

Selective Serotonin Reuptake Inhibitors									
Author, year	Setting	Design/ approach	Subjects	Intervention	Comparator	Sample size	Outcomes	Quality Assessment ¹	Results
Alpay 2001	Turkey	Prospective cohort study (with randomized design)	Patients with PMDD	50 mg/day sertraline continuously	50mg/day sertraline intermittently	94 patients	Tolerance to medication and response to treatment	Serious risk of bias in 2 domains (deviations from intended interventions and missing data)	71 patients were given sertraline on a continuous basis, and 23 took sertraline intermittently in the luteal phase of the cycle. Because of side effects, 44 of the continuous therapy and 22 of the intermittent therapy group stopped medication. At the end of 6-month follow-up, continuous use of sertraline was found to be significantly more tolerated than intermittent therapy.
Atmaca 2003	Turkey	Randomized, prospective, parallel group trial	Females between 24-45 years of age meeting DSM-IV criteria for PMDD	20-40 mg/day Fluoxetine	20-40 mg/day Vitex agnus castus (AC) extract	41 patients	Penn daily symptom report (DSR), Hamilton depression rating scale (HAM-D), and clinical global impression-severity of illness (CGI-SI)	Unclear risk of bias in 2 domains (allocation concealment and other sources of bias)	At endpoint, using the clinical criterion for improvement, a similar percentage of patients responded to fluoxetine (68.4%, n=13) and AC (57.9%, n=11). There was no statistically significant difference between the groups with respect to the rate of responders. This preliminary study suggests that patients with PMDD respond well to treatment with both fluoxetine and AC. However, fluoxetine was more effective for psychological symptoms while the extract diminished the physical symptoms.

¹ Quality Assessment Definitions

There are 4 main types of references, evaluated using a corresponding quality assessment tool:

- Guidelines: [AGREE-II](#)
 - The overall rating is generated by averaging the scores of all 23 items and will be on a scale of 1-7, with 7 being the highest quality
- Systematic Reviews/Meta-Analyses: [AMSTAR 2](#)
 - An overall rating of quality of the evidence will be rated as **High, Moderate, Low, or Critically Low-Quality Review**, based on 16 domains
- Randomized Control Trials: [Cochrane Collaboration's tool](#)
 - Each of the 7 domains will be rated as **low, high, or unclear risk of bias**, with a brief summary of the findings in the evidence table
- Observational Studies: [ROBINS-I](#)
 - For each of the 7 domains, the risk of bias will be judged as **low, moderate, serious, or critical risk of bias (or no information)**, with a brief summary of the findings in the evidence table

Cohen 2002	USA	Randomized controlled trial	Menstruating women aged 18-45 years	Fluoxetine 20mg or 10mg capsules	Placebo	260 women	PMDD symptoms rated daily using DRSP	High risk of bias in 2 domains (incomplete outcome data and other sources of bias)	Premenstrual daily dosing with fluoxetine effectively treats mood, physical, and social functioning symptoms associated with premenstrual dysphoric disorder. Fluoxetine 20 mg appears to have comparable tolerability with, and better efficacy than, fluoxetine 10 mg.
Cohen 2004	USA	Randomized controlled trial	Females aged 18-45 years meeting DSM-IV criteria for PMDD	Paroxetine CR 12.5 mg or paroxetine CR 25 mg once daily	Placebo	313 patients in ITT analysis	Mean luteal phase VAS-Mood score	Unclear risk of bias in 4 domains (allocation concealment, both blinding domains, and other sources of bias)	At end point, subjects treated with paroxetine CR demonstrated significant improvement in VAS-Mood scores compared with those who received placebo (paroxetine CR 12.5 mg mean treatment difference vs. placebo, 8.7 mm; 95% CI, 15.7, 1.7; p.015; paroxetine CR 25 mg mean treatment difference vs. placebo, 12.1 mm; 95% CI, 18.9, 5.3; p.001). Results were also significant across measures of physical symptoms and social functioning.
Dimmock 2000	Global	Systematic review and meta-analysis	Women with premenstrual syndrome	SSRIs	Placebo	15 RCTs including data on 904 women	Reduction in overall PMS symptoms	High-quality review	The overall standardized mean difference was 1.066 (95% CI 1.381 to 0.750), which corresponds to an odds ratio of 6.91 (3.90 to 12.2) in favor of SSRIs. SSRIs were effective in treating physical and behavioral symptoms. There was no significant difference in symptom reduction between continuous and intermittent dosing or between trials funded by pharmaceutical companies and those independently funded. Withdrawal due to side-effects was 2.5 times more likely in the active-treatment group than in the placebo group.
Eriksson 2008	Sweden	Randomized controlled trial	Women aged 18 or older with PMDD	10 mg/d escitalopram or 20 mg/d escitalopram	Placebo	151 women included in intent-to-treat analysis	Self-assessed severity of PMDD symptoms using VAS	Low risk of bias	Escitalopram was found to exert a marked and a dose-dependent symptom-reducing effect, 20 mg/d being clearly superior to 10 mg/d. Although the primary outcome parameter, that is, the sum of the symptoms of irritability, depressed mood, tension, and affective lability, was decreased by 90% with 20 mg/d escitalopram, the effect of active treatment on breast tenderness, food craving, and lack of energy was more

modest and not significantly different from that of placebo.

Freeman 2009	Pennsylvania, USA	Randomized controlled trial	Patients aged 18-45 years with persistent premenstrual symptoms	Short term sertraline 50 mg/day	Long-term sertraline 50 mg/day	174 patients	Relapse, defined as symptoms returning to the entry criterion level as assessed with daily ratings	High risk of bias in 2 domains (incomplete outcome data and other sources of bias)	The relapse rate was 41% during long-term treatment compared with 60% after short-term sertraline therapy, with a median time to relapse of 8 months vs 4months (hazard ratio, 0.58; 95% confidence interval, 0.34-0.98; P=.04).
Freeman 2004	Pennsylvania, USA	Randomized controlled trial	Patients aged 18-45 years with persistent premenstrual symptoms	Sertraline 50 or 100 mg/day continuously or only during luteal phase	Placebo	167 patients	Daily Symptom Rating Form score and patient global ratings of functioning	High risk of bias in 1 domain (incomplete outcome data); unclear bias in blinding domains	Both sertraline groups improved significantly more than the placebo group as assessed by total premenstrual Daily Symptom Rating Form scores for 3 treatment months. Daily Symptom Rating Form factors that were significantly more improved in the sertraline groups were mood and physical symptoms.
Freeman 2001	Pennsylvania, USA	Randomized controlled trial	Patients aged 18-45 years with PMDD	Venlafaxine 50-200 mg/day	Placebo	164 patients	Total premenstrual symptom scores as assessed by a daily symptom report (DSR) and the Hamilton Rating Scale for Depression	High risk of bias in other sources of bias domain. Unclear risk of bias in 2 domains (allocation concealment and blinding of outcome assessors).	Venlafaxine was significantly more effective than placebo in reducing PMDD symptoms as assessed by DSR scores (P<.001 for last observation carried forward and observed analyses). Sixty percent of venlafaxine versus 35% of placebo subjects improved>50% (P=.003). Forty-three percent of venlafaxine subjects versus 25% of placebo subjects experienced symptom remission, defined as reduction of DSR scores to the postmenstrual level (P=.034).
Freeman 2011	USA	Secondary analysis of 3 clinical trials	Women aged 18-45 years who met criteria for PMS or PMDD	Sertraline at different treatment lengths and dosing schedules	Alprazolam or placebo	447 women from 3 different trials	Symptom scores were calculated from the DSR (10), which lists 17 symptoms that include the 11 PMDD symptoms	Serious risk of bias in 1 domain (selection of participants)	The PMS and premenstrual dysphoric disorder diagnoses improved similarly with sertraline relative to placebo, while symptom-based subtypes had differential responses to treatment. The mixed symptom subtype had the strongest response to sertraline relative to placebo (DSR difference 33.80, 95% CI: 17.16, 50.44, P<0.001), and the physical symptom subtype had the poorest response to sertraline (DSR difference 9.50, 95% CI: -16.29,35.28, P=0.470).
Freeman 2000	USA	Secondary analysis of a	Patients aged 18-45 years experiencing	Sertraline 50 mg/day	Sertraline 100 or 150 mg/day	62 subjects	Premenstrual daily symptoms	High risk of bias in 2 domains (incomplete	Baseline postmenstrual symptom ratings were significantly and independently associated with posttreatment PMS symptoms in

		randomized controlled trial	premenstrual symptoms				scores rated on the DSR	outcome data, and selective outcome reporting); unclear risk of bias in all other domains.	multivariate analysis. Premenstrual and postmenstrual ratings of depression, medical history variables, and demographic variables were not significantly predictive of response to sertraline.
Freeman 2005	USA	Randomized controlled trial	Patients aged 18-45 years meeting DSM-IV criteria for PMDD	Luteal phase dosing of escitalopram 10 mg/day	Symptom-onset dosing of escitalopram 10 mg/day	27 patients	Premenstrual DSR score	High risk of bias in 1 domain (other sources of bias) and unclear risk of bias in 4 domains (sequence generation, allocation concealment, and both blinding domains)	Total premenstrual DSR scores significantly improved from baseline ($p=.003$), with a 57% decrease in the luteal phase group and a 51% decrease in the symptom-onset group. Clinical improvement was reported by 11 of 13 patients in the luteal phase group and 9 or 14 patients in the symptom-onset group.
Halbreich 2002	USA and Canada	Randomized controlled trial	Women aged 24-45 years meeting DSM-IV criteria for PMDD	50-100 mg/day of sertraline	Placebo	281 patients	Daily Record of Severity of Problems and Clinical Global Impression Severity and Improvement scales	High risk of bias in 2 domains (incomplete outcome data and other sources of bias); unclear allocation concealment and blinding	Luteal phase treatment with sertraline was significantly superior to the placebo, as demonstrated by end-point analysis of Clinical Global Impression Improvement scale scores (sertraline, 2.3 +/- 1.1, versus placebo, 2.7 +/- 1.1; $P<.001$), and cycle 3 DRSP change scores (sertraline, 27.6 +/-26.8, versus placebo, 17.6 +/- 23.3; $P<.002$).
Hofmeister 2016 (AAFP)	Global	Guideline	Women with premenstrual disorders	Various interventions such as CBT, CAM therapies, and hormonal and non-hormonal management	Different dosages and regimens for various interventions	Various studies on the efficacy and safety of PMS management options	Safety and efficacy of therapies on PMD symptoms	4.5 out of 7 on the AGREE tool	Selective serotonin reuptake inhibitors may be used as first-line treatment for severe symptoms of PMS and PMDD.
Hunter 2002	London, England	Randomized trial	Women meeting DSM-IV criteria for	Cognitive behavioral therapy (8 hourly-sessions over a 3-month period) or	Combined cognitive behavioral therapy and Fluoxetine	108 participants randomized (60 completed treatment)	Premenstrual score on the COPE diary measure	High risk of bias in 3 domains [blinding (both domains) and	Significant improvement occurred in all three treatment-groups after 6 months' treatment, assessed by the COPE. Fluoxetine was associated with a more rapid improvement. There were no group differences in the

			PMDD; aged 20-45 years	Fluoxetine (20mg daily)				incomplete outcome data]	percentage of DSM cases of PMDD posttreatment, but at follow-up CBT was associated with better maintenance of treatment effects compared with fluoxetine
Ismaili 2016 (ISPMD)	Global	Guideline	Patients with premenstrual disorders	SSRIs, CBT, combined oral contraceptive pill, estrogen, surgical treatment, and GnRH analogues	Placebo, no treatment, other treatments	Various studies on PMD treatments	Safety and efficacy of various therapies on PMD symptoms	4.65 out of 7	When a diagnosis of PMS/PMDD has been successfully made, SSRIs should be considered amongst the first line treatments. When a patient is going to be commenced on SSRI treatment, the common side effects which they may experience such as initial nausea and influence on sexual function should be discussed. Patients who are started on SSRIs should be offered a follow-up appointment face to face or by phone 1 week after treatment has been commenced in order to assess for increased anxiety.
Jackson 2015	North Carolina, USA	Randomized controlled trial	Female patients aged 18-45 years with premenstrual mood and anxiety symptoms and taking SSRI/SSNI	Quetiapine sustained-release (SR)	Placebo	20 women	Hamilton Depression and Anxiety Scales, Clinical Global Impression Scale, and PRISM	High risk of bias in 2 domains (selective outcome reporting and other sources of bias); unclear risk of bias in 4 domains (sequence generation, allocation concealment, and both blinding domains)	Although the study was underpowered, greater reductions in luteal phase mood ratings were observed in the quetiapine group on the 17-item Hamilton Depression Rating Scale, Clinical Global Impression improvement rating, and PRISM daily score. The quetiapine group showed most improvement in symptoms of mood lability, anxiety, and irritability
Jarvis 2008	Global	Systematic review	Patients with premenstrual syndrome or premenstrual dysphoric disorder	Pharmacologic and nonpharmacologic treatment	Placebo, no treatment, one treatment vs. another	Various studies on treatment of PMS/PMDD	Safety and efficacy of treatments	Critically low-quality review	Selective serotonin-reuptake inhibitors (SSRIs) have been proven safe and effective for the treatment of PMDD and are recommended as first-line agents when pharmacotherapy is warranted. Currently fluoxetine, controlled release paroxetine, and sertraline are the only Food and Drug Administration– approved agents for this indication. Anxiolytics, spironolactone, and nonsteroidal anti-

inflammatory drugs can be used as supportive care to relieve symptoms.

