

ARTICLE



The use of home remedies and complementary health approaches in endometriosis



BIOGRAPHY

Alexandra Sabrina Kohl Schwartz works as a Research Fellow at the University Hospital in Zurich and as a Consultant in Reproductive Medicine at the Women's University Hospital in Berne, Switzerland. Her main interests are endometriosis, implantation failure and long-term consequences of children conceived after reproductive treatment.

Alexandra Sabrina Kohl Schwartz^{1,2}, Elvira Gross¹, Kirsten Geraedts¹, Martina Rauchfuss³, Monika Maria Wölfler⁴, Felix Häberlin⁵, Stephanie von Orelli⁶, Markus Eberhard⁷, Patrick Imesch⁸, Bruno Imthurn¹, Brigitte Leeners^{1,*}

KEY MESSAGE

Many endometriosis-affected women use complementary health approaches or home remedies to relieve pain as they suffer from adverse effects of hormonal therapy and/or recurring pain and/or are unsatisfied with standard healthcare. Hence, to better meet the needs of patients, we recommend addressing individual treatment options in clinical practice.

ABSTRACT

Research question: Conventional treatments are often associated with adverse effects and endometriosis pain symptoms may reoccur despite treatment. Consequently, many women use complementary health approaches (CHA) and home remedies (HR) to relieve their pain. The aim of this study was to examine the frequency and the subjectively perceived efficacy of CHA/HR use by women affected by endometriosis.

Design: Retrospective evaluation using medical charts and a questionnaire. Women recruited in hospitals and in self-help groups were asked about the use of 'topical heat', 'repose/relaxation', 'movement/massages', 'homeopathy/phytotherapy', 'acupuncture/traditional Chinese medicine (TCM)' and 'kinesiology/physiotherapy'.

Results: From a total of 574 women with a confirmed diagnosis of endometriosis, 359 (62.5%) applied some form of CHA/HR. Women suffering from fatiguing disease symptoms more often selected alternative therapies (odds ratio [OR] 3.14, 95% confidence interval [CI] 1.39–7.11, $P = 0.006$) compared with women without these characteristics. Furthermore, women dissatisfied with healthcare provided by their treating physician, more frequently (OR 2.30, 95% CI 1.19–4.45, $P = 0.013$) chose the aforementioned alternative strategies.

Conclusion: As conventional therapies may not be sufficiently effective, women's needs should be closely examined, and individual treatment options should be discussed and initiated by clinicians to provide the best comprehensive treatment possible for endometriosis.

¹ University Hospital Zürich, Department of Reproductive Endocrinology, Zürich 8910, Switzerland

² University Women's Hospital, Division of Gynecological Endocrinology and Reproductive Medicine, Bern 3010, Switzerland

³ Charité Berlin, University Hospital, Department of Psychosomatics, Berlin 10117, Germany

⁴ University Hospital Graz, Department of Gynecology and Obstetrics, Graz 8036, Austria

⁵ Canton Hospital St. Gallen, Department of Gynecology and Obstetrics, St. Gallen 9007, Switzerland

⁶ Triemli Hospital Zürich, Department of Gynecology and Obstetrics, Zürich 8036, Switzerland

⁷ Canton Hospital Schaffhausen, Department of Gynecology and Obstetrics, Schaffhausen 8208, Switzerland

⁸ University Hospital Zürich, Department of Gynecology, Zürich 8910, Switzerland

KEYWORDS

Acupuncture/TCM
Complementary health approaches
Endometriosis
Home remedies
Topical heat

INTRODUCTION

Endometriosis is a benign gynaecological disease affecting 6–10% of women of reproductive age (Dunselman *et al.*, 2014; Giudice *et al.*, 2004; Guo, 2009), characterized by the growth of endometrial-like tissue outside the uterine cavity (Kennedy *et al.*, 2005; Kong *et al.*, 2014). The most common clinical symptoms are chronic pelvic pain, dysmenorrhoea, dyspareunia, irregular bleeding, reduced fertility and chronic fatigue (Bulun, 2009; Haemmerli *et al.*, 2018; Hansen *et al.*, 2014; Kohl Schwartz *et al.*, 2017; Leeners *et al.*, 2018; Ramin-Wright *et al.*, 2018). Pain symptoms and severity correlate poorly with lesion characteristics, while the physiology of nociception and pain syndromes is not yet fully understood (As-Sanie *et al.*, 2012; Stratton *et al.*, 2011). It is assumed that somatic mechanisms interact with psychological factors and are further modified by individual differences in pain perception (Brawn *et al.*, 2014; Leeners *et al.*, 2007; Liebermann *et al.*, 2018). Non-steroidal anti-inflammatory drugs (NSAID) are often applied as first-line analgesics (Allen *et al.*, 2009; Roshni *et al.*, 2012).

Standard treatment includes surgical excision and ablation of endometriosis lesions, which often leads to pain relief, but this may be only temporary in some cases. Approximately 25% of women undergo additional surgery within 4 years and about 50–60% report symptom recurrence at 5–7 years after surgery (Falcone *et al.*, 2008; Fedele *et al.*, 2008; Kavoussi *et al.*, 2016). Also, pregnancy is not a reliable way to manage the symptoms and reduce the progression of endometriosis (Leeners *et al.*, 2018). To account for this, various pharmacological approaches, particularly hormonal treatments such as combined oral contraceptives, progestin, progestogens (Fedele *et al.*, 2008; Vercellini *et al.*, 1999), gonadotrophin-releasing hormone (GnRH) agonists (Ling, 1999) and in selected cases aromatase inhibitors (Bulun, 2009) are applied to suppress disease recurrence. Typically, hormonal treatments exert their effect by inhibiting oestrogen production through follicular growth and by decreasing myometrial activity (Kennedy *et al.*, 2005; Roshni *et al.*, 2012; Soares *et al.*, 2012).

Persistence of pain is observed in many women either due to remodelling pain perception in the central nervous system (Bulun, 2009; Stratton *et al.*, 2011) or because of incomplete lesion removal (Abbott *et al.*, 2003; Vercellini *et al.*, 2009). Quiescent lesions (eventually neurologically inactive) are observed with the use of GnRH agonists, progestin or progestogens and can explain pain recurrence after the termination of medical treatment (Nisolle-Pochet *et al.*, 1988).

Medical options have improved recently and allow control of the disease in many women worldwide (Dunselman *et al.*, 2014). However, a recent systematic review showed that in other women the efficacy of medical treatment in endometriosis provides only limited or intermittent benefit from adjuvant hormonal treatment (Becker *et al.*, 2017). In addition to their limited efficacy, the aforementioned therapeutic strategies have further disadvantages, such as impairing the reproductive function of the pituitary–gonadal axis (Soares *et al.*, 2012). Further adverse effects include nausea, rare androgenic side-effects (such as acne or alopecia), weight gain and the risk of thrombosis in combined oral contraceptives (Dunselman *et al.*, 2014; Roshni *et al.*, 2012). Furthermore, GnRH agonists may induce a loss of bone density and worsen metabolic parameters including the lipid profile (Soares *et al.*, 2012). As disease symptoms may severely affect women's quality of life (Taylor *et al.*, 2012), while short-term as well as especially long-term therapeutic effects of currently available strategies are somewhat limited, dissatisfaction with only hormonal and/or surgical treatment is rising among patients (Roshni *et al.*, 2012). Taking this into consideration, women with endometriosis often search for further treatment options such as complementary health approaches (CHA), the term preferred by the National Centre for Complementary and Integrative Health (NCCIH), and home remedies (HR) to improve their physical as well as psychological well-being. Complementary health approaches and home remedies include, for example, the application of topical heat, repose, relaxation, movement, massage, kinesiology, physiotherapy, homeopathy, phytotherapy, acupuncture and traditional Chinese medicine (TCM).

