individual psychotherapy with somatosensory stimulation (Beissner et al. 2017; Meissner et al. 2016) and a multi-professional group intervention involving cognitive behaviour therapy (CBT) and physiotherapy (Lorençatto et al. 2007). In addition, yoga with breathing exercises and combined physical and psychological relaxation (Gonçalves et al. 2017) was effective in decreasing pain-related outcomes for women with endometriosis.

Four of the studies reporting positive treatment effects were limited by small sample size (Gonçalves et al. 2017; Hansen et al. 2016; Kold et al. 2012; Petrelluzzi et al. 2012), and three of the 11 studies lacked a control group comparison (Hansen et al. 2016; Kold et al. 2012; Petrelluzzi et al. 2012). Two of the 11 studies included a control group that was a waitlist rather than treatment-as-usual leading to difficulties in evaluating treatment (Beissner et al. 2017; Meissner et al. 2016).

**Table 1** Overview of study characteristics

Study	Country	Participants	Number	Age <sup>a</sup>	Recruitment method
Beissner et al. 2017	DE	Women with clinically proven endo and PPP	67	(18–40)	NR
Colwell 1997	US	Woman with endo, with PPP	1	40	Gynaecologist referral
Gonçalves et al. 2017	BR	Women with SC endo, with PPP	40	(18–50)	Outpatient units: Department of OBGYN, UH
Hansen et al. 2016	DK	Women with endo and PPP	10	(33–68)	Single tertiary referral centre
Hawkins and Hart 2003	US	Women with endo and PPP	5	NR	Community sample
Kold et al. 2012	DK	Women with endo and PPP	10	NR	Single tertiary referral centre
Lorençatto et al. 2007	BR	Women with SC endo and PPP	128	34.7 ± 7.6 (I), 32.8 ± 6.7 (C)	Outpatient unit: Department of OB, UH
Meissner et al. 2010	DE	Women with SC endo	47	25–54	Private TCM practice
Meissner et al. 2016	DE	Women with HC endo and PPP	67	18–40	NR
Petrelluzzi et al. 2012	BR	Women with SC and HC endo with PPP	26	18–50	Outpatient unit: Women’s Health Centre, UH
Zhao et al. 2012	CN	Women with SC endo with PPP	100	18–48	Department of OBGYN, UH

BR Brazil, CN China, DK Denmark, DE Germany, US United States of America, endo endometriosis, PPP persistent pelvic pain, ID interdisciplinary, VAS Visual Analogue Scale, COC combined oral contraceptive, SC surgically confirmed, HC histologically confirmed, NR not reported, I intervention, C control, OBGYN Obstetrics and Gynaecology, GYN gynaecologist, OB obstetrics, NR not reported, TCM Traditional Chinese Medicine, UH university hospital

<sup>a</sup> Age: mean (± SD), or (x-y): age range

Other limitations of the studies related to the Reporting of Results, with two studies reporting insufficient data to allow the calculation of effect sizes (Hawkins and Hart 2003; Meissner et al. 2010) or failing to measure psychological outcomes (Meissner et al. 2010).

## Discussion

### Efficacy of psychological interventions

The systematic review demonstrated the importance of evidence-based psychological interventions in the treatment of endometriosis-related symptomatology in reducing anxiety and symptoms of depression. Combined Mindfulness, psychoeducation and individual psychotherapy based on CBT showed significant improvements in pain coping and quality of life (Kold et al. 2012; Hansen et al. 2016). Progressive Muscle Relaxation (PMR) was also associated with significant reductions in psychological distress and pain intensity (Zhao et al. 2012).

An important finding was the use of physical interventions for endometriosis-related pain. In particular, physiotherapy, acupuncture and related techniques (somatosensory stimulation), yoga, controlled breathing techniques and PMR tend to be used to treat endometriosis-related pain. As the effectiveness of these techniques in reducing pain-related symptomatology among women with endometriosis is not well established, further research that tests these interventions with high-quality protocols is suggested.