Kleinstauben 2012	Global	Systematic review and meta-analysis	Patients aged between 18 and 45 years characterized by moderate to severe PMS or a diagnosis of PMDD or LLPDD	Psychotherapy or psychopharmacotherapy, or a combination of both	Waitlist, no treatment, or placebo	6 studies for psychotherapy; 16 studies for psychotropic drugs	Self- or clinician-rated psychological outcomes – primary outcome of mood or negative affect	Critically low-quality review	Dependent on outcome, 22 included studies obtained small to medium effect sizes for cognitive-behavioral interventions and for serotonergic antidepressants at post-assessment. For both cognitive-behavioral interventions and serotonergic antidepressants, efficacy in treatment of PMS was found not to be satisfactory.
Kornstein 2006	USA	Randomized controlled trial	Women with PMS aged 24-45 years	Sertraline (25 or 50 mg/day)	Placebo	269 patients included in intent-to-treat analysis	Daily Symptom Report (DSR) total score for PMS symptoms	High risk of bias in 2 domains (incomplete outcome data and other sources of bias); unclear risk of bias in 4 domains (sequence generation, allocation concealment, and both blinding domains)	Intermittent luteal-phase dosing with low doses of sertraline produced significant improvement across 2 menstrual cycles, based on total DSR scores, compared with placebo. Continuous and symptom-onset dosing were also effective in treating PMS symptoms, particularly at the lower dose of 25 mg/day.
Kwan 2009	Global	Systematic review	Women with PMS	Drug treatments, hormonal treatments, psych interventions, physical therapy, dietary supplements, and surgical treatments	Placebo	56 systematic reviews, RCTs, or observational studies that met inclusion criteria	Symptom severity assessed by various questionnaires or scales	Low-quality review	Drug treatments can be effective at reducing premenstrual symptoms, but some are associated with significant adverse effects. Good evidence that spironolactone improves mood and somatic symptoms in women with PMS. Alprazolam, metolazone, and NSAIDs may also be effective. Buspirone and gonadorelin analogues seem to improve overall self-rated symptoms. Other treatments such as clomipramine, danazol, and SSRIs may improve psych symptoms but are associated with serious adverse effects.
Landen 2001	Sweden	Randomized controlled trial	Participants between 18- and 45-years old meeting DSM-IV	10-30mg Buspirone or 100-300mg nefazodone; intermittently for cycle 1 and 2,	Placebo	63 patients included in intent-to-treat analysis	PMDD symptoms assessed by VAS	Unclear risk of bias in 5 domains (sequence generation, allocation	With respect to self-rated global improvement, buspirone ($P<0.001$) but not nefazodone was significantly superior to placebo. While buspirone appeared to reduce self-rated irritability (visual analogue scale)

			criteria for PMDD	continuous for cycle 3 and 4				concealment, both blinding domains, and other sources of bias)	more effectively than placebo, other self-rated symptoms did not differ markedly between the groups. The side-effects were mild, and sexual dysfunction was not significantly more common in patients given buspirone or nefazodone than in those given placebo.
Landen 2009	Sweden	Randomized crossover trial	Women aged 18 or older meeting DSM-IV criteria for PMDD	Paroxetine 20 mg/day	Placebo	22 women	Self-rated irritability using VAS	Unclear risk of bias in 3 domains (allocation concealment and both blinding domains)	The paroxetine cycles differed significantly from the placebo cycle as early as 14 h after drug intake with respect to the number of subjects experiencing sustained reduction in irritability. When the different cycles were compared with respect to irritability-rating scores for each time of assessment, the difference was significant at day 3. The side effect nausea had an even more rapid onset (4 h), but usually disappeared within 4 days.
Landen 2007	Sweden	Randomized controlled trial	Women over 18 years of age meeting DSM-IV criteria for PMDD	Paroxetine 10-20 mg/day continuously or during luteal phase	Placebo	167 patients included in ITT analysis	Severity of symptoms using VAS scales each day	Unclear risk of bias in 3 domains (allocation concealment and both blinding domains)	Continuous treatment with paroxetine reduced premenstrual symptoms effectively with a response rate of 85%. The effect size was highest for irritability (1.4) and lowest for lack of energy (0.5). Intermittent treatment was as effective as continuous treatment in reducing irritability, affect lability, and mood swings, but had a somewhat weaker effect on depressed mood and somatic symptoms.
Marjoribanks 2013	Global	Systematic review and meta-analysis	Women of any age with PMS or PMDD	SSRIs at any dose and in any dosing regimen for longer than 1 menstrual cycle	Placebo	31 studies included in review	Self-rated overall premenstrual symptoms measured using a validated prospective screening tool; adverse events	High-quality review	SSRIs reduced overall self-rated symptoms significantly more effectively than placebo. The effect size was moderate when studies reporting end scores were pooled (for moderate dose SSRIs: SMD -0.65, 95% CI -0.46 to -0.84). The effect size was small when studies reporting change scores were pooled (for moderate dose SSRIs: SMD -0.36, 95% CI -0.20 to -0.51).
Miner 2002	Australia, Europe, and Mexico	Randomized controlled trial	Women aged 18-45 years meeting criteria for PMDD	Fluoxetine 90mg given once (LPWDx1) or twice (LPWDx2)	Placebo	247 women included in analysis	Daily Record of Severity of Problems (DRSP)	High risk of bias in 1 domain (other sources of bias); unclear risk of bias in	At the end of the study, the LPWDx2 group had statistically significant improvements in DRSP total scores compared with LPWDx1 and placebo. Findings support the efficacy and tolerability of enteric-coated fluoxetine

				during the luteal phase				3 domains (allocation concealment and both blinding domains)	90mg given during the luteal phase of the menstrual cycle for the treatment of PMDD.
Nevatte 2013 (ISPMD)	Global	Guideline	Patients with premenstrual disorders	SSRIs, and other anti-depressants; benzodiazepine and buspirone	Placebo, no treatment, other treatments	Various studies on alternative therapies	Safety and efficacy of therapies on PMD symptoms	4.1 out of 7	Psychotropic medication such as SSRIs probably acts by dampening the influence of sex steroids on the brain.
Pearlstein 2000	USA	Randomized controlled trial	Women meeting DSM-IV criteria for PMDD	Flexible dosing of sertraline (up to 150mg/day)	Placebo	243 women	DRSP, SAS, and Q-LES-Q measuring psychosocial functioning	High risk of bias in 3 domains (incomplete outcome data, selective outcome reporting, and other sources of bias)	Sertraline was significantly more effective than placebo in improving psychosocial functioning as measured by the SAS, the Q-LES-Q, and the 3 DRSP items of impaired productivity, interference with social activities, and interference with relationship with others.
Pearlstein 2003	USA	Retrospective analysis of 2 clinical trials	Women 18-45 years of age meeting PMDD criteria	Fluoxetine 10-20mg/day during luteal phase (study 1) or fluoxetine enteric-coated 90mg administered either 14 or 7 days before menses, or at both 14 and 7 days before menses (study 2)	Placebo	260 women in study 1; 257 women in study 2.	PMDD symptom recurrence assessed by DRSP, Sheehan disability scale, PTS-C, and CGI-Severity	Moderate risk of bias in 2 domains (missing data and reported results)	Premenstrual dysphoric disorder symptoms significantly increased after fluoxetine discontinuation. The scores did not return to baseline; however, the fluoxetine group was no longer significantly superior to placebo.
RCOG/NICE 2017	Global	Guideline	Women with Premenstrual Disorders (PMS/PMDD)	Various interventions including CBT, CAM therapies, hormonal and nonhormonal medical management, and nutritional supplements	Different dosages and regimens for various interventions	Various studies on the efficacy and safety of PMS management options	Safety and efficacy of therapies on PMD symptoms	5.7 out of 7 on the AGREE tool	SSRIs should be considered one of the first-line pharmaceutical management options in severe PMS. When treating women with PMS, either luteal or continuous dosing with SSRIs can be recommended. SSRIs should be discontinued gradually to avoid withdrawal symptoms, if given on a continuous basis. Women with PMS treated with SSRIs should be warned of the possible adverse effects such as nausea, insomnia, somnolence, fatigue and reduction in libido. Spironolactone can be used in

									women with PMS to treat physical symptoms.
Reilly 2022	Global	Systematic review and meta-analysis	Women with PMDD or PMS diagnosed by prospective ratings of a validated scale	Intermittent dosing of SSRIs	Continuous dosing of SSRIs	8 studies included in SR	Response rate and dropout rate; SMD of symptom ratings	High-quality review	All included studies provided response rates, six provided dropout rates and 5 provided symptom scores. There was no statistically significant differences between intermittent and continuous dosing in terms of response rate (odds ratio: 1.0, 95% CI, 0.23-4.31, $I^2=71\%$), dropout rates (odds ratio 1.26, 95% CI: 0.39-4.09, $I^2=33\%$) or symptom change (standardized mean difference: 0.04, 95% CI: -0.27 to 0.35, $I^2=39\%$). All studies had a moderate or high risk of bias.
Roca 2002	USA	Randomized controlled trial	Patients with PMDD and healthy controls	Serotonin receptor antagonist metergoline (8mg) administered orally	Diphenhydramine (50mg) as active placebo	20 women	Vital signs and mood ratings before, during, and after procedure	Unclear risk of bias in all domains	The patients with premenstrual dysphoric disorder experienced a return of symptoms 24 hours after treatment with metergoline but not diphenhydramine (active placebo). The comparison women experienced no changes in mood.
Shah 2008	Global	Systematic review and meta-analysis	Women of any age who met diagnostic criteria for PMS	SSRI at any dose and any dosing regimen	Placebo	2,964 women from 19 articles	Change in overall premenstrual symptomatology measured by validated severity score	High-quality review	Findings demonstrate that SSRIs are effective for treating PMS and premenstrual dysphoric disorder (OR 0.40, 95% confidence interval [CI] 0.31-0.51). Intermittent dosing regimens were found to be less effective (OR 0.55, 95% CI 0.45-0.68) than continuous dosing regimens (OR 0.28, 95% CI 0.18-0.42). No SSRI was demonstrably better than another.
Steinberg 2012	USA	Open label, unrandomized controlled trial	Women with PMDD	Fluoxetine 20mg/day during luteal phase	No treatment	24 women	Visual analogue scale and premenstrual tension syndrome scale	Moderate risk of bias in 2 domains (confounding and outcome measures)	Hourly VAS scores significantly improved after SRI in irritability as well as sadness, anxiety, and mood swings. Compared with the symptomatic pretreatment baseline, PMTS scores significantly improved on the second day after the start of SRI ($p < .01$). An identical time course of symptom improvement occurred after both SRI and menses-onset.
Steiner 2003	USA and Canada	Randomized controlled trial	Participants aged 18-45 years with 5 or more DSM-III-R symptoms of	Fluoxetine 20 mg/day or 60 mg/day	Placebo	273 women with at least one treatment measure	Premenstrual Tension Scale	High risk of bias in 2 domains (incomplete outcome data and selective	A statistically significant improvement from baseline to the average treatment score for the work capacity subscale was detected for both fluoxetine groups compared to the placebo group. This beneficial