Gaining control over the situation and actively participating in the treatment against their disease also motivates women with endometriosis to seek additional treatment options (Fisher *et al.*, 2016a). CHA/HR represent easy and low-risk procedures, providing potential relief of endometriosis-related symptoms (Akin *et al.*, 2001; Roshni *et al.*, 2012). Despite its widespread use for minor ailments in the general population and potential benefits for pelvic pain symptoms (Chao *et al.*, 2015), little is known about the use of complementary health approaches among women with endometriosis and needs further research. An Australian longitudinal cross-sectional survey (Fisher *et al.*, 2016b) reported a higher use of 'vitamins/minerals', 'yoga/meditation' or 'acupuncture/TCM' in women with endometriosis compared with non-sufferers. However, the prevalence of endometriosis in this study was low (3.7%) and the diagnosis based on questionnaire information only.

The aim of this study was to investigate (i) the prevalence of CHA/HR use and (ii) the subjectively perceived efficacy of those treatments, as well as (iii) to define factors that influence the use of such therapies and (iv) to consider whether dissatisfaction with conventional treatment/treating physicians is associated with the use of CHA/HR.

MATERIALS AND METHODS

The study was designed as a multicentre cross-sectional study investigating the quality of life in women with endometriosis in Switzerland, Germany and Austria. The study was registered at ClinicalTrials.gov under NCT 02511626. The present analysis focuses on the use of complementary health approaches and home remedies in endometriosis. Women with a surgically and histologically confirmed diagnosis of endometriosis were investigated for different quality of life factors. The STROBE criteria were used to draft the manuscript (Von Elm *et al.*, 2007). The local ethics committee (Cantonal Ethics Committee Zürich, Switzerland, KEK_StV-Nr. 05/2008) approved the study. All women included in this analysis signed an informed consent, including the permission to collect data from medical charts for confirmation of diagnosis. The study was conducted according to the Declaration of Helsinki.

Recruitment

Women aged 18 to 59 years were eligible for recruitment between 2010 and 2016 in hospitals and associated private practices in Switzerland (including the University Hospital Zürich, Triemli Hospital Zürich, and district hospitals in Baden, Schaffhausen, Solothurn, St. Gallen, Winterthur and Walenstadt), Germany (Charité Berlin, Vivantes Humboldt Hospital Berlin, Albertinen Hospital Hamburg, University Hospital Aachen) and Austria (University Hospital Graz), summarized as the 'hospital group'. In addition, patients were recruited with the help of endometriosis self-help groups, summarized as the 'self-help group', in order to reduce selection bias and gain an insight into this specific subgroup of women diagnosed with endometriosis. The self-help groups were contacted via the German Endometriosis Society (www.endometriose-vereinigung.de), an organization in charge of coordination and support of all local self-help groups within Germany.

Patients having undergone surgery who were diagnosed with endometriosis and fulfilling inclusion criteria were invited to participate either by direct contact between study participants and healthcare professionals, e.g. during follow-up visits or by a letter. Inclusion criteria were exclusion of current pregnancy and ability to complete the questionnaire based on language and reason. After signed informed consent was given, surgical and histological reports from any treating clinic were collected for study participants including women recruited in self-help groups. Stage classification was carried out according to the revised American Society for Reproductive Medicine score (rASRM I–IV) ([Schenken et al., 1997](#)).

Based on the surgical reports, time interval since the initial diagnosis (in months) and number of endometriosis-related surgical interventions (1, 2, 3–4, 5–6, ≥7), were assessed by the study team. Data sets for questionnaires included in the statistical analysis had to contain at least 80% of answers for primary and secondary outcome measures, as defined below.

For the total 'quality of life in endometriosis' project women with endometriosis were compared with a control group without endometriosis. To detect a 10% difference between women

with and women without endometriosis an alpha of 0.05, a power of 0.8 and a sample size between 387 and 510 matched pairs was needed for the different aspects investigated. The focus of the present evaluation was the use of CHA/HR in women diagnosed with endometriosis. Therefore, all women with confirmed diagnosis fulfilling inclusion criteria ($n = 607$) irrespective of the presence of a control matching partner were included in this analysis.

Definitions

As suggested by the NCCIH, CHA/HR were defined as healthcare approaches developed outside of conventional Western medicine: 'repose/relaxation', 'movement/massages', 'homeopathy/phytotherapy', 'acupuncture/TCM' or 'kinesiology/physiotherapy'. 'Topical heat', being a home remedy, was classified separately. Special food/diets, nutritional supplements and vitamins were not evaluated. Infertility was defined as unsuccessfully trying to conceive through regular unprotected intercourse for at least 1 year before inclusion in the study. Hormonal therapies included systemic (combined oral contraceptives [COC], progestin, GnRH analogue) and local progestogen through levonorgestrel–intrauterine devices (LNG–IUD).

Outcome measures

All outcome measures were discriminated for both the hospital group and the self-help group, respectively. Primary outcome measures were frequency and perceived effectiveness of the use of CHA/HR to treat endometriosis-associated symptoms. Secondary outcome measures were the association between use of CHA/HR and confounders such as duration of disease, stage of disease, disease symptoms, e.g. chronic pain, fatigue and infertility, as well as satisfaction with conventional healthcare provided by physicians.

Questionnaire

A questionnaire was designed in German that focused on endometriosis in general: topics included questions on surgical and hormonal therapies as well as the use of CHA/HR. Chronic pain was investigated with a modified version of the validated standard questionnaires such as the Brief Pain Inventory ([Tan et al., 2004](#)) and Pain Disability Index ([Gronblad et al., 1993](#); [Tait et al., 1990](#)).

Questions related to socio-epidemiological data included age of

the participating women, nationality (Swiss/German/Austrian/others), level of education (low: no formal education, lower school education/medium: higher school education, apprenticeship/high: university degree), and duration of disease in months. Further questions investigated disease symptoms like dysmenorrhoea (never/not currently/yes currently), chronic pain (no/yes) and infertility for more than 1 year (no/yes). Regarding conventional therapies, women had to state whether they received/currently receive any hormonal therapy (systemic or LNG–IUD: no/yes), the type of prescribed treatment (progestin, COC, IUD, GnRH analogues), therapeutic effects (for each one: no/yes/not applicable) and use of analgesics (no/yes/not applicable). Further questions related to a woman's satisfaction with healthcare provided by physicians (no/yes), whether physicians were open-minded about CHA/HR (1 = 'not at all' to 7 = 'yes, absolutely') and whether women felt well supported regarding their pain issues (1 = 'not at all' to 7 = 'yes, absolutely'). Additional questions addressed the use of the different CHA/HR (investigated in categories 'topical heat', 'repose/relaxation', 'movement/massages', 'homeopathy/phytotherapy', 'acupuncture/TCM' and 'kinesiology/physiotherapy' (for each one: no/yes/not applicable). When making statements about the use of those modalities, the marked option 'not applicable' was defined as 'no'. Furthermore, eight questions focused on the therapeutic effects of CHA/HR (for each approach investigated: no/yes/not applicable) on endometriosis symptoms.

Only women with chronic pain issues were additionally asked the following questions: whether pain is endometriosis-related (no/yes), general duration of chronic pain (<3 years, 3–10 years, >10 years), location of the most intense chronic pain (lower gastrointestinal system, anus, vagina, others), whether it is menstrual cycle-dependent (no/yes) and presence of fatigue (no/yes).

The presence (yes/no) of co-occurring diseases (depression, arthritis and joint pain, bowel diseases, asthma, diabetes, malignancies, kidney diseases and cardiac diseases) was also assessed in the questionnaire. Included were all co-occurring diseases with a prevalence of ≥1% in the study population, regardless of whether or not they were

known comorbidities of endometriosis (depression, bowel diseases).

The use of CHA/HR was controlled for the effects of recruitment (self-help group versus hospital-recruited group), satisfaction with physician, chronic pain, fatigue, endometriosis stage (I/II versus III/IV), and duration of disease (time since diagnosis).

Women recruited in self-help groups were evaluated separately to adjust for specific motivations for participation in self-help groups, which might also influence the results, i.e. higher burden resulting from endometriosis-associated symptoms as well as higher dissatisfaction with standard treatment.

Statistics

Statistical analysis was performed using STATA statistical software Version 14 (Stata Corporation, College Station, TX, USA). To compare descriptive data from the hospital group and the self-help group, independent-sample t-tests for continuous data and chi-squared tests for categorical data were used. Binary logistic regression evaluated additional factors influencing the likelihood of CHA/HR use. The level of significance was $P < 0.05$.