Psychoeducation regarding endometriosis and its impacts was shown to be an important and effective intervention. This finding is consistent with a recent meta-analytic review showing that psychoeducation may reduce depression, anxiety and psychological distress in psychological disorders (Donker et al. 2009). Specifically, Donker and colleagues reported larger reductions in anxiety, depression and psychological distress for a psychoeducation intervention that involved evidence-based medical/psychological information addressing these symptoms ( $d = 0.25$  to  $0.61$ ) compared with small effects for psychoeducation using passive methods, such as leaflets ( $d = 0.20$ ). Future research is required to explore the most effective format of psychoeducation in regard to endometriosis-related symptoms.

The findings of this systematic review highlights the need for endometriosis to be conceptualised beyond a purely biopsychosocial model. While conceptualising endometriosis within a biopsychosocial framework would be consistent with the conceptualisation of other persistent pain conditions (e.g. Daniels and Khan 2010; and Gatchel 2004), this model may not adequately account for the interrelated aspects of women's experience of disease and may result in a simplified treatment approach that focusses on pain alone. Lehman et al. (2017)

propose that the biopsychosocial model of health be extended to view human health as an interaction between biological, psychological, interpersonal and macrosystem contextual dynamics that develop over the individual's lifespan. The dynamic model discussed by the authors is considered to be relevant in understanding the impacts, and required treatment areas, of endometriosis given the impact that the disease has in regard to biological, psychological, interpersonal and socio-cultural health and functioning.

### Gaps in the literature

One of the most striking findings of the current review was that only three of the 11 studies were rated as 'strong' for the criterion of Intervention Integrity (Hansen et al. 2016; Kold et al. 2012; Petrelluzzi et al. 2012). The researchers for these studies provided clear evidence-based intervention protocols that would facilitate repetition. The remaining eight studies either did not utilise evidence-based psychological interventions or did not provide adequate information regarding the intervention, significantly limiting the possibility of replicability. The level of practitioner adherence to the intervention protocol was rarely cited and, in some cases, the psychological intervention was delivered by individuals or researchers trained in other disciplines (e.g. music therapy), or professions (e.g. medical specialists for psychosomatic medicine and Chinese medicine). It is suggested that future research protocols are provided by Masters-level or higher psychologists with training and experience in the intervention to be delivered, and that a measure of protocol adherence is reported (Bawa et al. 2015).

Overall, the quality of the studies included was found to be 'weak' to 'moderate'. Although the 'gold standard' is to adhere to stringent research guidelines when assessing the effectiveness of psychological interventions, for women diagnosed with endometriosis, the capacity for this to occur at a consistently high standard may be impacted by a variety of factors. For example, factors such as variance in endometriosis-specific symptoms; diagnostic difficulties including duration, form and severity; financial and demographic access to treatment or suitably qualified professionals may continue to impact on the quality assessment or risk of bias for future research. The financial costs for women with endometriosis to self-fund and source psychological treatment to remove potential bias such as Allocation Bias or for researchers to fund independent psychologists to deliver the intervention to manage Blinding Bias are generally prohibitive.

The Australian Government has only recently announced a commitment to endometriosis research in the form of the development and planned implementation of the National Action Plan for Endometriosis (Perrott 2018, March 2), acknowledging the extensive costs associated with endometriosis at an individual, relational, societal and research level.