			LLPDD/PMDD					outcome reporting)	response to fluoxetine was evident by the first cycle of treatment.
Steiner 2005	Europe, Canada, USA	Randomized controlled trial	Female patients aged 18-45 years who met criteria for PMDD	Paroxetine CR 25 mg/day or paroxetine CR 12.5 mg/day	Placebo	366 women included in ITT analysis	Daily VAS symptom measure; PMTS-O, CGI-S	Unclear risk of bias in 4 domains (sequence generation, allocation concealment, and both blinding domains)	Patients treated with either dose of paroxetine CR demonstrated significantly greater improvements on the primary efficacy measure (change from baseline in mean luteal phase VAS-Mood scores) and on the majority of secondary efficacy measures compared with patients randomly assigned to placebo.
Steiner 2008	Canada	Randomized controlled trial	Female patients aged 18-45 years meeting DSM-IV criteria for PMDD	Luteal phase treatment of paroxetine 10mg or 20mg	Placebo	99 patients included in ITT population	Percent change from baseline at study endpoint on visual analog scale irritability score	High risk of bias in 1 domain (other sources of bias) and unclear risk of bias in 3 domains (allocation concealment and both blinding domains)	When compared with placebo, patients treated with paroxetine 20 mg attained a significant reduction in irritability (difference in median percent change: -23.9, 95% CI = -51.3 to -6.2, p = .014; difference in mean absolute change: -18.6, 95% CI = -32.5 to -4.6, p = .007). A statistically significant difference was not observed when the patients treated with the lower dose of paroxetine (10 mg) were compared with placebo. Treatment was well tolerated with no unexpected side effects.
Steiner 2001	Canada	Randomized controlled trial	Women with prospectively determined PMDD	Fluoxetine 20 or 60 mg/day	Placebo	320 women	PMDD symptoms evaluated by VAS and self-rated and observer PMTS scales	High risk of bias in 3 domains (incomplete outcome data, selective outcome reporting, and other sources of bias)	Fluoxetine treatment was statistically superior to placebo, with no significant differences between the two fluoxetine dosages in their effects on physical symptoms.
Tamayo 2004	Puerto Rico, USA	Prospective, open, uncontrolled study	Patients aged 18 or over diagnosed with PMDD	Fluoxetine 20 mg daily	N/A	30 patients	Calendar of Premenstrual Experiences (COPE) used to measure efficacy	Moderate risk of bias in 3 domains (confounding, missing data, measurement of outcomes)	According to response parameters established be-forehand in the protocol, 95% of the patients had a reduction higher than 50% at V9 in comparison with the initial COPE score in the luteal phase and a final score of <40 in the same scale.
Yonkers 2006	USA	Randomized controlled trial	Women aged 18-48 years with PMDD	Paroxetine CR 25 mg	Placebo	20 women	Change in the mean luteal-phase DRSP scores from baseline to	Unclear risk of bias in 5 domains (sequence generation, allocation	Daily Record of Severity of Problems scores were lower in the paroxetine group compared with the placebo group, although the differences were not statistically significant. However, the mean on-treatment Inventory of

							cycle 1 and cycle 2	concealment, both blinding domains, and other sources of bias)	Depressive Symptomatology (clinician-rated) score for the paroxetine group was 17.9 ± 8.3 compared with 31.5 ± 11.2 in the placebo group (adjusted mean difference = 13.6, $P = 0.009$).
Yonkers 2015	USA	Randomized controlled trial	Women with PMDD aged 18-40 years	Sertraline hydrochloride 50 to 100 mg/day during symptomatic interval	Placebo	252 participants	Premenstrual Tension Scale score	High risk of bias in 1 domain (incomplete outcome data). Low risk of bias in other domains	The mean (SD) estimated difference in IDS-C scores between baseline (35.4 [10.7] for sertraline; 32.8 [10.4] for placebo) and the end point (15.3 [10.7] for sertraline; 17.8 [11.0] for placebo) favored the sertraline group by 5.14 (95% CI, 1.97-8.31) points ($P =$.02). Compared with the placebo group, those assigned to sertraline showed greater improvement on the total DRSP score (estimated mean difference, 1.09 [95% CI, 0.96-1.25] points; $P = .02$) and Anger/Irritability DRSP subscale score (1.22 [95% CI, 1.05-1.41] points; $P < .01$) and were more likely to respond to treatment (77 of 115 patients [67.0%] for sertraline and 65 of 124 [52.4%] for placebo; $\chi^2_1 = 5.23$; $P = .02$).
Yonkers 2013	USA	Randomized controlled trial	Women aged 18-48 with moderate to severe PMS	Fluoxetine 10mg twice a day or calcium carbonate 600 mg twice a day	Placebo	39 women	Daily ratings of premenstrual symptoms	High risk of bias in 1 domain (incomplete outcome data). Low risk of bias in other domains	Symptom improvement was greatest for the fluoxetine group, although significance was achieved only for the Daily Record of Severity of Problems ($B = -0.28$; 95% confidence interval = -1.70 to -0.35; $P = 0.02$) and the Clinical Global Impression-Improvement ($B =$ -1.03; 95% confidence interval = -1.70 to -0.35; $P = 0.04$). The Cohen d effect sizes for fluoxetine relative to placebo were between 0.80 and 2.08, whereas the effect sizes for calcium were only between 0.10 and 0.4.
Yonkers, Pearlstein 2005	USA	Secondary analysis of 2 clinical trials	Women aged 24-45 years with PMDD	Study 1: continuous dosing of sertraline 50- 150 mg/day	Study 2: intermittent dosing of sertraline 50- 150 mg/day	Study 1: 281 patients; Study 2: 251 patients	Daily Record of Severity of Problems	Moderate risk of bias in 4 domains (confounding, missing data, measurement of outcomes, and reported results)	The baseline (pretreatment) to on- treatment effect sizes were similar for continuous vs. luteal phase dosing on the first day of menses (0.73 vs. 0.89), second day of menses (0.40 vs. 0.55), and third day of menses (0.42 vs. 0.44), respectively. Subjects who abruptly discontinued sertraline had fewer symptoms indicative of withdrawal at Day 3 ($p < 0.01$) and no difference during Days 4–5 compared

to subjects abruptly discontinuing placebo.

Hormonal Medical Management

<i>Author, year</i>	<i>Setting</i>	<i>Design/ approach</i>	<i>Subjects</i>	<i>Intervention</i>	<i>Comparator</i>	<i>Sample size</i>	<i>Outcomes</i>	<i>Quality Assessment</i>	<i>Results</i>
Abraham 2003	Australia	Prospective cohort study	Women aged 18-41 years with regular menstrual cycles	Monophasic and triphasic oral contraceptives	Non-hormonal contraceptives	119 women	Menstrual cycle experiences using daily diaries	Moderate risk of bias in 2 domains (selection of participants and measurement of outcomes)	There were no significant differences between the three groups in cyclic changes for any physical rating, but there were for tiredness or fatigue (non-OC users reported experiencing tiredness or fatigue more frequently than the OC users) and sadness or depression (non-OC users experienced sadness or depression less frequently than OC users during the early part of the cycle, followed by a sharp rise from early premenstrual to the menstrual phase). There were no significant cyclic differences in ratings between the monophasic and triphasic groups.
Borenstein 2003	USA	Open-label cohort survey study	Women using oral contraception	Drospirenone 3mg and ethinyl estradiol 30ug	N/A	858 women	Premenstrual symptoms using Moos Menstrual Distress Questionnaire (MDQ) via survey at baseline and follow up	Serious risk of bias in 1 domain (missing data); moderate risk of bias in 3 domains (confounding, selection, and measurement of outcomes)	Negative affect and water retention domains of MDQ significantly improved from baseline in all phases of the menstrual cycle ($p=.000$). All individual MDQ items improved significantly in the late luteal phase and during menses ($p=.000$), and the majority (76.9%) improved significantly in the remainder of the cycle ($p<.05$).
Coffee 2006	USA	Prospective cohort study	Combination oral contraceptive users between the ages of 18-48	Monophasic OC containing 3mg drospirone and 30ug ethinyl estradiol (DRSP/EE)	N/A	111 patients	Scott and White (S&W) Mood Scale and Penn Daily Symptom Report (DSR17) for premenstrual symptom measurements	Moderate risk of bias in 4 domains (confounding, selection, missing data, and outcome measures)	A 168-day extended regimen of DRSP/EE led to a decrease in premenstrual-type symptoms compared with the 21/7-day regimen.
Comasco 2021	Sweden	Randomized controlled trial	Women 18-46 years of age meeting criteria for PMDD	5mg/day of ulipristal acetate (UPA) for 3 28-day cycles	Placebo for 3 28-day cycles	95 women were randomized (17 of those dropped out)	Change in premenstrual total score on DRSP from baseline to end of treatment	High risk of bias in 1 domain (incomplete outcome data)	The mean improvement in DRSP score after 3 months was 41% (SD=18) in the UPA group, compared with 22% (SD=27) in the placebo group (mean difference -18%; 95% CI=-29, -8).

DeWit 2021	Global	Systematic review and meta-analysis	Premenopausal women with PMS or PMDD	A specific combined oral contraceptive regimen	Another combined oral contraceptive regimen or nonhormonal or hormonal contraceptives or placebo	9 studies included in quantitative synthesis	Depressive symptoms using a validated scale	High-quality review	The pairwise meta-analysis revealed that combined oral contraceptives were more efficacious than placebo in treating overall premenstrual symptomatology (standardized mean difference, 0.41; 95% credible interval, 0.17-0.67), but not premenstrual depressive symptoms specifically (standardized mean difference, 0.22; 95% credible interval, 0.06 to 0.47). However, none of the combined oral contraceptives were more effective than each other in reducing premenstrual depressive symptoms and overall premenstrual symptomatology.
Di Carlo 2001	Naples, Italy	Randomized controlled trial	Patients with PMS, aged 23-29 years	Tibolone 2.5 mg/day + Leuprolide acetate depot 3.75 mg IM	Placebo + Leuprolide acetate depot 3.75mg IM	30 patients	The mean severity of each symptom and sign of PMS was evaluated using a visual analog scale during the last 7 days of each treatment cycle in comparison with the last 7 days of the cycle before treatment	Unclear risk of bias in 4 domains (allocation concealment, both blinding domains, and other sources of bias)	Mean scores for each of the adverse psychological/physical and positive psychological symptoms were significantly improved during treatment. No statistically significant difference was detected between patients treated with tibolone and placebo. A significantly lower number of hot flushes per day was observed in groups treated with GnRH-a and tibolone in comparison with GnRH-a and placebo.
Eisenlohr Moul 2017	North Carolina, USA	Randomized controlled trial	Women with premenstrual dysphoria (PMD), aged 18-40	Continuous DROS/EE 3 mg/20 mcg or intermittently dosed DROS/EE 3 mg/20 mcg	Placebo	55 women	Daily Record of Severity of Problems (DRSP) measurements for PMD symptoms	High risk of bias in 1 domain (incomplete outcome data)	All three groups demonstrated similar, robust reductions in premenstrual symptoms over time. A marked placebo response was observed.
Ford 2012	Global	Systematic review and meta-analysis	Participants of reproductive age diagnosed with PMS	Progesterone	Placebo	2 studies with a total of 280 participants	Changes in severity of luteal phase symptoms	Moderate-quality review	The trials did not show that progesterone is an effective treatment for PMS nor that it is not. Neither trial distinguished a subgroup of women who benefited, nor examined claimed success with high doses.
Halbreich 2012	USA and Canada	Randomized controlled trial	Women with PMDD aged 18-49 years	Levonorgestrel (LNG) 90 mcg/ethinyl estradiol (EE) 20 mcg	Placebo	367 subjects received one or more dose of study medication	PMDD symptoms measured by Daily Record of Severity of	High risk of bias in 1 domain (incomplete outcome data)	Mean DRSP change from baseline to late luteal phase was significantly greater with LNG/EE than placebo at the late luteal phase of the first estimated cycle (-30.52 ± 1.73 [SE] vs. -22.47 ± 1.77 ; $p=0.001$) and the

							Problems (DRSP)		worst 5 days during the last on-therapy estimated cycle (-26.77 ± 1.83 vs. -20.89 ± 1.82 ; $p=.016$). Other primary end points were not statistically significant. Significantly more subject taking LNG/EE (52%) than placebo (40%) responded ($\geq 50\%$ improvement in the DRSP 7-day late luteal phase score and CGI Severity score of ≥ 1 improvement) at last on-therapy cycle ($p=.025$).
Hofmeister 2016 (AAFP)	Global	Guideline	Women with premenstrual disorders	Various interventions such as CBT, CAM therapies, and hormonal and non-hormonal management	Different dosages and regimens for various interventions	Various studies on the efficacy and safety of PMS management options	Safety and efficacy of therapies on PMD symptoms	4.5 out of 7 on the AGREE tool	Oral contraceptives are effective for treatment of PMS and PMDD.
Kwan 2009	Global	Systematic review	Women with PMS	Drug treatments, hormonal treatments, psych interventions, physical therapy, dietary supplements, and surgical treatments	Placebo	56 systematic reviews, RCTs, or observational studies that met inclusion criteria	Symptom severity assessed by various questionnaires or scales	Low-quality review	We don't know whether progesterone is effective in reducing symptoms of PMS. There is some evidence that progesterone-like drugs reduce premenstrual symptoms, but both are associated with several adverse effects. Oral contraceptives containing drospirenone are likely to be effective in reducing symptoms of PMS.
Kwan 2015	USA	Systematic review	Women of reproductive age with PMS	Continuous hormonal treatments	Placebo, no treatment, other treatment	1 SR and 3 RCTs included in review	Premenstrual symptoms and adverse effects	Low-quality review	In this systematic overview, we categorized the efficacy for three interventions based on information relating to the effectiveness and safety of continuous combined oral contraceptives, continuous transdermal estradiol, and continuous subcutaneous estradiol implant.
Leminen 2012	Finland	Secondary analysis of a randomized controlled trial	Women aged 35-49 years	LNG-IUS	Hysterectomy	236 women	Occurrence of premenstrual symptoms evaluated by questionnaires at baseline and at follow up	High risk of bias 1 domain (selective outcome reporting)	Premenstrual symptoms decreased significantly in both groups by six months ($p \leq 0.028$) without significant differences between the groups, except that in the LNG-IUS group the decrease of breast tenderness was seen first by 12 months ($p=0.048$). Even though 42% of the women assigned to treatment with LNG-IUS were hysterectomized during the follow-up period, the results of