RESULTS

Out of 847 invited women with endometriosis, 748 (88.3%) agreed to participate and 654 (77.2%) returned a completed questionnaire, 607 (92.8%) of which were sufficiently complete (>80%) with regard to the data evaluated in the present study. A further 14 questionnaires had to be excluded due to lack of consent to collect information from the medical charts and 19 because of inaccessibility of surgical reports, leaving 574 (67.8%) women with surgically and histologically confirmed endometriosis for the present evaluation. Overall, 88.3% (507/574) of participants were recruited in hospitals and associated private practices in Switzerland, Germany and Austria, and 11.7% (67/574) through endometriosis self-help groups.

Socio-epidemiological factors and characteristics of endometriosis are summarized in [TABLE 1](#). Participants enrolled through self-help groups ($n = 67$) were significantly older ($P = 0.005$), had a higher level of education ($P = 0.004$), a more advanced

stage of disease ($P = 0.049$), a longer time interval since initial diagnosis ($P < 0.005$) and more endometriosis-related surgical interventions ($P = 0.005$) than participants enrolled through hospitals ($n = 507$). Women recruited in the hospital reported significantly ($P = 0.001$) fewer co-occurring chronic diseases (32.5% [165/507]) than women from the self-help groups (52.2% [35/67]). In the hospital group, 12.6% (64/507) and in the self-help group, 26.9% (18/67; $P = 0.018$), stated they suffered from depression. Bowel diseases affected 8.3% (42/507) and 19.4% (13/67; $P = 0.021$), respectively.

Pain

Chronic pain was indicated by 56.8% ($n = 326$) of women. For 81.9% (267/326) of these women, chronic pain was perceived to be endometriosis-related. Overall, 88.7% (289/326) of the women reported pain in the lower abdomen/pelvis. Additional pain locations were the vagina in 32.2% (105/326) and the anal region in 45.4% (148/326). In 53.7% (175/326) of the study participants, pain occurred predominantly monthly, beginning with the onset of menstrual bleeding. Women in self-help groups suffered significantly more often from chronic pain (85.1% versus 53.1%, $P < 0.001$) and fatigue syndrome (76.1% versus 47.1%, $P < 0.001$) than women in the hospital-recruited group.

Conventional pain management

[TABLE 2](#) provides a summary of conventional hormonal treatments. Overall, 75.1% of women received post-operative hormonal therapy. The rate of progestin (40.8%), COC (40.6%) and GnRH analogue use (35.7%) were similar, but a positive therapeutic effect was perceived by only 39.7% (progestins) to 45.1% (COC) of women. Women recruited through self-help groups received hormonal therapies significantly more often (91.0% versus 73.0%, $P = 0.004$), but women recruited in hospitals rated them as significantly more effective (41.1–46.2%, $P < 0.001$, depending on the kind of hormone) than women recruited through the self-help groups (32.4–39.5%, $P < 0.001$). Analgesics were used more (55.2% versus 41.6%, $P = 0.019$) and perceived more effective (83.8% versus 67.3%, $P < 0.001$) by women recruited in self-help groups compared with the hospital group.

Primary outcome measures

From a total of 574 women with a confirmed diagnosis of endometriosis, 359 (62.5%) applied some form of CHA/HR. Prevalence and perceived therapeutic effect of CHA/HR as pain management are shown in [TABLE 3](#). Out of all CHA/HR listed, therapies with 'topical heat', followed by 'repose', were selected most frequently by all participants (48.6% and 43.0%, respectively). 'Homeopathy/phytotherapy', 'acupuncture/TCM' and 'movement/massage' were selected by approximately one-quarter of all participants. Women recruited through self-help groups made significantly more often use of acupuncture/TCM (35.8% versus 21.1%, $P = 0.022$), homeopathy/phytotherapy (40.3% versus 20.5%, $P = 0.001$), topical heat (68.7% versus 46.0%, $P = 0.002$) and repose (70.2% versus 39.5%, $P < 0.001$) than those recruited in a hospital setting.

The majority of women from both groups rated the CHA/HR chosen by them as an effective pain treatment. Women in the self-help group rated 'repose' (91.5% versus 65.0%, $P = 0.009$) and 'homeopathy/phytotherapy' (59.3% versus 37.5%, $P = 0.041$) significantly more often as an effective therapy than women in the hospital group.

Secondary outcome measures

[TABLE 4](#) shows the reasons for choosing a particular CHA/HR taking into consideration the different characteristics of endometriosis. When adjusted for other confounders, women recruited through self-help groups did not apply CHA/HR more often than women recruited in hospitals. Fatigue (OR 3.14; 95% CI 1.39–7.11; $P = 0.006$) and dissatisfaction with medical support by physician (OR 2.3; 95% CI 1.19–4.45; $P = 0.013$) were significantly associated with the use of CHA/HR.

Dissatisfaction with conventional treatment

A total of 19.0% (109/574) of women felt well supported by their physician in dealing with endometriosis-associated pain, while 13.8% (79/574) did not at all. Women in the self-help group were significantly more frequently dissatisfied (45.0% versus 20.9%, $P < 0.001$) with the treatment provided by their physicians. 11.0% (63/574) of the total study group reported that their physicians were very open towards the use of CHA/

TABLE 1 DESCRIPTIVE STATISTICS OF STUDY COHORT

		Hospital group (n = 507)	Self-help group (n = 67)	P-value
Age	Mean years (SD)	37.4 (7.2)	42.4 (6.0)	0.005 ^a
Nationality	Swiss	236 (46.6)	–	<0.001 ^b
	German	196 (38.7)	66 (98.5)	
	Austrian	8 (1.6)	–	
	Others	60 (11.8)	1 (1.5)	
	Missing	7 (1.4)		
Educational level ^c	Low	61 (12.0)	11 (16.4)	0.004 ^a
	Medium	216 (42.6)	17 (25.4)	
	High	203 (40.0)	39 (58.2)	
	Missing	27 (5.3)		
Duration of disease	Mean months (SD)	44.5 (75.6)	81.2 (58.3)	<0.001 ^a
rASRM stage	Stage I/II	199 (39.3)	18 (26.9)	0.049 ^b
	Stage III/IV	308 (60.8)	49 (73.1)	
Surgical interventions	1	274 (54.0)	14 (20.9)	0.005 ^b
	2	135 (26.6)	27 (40.3)	
	3–4	43 (8.5)	19 (28.4)	
	5–6	14 (2.8)	5 (7.5)	
	≥7	3 (0.6)	2 (3.0)	
	Missing	38 (7.5)		
Chronic pain	Yes	269 (53.1)	57 (85.1)	<0.001 ^b
Duration of chronic pain	<3 years	60 (9.9)	5 (7.5)	<0.001 ^b
	3–10 years	107 (21.1)	24 (35.8)	
	>10 years	103 (20.3)	27 (40.3)	
	Missing	247 (48.7)	11 (16.4)	
Fatigue	Yes	239 (47.1)	51 (76.1)	<0.001 ^b
Infertility	Yes	216 (42.6)	35 (52.2)	NS
Satisfaction with physician	Yes	228 (45.0)	14 (20.9)	<0.001 ^b

Data are presented as n (%) unless otherwise stated.

NS = non-significant; rASRM = revised American Society of Reproductive Medicine score; SD = standard deviation.

^a t-test.

^b Chi-squared test.

^c Level of education (low: no formal education, lower school education/medium: higher school education, apprenticeship/high: university degree).

HR, whereas 27.2% (156/574) of the women reported the opposite. Women dissatisfied with the treatment provided by their physicians used 'topical heat' (OR 2.40; 95% CI 1.35–4.28), 'repose/relaxation' (OR 2.16; 95% CI 1.25–3.75) and 'movement/massage' (OR 1.98; 95% CI 1.11–3.54) significantly more often. There was no difference for use of 'homeopathy/phytotherapy', 'acupuncture/TCM' and 'kinesiology/physiotherapy' between women dissatisfied and satisfied with their physicians' treatment (TABLE 4).