**Table 2** Study aims, design, treatment, measures and outcomes

Study	Aims	Design	N sessions (frequency) format	Components (session length, in minutes)	Measures	Outcomes <sup>a</sup>
Beissner et al. 2017	To investigate the effect of somatosensory stimulation and psychotherapy on pain, anxiety and depression among women with endo	RCT with waitlist control, unblinded	≥ 4 (NR) IN	IPSS (60)	NRS SF-12 HADS STAI	Pain (maximal, global pain) Summary of physical and mental health Anxiety and depression
Colwell 1997	To use music to cue relaxation and redirect attention from pain to improve pain coping and reduce reliance on pain medication	Single-case study	11 (W) IN	S + MUI + PMR + MR + S (60)	VAS McGill PQ PCQ	Pain (daily frequency, severity) Pain subscales Pain
Gonçalves et al. 2017	To compare the effect of participation in a yoga intervention versus control group on outcomes of PPP, QoL and menstrual patterns among women with endo	RCT, unblinded	16 (2 per W) GR	PPR + YB + PPR + R (90)	EHP-30 VAS Menstrual diary	Endometriosis QoL (Core and Supplementary subscales) Pain (daily) Menstrual patterns
Hansen et al. 2016	To evaluate long-term effects of mindfulness intervention on persistent pain and QoL among women with endo and PPP	FU, single-arm observational study	10 (NR) IN/GR	MI + PE + IP (90)	EHP-30 SF-36 5-point pain rating scale WHYMPI	Endometriosis QoL (5 Core, 3 Supplementary subscales) Health-related QoL Rating of changes in pain since original study Pain (subscales 1–4)
Hawkins and Hart 2003	To explore the impact of thermal biofeedback and relaxation training on PPP and dysmenorrhea in women with endo	Multiple-case study	5 (2 per W) IN	SR + PMR + TABF(40)		
Kold et al. 2012	To investigate the effect of a mindfulness intervention on pain, QoL and functional capacity of women with endo and PPP	Single-arm, PPT, FU observational pilot study	10 (NR) IN/GR	MI + PE + IP (90)	EHP-30 SF-36	Endometriosis QoL (5 Core, 3 Supplementary subscales) Health-related QoL
Lorençatto et al. 2007	To evaluate effectiveness of a multi-professional group intervention on pain and depression in women with endo	Two-arm retrospective PPT study	10 (W) GR	TAU + PHYS + CBT + QAD (150)	VAS BDI-II	Pain (daily) Depression
Meissner et al. 2010	To assess effectiveness of combined therapy (SART) on endo-associated symptoms in women with endo	FU on single-arm PPT study	12 (Median) (NR) IN	SART (NR)	Pain diary VAS	N days of pain during menstruation Daily pain
Meissner et al. 2016	To investigate the effect of somatosensory stimulation and psychotherapy on pain, anxiety and depression among women with endo	RCT, unblinded	≥ 4 (NR) IN	IPSS (60)	SF-12 NRS STAI HADS FW-7	Health-related QoL Pain (average, maximum) Anxiety and stress Depression and anxiety Functional wellbeing
Petrelluzzi et al. 2012	To evaluate the effectiveness of mind-body intervention on stress, QoL and PPP in women with endo	Single-arm PPT study	9 (W) GR	CBT + PHYS (150)	VAS SF-36 PSQ	Pain intensity Health-related QoL Perceived stress
Zhao et al. 2012	To investigate the effects of PMR on anxiety, depression and QoL of women with endo	RCT, unblinded	24 (2 per W) GR	PE + PMR (40)	STAI HADS-D	Anxiety, stress Depression

**Table 2** (continued)

Treatment	Aims	Design	N sessions (frequency) format	Components (session length, in minutes)	Measures	Outcomes <sup>a</sup>
					SF-36	Health-related QoL

*Endo* endometriosis, *SART* systemic autoregulation therapy (a combination of traditional Chinese medicine and hypnotherapy), *RCT* randomised control trial, *FU* follow-up, *PPT* pre- and post-test, *IN* individual format, *NR* not reported, *MIS* minimally invasive surgery, *MED* medical management,  $\pm$  *PP* with or without Pain Program, *IPSS* individual psychotherapy with somatosensory stimulation, *W* weekly, *S* Somatron (Vibro acoustic reclining chair), *MUJ* music imagery, *PMR* progressive muscle relaxation, *MR* music rehearsal, *GR* group format, *PPR* physical and psychological relaxation, *YB* yoga and breathing, *R* reflection, *MI* mindfulness, *V* visualisation, *PE* psychoeducation, *IP* individual psychotherapy, *SR* scripted relaxation, *TABF* thermal and audio biofeedback, *TAU* treatment as usual, *CBT* cognitive behaviour therapy, *PHYS* physiotherapy exercises, *QAD* question and answer session with doctor, *SART* systemic autoregulation therapy (a combination of traditional Chinese medicine and hypnotherapy), *EHP-30* Endometriosis Health Profile 30-item scale, *NRS* Numerical Rating Scale, *PHQ-9* Patient Health Questionnaire 9-item scale, *GAD-7* Generalised Anxiety Disorder 7-item scale, *SF-12* Short-Form Health Survey 12-item scale, *HADS* Hospital Anxiety and Depression Scale, *STAI* State-Trait Anxiety Inventory, *VAS* Visual Analogue Scale, *McGill PQ* McGill Pain Questionnaire, *PCQ* Pain Coping Questionnaire, *SF-36* 36-item Short Form Survey, *WHYMPI* West Haven-Yale Multidimensional Pain Inventory, *BDI* Beck Depression Inventory, *FW-7* functional wellbeing 7-item scale, *PSQ* Perceived Stress Questionnaire, *CPP* chronic pelvic pain, *QoL* quality of life