									intention-to-treat and actual treatment analyses were comparable.
Lombardi 2004	Italy	Prospective cohort study	Women aged between 18-32 years	Women with PMS	Women without PMS	40 women	Evaluation of cyclic symptoms using Calendar or Premenstrual Experience (COPE); hormonal basal evaluation via blood samples	Moderate risk of bias in 2 domains (confounding and reported results)	In the PMS group, significantly lower allopregnanolone levels were found in the luteal phase, while progesterone was lower in the PMS group in both phases. In the PMS group, higher free testosterone levels were found during the luteal phase and higher DHEA levels in both the follicular and the luteal phases. The present data confirm reduced allopregnanolone levels in the luteal phase in PMS patients, together with higher levels of DHEA and free testosterone.
Lopez 2012	Global	Systematic review	Women of reproductive age with or without previous diagnosis of PMDD or PMS	Oral contraceptive containing drospirenone	Placebo or another combined oral contraceptive	5 trials with a total of 1920 women	Affective and physical premenstrual symptoms recorded prospectively	Moderate-quality review	Drospirenone 3mg plus ethinyl estradiol 20µg may help treat premenstrual symptoms in women with severe symptoms, that is, premenstrual dysphoric disorder. The placebo also had a large effect. We do not know whether the combined oral contraceptive works after three cycles, helps women with less severe symptoms, or is better than other oral contraceptives.
Ma 2023	Global	Systematic review and meta-analysis	Women of reproductive age with PMS or PMDD	Combined oral contraceptives contain drospirenone	Any other COC or placebo	5 studies included in meta-analysis	End scores, or change scores for psychological and somatic premenstrual symptoms, and functional impairment, measured via any validated prospective symptom rating tool	High-quality review	5 RCTs were included; the evidence was very low to moderate quality; the main limitations were serious risk of bias due to poor reporting of study methods, and serious inconsistency and imprecision. COCs containing drospirenone and EE may improve overall premenstrual symptoms (SMD -0.41, 95% CI -0.59 to -0.24); and functional impairment due to premenstrual symptoms in terms of productivity (MD -0.32, 95%CI -0.55 to -0.08), social activities (MD -.029, 95%CI -0.54 to -0.04), and relationships (MD -0.30, 95% CI -0.54 to -0.06). Authors were uncertain of the effect of drospirenone plus EE on premenstrual mood symptoms.
Marr, Heinemann 2011	USA	Secondary analysis of a randomized controlled trial	Women with PMDD aged 18-40 years	EE 20 mcg/ drospirenone 3 mg	Placebo	449 women included in intent-to-treat analysis	DRSP scale completed daily during study	High risk of bias in 2 domains (incomplete outcome data, and other	The decrease in mean scores for all 3 DRSP functional impairment items (work, partnership, and social activities) from baseline to cycle 3 mirrored changes in the total DRSP symptom score; the greatest

								sources of bias)	decreases were observed in cycle 1 with further small reductions through to cycle 3. The proportional mean decreases from baseline to cycle 1 for the 3 functional items ranged from 47% to 48%. For all 3 functional items, the mean reductions from baseline to cycle 1 (but not from cycle 1 to cycles 2 and 3) were significantly greater with EE/drospirenone than with placebo (P<0.05).
Marr, Niknian 2011	USA	Sub analysis of randomized controlled trial	Women with PMDD aged 18-40 years	EE 20 mcg/drospirenone 3 mg	Placebo	449 women included in intent-to-treat analysis	DRSP scale completed daily during study	High risk of bias in 2 domains (incomplete outcome data, and other sources of bias)	Daily Record of Severity of Problems scores for each symptom cluster were significantly reduced from baseline with both EE 20 mcg/drospirenone 3 mg 24/4 and placebo (p<.0001 for all). The greatest symptom improvements were achieved within the first cycle of treatment and continued throughout cycles 2 to 3. The mean between-treatment difference was significant in favor of EE 20 mcg/drospirenone 3 mg 24/4 for all three symptom clusters in all three treatment cycles (p≤.0001vs. placebo in percent change from baseline)
Naheed 2017	Global	Systematic review and meta-analysis	Women of reproductive age with diagnosis of PMS	Non-contraceptive estrogen-containing preparations	Placebo or alternative treatment, or different dosages	5 studies with a total of 258 participants included in meta-analysis	Effectiveness assessed by prospective screening tools; adverse events	High-quality review	This review found very low-quality evidence to suggest that oral unopposed estrogen given in the luteal phase of the menstrual cycle is probably ineffective for controlling the symptoms of PMS and may even make them worse. There was very low-quality evidence to support the effectiveness of continuous estrogen plus progesterone, with a small to moderate effect size.
Nevatte 2013 (ISPMO)	Global	Guideline	Patients with premenstrual disorders	Interventions that suppress ovulation	Placebo, no treatment, other treatments	Various studies on alternative therapies	Safety and efficacy of therapies on PMO symptoms	4.1 out of 7	Oral contraceptives, gonadotropin-releasing hormone agonists, danazol, and estradiol all most likely function by ovulation suppression.
Nguyen 2017	USA	Randomized crossover trial	Women aged 23-48 years	4 weeks of estradiol	4 weeks progesterone	30 women, 15 with PMDD, 15 healthy controls	Liquid chromatography/tandem mass spectrometry measuring steroid metabolites	High risk of bias in 1 domain (selective outcome reporting) and unclear risk of bias in 5 domains	Both groups had significant increases in several steroid metabolites compared with the Lupron alone condition after treatment with E2 (that is, estrone-SO4(q= 0.039 and q= 0.002, respectively) and estradiol-3-SO4(q= 0.166 and q= 0.001, respectively)) and after treatment with P4 (that is, allopregnanolone (q=

								(sequence generation, allocation concealment, blinding, and other sources of bias)	0.001 for both PMDD and controls), pregnanediol (q= 0.077 and q= 0.030, respectively) and cortexone (q= 0.118 and q= 0.157, respectively). Only sulfated steroid metabolites showed significant diagnosis-related differences. During Lupron plus E2 treatment, women with PMDD had a significantly attenuated increase in E2-3-sulfate (q= 0.035) compared with control women, and during Lupron plus P4 treatment a decrease in DHEA-sulfate (q= 0.07) compared with an increase in controls.
Pearlstein 2005	USA	Randomized controlled crossover trial	Women aged 18-40 with PMDD	Drospirenone 3mg + ethinyl estradiol (EE) 30 ug	Placebo	64 women	DRSP scores for measuring symptoms of PMDD	High risk of bias in 2 domains (incomplete outcome data, and other sources of bias)	The mean decrease from baseline for total Daily Record of Severity of Problems (DRSP) scores while using drospirenone/EE was significantly greater than for placebo (-12.47, 95% CI =-18.28, -6.66; p<.001). A positive response (i.e., a score of 1 or 2 in the Clinical Global Impressions-Improvement scale) occurred in 61.7% and 31.8% of subjects while taking drospirenone/EE and placebo, respectively (p =.009).
RCOG/NICE 2017	Global	Guideline	Women with Premenstrual Disorders (PMS/PMDD)	Various interventions including CBT, CAM therapies, hormonal and nonhormonal medical management, and nutritional supplements	Different dosages and regimens for various interventions	Various studies on the efficacy and safety of PMS management options	Safety and efficacy of therapies on PMD symptoms	5.7 out of 7 on the AGREE tool	When treating women with PMS, drospirenone-containing COCs may represent effective treatment for PMS and should be considered as a first-line pharmaceutical intervention. When treating women with PMS, emerging data suggest use of the contraceptive pill continuously rather than cyclically.
Ross 2003	Australia	Prospective cohort study	Women 18-45 years of age	Oral contraceptive (OC) use	Non-OC use	181 women	Moos Menstrual Distress Questionnaire for 70 days	Serious risk of bias in 2 domains (confounding and missing data); Moderate risk of bias in 2 domains (selection and outcome measures)	OC use did not alter the incidence or severity of premenstrual change. Overall differences in symptom severity, however, were noted, with monophasic OC users reporting higher levels of fluid retention and somatic symptoms than the triphasic OC group.

Sadler 2010	UK	Cross-sectional survey	Women aged 20-34 years	Hormonal contraceptive use	No hormonal contraceptive use	974 women	Premenstrual symptoms identified by diaries and lifestyle factors measured by survey	Serious risk of bias in 1 domain (missing data) and moderate risk of bias in 3 domains (classification, deviations, and outcomes)	No associations were found between premenstrual symptoms and diet, alcohol or strenuous exercise, nor after adjustment for other factors, with age, smoking or body mass index. Use of any form of hormonal contraceptives was associated with a lower prevalence of premenstrual symptoms (prevalence ratio 0.66 (95%CI:0.52 to 0.84).
Schmidt 2017	Maryland, USA	Prospective controlled crossover trial	Women aged 30-50 years meeting criteria for PMDD who experienced symptom remission after 2-3 months of GnRH agonist-induced ovarian suppression (leuprolide)	3 months estradiol/progesterone replacement	1 month of placebo	12 women	Rating for Premenstrual Tension observer and self-ratings completed every 2 weeks during clinical visits	Moderate risk of bias in 3 domains (selection, missing data, and measurement of outcomes)	Both self- and observer-rated scores on the Rating for Premenstrual Tension were significantly increased (more symptomatic) during the first month of combined estradiol/progesterone compared with the last month of leuprolide alone, the placebo month, and the second and third months of estradiol/progesterone.
Segebladh 2009	Sweden	Randomized crossover trial	Women with PMDD between 25 and 47 years of age	Add-back hormone replacement (1.5 mg estradiol and 400 mg progesterone or 0.5 mg estradiol and 400 mg progesterone)	1.5mg estradiol and placebo	27 women included in analysis	Daily symptom ratings for mood and physical symptoms	Low risk of bias	The highest dose of estradiol in combination with progesterone was associated with the most pronounced symptom recurrence, both in comparison with a lower dose of estradiol together with progesterone and estradiol-only treatment.
Sveindottir 2000	Iceland	Prospective cohort study	Women 20-40 years of age	OC users	Non-OC users	83 women included in analysis	Women's Daily Health Diary for assessing menstrual cycle experiences	Moderate risk of bias in 4 domains (confounding, selection, missing data, and outcome measures)	Cyclicity was never displayed by 9.6% of participants; 80.7% displayed expected cyclicity and 72.3% unexpected cyclicity at least once. Cyclicity in somatic symptoms was most often demonstrated by participants. Expected and unexpected cyclicity in summary symptom scores in well-being and in psychoemotional symptoms was very similar among participants. There was not much difference in cyclicity between non OC users and OC users. Fifty-one percent of the participants

									were self-defined with premenstrual syndrome with 2%-6% of them meeting the criteria of premenstrual dysphoric disorder.
Tommaselli 2003	Italy	Prospective randomized study	Women affected by PMS and unaffected controls	Leuprolide acetate 3.75 mg plus tibolone 2.5 mg/day at onset of vasomotor symptoms	Leuprolide acetate 3.75 mg plus placebo at onset of vasomotor symptoms	48 women	Serum leptin, estradiol and progesterone levels, PMS signs and symptoms	High risk of bias in 2 domains (both blinding domains)	No differences in leptin levels among the three groups and within the same group at all time evaluated were observed. Estradiol and progesterone concentrations were significantly lower in all groups during treatment in comparison with pretreatment values.
Wyatt 2001	Global	Systematic review and meta-analysis	Women with premenstrual syndrome	Progesterone or progestogen therapy	Placebo	14 trials included in analysis	Proportion of women whose symptoms showed improvement with progesterone or progestogen therapies	High-quality review	Overall standardized mean difference for all trials that assessed efficacy of progesterone (by both routes of administration) was -0.028 (95% confidence interval -0.017 to -0.040). The odds ratio was 1.05 (1.03 to 1.08) in favor of progesterone, indicating no clinically important difference between progesterone and placebo. For progestogens the overall standardized mean was -0.036 (-0.014 to -0.060), which corresponds to an odds ratio of 1.07 (1.03 to 1.11) showing a statistically, but not clinically, significant improvement for women taking progestogens.
Wyatt 2004	Global	Systematic review and meta-analysis	Patients with a diagnosis of premenstrual syndrome	GnRHa (nasal spray, intravenous, depot)	Placebo	7 RCTs included in analysis	Reduction in overall premenstrual syndrome symptoms	Moderate-quality review	Overall standardized mean difference for all trials that assessed the efficacy of GnRHa was 1.19 (95% confidence interval [CI] 1.88 to 0.51). The equivalent odds ratio was 8.66 (95% CI 2.52 to 30.26) in favor of GnRHa. GnRHa were more efficacious for physical than behavioral symptoms, although the difference was not statistically significant. The addition of hormonal add-back therapy to GnRHa did not appear to reduce the efficacy of GnRHa alone; standardized mean difference 0.12 (95% CI 0.35 to 0.58).
Yonkers, Brown 2005	USA	Randomized controlled trial	Patients aged 18-40 years with diagnosis of PMDD	Drospirenone 3 mg + ethinyl estradiol 20 mcg	Placebo	449 patients included in intent-to-treat analysis	Scores on the total Daily Record of Severity of Problems	High risk of bias in 1 domain (other sources of bias) and unclear risk of bias in 1 domain	Scores on the total Daily Record of Severity of Problems decreased by -37.49 in the drospirenone/ethinyl estradiol group and by -29.99 in the placebo group (adjusted mean difference -7.5, 95% confidence interval [CI] -11.2 to -3.8; P < .001 by rank analysis of covariance).