DISCUSSION

This is a large cross-sectional study focusing on the use of CHA/HR in

women with endometriosis. The association between endometriosis-related symptoms and the use of CHA/HR was examined with detailed questions on perceived symptoms and evaluation of various confounders. This is the first study to provide a comprehensive overview of the use of CHA/HR by endometriosis-affected women to relieve pain as they suffer from the adverse effects of hormonal therapy and/or recurring pain or are unsatisfied with standard healthcare.

Although hormonal treatment showed a beneficial effect for many participants in this study, more than half of the women recruited in hospitals and even more women recruited through self-help

groups did not rate hormonal treatment as satisfying in terms of pain reduction. This is in line with the results from a recent systemic review (Becker et al., 2017) regarding hormonal treatment for endometriosis. Women reported no or little alleviation of pain severity after hormonal treatment: 11% after danazol (Barbieri et al., 1982), up to 20% after GnRH analogues (Agarwal et al., 1997) and 3–24% after progestin use (Harrison et al., 2000; Strowitzki et al., 2010). When asked about treatment satisfaction, COC users were dissatisfied in 28% and 50% had persistent pain despite COC use (Vercellini et al., 2010), while among progestin users 27% were dissatisfied and 34% had persistent pain (Vercellini et al., 2016).

TABLE 2 MEDICAL THERAPIES AND PERCEIVED THERAPEUTIC EFFECT

		Study cohort (n = 574)	Hospital group (n = 507)	Self-help group (n = 67)	P-value
Hormonal treatment use	Yes	431 (75.1)	370 (73.0)	61 (91.0)	0.004 ^a
	Missing		40 (7.9)		
Type of hormonal therapy ever used	Progestin	234 (40.8)	197 (38.9)	37 (55.2)	<0.001 ^a
	COC	233 (40.6)	195 (38.5)	38 (56.7)	<0.001 ^a
	LNG-IUD	58 (10.1)	53 (10.5)	5 (7.5)	<0.001 ^a
	GnRH analogue	205 (35.7)	162 (32.0)	43 (64.2)	<0.001 ^a
Therapeutic effect of progestin		93/234 (39.7)	81/197 (41.1)	12/37 (32.4)	<0.001 ^a
Therapeutic effect of COC		105/233 (45.1)	90/195 (46.2)	15/38 (39.5)	<0.001 ^a
Therapeutic effect of IUD		24/58 (41.4)	24/53 (45.3)	–	<0.001 ^a
Therapeutic effect of GnRH analogue		87/205 (42.4)	71/162 (43.8)	16/43 (37.2)	<0.001 ^a
Analgesics use		248 (43.2)	211 (41.6)	37 (55.2)	0.019 ^a
Therapeutic effect of analgesics		173/248 (69.8)	142/211 (67.3)	31/37 (83.8)	<0.001 ^a

Data are presented as n (%) unless otherwise stated.

COC = combined oral contraceptives; GnRH = gonadotrophin-releasing hormone; LNG-IUD = levonorgestrel-intrauterine device.

^a Chi-squared test.

TABLE 3 USE AND THERAPEUTIC EFFECT OF CHA/HR

Use of CHA/HR	Study cohort (n = 574)	Hospital group (n = 507)	Self-help group (n = 67)	P-value
Topical heat	279 (48.6)	233 (46.0); 0.41–0.50	46 (68.7); 0.57–0.79	0.002 ^a
Repose	247 (43.0)	200 (39.5); 0.33–0.46	47 (70.2); 0.57–0.83	<0.001 ^a
Movement/massage	146 (25.4)	130 (25.6); 0.18–0.33	16 (23.9); 0.03–0.45	NS
Homeopathy/phytotherapy	131 (22.8)	104 (20.5); 0.13–0.28	27 (40.3); 0.22–0.59	0.001 ^a
Acupuncture/TCM	131 (22.8)	107 (21.1); 0.13–0.29	24 (35.8); 0.17–0.55	0.022 ^a
Kinesiology/physiotherapy	73 (12.7)	62 (12.2); 0.04–0.20	11 (16.4); –0.05–0.38	NS
Therapeutic effect of CHA/HR				
Topical heat	224 (80.3)	183 (78.5); 0.73–0.84	41 (89.1); 0.80–0.98	NS
Repose	173 (70.0)	130 (65.0); 0.66–0.81	43 (91.5); 0.83–0.99	0.009 ^a
Movement/massage	101 (69.2)	90 (69.2); 0.60–0.79	11 (68.8); 0.41–0.96	NS
Homeopathy/phytotherapy	55 (42.0)	39 (37.5); 0.22–0.53	16 (59.3); 0.35–0.83	0.041 ^a
Acupuncture/TCM	58 (44.3)	44 (41.1); 0.27–0.56	14 (58.3); 0.32–0.84	NS
Kinesiology/physiotherapy	30 (41.1)	23 (37.1); 0.17–0.58	7 (63.6); 0.28–0.99	NS

Data are presented as n (%), and 95% CI unless otherwise stated.

CHA = complementary health approaches; HR = home remedies; NS = non-significant; TCM = traditional Chinese medicine.

^a Chi-squared test.

Just under half of the affected women in this study used additional analgesics and topical heat or repose to alleviate disease symptoms. Around one-quarter of women applied homeopathy/phytotherapy or acupuncture/TCM, with an estimated beneficial effect in about half of the users. As we are the first to report the use of CHA/HR in the context of endometriosis, there are few other data for a direct comparison with our results. In this study, home remedies were used more often than complementary health approaches. This shows that although women actively

seek to reduce disease symptoms, the majority use well-known natural approaches and a smaller percentage tries additional complementary health approaches. Overall, women's assessment of the efficacy of different CHA/HR modalities is positive and rated more effective than standard hormonal therapies.

Specific background factors that might increase the motivation to participate in a self-help group, such as age, duration of the disease, satisfaction with previous treatment and a higher prevalence of

co-occurring chronic diseases, might influence the use of CHA/HR (*Chen and Michalsen, 2017; Drossman et al., 2010; Sukhato et al., 2017*). However, in contrast to our expectations, women recruited in self-help groups did not use CHA/HR particularly often. Therefore, CHA/HR application seems not to be a strategy only in a selected group, which probably experiences a particularly strong burden of endometriosis-related symptoms and co-occurring diseases, but a potential treatment option for about half of the women diagnosed with endometriosis.

TABLE 4 LOGISTIC REGRESSION ANALYSIS OF FACTORS INFLUENCING THE LIKELIHOOD OF THE USE OF ANY AND THE DIFFERENT METHODS OF COMPLEMENTARY HEALTH APPROACHES AND HOME REMEDIES AFTER CORRECTION FOR DIFFERENT DISEASE CHARACTERISTICS: TOPICAL HEAT, REPOSE, MOVEMENT/MASSAGE, HOMEOPATHY/PHYTOTHERAPY, ACUPUNCTURE/TCM, KINESIOLOGY/PHYSIOTHERAPY

	OR (95% CI)	P-value
Use of any method		
Self-help group participants	2.03 (0.65–6.35)	NS
Dissatisfaction with physician	2.30 (1.19–4.45)	0.013
Chronic pain	1.24 (0.35–4.45)	NS
Fatigue	3.14 (1.39–7.11)	0.006
rASRM stage I/II	Ref.	
rASRM stage III/IV	1.56 (0.82–3.00)	NS
Time since diagnosis <2 years	Ref.	
Time since diagnosis 2 to <5 years	1.77 (0.81–3.87)	NS
Time since diagnosis 5 to <10 years	1.48 (0.61–3.62)	NS
Time since diagnosis ≥10 years	1.61 (0.49–5.34)	NS
Topical heat		
Self-help group participants	1.67 (0.71–3.90)	NS
Dissatisfaction with physician	2.40 (1.35–4.28)	0.003
Chronic pain	1.39 (0.38–5.01)	NS
Fatigue	1.61 (0.73–3.58)	NS
rASRM stage I/II	Ref.	
rASRM stage III/IV	0.82 (0.46–1.45)	NS
Time since diagnosis <2 years	Ref.	
Time since diagnosis 2 to <5 years	2.20 (1.11–4.34)	0.023
Time since diagnosis 5 to <10 years	1.14 (0.55–2.34)	NS
Time since diagnosis ≥10 years	3.08 (1.05–9.00)	0.039
Repose/relaxation		
Self-help group participants	2.13 (0.94–4.82)	NS
Dissatisfaction with physician	2.16 (1.25–3.75)	0.006
Chronic pain	0.87 (0.26–2.94)	NS
Fatigue	1.92 (0.87–4.20)	NS
rASRM stage I/II	Ref.	
rASRM stage III/IV	1.34 (0.78–2.30)	NS
Time since diagnosis <2 years	Ref.	
Time since diagnosis 2 to <5 years	0.94 (0.50–1.77)	NS
Time since diagnosis 5 to <10 years	0.90 (0.43–1.86)	NS
Time since diagnosis ≥10 years	1.32 (0.52–3.36)	NS
Movement/massage		
Self-help group participants	0.56 (0.28–1.13)	NS
Dissatisfaction with physician	1.98 (1.11–3.54)	0.021
Chronic pain	0.62 (0.16–2.41)	NS
Fatigue	1.82 (0.74–4.47)	NS
rASRM stage I/II	Ref.	
rASRM stage III/IV	0.91 (0.53–1.58)	NS
Time since diagnosis <2 years	Ref.	
Time since diagnosis 2 to <5 years	2.30 (1.22–4.32)	0.010
Time since diagnosis 5 to <10 years	1.50 (0.73–3.07)	NS
Time since diagnosis ≥10 years	1.65 (0.71–3.82)	NS