<sup>a</sup> Outcomes codes: *EHP-30* Core subscales: Pain, Control and powerlessness, Social support, Emotional wellbeing, Self-image. *EHP-30* Supplementary modules: Work, Relationships with children, Sexual relationships, Feelings about medical profession, Feelings about treatment, Feelings about infertility; *McGill PQ*: sensory, affective, evaluative, miscellaneous; *Pain rating index*: Present pain index; *PCQ*: self-management, helplessness, social support, medical remedies; *SF-36* subscales: Role physical, Role emotional, Bodily pain, Social functioning, Physical functioning, Mental health, General health, Vitality (energy/fatigue); *WHYMPI*: Pain severity, Interference, Life control, Affective distress

The funds are intended to support research that focuses on the early detection and diagnosis of endometriosis, and by supporting women with more effective treatments. As highlighted in the current review, high-quality psychological interventions may expand treatment options to more fully address the psychological and pain-related sequelae of endometriosis, as well as the impacts of disease burden on quality of life of affected women.

### Recommendations for psychological interventions for endometriosis-related symptoms

In view of the current findings, numerous recommendations are made as guidelines for psychological practice. It is suggested that practitioners conduct a comprehensive assessment that is based on a biopsychosociocultural conceptualization of endometriosis. It is also important that assessment takes into account the variability in symptoms experienced by women with endometriosis. A useful guide to a cognitive behavioural approach to assessment is provided by Weijenborg et al. (2009). Furthermore, it is recommended that measures such as the visual analogue scale (VAS) and the Endometriosis Health Profile (EHP-30) be used in initial assessment (Bourdel et al. 2015), with the Pain catastrophising questionnaire (PCS) and Pain Coping Questionnaire (PCQ) incorporated to assess the impact of persistent pelvic pain on coping and catastrophising.

Consistent with evidence-based psychological interventions reported in articles of ‘moderate’ quality, it is suggested that appropriate interventions for endometriosis-related pain and psychological distress may include elements of cognitive behaviour therapy (CBT), acceptance and commitment therapy (ACT) and Mindfulness-Based Stress Reduction (MBSR) either alone or in combination. Although the findings reported in the articles of ‘moderate’ quality are promising, further well-designed research is recommended to establish the efficacy of these therapeutic modalities in regard to endometriosis-related symptoms.

Given the findings that women diagnosed with endometriosis experience lower quality of life than their endometriosis-free peers, psychological interventions with the potential to improve quality of life are important. As MBSR interventions of ‘mixed’ quality have been associated with improvements in quality of life within a persistent pain population, further clarification of their effectiveness for women diagnosed with endometriosis is clearly warranted.

Given the high prevalence of persistent pain experienced by women diagnosed with endometriosis, a psychological treatment package that incorporates a pain management component is essential. Although the current review did not reveal a sound presentation of a CBT intervention for endometriosis, research investigating the use of CBT for other forms of persistent pain is promising. Glombiewski et al. (2010) reported