Yonkers 2017	USA	Prospective cohort study	Women aged between 18- 48 years	Cyclic hormonal contraception (CHC) users	Non-CHC users	742 women included in analysis	Daily Rating of Severity of Problems to catalog daily symptoms	(incomplete outcome data)	Moderate risk of bias in 2 domains (selection and measurement of outcomes)	Both cohorts showed a significant two-way interaction between CHC use and symptom change scores($p<0.01$) and a significant main effect of perimenstrual window ($p<0.0001$). Overall menstrual cycle symptom change was greater for the nonhormonal contraception versus hormonal contraception group. In the Screened Cohort, change scores were greater in the nonhormonal group specifically for depression ($p=0.04$); anger or irritability ($p<0.01$); and physical symptoms ($p<0.01$).
-----------------	-----	-----------------------------	---------------------------------------	---	---------------	--------------------------------------	--	---------------------------------	---	--

Cognitive Behavioral Therapy

<i>Author, year</i>	<i>Setting</i>	<i>Design/ approach</i>	<i>Subjects</i>	<i>Intervention</i>	<i>Comparator</i>	<i>Sample size</i>	<i>Outcomes</i>	<i>Quality Assessment</i>	<i>Results</i>
Basogul 2020	Turkey	Randomized controlled trial	Female students receiving 110 points or more on the PMS scale	Psychoeducation based on a cognitive-behavioral approach for 5 sessions over a 4 week period	Control group (no treatment)	88 participants	Physical, emotional, and behavioral symptoms of PMS using PMS scale	High risk of bias in 2 domains (blinding of participants and personnel, and outcome assessors)	There was a significant difference between the pretest and posttest total mean scores of the intervention group that received psychoeducation ($p<0.05$). There was also a significant difference in depressive thoughts, irritability, and fatigue mean scores between the two groups ($p<0.05$).
Busse 2009	Global	Systematic review and meta-analysis	Women who presented with premenstrual syndrome	Cognitive behavioral therapy, education therapy, or self-monitoring of symptoms	Waitlist, placebo pill, no treatment, symptom monitoring by spouse	9 RCTs (n=at least 435)	Anxiety, behavioral changes, depression, effect on daily living, sexual relations, and water retention and edema	Low-quality review	Evidence from low-quality randomized trials suggested that cognitive behavioral therapy may have beneficial effects in managing symptoms associated with premenstrual syndrome.
Han 2019	Global	Systematic review and meta-analysis	Women of reproductive age experiencing PMS	Psychosocial intervention utilizing cognitive, behavioral, or social mechanisms	Usual care or care without psychosocial intervention	11 studies included in meta-analysis	Measurement of severity of PMS including somatic and psychological symptoms	Low-quality review	Pooled effects of 11 psychosocial interventions (n=324) showed statistically significant beneficial effects on the severity of PMS (SMD -0.29, 95% CI -0.45 to -0.13, $I^2=27\%$). Participants who received coping skills training had significantly low severity of PMS than the control group (SMD -0.53, 95% CI -0.77 to -0.28, $p<.001$, $I^2=3\%$). There were no effects found for education program nor social support intervention.
Hofmeister 2016 (AAFP)	Global	Guideline	Women with premenstrual disorders	Various interventions such as CBT, CAM therapies, and hormonal and non-hormonal management	Different dosages and regimens for various interventions	Various studies on the efficacy and safety of PMS management options	Safety and efficacy of therapies on PMD symptoms	4.5 out of 7 on the AGREE tool	Cognitive behavior therapy may improve PMS and PMDD symptoms.
Hunter 2002	London, England	Randomized trial	Women meeting DSM-IV criteria for PMDD; aged 20-45 years	Cognitive behavioral therapy (8 hourly-sessions over a 3-month period) or	Combined cognitive behavioral therapy and Fluoxetine	108 participants randomized (60 completed treatment)	Premenstrual score on the COPE diary measure	High risk of bias in 3 domains (blinding (both domains) and incomplete outcome data]	Significant improvement occurred in all three treatment-groups after 6 months' treatment, assessed by the COPE. Fluoxetine was associated with a more rapid improvement. There were no group differences in the percentage of DSM cases of PMDD

				Fluoxetine (20 mg daily)					posttreatment, but at follow-up CBT was associated with better maintenance of treatment effects compared with fluoxetine.
Kleinstauber 2012	Global	Systematic review and meta-analysis	Patients aged between 18 and 45 years characterized by moderate to severe PMS or a diagnosis of PMDD or LLPDD	Psychotherapy or psychopharmacotherapy, or a combination of both	Waitlist, no treatment, or placebo	6 studies for psychotherapy; 16 studies for psychotropic drugs	Self- or clinician-rated psychological outcomes – primary outcome of mood or negative affect	Critically low-quality review	Dependent on outcome, 22 included studies obtained small to medium effect sizes for cognitive-behavioral interventions and for serotonergic antidepressants at post-assessment. For both cognitive-behavioral interventions and serotonergic antidepressants, efficacy in treatment of PMS was found not to be satisfactory.
Kwan 2009	Global	Systematic review	Women with PMS	Drug treatments, hormonal treatments, psych interventions, physical therapy, dietary supplements, and surgical treatments	Placebo	56 systematic reviews, RCTs, or observational studies that met inclusion criteria	Symptom severity assessed by various questionnaires or scales	Low-quality review	There is not enough evidence for us to assess the efficacy of CBT in treating psychological symptoms of PMS.
Lustyk 2009	Global	Systematic review	Individuals with PMS or PMDD	Cognitive-behavioral therapy	Pharmacotherapy	7 studies (3 RCTs)	Measurements of PMS/PMDD symptoms	Critically low-quality review	This review revealed a dearth of evidence providing statistically significant CBT intervention effects. Issues such as overall time investment, latency to treatment effects, and complementary and combined therapies are considered.
Nevatte 2013 (ISPMD)	Global	Guideline	Patients with premenstrual disorders	CBT	Placebo, no treatment, other treatments	Various studies on alternative therapies	Safety and efficacy of therapies on PMD symptoms	4.1 out of 7	The strongest evidence for efficacy of non-pharmacological treatments for PMDs exists for calcium, chasteberry and cognitive-behavior therapy.
RCOG/NICE 2017	Global	Guideline	Women with Premenstrual Disorders (PMS/PMDD)	Various interventions including CBT, CAM therapies, hormonal and nonhormonal medical management, and nutritional supplements	Different dosages and regimens for various interventions	Various studies on the efficacy and safety of PMS management options	Safety and efficacy of therapies on PMD symptoms	5.7 out of 7 on the AGREE tool	When treating women with severe PMS, CBT should be considered routinely as a treatment option.
Ussher 2017	Australia	Randomized controlled trial	Participants aged between 20-45 who	Couple-based or one-to-one	Waitlist control	83 allocated across the 3 groups, 63	Screening tools for PMS symptoms	High risk of bias in 1 domain	Repeated measures analysis of variance found a significant time by group interaction identifying that

			met the criteria for a premenstrual disorder diagnosis and were in a relationship (heterosexual or lesbian)	CBT intervention		completed post-intervention measures	(PSST, SEPQ, HADS, DAS, STSS), subjective experience of premenstrual change and intervention, interviews	(incomplete outcome data). Blinding was not possible – unclear if it would impact results	women in the two CBT conditions reported lower total premenstrual symptoms, emotional reactivity/mood, and premenstrual distress, in comparison to the waitlist control. Significantly higher active behavioral coping post-intervention was found in the couple condition than in the one-to-one and waitlist control group.
Weise 2019	Germany	Randomized controlled trial	Women 18-45 years of age who fulfilled DSM-5 criteria for PMDD	Internet-based CBT program	Waitlist control	174 women were randomized; 152 completed post assessment	Impairment measure (PMS-I) and impact on everyday life and symptom severity (symptom diary)	High risk of bias in 1 domain (incomplete outcome data). Blinding was not possible – unclear if it would impact results	Significant time × group interaction effects on functional impairment and psychological impairment, impact on everyday life, symptom intensity, and symptom disability in favor of the TG indicated the efficacy of the treatment.

Exercise									
Author, year	Setting	Design/ approach	Subjects	Intervention	Comparator	Sample size	Outcomes	Quality Assessment	Results
Nevatte 2013 (ISPMD)	Global	Guideline	Patients with premenstrual disorders	Exercise, vitamin B6, calcium and other dietary interventions	Placebo, no treatment, other treatments	Various studies on alternative therapies	Safety and efficacy of therapies on PMD symptoms	4.1 out of 7	Although no RCTs of exercise have been conducted in women with prospectively confirmed PMDs, exercise has been reported to improve premenstrual dysphoria, fatigue and bloating (Daley2009). It is commonly considered that exercise improves premenstrual symptoms through elevation of beta-endorphin levels and improved well-being however there is no evidence to confirm this.
Pal 2022	Global	Systematic review and meta-analysis	Subjects diagnosed with premenstrual syndrome	Yoga	No treatment	11 studies included in meta-analysis	Global measures of PMS, physical symptoms, affective symptoms, pulse rate	Low-quality review	The studies were heterogenous in terms of the design, yoga regimes, nature of interventions and tools used for outcome measures. It was found that yoga was beneficial in the management of PMS. This benefit was also seen when all the sub-domains of PMS were individually examined except physical sub-domain.
Stoddard 2007	California, USA	2 studies: Cross-sectional study (a) and prospective study (b)	(a) and (b) Women with regular menstrual cycles between 24-33 years of age	(a) usual exercise (b) exercise training program	(a) sedentary (less than 1 h/week of exercise) (b): N/A	(a) 54 women (b) 14 women	(a) and (b) premenstrual distress (PD) symptom questionnaire, hormone levels	(a) Moderate risk of bias in 4 domains (confounding, selection, missing data, outcome measures) (b) Moderate risk of bias in 2 domains (confounding, and deviations)	In the cross-sectional study, exercising women reported lower Pain symptoms, and had lower peak E1G levels than did sedentary women. The baseline PD symptoms loneliness, crying, and skin blemishes with were statistically significantly and positively correlated with pregnanediol glucuronide levels in the cross-sectional study. In the prospective study, exercise reduced the global PD symptom score, including the Water Retention and Pain scales, and reduced pregnanediol glucuronide and peak E1G levels.

Yesildere-Saglam 2020	Global	Systematic review	Women with premenstrual syndrome	Exercise of any type and duration	Any comparison (placebo, other therapy, no treatment)	17 studies included in review	Physical and psychological premenstrual symptoms	Critically low-quality review	It can be said that exercise is effective in improving physical symptoms such as pain, constipation, breast sensitivity, and psychological symptoms such as anxiety and anger. However, although there is no clarity regarding other symptoms, exercise has a symptom-reducing effect
-----------------------	--------	-------------------	----------------------------------	-----------------------------------	---	-------------------------------	--	-------------------------------	---

Nutritional Supplements (eg, calcium)

Author, year	Setting	Design/ approach	Subjects	Intervention	Comparator	Sample size	Outcomes	Quality Assessment	Results
Arab 2019	Global	Systematic review and meta-analysis	Individuals with PMS	Vitamin D	Various doses, placebo, other supplements, other therapies	7 studies included in meta-analysis	Association between vitamin D and PMS or its symptoms	Low-quality review	Although no significant association between serum 25(OH)D and PMS (weighted mean difference (WMD)=3.35; 95% CI, -7.80 to 1.11; p=0.14) was indicated in observational studies, vitamin D supplementation was effective in ameliorating PMS symptoms based upon findings from interventional studies.
Bryant 2005	UK	Placebo-controlled, cross-over study	Women aged 18-35 years	Active soy isoflavones	Milk protein placebo	23 women completed study	Presence, severity, and timing of PMS symptoms using Penn daily symptom report (DSR)	High risk of bias in 3 domains (sequence generation, allocation concealment, and incomplete outcome data)	After two cycles of ISP containing IF intervention, total symptoms (F(2,36)8·20, P=0·000) and physical symptoms (F(2,36)8·18, P=0·000) were significantly reduced compared with baseline after both active and placebo treatments, although differences between active and placebo treatment were non-significant. Specific premenstrual symptoms, headache (F(2,32)4·10, P=0·026) and breast tenderness (F(2,32)4·59, P=0·018), were reduced from baseline after soy IF, but not milk protein placebo. Cramps (F(2,32)4·15, P=0·025) and swelling (F(2,32)4·64, P=0·017) were significantly lower after active treatment compared with placebo.
De Souza 2000	UK	Randomized, double-blind crossover study	Women suffering adverse premenstrual symptoms	Daily supplement of 200mg magnesium, 50mg vitamin B6, or both	Placebo	44 participants included in analysis	Daily symptoms using 30-item menstrual diary; food frequency questionnaire	High risk of bias in 1 domain (incomplete outcome data); unclear risk of bias in blinding domains and allocation concealment	ANOVA showed no overall difference between individual treatments, but predefined treatment comparisons using factorial contrasts in ANOVA showed a significant effect of 200mg/day Mg 150mg/day vitamin B6 on reducing anxiety-related premenstrual symptoms (nervous tension, mood swings, irritability, or anxiety) (p=0.040). Urinary Mg output was not affected by treatment. A small synergistic effect of a daily dietary supplementation with a combination of Mg 1 vitamin B6 in the reduction of mild premenstrual anxiety-related symptoms was demonstrated during