(continued on next page)

Table 4 – (continued)

	OR (95% CI)	P-value
Homeopathy/phytotherapy		
Self-help group participants	1.83 (0.92–3.65)	NS
Dissatisfaction with physician	0.94 (0.52–1.69)	NS
Chronic pain	0.42 (0.10–1.65)	NS
Fatigue	2.46 (0.92–6.58)	NS
rASRM stage I/II	Ref.	
rASRM stage III/IV	0.74 (0.42–1.32)	NS
Time since diagnosis <2 years	Ref.	
Time since diagnosis 2 to <5 years	2.32 (1.18–4.55)	0.015
Time since diagnosis 5 to <10 years	4.40 (2.10–9.25)	<0.001
Time since diagnosis ≥10 years	2.76 (1.14–6.67)	0.025
Acupuncture/TCM		
Self-help group participants	1.15 (0.58–2.29)	NS
Dissatisfaction with physician	1.18 (0.65–2.12)	NS
Chronic pain	1.81 (0.34–9.50)	NS
Fatigue	1.60 (0.63–4.08)	NS
rASRM stage I/II	Ref.	
rASRM stage III/IV	0.80 (0.45–1.40)	NS
Time since diagnosis <2 years	Ref.	
Time since diagnosis 2 to <5 years	2.15 (1.09–4.23)	0.027
Time since diagnosis 5 to <10 years	3.76 (1.80–7.83)	<0.001
Time since diagnosis ≥10 years	2.71 (1.15–6.39)	0.023
Kinesiology/physiotherapy		
Self-help group participants	0.83 (0.36–1.93)	NS
Dissatisfaction with physician	1.50 (0.73–3.08)	NS
Chronic pain	0.81 (0.15–4.44)	NS
Fatigue	1.19 (0.41–3.50)	NS
rASRM stage I/II	Ref.	
rASRM stage III/IV	0.90 (0.46–1.75)	NS
Time since diagnosis <2 years	Ref.	
Time since diagnosis 2 to <5 years	1.38 (0.60–3.19)	NS
Time since diagnosis 5 to <10 years	2.76 (1.20–6.38)	0.017
Time since diagnosis ≥10 years	2.55 (0.94–6.90)	NS

CI = confidence interval; NS = non-significant; OR = odds ratio; rASRM = revised American Society of Reproductive Medicine score; TCM = traditional Chinese medicine.

In line with our results is the longitudinal study by *Fisher et al. (2016b)*, where endometriosis-affected women were more likely than non-sufferers to have consulted a massage therapist or acupuncturist and to have used vitamins/minerals, yoga/meditation or Chinese medicines. However, in this study prevalence of endometriosis was very low (3.7%) and diagnosis was based on self-reporting, probably leading to selection of more severe cases and inclusion/exclusion of women not aware of their correct diagnosis. A recent broad meta-

analysis study by *Chen and Michalsen (2017)* comes to the conclusion that the demand for complementary and integrative medicine approaches in the treatment of chronic pain conditions is high (prevalence about 30%) and continuously increasing. Evidence for the effectiveness of various complementary approaches, e.g. physical therapy and acupuncture in chronic pain conditions, was stated. In rheumatoid arthritis, mind-body interventions may improve quality of life and psychological well-being. Most of these interventions

support active self-care and seem to be useful for comprehensive chronic pain management; our findings support that such association is also relevant in the context of endometriosis.

Maximum self-perceived effectiveness ratings (defined as effectiveness, satisfaction or improvement) for complementary health approaches or alternative medicine used to address pain symptoms are reported to reach 79% (*Fisher et al., 2016a; Missmer et al., 2011*). This is also reflected in our findings

for home remedies, movement/massage and analgesic use. However, with estimated effectiveness rates between 41.4% and 80.3% for all alternative strategies combined in this study, this highlights the importance of additional treatment resources for women with endometriosis.

Empirical data on motives and factors influencing the use of complementary health approaches in women are sparse (Fisher et al., 2016b). We are the first to analyse these approaches. Fatigue is an underestimated symptom of endometriosis, even though it affects the majority of women suffering from it (Ramin-Wright et al., 2018). In this study, suffering from fatigue and dissatisfaction with medical care increased the likelihood of using any CHA/HR. Interestingly, women in this study suffering from chronic pain did use CHA/HR more often (OR 1.84) but not significantly more than women without chronic pain. We assume that women suffering from pain were more likely to follow standard treatment, including hormones and analgesics. Taking symptom recurrence and insufficient therapeutic effect of conventional medicine (Kavoussi et al., 2016) into account, the positive correlation between burdensome long-term symptoms such as fatigue and the use of CHA/HR are comprehensible.

In addition, women recruited through self-help groups were more likely to try topical heat, repose, homeopathy/phytotherapy and acupuncture/TCM to treat their endometriosis symptoms than women recruited at hospitals, which might be an effect of a more severe disease and/or higher dissatisfaction with conventional treatment options as well as support provided by healthcare professionals.

In this study, topical heat was the modality applied most often and perceived to be most effective by the affected women. Although a systematic evaluation of the effect of this well-known home remedy on pain reduction and its underlying physiology is missing (Akin et al., 2001), this approach seems to be as effective as NSAID use (Osayande et al., 2014).

Repose has a prevalence of 43.0% in this study and 70.0% of its users consider this approach helpful. The wide

range of repose techniques, ranging from hypnosis, reducing physical and mental activity to specific meditation techniques (Fisher et al., 2016a; Leong, 2014; Teixeira, 2008) precludes a direct comparison. However, several studies have confirmed a positive effect of relaxation techniques for different chronic pain conditions (La Cour et al., 2015; Teixeira, 2008) and also for chronic pelvic pain (Fox et al., 2011).

Between 1.4 and 61.0% of women use massages to alleviate dysmenorrhoea and premenstrual syndrome (PMS) (Fisher et al., 2016a). In our study, one-quarter of study participants used massage or physical therapies for endometriosis-related symptoms and the majority (69.2%) rated them as beneficial. Lower abdomen and back massages with essential oils may increase blood circulation, reduce spasms and consequently lead to pain reduction (Hur et al., 2012; Roshni et al., 2012). Other approaches, such as yoga or body therapies, may improve spinal flexibility and strengthen the pelvic floor, consequently reducing pelvic pain (Rakhshaei, 2011; Roshni et al., 2012). Known risks of movement therapies are low, however manual interventions should be performed by a specialized therapist, to avoid a misapplication (Yin et al., 2014).

Reported prevalence rates for the use of homeopathy range from 0.9% to 14.0% (Fisher et al., 2016a). Taking into account that in our study homeopathy also includes women using phytotherapy, this compares well with our results. Although clinical studies on herbs show promising effects, evidence of a therapeutic effect of these strategies are lacking (Wieser et al., 2007). In our cohort, estimated efficacy of homeopathy/phytotherapy was lower than that attributed to 'topical heat' or 'repose'.