	Beissner, et al., 2017	Colwell, 1997	Gonçalves et al., 2017	Hansen, et al., 2016	Hawkins & Hart, 2003	Kold, et al., 2012	Lorençatto, et al., 2007	Meissner, et al., 2010	Meissner, et al., 2016	Petrelluzzi, et al., 2012	Zhao, et al., 2012
<b>SF-12</b>	✓								✓		
<b>SF-36</b>											
Role Physical				✓		✓				✓	✓
Role Emotional				✓		✓				✓	✓
Bodily Pain				✓		✓				✓	✓
Social Functioning				✓		✓				✓	✓
Physical Functioning				✓		✓				✓	✓
Mental Health				✓		✓				✓	✓
General Health				✓		✓				✓	✓
Vitality (energy/fatigue)				✓		✓				✓	✓
<b>EHP-30 (Core)</b>											
Pain			✓	✓		✓					
Control and powerlessness			✓	✓		✓					
Social Support			✓	✓		✓					
Emotional-wellbeing			✓	✓		✓					
Self-image			✓	✓		✓					
<b>EHP-30 (Supp)</b>											
Work			✓	✓		✓					
Relationships with children		✓	✓	✓		✓					
Sexual relationship			✓	✓		✓					
Feelings about medical profession			✓			✓					
Feelings about treatment			✓			✓					
Feelings about infertility			✓			✓					
VAS - Pain intensity or severity			✓							✓	
VAS - daily pain			✓					✓			
NRS - average pain level	✓								✓		
NRS - maximum pain level	✓								✓		
Pain duration (days) during menstruation								✓			
<b>CPP severity</b>											
Physician/emergency room visits											
McGill Pain Questionnaire		✓			✓						
5-point pain rating scale				✓							
<b>WHYMPI</b>											
PSQ											
PSI										✓	
<b>PHQ-9</b>											
GAD-7											
STAI	✓								✓		✓
PCS											
BDI							✓				
HADS- A	✓								✓		
HADS- D	✓								✓		✓

**Fig. 2** Variability in outcomes and domains of included studies

	Selection Bias	Allocation Bias	Confounders	Blinding	Data Collection	Attrition Bias	Statistical Analysis	Integrity of Intervention	Contamination
Beissner, et al., 2017	Yellow	Yellow	Yellow	Red	Yellow	Yellow	Green	Yellow	Red
Colwell, 1997	Green	Red	Red	Red	Yellow	NA	Red	Yellow	Yellow
Gonçalves, et al., 2017	Yellow	Green	Yellow	Red	Green	Red	Green	Yellow	Yellow
Hansen, et al., 2016	Yellow	Red	Green	Red	Green	Green	Red	Green	Green
Hawkins & Hart, 2003	Green	Red	Red	Red	Yellow	Red	Red	Yellow	Red
Kold, et al., 2012	Red	Red	Red	Green	Yellow	Green	Yellow	Green	Green
Lorençatto, et al., 2007	Yellow	Green	Yellow	Red	Yellow	Yellow	Green	Yellow	Green
Meissner, et al., 2010	Yellow	Red	Red	Yellow	Red	Green	Red	Red	Green
Meissner, et al., 2016	Green	Green	Yellow	Red	Green	Yellow	Green	Yellow	Yellow
Petrelluzzi, et al., 2012	Yellow	Red	Red	Red	Green	Green	Yellow	Green	Yellow
Zhao, et al., 2012	Yellow	Green	Yellow	Red	Green	Green	Yellow	Green	Green

**Fig. 3** Quality and risk of bias assessment for the nine criteria. Key: ‘strong’ quality and ‘low’ risk of bias, color green; ‘moderate’ quality and ‘moderate’ risk of bias, color yellow; ‘low’ quality and ‘high’ risk of bias, color red. Overall ratings: Studies achieving seven or more ‘strong’

criteria were classified as ‘strong’ overall; studies achieving five or six ‘strong’ criteria were classified as ‘moderate’ overall; studies achieving four or less ‘strong’ criteria were classified as ‘weak’ overall

that CBT was more effective in reducing pain intensity in comparison with small combined effect sizes found for all other psychological interventions. In another meta-analysis on a range of persistent pain conditions (excluding headache), CBT was associated with improved mood and pain catastrophising at post-treatment in comparison to a treatment-as-usual control group, with small and moderate size effects reported, respectively ( $d = -0.38$ , and  $d = -0.53$ ; Williams et al. 2012).

Further consideration of PMR for endometriosis-related pain is warranted based on the effectiveness of PMR in reducing psychological distress and pain intensity with ‘moderate’ quality evidence in the current review. Within a persistent pain population, Gay et al. (2002) conducted a randomised controlled trial comparing the effects of PMR, hypnosis and usual care on pain outcomes. In comparison to the control group, hypnosis was associated with the largest treatment gains ( $d = 1.34$ ) and was more effective than PMR in reducing pain ( $d = 0.59$ ), but PMR was more effective in reducing pain than usual care, with large effect sizes reported ( $d = 0.76$ ). As PMR and hypnosis interventions of ‘moderate’ quality have been found to be effective in pain reduction in other forms of persistent pain, it is suggested that research protocols are developed to test the effectiveness of PMR and hypnosis in a sample of women with endometriosis.