									treatment of 44 women for one menstrual cycle.
Derman 2004	Ankara, Turkey	Cross-sectional study	Adolescent girls, aged 10-17 years with menstrual cycles	Various nutritional supplements and milk consumption	No supplementation or other supplements	171 adolescent girls	Questionnaire about PMS criteria, dysmenorrhea, menstrual cycle, and daily nutrition	Serious risk of bias in 2 domains (confounding, and participant selection); moderate risk of bias in 3 domains (classification, deviation, and measurement of outcomes)	One hundred and five adolescent girls out of 171 (61.4%) met DSM-IV criteria for PMS. There was an association between dysmenorrhea and PMS in 60 (57.1%). Half of the girls, i.e. 52 (49.5%) had mild, 39 (37.1%) had moderate and 14 (13.4%) had severe PMS. The most common symptom of PMS was negative affect particularly in the form of stress (87.6%) and nervousness (87.6%). There was a statistically significant negative relationship between milk consumption and the following: abdominal bloating, cramps, craving for some foods and increased appetite.
Hofmeister 2016 (AAFP)	Global	Guideline	Women with premenstrual disorders	Various interventions such as CBT, CAM therapies, and hormonal and non-hormonal management	Different dosages and regimens for various interventions	Various studies on the efficacy and safety of PMS management options	Safety and efficacy of therapies on PMD symptoms	4.5 out of 7 on the AGREE tool	Calcium supplementation of 1,000 to 1,200 mg per day may improve PMS symptoms.
Kwan 2009	Global	Systematic review	Women with PMS	Drug treatments, hormonal treatments, psych interventions, physical therapy, dietary supplements, and surgical treatments	Placebo	56 systematic reviews, RCTs, or observational studies that met inclusion criteria	Symptom severity assessed by various questionnaires or scales	Low-quality review	We don't know how effective physical therapy techniques (bright light therapy, chiropractic manipulation, exercise, reflexology, relaxation, and acupuncture) are in relieving symptoms of PMS. We found evidence that pyridoxine (vitamin B6) reduces overall symptoms of PMS. Calcium supplements may also be effective. We don't know whether other supplements (evening primrose oil or magnesium) are a useful treatment for PMS.
Nevatte 2013 (ISPMD)	Global	Guideline	Patients with premenstrual disorders	Exercise, vitamin B6, calcium and other dietary interventions	Placebo, no treatment, other treatments	Various studies on alternative therapies	Safety and efficacy of therapies on PMD symptoms	4.1 out of 7	The strongest evidence for efficacy of non-pharmacological treatments for PMDs exists for calcium, chasteberry and cognitive-behavior therapy

Quaranta 2007	Italy	Open-label intervention study	Women aged 18-45 years affected by PMS	Modified-release magnesium 250mg tablet	No treatment	40 patients included in ITT analysis	Improvement in PMS symptoms measured by MMDQ by investigator and monthly diary	Moderate risk of bias in 1 domain (outcome measurement); low risk of bias in all other domains	MS symptoms improved during magnesium treatment. After 3 months, the mean total PMS score as assessed by the investigator using MMDQ, was significantly lower than before therapy ($p < 0.0001$). During the same period, the mean PMS scores, as recorded in patients' diaries, also showed significant improvements ($p < 0.0001$ for all subscales). The relative decreases in total PMS scores, as assessed by investigator and patient, were 35.1% and 33.5%, respectively.
RCOG/NICE 2017	Global	Guideline	Women with Premenstrual Disorders (PMS/PMDD)	Various interventions including CBT, CAM therapies, hormonal and nonhormonal medical management, and nutritional supplements	Different dosages and regimens for various interventions	Various studies on the efficacy and safety of PMS management options	Safety and efficacy of therapies on PMD symptoms	5.7 out of 7 on the AGREE tool	In a systematic review, two studies ($n=499$) revealed consistent evidence for calcium in alleviating both physical and psychological symptoms of PMS. The evidence for both vitamin B6 and Vitex was contradictory in this review and therefore advice could not be given for either. Due to the lack of power, reliable recommendations cannot be provided.
Retallick-Brown 2020	New Zealand	Pilot randomized controlled trial	Women over the age of 18 meeting the diagnosis of PMS	Vitamin B6 (80 mg/day)	Broad-spectrum micronutrient formula	78 included in ITT analysis	DRSP questionnaire	High risk of bias in 1 domain (selective outcome reporting)	Linear-mixed model analyses indicated both treatments produced comparable reduction in PMS symptoms with medium effect sizes (ES) across all PMS variables as measured by the DRSP (micronutrient ES=0.50–0.56; B6 ES=0.43–0.56), with 72% of the micronutrient and 60% of the vitamin B6 group identified as in full remission in PMS symptoms after three cycles. The micronutrient-treated participants showed greater improvement than the B6 group (between group $d=0.51$, $p<0.05$) in health-related quality of life.
Thys-Jacobs 1989	USA	Randomized crossover trial	Women with premenstrual syndrome evaluated prospectively one menstrual cycle prior to treatment	Elemental calcium (3 months and then 3 months placebo)	Placebo (3 months and then 3 months calcium)	33 women	Symptom scores measured daily (14 daily symptom self-assessment questionnaires)	High risk of bias due to incomplete outcome data; unclear risk of bias in 3 domains (sequence generation, allocation concealment, and other	Multivariate repeated measures analysis of variance on symptom ratings derived from daily PMS symptom scores demonstrated a reduction in symptoms on calcium treatment during both the luteal ($p=0.011$) and the menstrual phases ($p=0.032$) of the reproductive cycle. Calcium supplementation had no effect during the intermenstrual phase. Retrospective assessment of overall symptoms confirmed this

								sources of bias)	reduction: 73% of the women reported fewer symptoms during the treatment phase on calcium, 15% preferred placebo, and 12% had no clear preference.
Thys-Jacobs 1998	USA	Randomized controlled trial	Healthy premenopausal women with a diagnosis of PMS prospectively documented for 2 menstrual cycles	1200 mg elemental calcium per day for 3 menstrual cycles	Placebo daily for 3 menstrual cycles	466 patients	Daily documentation of symptoms, adverse effects, and compliance with medication. Primary outcome measure was the 17-parameter symptom complex score	Unclear risk of bias in 3 domains (sequence generation, allocation concealment, other sources of bias)	There were no differences between groups in the mean screening symptom complex score of the luteal (P= .659), menstrual (P= .818), or intermenstrual phase (P= .726) of the menstrual cycle. During the luteal phase of the treatment cycle, a significantly lower mean symptom complex score was observed in the calcium-treated group for both the second (P= .007) and third (P< .001) treatment cycles. By the third treatment cycle calcium effectively resulted in an overall 48% reduction in total symptom scores from baseline compared with a 30% reduction in placebo. All 4 symptom factors were significantly reduced by the third treatment cycle.
Whelan 2009	Global	Systematic review	Women with PMS or PMDD	Therapies containing only one herb, vitamin, or mineral	Other recognized therapy or placebo	29 RCTs included in review	Change in severity of PMS/PMDD symptoms	Low-quality review	Data supports the use of calcium for PMS and suggests that chasteberry and vitamin B6 may be effective. Preliminary data shows some benefit with ginkgo, magnesium pyrrolidone, saffron, St. John's Wort, soy and vitamin E. No evidence of benefit with evening primrose oil or magnesium oxide was found.
Yonkers 2013	USA	Randomized controlled trial	Women between 18 and 40 years of age, with moderate to severe PMS	Fluoxetine 10 mg twice daily or Calcium 600 mg twice daily	Placebo	39 women	Daily ratings of premenstrual symptoms	Unclear risk of bias in 1 domain (incomplete outcome data)	Symptom improvement was greatest for the fluoxetine group, although significance was achieved only for the Daily Record of Severity of Problems (B= -0.28; 95% confidence interval= -1.70 to -0.35; P=0.02) and the Clinical Global Impression-Improvement (B= -1.03; 95% confidence interval= -1.70 to -0.35; P= 0.04). The Cohen d effect sizes for fluoxetine relative to placebo were between 0.80 and 2.08, whereas the effect sizes for calcium were only between 0.10 and 0.4.

Acupuncture

Author, year	Setting	Design/ approach	Subjects	Intervention	Comparator	Sample size	Outcomes	Quality Assessment	Results
Armour 2018	Global	Systematic review and meta-analysis	Women of any age who met diagnostic criteria for PMS or PMDD	Various forms of acupuncture	Sham acupuncture or sham acupressure, no treatment, or other conventional treatments	5 trials included in meta-analysis	Overall premenstrual symptoms; adverse events	High-quality review	The limited evidence available suggests that acupuncture and acupressure may improve both physical and psychological symptoms of PMS when compared to a sham control. There was insufficient evidence to determine whether there was a difference between the groups in rates of adverse events.
Cho 2010	Global	Systematic review	Women of any age meeting the diagnostic criteria for PMS or PMDD	All forms of acupuncture techniques	No acupuncture, placebo, pharmacologic treatment, or non-conventional interventions	9 RCTs included in review	Any scales for overall symptoms or particular symptoms of PMS; adverse events	Moderate-quality review	Four studies reported a significant difference in reduction of PMS symptoms for acupuncture treatment compared with pharmacological treatment. Two studies reported the improvements in primary symptoms within the acupuncture and herbal medications groups compared with baseline. Only two RCTs reported information regarding acupuncture-related adverse events, which included one case of a small subcutaneous hematoma.
Hofmeister 2016 (AAFP)	Global	Guideline	Women with premenstrual disorders	Various interventions such as CBT, CAM therapies, and hormonal and non-hormonal management	Different dosages and regimens for various interventions	Various studies on the efficacy and safety of PMS management options	Safety and efficacy of therapies on PMD symptoms	4.5 out of 7 on the AGREE tool	There is insufficient evidence to recommend treatment with vitamin D, herbal remedies, or acupuncture, but there are data to suggest benefit from cognitive behavior therapy.
Jang 2014	Global	Systematic review	Participants diagnosed with PMS or PMDD	Acupuncture or herbal medicine	Control group, placebo, or pharmaceutical medicine	19 RCTs included in analysis	Measures of PMS symptoms before and after treatment	Moderate-quality review	Experimental groups with Acupuncture and herbal medicine treatment (all herbal medicine except <i>Cirsium japonicum</i>) had significantly improved results regarding PMS/PMDD.
Jing 2009	Global	Systematic review and meta-analysis	Women of reproductive age diagnosed with PMS	Chinese herbal medicine	Placebo, no intervention, acupuncture, western medication, or other intervention	2 RCTs included in analysis	PMS scoring systems; improvement of overall symptoms	Moderate-quality review	It is rare in PMS management that efficacy claims are substantiated by clinical trials. One of the identified trials was well designed and reported on the effectiveness of Jingqianping in the treatment of premenstrual syndrome. However, currently there is insufficient evidence to support the use of Chinese herbal medicine for

									PMS and further, well-controlled trials are needed before any final conclusions can be drawn.
Kim 2011	Global	Systematic review and meta-analysis	Women meeting diagnostic criteria for PMS or premenstrual tension syndrome	Needle acupuncture	Sham acupuncture, usual care, waiting list, or no treatment	8 studies included in analysis	Changes or improvements in PMS symptoms	Moderate-quality review	The pooled results demonstrated that acupuncture is superior to all controls (eight trials, pooled RR 1.55, 95% CI 1.33–1.80, $P < 0.00001$). A meta-analysis comparing the effects of acupuncture with different doses of progestin and/or anxiolytics supported the use of acupuncture (four trials, RR 1.49, 95% CI 1.27–1.74, $P < 0.00001$). In addition, acupuncture significantly improved symptoms when compared with sham acupuncture (two trials, RR 5.99, 95% CI 2.84–12.66, $P < 0.00001$).
Kwan 2009	Global	Systematic review	Women with PMS	Drug treatments, hormonal treatments, psych interventions, physical therapy, dietary supplements, and surgical treatments	Placebo	56 systematic reviews, RCTs, or observational studies that met inclusion criteria	Symptom severity assessed by various questionnaires or scales	Low-quality review	We don't know how effective physical therapy techniques (bright light therapy, chiropractic manipulation, exercise, reflexology, relaxation, and acupuncture) are in relieving symptoms of PMS. We found evidence that pyridoxine (vitamin B6) reduces overall symptoms of PMS. Calcium supplements may also be effective. We don't know whether other supplements (evening primrose oil or magnesium) are a useful treatment for PMS.
RCOG/NICE 2017	Global	Guideline	Women with Premenstrual Disorders (PMS/PMDD)	Various interventions including CBT, CAM therapies, hormonal and nonhormonal medical management, and nutritional supplements	Different dosages and regimens for various interventions	Various studies on the efficacy and safety of PMS management options	Safety and efficacy of therapies on PMD symptoms	5.7 out of 7 on the AGREE tool	Women with PMS should be informed that there is conflicting evidence to support use of some complementary medicines. An integrated holistic approach should be used when treating women with PMS.