In TCM, disruption of the flow of vital energy qi is attributed to causing disease and pain. The sensory stimulation through needles, e.g. acupuncture, is applied to unblock energy channels and provide cure for an associated disease (Lund et al., 2016). TCM has been proposed to modify hormonal parameters, cure endometriosis, pelvic inflammatory disease, relieve mental stress and regulate the immune system (Xia et al., 2017). In TCM, endometriosis is thought to result from a perturbed

energy regulation (Rubi-Klein et al., 2010; Wieser et al., 2007). In addition, medical herbs and other botanicals are used to reduce inflammation and pain (Kong et al., 2014). Prevalence rates for the use of acupuncture in endometriosis range between 0.1 and 31.0% and those of TCM around 28.8% (Fisher et al., 2016a), which is in agreement with our results. Our findings of nearly half of the women who reported a beneficial effect of acupuncture/TCM are supported by several other studies, which have also shown a favourable effect of acupuncture in endometriosis-related pain (Highfield et al., 2006; Rubi-Klein et al., 2010; Wayne et al., 2008; Xiang et al., 2002) and in general quality of life (Rubi-Klein et al., 2010; Wayne et al., 2008). A Cochrane review on acupuncture for pain in endometriosis published in 2011 only included one study with defined pain scores and cure rates according to the Guideline for Clinical Research on New Chinese Medicine: dysmenorrhoea scores were lower in the acupuncture group (mean difference -4.81 points, 95% CI -6.25 to -3.37, $P < 0.001$) (Zhu et al., 2011). Although it is still a matter of controversy (Lund et al., 2016; White, 2006), TCM application is relatively safe, with few side-effects such as subcutaneous bleeding and haematomas (2.64%), discomfort (0.78%) and residual pain at insertion points (0.67%) reported in the literature (Furuse et al., 2017).

Herbal medicine, homeopathy and massage are widely used to treat dysmenorrhoea and PMS (Fisher et al., 2016b). The use of homeopathy/phytotherapy and movement/massage is similar to our study. Adverse effects of herbal medicines should be considered when using such substances in endometriosis therapy. The desired anti-angiogenic effect could eventually affect implantation and lower chances of fertility (Laschke et al., 2012).

The feeling of not being taken seriously regarding pain experience and management (Cox et al., 2003; Leeners et al., 2007) is a frequent problem that women diagnosed with endometriosis have to face. While our study rates standard medical practitioners as restrained and uninformed with respect to the use of CHA/HR, other studies report that nearly a third of pain patients cite their physician to be a good source of information on complementary health approaches (Domoney et al.,

2003). As we have no information on the recommendations of healthcare professionals to our study participants, we unfortunately cannot evaluate how such information might have influenced the use of CHA/HR in our study. However, the majority of users of complementary health approaches are self-prescribing and without professional guidance, often using different therapies simultaneously (Fisher et al., 2016b). Gaining control over the situation and actively participating in treatment is known to ameliorate pain conditions (Pellino et al., 1998). Self-rated satisfaction with treatment of pelvic problems increases with a lower rate of conventional medical interventions and a higher use of complementary health approaches (Kuppermann et al., 2007).

We are the first to address the use of CHA/HR in a large number of accurately diagnosed women with endometriosis recruited in different patient settings, such as university care centres, regional hospitals and self-help groups. This diverse distribution of recruiting centres offers a considerably representative sample of the general endometriosis-affected population. As the response rate of 67.7% is very high, selection bias towards either women with particularly strong or particularly weak disease symptoms is unlikely, which is also supported by the distribution of disease stages in this study. While many women diagnosed with endometriosis suffer from severe pain symptoms and a decreased quality of life, others experience fewer pain symptoms and a quality of life similar to that of the general population (Vercellini et al., 2007).

As most studies focus on the presence of disease symptoms, endometriosis-affected women with few symptoms and a satisfactory quality of life are under-represented in most scientific studies conducted at university care centres. Our diverse recruitment strategy is a highly relevant strength, used to reduce selection bias. Our population covers a large variety of women differing in endometriosis stages, duration of disease and symptoms. However, inclusion of only German-speaking, mainly Caucasian women limits the generalizability of our results. An important strength of the study is the verification of diagnosis according to surgery reports as well as histological evaluations and classified according to the rASRM criteria by two

blinded and independent investigators, allowing a reliable classification of endometriosis lesions. Another limitation is the use of a non-standardized questionnaire. Furthermore, apart from reports on endometriosis-related surgery, no other medical records were reviewed. In our study pain occurrence and pain treatment were assessed retrospectively, which could harbour the risk of recall bias, e.g. result in over- as well as under-estimation of pain symptoms and the resulting associations with CHA/HR. Current disease symptoms may influence pain reporting and a lack of earlier treatment effects may be neglected. However, pain symptoms seem to be adequately reported, even when assessed after several months (Brauer et al., 2003).

As we asked for lifetime use of medication, we cannot give any information on time duration or relations between conventional and complementary health approaches. Also, future studies should address each complementary health approach separately.

Our study shows that the majority of women with endometriosis seek additional treatment strategies such as CHA/HR to deal with and/or cure symptoms of the disease, as they seem to provide a better therapeutic effect than hormonal therapies. Home remedies are used more frequently than specific complementary health approaches and are rated as particularly effective. Persisting disease symptoms after conventional therapies and dissatisfaction with medical support seemed to be key factors when deciding to use CHA/HR. Therefore, women's needs should be carefully investigated within medical counselling and women should be offered a more active role in developing adequate individual treatment strategies. Consequently, the aim should be pain reduction, better quality of life and an increased treatment satisfaction in women with endometriosis.

ACKNOWLEDGEMENTS

We would like to thank the boards of the various self-help groups on endometriosis for their support in developing the questionnaire, as well as for the recruitment of study participants. Furthermore, we would like to thank Vera Mitter and Burkhardt

Seifert for the statistical consulting and Jarmila Zdanowicz for language editing of the manuscript. The authors thank Theodosia Charpidou, Brigitte Alvera, Lina Sperschneider, Anna Dietlicher, Franka Grischott, Nicole Kuenzle, Judith Kurmann, Christina Liebermann, Sarah Schaerer, Elena Lupi and Franziska Graf for their assistance in data collection.