As discussed, CBT has been associated with improved mood, improved pain coping, reduced pain catastrophisation, reduced fatigue and improved pain intensity. PMR has been reported as reducing pain, and MBSR has been reported as improving quality of life by increasing pain acceptance. The decision to adopt one or other treatment modality would be based on the presentation of the individual and clinician’s familiarity and experience with the intervention. Choice of

treatment modality may also be guided by the clinical presentation and type of endometriosis-related symptoms experienced by the client. For example, incorporating elements of ACT may be appropriate where the experience of endometriosis-related symptoms is associated with aspects of loss or grief (e.g. infertility) or for increasing acceptance of pain and engagement in value-directed decision making (e.g. McCracken et al. 2004). A definitive decision to adopt a CBT versus ACT approach to managing the endometriosis symptoms is not easily answered as ACT has its roots in CBT (McCracken and Vowles 2004), and the two modalities, while having some differences also share a number of commonalities (e.g. behavioural avoidance versus experiential avoidance). A selection of evidence-based techniques informed by the clinical case conceptualisation rather than the overarching therapeutic modality may be warranted.

**Limitations and recommendation for further research**

The current review was limited by a search strategy that was broader than required, evident in the 15,814 results identified via database searching returning only 11 studies meeting inclusion criteria. The reason for a broad search strategy was to ensure that studies were not missed; however, this outcome may have been achieved with a search string that was less comprehensive. A second limitation relates to the overall finding of ‘low’ quality of evidence and moderate-to-high risk of bias in the existing literature. Although consistent with the broader persistent pain literature, this suggests that the development of future research protocols with high levels of Intervention Integrity and appropriately funded randomised controlled trials to test them are an essential next step for researchers.

**Table 3** Results and limitations of studies

Study	Outcome <sup>a</sup>	Results	Limitations
Beissner et al. 2017	NRS (Pain) Maximal global 0.8 Average global 1.18	SF-12 Physical health sum 1.11 Mental health sum 0.57	Limited detail regarding psychological treatment components reducing replicability. Wide variability in N treatment sessions. Waitlist control rather than matched control group. Participants lost to attrition were not included as an intention-to-treat analysis Single-case study. PCS less comprehensive than other QoL measures, no measure of psychological outcomes
Colwell 1997	McGill PQ § Pain rating index -23 Present Pain index -20 EHP-30 Pain -1.043 Control -1.22 Emotional wellbeing -0.27 Self-image -0.08 Work -0.64 Treatment -0.55 SF-36 Social functioning 0.56	PCS § Self-management -50 Helplessness -40 Social Support -33 Medical remedies -33	Small sample size. Women in the treatment group had attended significantly more years of schooling, and a smaller number of cases were working, compared to the control group (13 vs. 50%). No follow-up data
Gonçalves et al. 2017		Groups improved across QOL domains. Treatment group experienced moderate to large improvements in pain, control, powerlessness, work, feelings towards treatment	
Hansen et al. 2016		The significant gains at 12-month FU reported in the original study were sustained at 6-year FU, and social functioning improved. Nine out of 10 original participants continued to use techniques learned in the original intervention	No control group, small sample size. Study conducted within a tertiary referral centre, limiting generalisability of results
Hawkins and Hart 2003	WHYMPI IDR	Reported 4 out of 5 participants able to successfully warm their hands, and significant individual improvements in pain-related interference in different areas of their lives. Gains were reported as sustained during return to baseline phase	Small sample size, no control group. Diverse results across participants make quantifying results difficult
Kold et al. 2012	SF-36 Role physical 1.11 Bodily pain 1.79 Physical health composite 2.43	EHP-30 Pain -1.68 Control and powerlessness -1.43 Emotional wellbeing -1.01 Work life -1.46 BDI Depression -0.57	Small sample size, no control group. Study conducted within a tertiary referral centre, limiting generalisability of results
Lorençatto et al. 2007	VAS Daily Pain -0.54	A significant moderate effect reported as reduction in pain and depression for the intervention group. Pain and depression positively correlated for both groups	Variability in group size may bias per session. Elements of psychological intervention described briefly, but limited protocol detail. Intervention data was retrospective, but control group data was prospectively recorded. Baseline differences in depression and