Complementary Alternative Therapies (eg, *Vitex agnus castus*)

Author, year	Setting	Design/ approach	Subjects	Intervention	Comparator	Sample size	Outcomes	Quality Assessment	Results
Atmaca 2003	Turkey	Randomized, prospective, parallel group trial	Females between 24-45 years of age meeting DSM-IV criteria for PMDD	20-40 mg/day fluoxetine	20-40 mg/day <i>Vitex agnus castus</i> (AC) extract	41 patients	Penn daily symptom report (DSR), Hamilton depression rating scale (HAM-D), and clinical global impression-severity of illness (CGI-SI)	Unclear risk of bias in 2 domains (allocation concealment and other sources of bias)	At endpoint, using the clinical criterion for improvement, a similar percentage of patients responded to fluoxetine (68.4%, n=13) and AC (57.9%, n=11). There was no statistically significant difference between the groups with respect to the rate of responders. This preliminary study suggests that patients with PMDD respond well to treatment with both fluoxetine and AC. However, fluoxetine was more effective for psychological symptoms while the extract diminished the physical symptoms.
Berger 2000	Switzerland	Prospective, multicenter trial	Patients diagnosed with PMS	1 tablet of 20 mg <i>vitex agnus castus</i> L extract Ze 440 for 3 menstrual cycles	3 cycles without treatment	43 patients	Moos' menstrual distress questionnaire (MMDQ)	Moderate risk of bias in 2 domains (confounding and missing data); low risk of bias in all other domains	At the end of the study, PMS-related symptoms were reduced by treatment. There was a significant score reduction (42.5%) of the MMDQ as the main effect parameter ($p < 0.001$). Symptoms gradually returned after treatment cessation. However, a difference from baseline remained (20%; $p < 0.001$) up to 3cycles thereafter.
Canning 2010	UK	Randomized controlled trial	Women aged 18-45 years prospectively diagnosed with PMS	<i>Hypericum perforatum</i> tablets 900mg/day for 2 menstrual cycles	Placebo for 2 menstrual cycles	36 women	Symptoms rated daily using Daily Symptom Report	High risk of bias in 1 domain (selective outcome reporting)	<i>Hypericum perforatum</i> was statistically superior to placebo in improving physical and behavioral symptoms of PMS ($p < 0.05$). There were no significant effects of <i>Hypericum perforatum</i> compared with placebo treatment for mood- and pain-related PMS symptoms ($p > 0.05$).
Cerqueira 2017	Global	Systematic review	Individuals with PMS or PMDD	<i>Vitex agnus castus</i> (VAC)	Placebo or active treatment	9 articles included in review	Various methods of assessing PMS symptoms and efficacy of VAS	Critically low-quality review	Three different preparations of VAC were tested, and there was significant variability in the measurement of treatment outcomes between the studies. Nevertheless, all eight studies were positive for VAC in the treatment of PMS or PMDD and VAC was overall well tolerated
Chou 2008	Australia	Randomized placebo-	Women with PMS symptoms	Chinese herbal medication	Placebo	61 women completed trial	Menstrual distress questionnaire	Low risk of bias in all domains	The results of the study indicate that Chinese herbal medicine can lower the symptoms occurrence and

		controlled clinical trial	aged 18 and over	(herbal granules)			(MDQ) and menstrual symptom diary (MSD)		severity of PMS significantly, and the effect of the treatment can last up to three months after herbal treatment has ceased.
Csupor 2019	Global	Meta-analysis of RCTs	Individuals with premenstrual syndrome	Vitex agnus castus (chasteberry; VAC)	Placebo	3 trials included in final analysis	Binarized results of efficacy	High-quality review	VAC preparations were confirmed to be effective in the reduction of PMS symptoms: women taking VAC were 2.57 (95% CI 1.52-4.35) times more likely to experience a remission in their symptoms compared to those taking the placebo. Although several clinical trials have been carried out with VAC, the majority of the studies cannot be used as evidence for efficacy due to incomplete reporting, especially concerning the description of the used medication.
Dante 2011	Global	Systematic review	Individuals with PMS or PMDD	Herbal treatments, including vitex agnus castus, oenotera biennis, hypericum perforatum, ginkgo biloba, crocus sativus	Placebo or other treatment	10 RCTs included	Various menstrual symptom assessments	Moderate-quality review	Vitex agnus castus was the more investigated remedy (four trials, about 500 women), and it was reported to consistently ameliorate PMS better than placebo. Single trials also support the use of either Ginkgo biloba or Crocus sativus. On the contrary, neither Evening primrose oil nor St. John Worth show an effect different than placebo. None of the herbs was associated with major health risks, although the reduced number of tested patients does not allow definitive conclusions on safety.
Gianfranco 2011	Italy	Randomized controlled trial	Patients aged 18-45 years	4 g myo-inositol 3 times per day in powder form	1.2 g of myo-inositol 3 times per day in soft gel capsule form	71 patients	Premenstrual score from HAM-D scale, DSR scale, CGI-SI scale taken at baseline and end point of each phase	Low risk of bias in 1 domain (selective outcome reporting); unclear risk of bias in all other domains	Results showed a significant improvement of three different scales: a reduction in the Daily Symptoms Records scale and an improvement of the Hamilton Depression Rating and Clinical Global Impression—Severity of Illness scales. Results were similar for both formulations.
Hernandez-Reif 2000	Florida, USA	Randomized controlled trial	Women aged between 19 and 45 years with PMDD	Massage therapy	Relaxation therapy	24 women	Menstrual symptom assessments including CES-D, MDQ, STAI, POMS, and VAS	Unclear risk of bias in all domains, except selective outcome reporting	The massage group showed decreases in anxiety, depressed mood and pain immediately after the first and last massage sessions. The longer term (5 week) effects of massage therapy included a reduction in pain and water retention and overall menstrual distress. However, no long-term changes were observed in the

									massaged group's activity level or mood.
Hofmeister 2016 (AAFP)	Global	Guideline	Women with premenstrual disorders	Various interventions such as CBT, CAM therapies, and hormonal and non-hormonal management	Different dosages and regimens for various interventions	Various studies on the efficacy and safety of PMS management options	Safety and efficacy of therapies on PMD symptoms	4.5 out of 7 on the AGREE tool	There is insufficient evidence to recommend treatment with vitamin D, herbal remedies, or acupuncture, but there are data to suggest benefit from cognitive behavior therapy.
Jang 2004	Iksan, Korea	Randomized placebo-controlled trial	College women with symptoms of PMS	Qi therapy	Placebo (sham qi therapy)	36 women	Premenstrual symptoms diary including negative feelings, pain, autonomic nervous system reactions, water retention, and behavioral changes	Unclear risk of bias in 2 domains (allocation concealment and other sources of bias)	There were significant improvements in the symptoms of negative feeling, pain, water retention, and total PMS symptoms in subjects receiving qi therapy compared to placebo controls.
Jing 2009	Global	Systematic review and meta-analysis	Women of reproductive age diagnosed with PMS	Chinese herbal medicine	Placebo, no intervention, acupuncture, western medication, or other intervention	2 RCTs included in analysis	PMS scoring systems; improvement of overall symptoms	Moderate-quality review	It is rare in PMS management that efficacy claims are substantiated by clinical trials. One of the identified trials was well designed and reported on the effectiveness of Jingqianping in the treatment of premenstrual syndrome. However, currently there is insufficient evidence to support the use of Chinese herbal medicine for PMS and further, well-controlled trials are needed before any final conclusions can be drawn.
Krasnik 2005	Global	Systematic review and meta-analysis	Patients with PMDD	Bright light therapy	Placebo	4 studies included in analysis	Change in depressive symptoms scores measured by HADS and BDI	Low-quality review	Four crossover trials studying a total of 55 participants met inclusion criteria. Three trials showed similar results; one fully unblinded trial showed a much larger effect. The pooled effect size from the random-effects model of the 3 higher quality trials was 0.20 (95% CI 0.48 to 0.07).
Kwan 2009	Global	Systematic review	Women with PMS	Drug treatments, hormonal treatments, psych interventions, physical therapy, dietary supplements,	Placebo	56 systematic reviews, RCTs, or observational studies that met inclusion criteria	Symptom severity assessed by various questionnaires or scales	Low quality review	We don't know how effective physical therapy techniques (bright light therapy, chiropractic manipulation, exercise, reflexology, relaxation, and acupuncture) are in relieving symptoms of PMS. We found evidence that pyridoxine (vitamin B6) reduces overall symptoms of PMS. Calcium supplements may also be

				and surgical treatments					effective. We don't know whether other supplements (evening primrose oil or magnesium) are a useful treatment for PMS.
Momoeda 2014	Japan	Nonrandomized, noncontrolled, cohort study	Female patients aged 18-44 years with PMS	Prefemin containing 20mg of Vitex agnus-castus (VAC) extract	N/A	69 patients	Efficacy profile based on intensity of 10 PMS symptoms measured by visual analog scale	Moderate risk of bias in 3 domains (confounding, missing data, and outcome measures)	After the first menstrual cycle, a statistically significant decrease in total VAS score was observed ($P<0.001$), and the score continued to diminish for the following two cycles. Each of the ten symptom scores decreased significantly in this manner.
Nemets 2002	Israel	Randomized controlled crossover trial	Patients with PMDD	Inositol	Placebo	11 female patients	Ten rating scales to assess premenstrual symptoms	High risk of bias in 1 domain (selective outcome reporting) and unclear risk of bias in all other domains	Inositol was not found to be superior to placebo in this study in any of the scales used. Side effects were few and included mild and transient bloating in two patients on inositol and no complaints on placebo.
Nevatte 2013 (ISPMDD)	Global	Guideline	Patients with premenstrual disorders	Chasteberry/VAC, St. John's Wort, ginkgo biloba, saffron	Placebo, no treatment, other treatments	Various studies on alternative therapies	Safety and efficacy of therapies on PMD symptoms	4.1 out of 7	The strongest evidence for efficacy of non-pharmacological treatments for PMDs exists for calcium, chasteberry and cognitive-behavior therapy.
Ooi 2020	Global	Systematic review and meta-analysis	Premenopausal women experiencing breast tenderness/pain during premenstrual periods	VAC	Placebo, no treatment, wait list	10 articles included in analysis	Changes in breast tenderness/pain before and after study	High quality review	A conservative meta-analysis included only six studies ($n=718$, $VAC=356$, $placebo=362$) and revealed a moderate effect size ($SMD: 0.67$, $95\% CI: 0.5-0.85$) favoring VAC over a placebo.
RCOG/NICE 2017	Global	Guideline	Women with Premenstrual Disorders (PMS/PMDD)	Various interventions including CBT, CAM therapies, hormonal and nonhormonal medical management, and nutritional supplements	Different dosages and regimens for various interventions	Various studies on the efficacy and safety of PMS management options	Safety and efficacy of therapies on PMD symptoms	5.7 out of 7 on the AGREE tool	Women with PMS should be informed that there is conflicting evidence to support use of some complementary medicines. An integrated holistic approach should be used when treating women with PMS.
Schellenberg 2001	Germany	Randomized controlled trial	Women with premenstrual syndrome	Agnus castus (ZE 440)	Placebo	170 women	Change from baseline to end of third cycle in premenstrual syndrome symptoms	Low risk of bias in all domains	Improvement in the main variable was greater in the active group compared with placebo group ($P < 0.001$). Analysis of the secondary variables showed significant ($P < 0.001$) superiority of active treatment in each of the three global impression items.

									Responder rates were 52% and 24% for active and placebo, respectively. Seven women reported mild adverse events (four active; three placebo), none of which caused discontinuation of treatment.
Schellenberg 2012	Germany	Randomized controlled trial	Patients with PMS diagnosis according to DSM III-R criteria	3 doses of Vitex agnus castus fruit extract Ze 440 (8 mg, 20 mg, 30 mg)	Placebo	142 female patients	Visual analog scales (VAS) for the symptoms of irritability, mood alteration, anger, headache, bloating and breast fullness.	Unclear risk of bias in 2 domains (allocation concealment and other sources of bias)	Each of the treatments was well tolerated. Improvement in the total symptom score (TSS) in the 20 mg group was significantly higher than in the placebo and 8 mg treatment group. The higher dose of 30 mg, on the other hand, did not significantly decrease symptom severity compared to the 20 mg treatment, providing a rational for the usage of 20 mg. Corresponding results were observed with the single PMS symptom scores.
Solt Kirca 2022	Turkey	Randomized controlled trial	Subjects between 18 and 30 years of age, having regular menstruation and a score of 45 or above on the PMSS (premenstrual syndrome scale)	Music medicine (participants listened to personalized music playlists 3 times a week for 30 minutes each time during the menstrual cycle)	Control group – no treatment	97 women	PMSS scores and World Health Organization quality of life questionnaire (WHOQOL-BREF)	High risk of bias in 2 domains (blinding of participants and personnel, and blinding of outcome assessors)	Comparing the two groups, music significantly reduced the premenstrual syndrome level after application (PMSS -1123.23 ± 32.06 vs. 105.90 ± 27.55, respectively, PMSS-294.21 ± 28.42 vs. 119.44 ± 27.29, respectively, p<.05). Comparing the music medicine and control groups had significantly increased WHOQOL-BREF scores (Physical, psychological, and environmental) after the application (13.71 vs.13.14;14.33 vs. 15.44 vs. 14.66, respectively, p<.05).
Stevinson 2000	UK	Prospective uncontrolled observational study	Women with premenstrual syndrome	Hypericum tablets	N/A	19 women	Daily Symptom Ratings score daily	Moderate risk of bias in 2 domains (confounding and outcome measures)	There were significant reductions in all outcome measures. The degree of improvement in overall premenstrual syndrome scores between baseline and the end of the trial was 51%, with over two-thirds of the sample demonstrating at least a 50% decrease in symptom severity.
Uzuncakmak 2018	Turkey	Randomized controlled trial	Participants scoring above 110 on PMS scale and experiencing at least 5 symptoms of PMS every month	Aromatherapy by steam inhalation with lavender oil started at least 10 days before menstrual cycle each day until their menstrual cycle	Control group – no treatment	77 participants	Premenstrual Syndrome Scale	High risk of bias in 2 domains (blinding of participants and personnel, and blinding of outcome assessors)	When PMS mean scores of the intervention and control groups during 3 follow-up periods were compared, it was found that there is a statistically significant difference between intervention and control groups (p < 0.05). It was determined that there is a statistically significant difference between the groups in terms of PMS scale and sub-dimensions of anxiety,