REFERENCES

- Abbott, J.A., Hawe, J., Clayton, R.D., Garry, R. **The effects and effectiveness of laparoscopic excision of endometriosis: a prospective study with 2-5 year follow-up.** Hum. Reprod. 2003; 18: 1922-1927
- Agarwal, S.K., Hamrang, C., Henzl, M.R., Judd, H.L. **Nafarelin versus leuprolide acetate depot for endometriosis. Changes in bone mineral density and vasomotor symptoms.** Nafarelin Study Group. J. Reprod. Med. 1997; 42: 413-423
- Akin, M.D., Weingand, K.W., Hengehold, D.A., Goodale, M.B., Hinkle, R.T., Smith, R.P. **Continuous low-level topical heat in the treatment of dysmenorrhoea.** Obstetrics and Gynecology. 2001; 97: 343-349
- Allen, C., Hopewell, S., Prentice, A., Gregory, D. **Nonsteroidal anti-inflammatory drugs for pain in women with endometriosis.** Cochrane Database of Systematic Reviews. 2009
- As-Sanie, S., Harris, R.E., Napadow, V., Kim, J., Neshewat, G., Kairys, A., Williams, D., Clauw, D.J., Schmidt-Wilcke, T. **Changes in regional gray matter volume in women with chronic pelvic pain: A voxel-based morphometry study.** Pain. 2012; 153: 1006-1014
- Barbieri, R.L., Evans, S., Kistner, R.W. **Danazol in the treatment of endometriosis: analysis of 100 cases with a 4-year follow-up.** Fertil. Steril. 1982; 37: 737-746
- Becker, C.M., Gattrell, W.T., Gude, K., Singh, S.S. **Reevaluating response and failure of medical treatment of endometriosis: a systemic review.** Fertil. Steril. 2017; 108: 125-136
- Brawn, J., Morotti, M., Zondervan, K.T., Becker, C.M., Vincent, K. **Central changes associated with chronic pelvic pain and endometriosis.** Human Reproduction Update. 2014; 20: 737-747
- Brauer, C., Thomsen, J.F., Loft, I.P., Mikkelsen, S. **Can we rely on retrospective pain assessments?.** Am. J. Epidemiol. 2003; 157: 552-557
- Bulun, S.E. **Endometriosis.** New England Journal of Medicine. 2009; 360: 268-279
- Chao, M.T., Abercrombie, P.D., Nakagawa, S., Gregorich, S.E., Learman, L.A., Kuppermann, M. **Prevalence and use of complementary health approaches among women with chronic pelvic pain in a prospective cohort study.** Pain. Med. 2015; 16: 328-340
- Chen, L., Michalsen, A. **Management of chronic pain using complementary and integrative medicine.** BMJ. 2017; 357: j1284
- Cox, H., Henderson, L., Wood, R., Cagliarini, G. **Learning to take charge: Women's experiences of living with endometriosis.** Complementary Therapies in Nursing and Midwifery. 2003; 9: 62-68
- Domoney, C.L., Vashisht, A., Studd, J.W.W. **Use of complementary therapies by women attending a specialist premenstrual syndrome clinic.** Gynecological Endocrinology. 2003; 17: 13-18
- Drossman, D.A., Camilleri, M., Mayer, E.A., Whitehead, W.E. **AGA technical review on irritable bowel syndrome.** Gastroenterology. 2002; 6: 2108-2131
- Dunselman, G.A., Vermeulen, N., Becker, C., Calhaz-Jorge, C., D'Hooghe, T., De Bie, B., Heikinheimo, O., Horne, A.W., Kiesel, L., Nap, A., Prentice, A., Saridogan, E., Soriano, D., Nelen, W. **European Society of Human Reproduction and Embryology. ESHRE guideline: Management of women with endometriosis.** Human Reproduction. 2014; 29: 400-412
- Falcone, T., Shakiba, K., Bena, J.F., McGill, K.M., Minger, J. **Surgical treatment of endometriosis: A 7-year follow-up on the requirement for further surgery.** Obstetrics and Gynecology. 2008; 111: 1285-1292
- Fedele, L., Somigliana, E., Frontino, G., Benaglia, L., Vigano, P. **New drugs in development for the treatment of endometriosis.** Expert Opin. Investig. Drugs. 2008; 17: 1187-1202
- Fisher, C., Sibbritt, D., Hickman, L., Adams, J. **A critical review of complementary and alternative medicine use by women with cyclic perimenstrual pain and discomfort: a focus upon prevalence, patterns and applications of use and users' motivations, information seeking and self-perceived efficacy.** Acta Obstetrica et Gynecologica Scandinavica. 2016a; 95: 861-871
- Fisher, C., Adams, J., Hickman, L., Sibbritt, D. **The use of complementary and alternative medicine by 7427 Australian women with cyclic perimenstrual pain and discomfort: a cross-sectional study.** BMC Complement Altern. Med. 2016b; 16: 129
- Fox, S.D., Flynn, E., Allen, R.H. **Mindfulness meditation for women with chronic pelvic pain: A pilot study.** Journal of Reproductive Medicine. 2011; 56: 158-162
- Furuse, N., Shinbara, H., Uehara, A., Sugawara, M., Yamazaki, T., Hosaka, M., Ymashita, H. **A Multicentre Prospective Survey of Adverse Events Associated with Acupuncture and Moxibustion in Japan.** Medical Acupuncture. 2017; 29: 155-162
- Giudice, L.C., Kao, L.C. **Endometriosis.** Lancet. 2004; 364: 1789-1799
- Gronblad, M., Hupli, M., Wennerstrand, P., Jarvinen, E., Lukinmaa, A., Kouri, J.P., Karaharju, E.O. **Intercorrelation and test-retest reliability of the Pain Disability Index (PDI) and the Oswestry Disability Questionnaire (ODQ) and their correlation with pain intensity in low back pain patients.** Clinical Journal of Pain. 1993; 9: 189-195
- Guo, S.W. **Recurrence of endometriosis and its control.** Human Reproduction Update. 2009; 15: 441-461
- Haemmerli, S., Kohl Schwartz, A.S., Geraedts, K., Imesch, P., Rauchfuss, M., Woelfler, M.M., Haeblerlin, F., von Orelli, S., Eberhard, M., Imthurn, B., Leeners, B. **Does endometriosis affect sexual activity and satisfaction of the male partner? J. Sex Med.** 2018. doi:10.1016/j.jsxm.2018.03.087
- Hansen, K.E., Kesmodel, U.S., Baldrsson, E.B., Kold, M., Forman, A. **Visceral syndrome in endometriosis patients.** European Journal of Obstetrics Gynecology and Reproductive Biology. 2014; 179: 198-203
- Harrison, R.F., Barry-Kinsella, C. **Efficacy of medroxyprogesterone treatment in infertile women with endometriosis: a prospective, randomized, placebo-controlled study.** Fertil. Steril. 2000; 74: 24-30
- Highfield, E.S., Laufer, M.R., Schnyer, R.N., Kerr, C.E., Thomas, P., Wayne, P.M. **Adolescent endometriosis-related pelvic pain treated with acupuncture: Two case reports.** Journal of Alternative and Complementary Medicine. 2006; 12: 317-322
- Hur, M.H., Lee, M.S., Seong, K.Y., Lee, M.K. **Aromatherapy massage on the abdomen for alleviating menstrual pain in high school girls: A preliminary controlled clinical study.** Evidence-based Complementary and Alternative Medicine. 2012; 2012
- Kavoussi, S.K., Lim, C.S., Skinner, B.D., Lebovic, D.I., As-Sanie, S. **New paradigms in the diagnosis and management of endometriosis.** Current Opinion in Obstetrics and Gynecology. 2016; 28: 267-276
- Kennedy, S., Bergqvist, A., Chapron, C., D'Hooghe, T., Dunselman, G., Greb, R., Hummelshoj, L., Prentice, A., Saridogan, E. **ESHRE Special Interest Group for Endometriosis and Endometrium Guideline Development Group. ESHRE guideline for the diagnosis and treatment of endometriosis.** Human Reproduction. 2005; 20: 2698-2704
- Kohl Schwartz, A.S., Woelfler, M., Mitter, V., Rauchfuss, M., Haeblerlin, F., Eberhard, M., von Orelli, S., Imthurn, B., Imesch, P., Fink, D., Leeners, B. **Endometriosis, especially mild disease: a risk factor for miscarriages.** Fertil. Steril. 2017; 108: 806-814
- Kong, S., Zhang, Y.H., Liu, C.F., Tsui, I., Guo, Y., Ai, B.B., Han, F.J. **The complementary and alternative medicine for endometriosis: A review of utilization and mechanism.** Evidence-based Complementary and Alternative Medicine. 2014; 2014
- Kuppermann, M., Learman, L.A., Schembri, M., Gregorich, S., Jacoby, A., Jackson, R.A., Gates, E., Wassel-Fyr, C., Lewis, J., Washington, A.E. **Effect of noncancerous pelvic problems on health-related quality of life and sexual functioning.** Obstetrics and Gynecology. 2007; 110: 633-642
- La Cour, P., Petersen, M. **Effects of Mindfulness Meditation on Chronic Pain: A Randomized Controlled Trial.** Pain Medicine (United States). 2015; 16: 641-652
- Laschke, M.W., Menger, M.D. **Anti-angiogenic treatment strategies for the therapy of endometriosis.** Hum Reprod Update. 2012; 18: 682-702
- Leeners, B., Imthurn, B. **Psychosomatic aspects of endometriosis Current state of scientific knowledge and clinical experience.** Gyn- geburtsliche Rundschau. 2007; 47: 132-139
- Leeners, B., Damaso, F., Ochsenbein-Kölble, N., Farquhar, C. **The effect of pregnancy on endometriosis-facts or fiction? Hum. Reprod. Update.** 2018; in press
- Leong, F.C. **Complementary and alternative medications for chronic pelvic pain.** Obstetrics and Gynecology Clinics of North America. 2014; 41: 503-510
- Liebermann, C., Kohl Schwartz, A.S., Charpidou, T., Geraedts, K., Rauchfuss, M., Woelfler, M.M., von Orelli, S., Haeblerlin, F., Eberhard, M., Imesch, P., Imthurn, B., Leeners, B. **Maltreatment during childhood: a risk factor for the development of endometriosis? Hum. Reprod.** 2018; in press
- Ling, F.W. **Randomized controlled trial of depot leuprolide in patients with chronic pelvic pain and clinically suspected endometriosis. Pelvic Pain Study Group.** Obstet. Gynecol. 1999; 93: 51-58
- Lund, I., Lundeberg, T. **Is acupuncture effective in the treatment of pain in endometriosis? Journal of Pain Research.** 2016; 9: 157-165
- Missmer, S.A., Bove, G.M. **A pilot study of the prevalence of leg pain among women with**