**Table 3** (continued)

Study	Outcome <sup>a</sup>	Results	Limitations
Meissner et al. 2010	VAS Daily Pain IDR Pain duration N days during menstruation IDR	Significant reduction in median pain severity and pain duration. Decreases in VAS pain scores were larger in participants with longer treatment durations	pain between groups, with the control group reporting less pain and depression SART not a recognised evidence-based therapy, hypnotherapy component not consistent with evidence base. Retrospective study design. No post-test assessment carried out. Wide variability in time to follow-up. Outcomes were pain related, not psychological Use of waitlist control rather than TAU creates difficulty for evaluating treatment. Variability in number of treatment sessions. Treatment components according to individual requirements. Limited detail provided for psychological treatment protocol beyond treatment components, limiting replicability No control group, small sample size
Meissner et al. 2016	NRS (Pain) Maximal global 0.8 Average global 1.18 Maximal pelvic 0.55 Maximal dyschezia 1.10 Maximal dyspareunia 0.61	SF-12 Physical health sum 1.11 Mental health sum 0.57	
Perrelluzzi et al. 2012	SF-36 Vitality 0.41 Physical Functioning 0.34	FW-7 Functional wellbeing 0.85	Effect of intervention reported as a reduction in pain, and improved physical health and depression. When intervention was delivered to waitlist control, results were of a similar magnitude across groups. Results stable at 24-month follow-up when groups were combined Intervention reported as significantly improving energy and daily functioning, and reducing perceived stress. Small but non-significant reduction in pelvic pain from moderate to mild Both groups QoL significantly improved over time. Intervention group experienced significant improvements in anxiety, depression and QoL
Zhao et al. 2012	STAI State anxiety 1.38 Trait anxiety 1.49	HADS-D Depression 0.91	Reasons for participant attrition not reported. Control group did not receive 'sham' group intervention. Study excluded patients with a family history of mental illness, or current mental illness
		HADS Depression 1.19 Anxiety 0.68	
		STAI Anxiety, stress 0.68	
		SF-36 QOL overall 0.89 Physical function 0.82 Role physical 0.59 Bodily pain 0.88 General Health 0.84 Vitality 0.84 Social function 0.51 Role emotional 0.98 Mental health 0.88	

Only significant pre-post changes reported. Effect sizes for Cohen's *d* calculated using the Campbell Collaboration Effect Size Calculator (Wilson n.d.), and reported as small = 0.2, medium = 0.5 and large = 0.8

IDR insufficient data reported to calculate effect size

<sup>a</sup> Outcome codes: § = percentage of change pre-post-test

Overall, well-controlled studies investigating psychological interventions that include PMR, CBT and MBSR interventions have been highlighted in the current review as requiring further research with an adequate sample size and reported power calculation, as well as clear protocols to allow studies to be replicated. In particular, as the presence of persistent pain and psychological distress experienced by women with endometriosis is consistent, regardless of individual diagnostic or demographic variations (e.g. Cano-García et al. 2017; Nnoaham et al. 2011; Riazzi et al. 2014), it is further suggested that multiple-component studies that replicate the intervention delivered in the study of Cano-García and colleagues (Cano-García et al. 2017) are carried out.

Furthermore, a psychological intervention that specifically targets pain-related cognitions and pain catastrophising is also justified (Chiantera et al. 2017). This suggestion is based on the finding that pain catastrophising is a 'strong' predictor of persistent pelvic pain at 1-year post medical and/or surgical treatment follow-up (e.g. Allaire et al. 2018), and that pain-related cognitions and pain catastrophising have been found to predict pain coping, both pre- and post-operatively (Carey et al. 2014). Given the number of diagnostic and treatment-based surgeries women with endometriosis undergo, a treatment program that results in realistic beliefs regarding treating or surgical outcomes is warranted.

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