- endometriosis.** *Journal of Bodywork and Movement Therapies.* 2011; 15: 304–308
- Nisolle-Pochet, M., Casanas-Roux, F., Donnez, J. **Histologic study of ovarian endometriosis after hormonal therapy.** *Fertil. Steril.* 1988; 49: 423–426
- Osayande, A.S., Mehulic, S. **Diagnosis and initial management of dysmenorrhoea.** *American Family Physician.* 2014; 89: 341–346
- Pellino, T.A., Ward, S.E. **Perceived control mediates the relationship between pain severity and patient satisfaction.** *J Pain Symptom Manage.* 1998; 15: 110–116
- Rakhshaei, Z. **Effect of Three Yoga Poses (Cobra, Cat and Fish Poses) in Women with Primary Dysmenorrhoea: A Randomized Clinical Trial.** *Journal of Pediatric and Adolescent Gynecology.* 2011; 24: 192–196
- Ramin-Wright, A., Kohl Schwartz, A.S., Geraedts, K., Rauchfuss, M., Woelfler, M.M., Haeblerlin, F., von Orelli, S., Eberhard, M., Imthurn, B., Imesch, P., Fink, D., Leeners, B. **Fatigue – an underestimated symptom in endometriosis.** *Human Reproduction.* 2018; in press.
- Roshni, P., Suneetha Susan Cleave, A., Suresh, P.K. **Complementary and alternative medicine (CAM) therapies for management of pain related to endometriosis.** *International Research Journal of Pharmacy.* 2012; 3: 30–34
- Rubi-Klein, K., Kucera-Sliutz, E., Nissel, H., Bijak, M., Stockenhuber, D., Fink, M., Wolkenstein, E. **Is acupuncture in addition to conventional medicine effective as pain treatment for endometriosis?: A randomized controlled crossover trial.** *European Journal of Obstetrics Gynecology and Reproductive Biology.* 2010; 153: 90–93
- Schenken, R.S., Guzick, D.S. **Revised endometriosis classification: 1996.** *Fertil Steril.* 1997; 67: 815–816
- Soares, S.R., Martinez-Varea, A., Hidalgo-Mora, J.J., Pellicer, A. **Pharmacologic therapies in endometriosis: A systematic review.** *Fertility and Sterility.* 2012; 98: 529–555
- Stratton, P., Berkley, K.J. **Chronic pelvic pain and endometriosis: Translational evidence of the relationship and implications.** *Human Reproduction Update.* 2011; 17: 327–346
- Strowitzki, T., Marr, J., Gerlinger, C., Faustmann, T., Seitz, C. **Dienogest is as effective as leuprolide acetate in treating the painful symptoms of endometriosis: a 24-week, randomized, multicentre, open-label trial.** *Hum. Reprod.* 2010; 25: 633–641
- Sukhato, K., Lotrakul, M., Dellow, A., Ittasakul, P., Thakkinstant, A., Anothaisintawee, T. **Efficacy of home-based non-pharmacological interventions for treating depression: a systematic review and network meta-analysis of randomized controlled trials.** *BMJ Open.* 2017; 7:e014499
- Tait, R.C., Chibnall, J.T., Krause, S. **The Pain Disability Index: Psychometric properties.** *Pain.* 1990; 40: 171–182
- Tan, G., Jensen, M.P., Thornby, J.I., Shanti, B.F. **Validation of the brief pain inventory for chronic nonmalignant pain.** *Journal of Pain.* 2004; 5: 133–137
- Taylor, R.N., Hummelshoj, L., Stratton, P., Vercellini, P. **Pain and endometriosis: aetiology, impact, and therapeutics.** *Middle East Fertility Society Journal.* 2012; 17: 221–225
- Teixeira, M.E. **Meditation as an intervention for chronic pain: an integrative review.** *Holistic nursing practice.* 2008; 22: 225–234
- Vercellini, P., Aimi, G., Panazza, S., De Giorgi, O., Pesole, A., Crosignani, P.G. **A levonorgestrel-releasing intrauterine system for the treatment of dysmenorrhoea associated with endometriosis: a pilot study.** *Fertil. Steril.* 1999; 72: 505–508
- Vercellini, P., Barbara, G., Somigliana, E., Bianchi, S., Abbiati, A., Fedele, L. **Comparison of contraceptive ring and patch for the treatment of symptomatic endometriosis.** *Fertil. Steril.* 2010; 93: 2150–2161
- Vercellini, P., Bracco, B., Mosconi, P., Roberto, A., Alberico, D., Dhrouha, D., Somigliana, E. **Norethindrone acetate or dienogest for the treatment of symptomatic endometriosis: a before and after study.** *Fertil. Steril.* 2016; 105: 734–743
- Vercellini, P., Fedele, L., Aimi, G., Pietropaolo, G., Consonni, D., Crosignani, P.G. **Association between endometriosis stage, lesion type, patient characteristics and severity of pelvic pain symptoms: a multivariate analysis of over 1000 patients.** *Hum. Reprod.* 2007; 22: 266–271
- Vercellini, P., Somigliana, E., Vigano, P., Abbiati, A., Barbara, G., Fedele, L. **Chronic pelvic pain in women: aetiology, pathogenesis and diagnostic approach.** *Gynecol. Endocrinol.* 2009; 25: 149–158
- Von Elm, E., Altman, D.G., Egger, M., Pocock, S.J., Gøtzsche, P.C., Vandenbroucke, J.P. **The Strengthening of Reporting of Observational Studies in Epidemiology (STROBE) Statement: Guidelines for reporting observational studies.** *Bulletin of the World Health Organization.* 2007; 85: 867–872
- Wayne, P.M., Kerr, C.E., Schnyer, R.N., Legedza, A.T.R., Savetsky-German, J., Shields, M.H., Buring, J.E., Davis, R.B., Conboy, L.A., Highfield, E., Parton, B., Thomas, P., Laufer, M.R. **Japanese-Style Acupuncture for Endometriosis-Related Pelvic Pain in Adolescents and Young Women: Results of a Randomized Sham-Controlled Trial.** *Journal of Pediatric and Adolescent Gynecology.* 2008; 21: 247–257
- White, A. **The safety of acupuncture—Evidence from the UK.** *Acupuncture in Medicine* 2006; 24: S53–S57
- Wieser, F., Cohen, M., Gaedert, A., Yu, J., Burks-Wicks, C., Berga, S.L., Taylor, R.N. **Evolution of medical treatment for endometriosis: Back to the roots?** *Human Reproduction Update.* 2007; 13: 487–499
- Xia, J.F., Inagaki, Y., Zhang, J.F., Wang, L., Song, P.P. **Chinese medicine as complementary therapy for female infertility.** *Chinese Journal of Integrative Medicine* 2017; 23: 245–252
- Xiang, D., Situ, Y., Liang, X., Cheng, L., Zhang, G. **Ear acupuncture therapy for 37 cases of dysmenorrhoea due to endometriosis.** *Journal of Traditional Chinese Medicine.* 2002; 22: 282–285
- Yin, P., Gao, N., Wu, J., Litscher, G., Xu, S. **Adverse events of massage therapy in pain-related conditions: a systematic review.** *Evid Based Complement Alternat Med.* 2014:480956
- Zhu, X., Hamilton, K.D., McNicol, E.D. **Acupuncture for pain in endometriosis.** *Cochrane database of systematic reviews (Online).* 2011; 9:CD007864

Received 3 February 2018; received in revised form 17 October 2018; accepted 31 October 2018.