									depressive affect, nervousness, pain, bloating, depressive thoughts mean scores of pre-test and 3rd follow-up ($p < 0.05$).
Van Die Burger 2013	Global	Systematic review	Females with reproductive disorders	Vitex agnus-castus extract	Placebo or other treatment	12 studies included (10 on PMS or PMDD)	Symptoms of PMDD and PMS using self-rating scales and symptom diaries	Moderate-quality review	For premenstrual syn-drome, seven of eight trials found Vitex extracts to be superior to placebo (5 of 6 studies), pyridoxine (1), and magnesium oxide (1). In premenstrual dysphoric disorder, one study reported Vitex to be equivalent to fluoxetine, while in the other, fluoxetine outperformed Vitex.
Verkaik 2017	Global	Systematic review and meta-analysis	Patients with premenstrual syndrome	Vitex agnus castus	Placebo, dietary supplements, or herbal preparations	14 studies included in analysis	PMDD or PMS symptoms, both physical and psychiatric	High-quality review	Thirteen studies with placebo, dietary supplements, or herbal preparations as controls reported positive effects of Vitex agnus castus on total premenstrual syndrome symptoms. Unfortunately, most of the trials are associated with a high risk of bias. The pooled effect of Vitex agnus castus in placebo-controlled trials was large (Hedges g , -1.21; 95% confidence interval, -1.53 to -0.88), but heterogeneity was extremely high (I^2 , 91%).
Whelan 2009	Global	Systematic review	Women with PMS or PMDD	Therapies containing only one herb, vitamin, or mineral	Other recognized therapy or placebo	29 RCTs included in review	Change in severity of PMS/PMDD symptoms	Low-quality review	Preliminary data shows some benefit with ginkgo, magnesium pyrrolidone, saffron, St. John's Wort, soy and vitamin E. No evidence of benefit with evening primrose oil or magnesium oxide was found

Non-Hormonal Medical Therapies (eg, NSAIDs)

<i>Author, year</i>	<i>Setting</i>	<i>Design/ approach</i>	<i>Subjects</i>	<i>Intervention</i>	<i>Comparator</i>	<i>Sample size</i>	<i>Outcomes</i>	<i>Quality Assessment</i>	<i>Results</i>
Backstrom 2021	Europe (12 centers)	Randomized controlled trial	Patients with PMDD verified prospectively with a regular menstrual cycle	Subcutaneously administered sepranolone (10 mg/dose or 16 mg/dose) taken every 48h during the 14 premenstrual days of 3 consecutive menstrual cycles	Placebo (diluted intralipid)	202 women	Total symptom scores of 21 questions (Sum21) on the validated daily rating scale (DRSP) containing symptoms from DSM-5 for PMDD	Unclear risk of bias in 2 domains (sequence generation and allocation concealment)	The analysis of Sum21 showed a large treatment effect of all three treatments but no statistically significant difference to placebo. However, the ratings of distress showed a significant treatment effect of sepranolone compared to placebo ($p = 0.037$) and the ratings of impairment showed a trend to greater treatment effect of sepranolone compared to placebo. Many women with PMDD had symptoms during a longer period than the late luteal phase. It has previously been shown that 9 premenstrual days may be more representative for comparison of PMDD symptom periods than the 5 worst premenstrual days. A post hoc analysis was undertaken in the per protocol population investigating the treatment effect during 9 premenstrual days in the third treatment cycle. The Sum21 results of this analysis showed that the sepranolone 10 mg was significantly better than placebo ($p = 0.008$). Similar significant treatment effects were found for the impairment and distress scores. A significantly larger number of individuals experienced no or minimal symptoms (Sum21 < 42 points) with the 10 mg sepranolone treatment compared to placebo ($P=0.020$).
Bixo 2017	Sweden	Randomized controlled trial	Healthy women for phase I, women with PMDD for phase II	UC1010 (10 mg or 16 mg) subcutaneously every second day during the luteal phase	Placebo during one menstrual cycle	26 women in phase I, 126 women in phase II	Total DRSP score	High risk of bias in 2 domains (incomplete outcome data and other sources of bias)	106 of the 126 women completed the phase II study. Within this group, a significant treatment effect with UC1010 compared to placebo was obtained for the Total DRSP score ($p = 0.041$) and borderline significance ($p = 0.051$) for the sum of Negative mood score. This explorative study indicates promising results for UC1010 as a potential treatment for PMDD. The effect size was comparable to that of SSRIs and drospirenone containing oral contraceptives. UC1010 was well tolerated and deemed safe.

Facchinetti 1989	Italy	Randomized controlled trial	Patients having menses every 22-33 days suffering from premenstrual syndrome	Naproxen sodium (550 mg tablets) for 6 cycles	Placebo for 3 cycles, then naproxen sodium (550 mg) for 3 cycles	28 patients	Menstrual distress questionnaire (MDQ) given prospectively, after the 3 rd cycle, and after the 6 th cycle	Unclear risk of bias in 5 domains (sequence generation, allocation concealment, participant blinding, outcome assessor blinding, and other sources of bias)	Both menstrual and premenstrual "pain" decreased during active drug treatment, while placebo was ineffective. We also obtained a significant improvement of premenstrual "behavioral changes" which is probably related to the relief of painful symptomatology.
Jarvis 2008	Global	Systematic review	Patients with premenstrual syndrome or premenstrual dysphoric disorder	Pharmacologic and nonpharmacologic treatment	Placebo, no treatment, one treatment vs. another	Various studies on treatment of PMS/PMDD	Safety and efficacy of treatments	Critically low-quality review	Naproxen sodium 275–550 mg twice daily has been shown in several small randomized trials to improve all physical symptoms of PMS except breast tenderness; it may also modify mood symptoms, likely related to relief of pain. Although not evaluated for their effectiveness in PMS/PMDD, all NSAIDs are presumed to relieve PMS symptoms due to their anti-inflammatory properties and can be taken as needed, up to 1–2 days before the onset of menses and until symptoms resolve. Adverse effects of NSAIDs, such as nausea, gastric ulceration, and renal dysfunction, may limit their use in some patients. ²² Acetaminophen may also help to decrease pain and be a good alternative for patients who cannot tolerate NSAID.
Kwan 2009	Global	Systematic review	Women with PMS	Drug treatments, hormonal treatments, psych interventions, physical therapy, dietary supplements, and surgical treatments	Placebo	56 systematic reviews, RCTs, or observational studies that met inclusion criteria	Symptom severity assessed by various questionnaires or scales	Low-quality review	Drug treatments can be effective at reducing premenstrual symptoms, but some are associated with significant adverse effects. Good evidence that spironolactone improves mood and somatic symptoms in women with PMS. Alprazolam, metolazone, and NSAIDs may also be effective. Bupirone and gonadorelin analogues seem to improve overall self-rated symptoms. Other treatments such as clomipramine, danazol, and SSRIs may improve psych symptoms but are associated with serious adverse effects.

Landen 2001	Sweden	Randomized controlled trial	Participants between 18- and 45-years old meeting DSM-IV criteria for PMDD	10-30mg Buspirone or 100-300mg nefazodone; intermittently for cycle 1 and 2, continuous for cycle 3 and 4	Placebo	63 patients included in intent-to-treat analysis	PMDD symptoms assessed by VAS	Unclear risk of bias in 5 domains (sequence generation, allocation concealment, both blinding domains, and other sources of bias)	With respect to self-rated global improvement, buspirone ($P<0.001$) but not nefazodone was significantly superior to placebo. While buspirone appeared to reduce self-rated irritability (visual analogue scale) more effectively than placebo, other self-rated symptoms did not differ markedly between the groups. The side-effects were mild, and sexual dysfunction was not significantly more common in patients given buspirone or nefazodone than in those given placebo.
Le Melledo 2000	Alberta, Canada	Randomized crossover trial	Women with or without PMDD	Flumazenil (2mg) intravenously	Placebo	21 women	Panic symptom scale	Unclear risk of bias in 5 domains (sequence generation, allocation concealment, both blinding domains, and other sources of bias)	Flumazenil induced a much greater panic response in the women with premenstrual dysphoric disorder than in the comparison subjects.
Martinez 2016	USA	2 separate randomized controlled crossover trials	Women with or without PMDD, aged 30-50 years	Dutasteride 0.5 mg/day (trial 1) or 2.5 mg/day (trial 2)	Placebo	16 women	DRF measuring symptoms of irritability, sadness, and anxiety	Unclear risk of bias in 3 domains (allocation concealment and both blinding domains)	In the low-dose group, no significant effect of dutasteride on PMDD symptoms was observed compared with placebo (ie, symptom cyclicity maintained), and plasma allopregnanolone levels increased in women with PMDD from follicular to the luteal phases, suggesting the absence of effect of the low-dose dutasteride on 5 α -reductase. In contrast, the high-dose group experienced a statistically significant reduction in several core PMDD symptoms (ie, irritability, sadness, anxiety, food cravings, and bloating) on dutasteride compared with placebo.
Mira 1986	Australia	Randomized controlled trial	Subject suffering from severe premenstrual symptoms for at least 2 years	Mefenamic acid (250mg; active medication 2 cycles, placebo 2 cycles, active medication 2 cycles)	Placebo (containing lactose; placebo 2 cycles, active medication 2 cycles, placebo 2 cycles)	15 subjects	Number of mood, physical, and performance symptoms measured by questionnaire	Unclear risk of bias in 3 domains (sequence generation, allocation concealment,	Mefenamic acid significantly improved many of the physical, mood, and performance symptoms associated with PMS. The physical symptoms that showed marked improvement were fatigue, headache, and general aches and pains ($P<0.001$). Most mood symptoms were improved, the most

								other sources of bias)	significant being freedom from mood swings (p<.005).
Nevatte 2013 (ISPMD)	Global	Guideline	Patients with premenstrual disorders	SSRIs, and other anti-depressants; benzodiazepine and buspirone	Placebo, no treatment, other treatments	Various studies on alternative therapies	Safety and efficacy of therapies on PMD symptoms	4.1 out of 7	If anxiety/tension and irritability are the patient's predominant symptoms of PMD, treatment with anxiolytics, such as benzodiazepines, may seem appropriate.
RCOG/NICE 2017	Global	Guideline	Women with Premenstrual Disorders (PMS/PMDD)	Various interventions including CBT, CAM therapies, hormonal and nonhormonal medical management, and nutritional supplements	Different dosages and regimens for various interventions	Various studies on the efficacy and safety of PMS management options	Safety and efficacy of therapies on PMD symptoms	5.7 out of 7 on the AGREE tool	Spironolactone can be used in women with PMS to treat physical symptoms.
Roca 2002	USA	Randomized controlled trial	Patients with PMDD and healthy controls	Serotonin receptor antagonist metergoline (8mg) administered orally	Diphenhydramine (50mg) as active placebo	20 women	Vital signs and mood ratings before, during, and after procedure	Unclear risk of bias in all domains	The patients with premenstrual dysphoric disorder experienced a return of symptoms 24 hours after treatment with metergoline but not diphenhydramine (active placebo). The comparison women experienced no changes in mood,

Educational and Self-Help Strategies

Author, year	Setting	Design/ approach	Subjects	Intervention	Comparator	Sample size	Outcomes	Quality Assessment	Results
Ayaz-Alkaya 2020	Turkey	Randomized controlled trial	Adults with PMS	Health Belief Model (HBM)-based education program	No treatment	60 subjects	Mean difference in scores from Premenstrual Syndrome Scale and questionnaire for other PMS related factors	High risk of bias in 2 domains (blinding of participants and blinding of outcome assessors)	There was a statistically significant difference between the pre-test mean scores and the first, second, and third follow-up mean scores; and between the first follow-up mean score and the second and the third follow-up mean scores in the repeated measurements of the intervention group ($p < .05$). The mean scores of the intervention group were found to be significantly lower than the control group in the second and third follow-ups ($p < .05$).
Han 2019	Global	Systematic review and meta-analysis	Women of reproductive age experiencing PMS	Psychosocial intervention utilizing cognitive, behavioral, or social mechanisms	Usual care or care without psychosocial intervention	11 studies included in meta-analysis	Measurement of severity of PMS including somatic and psychological symptoms	Low-quality review	Pooled effects of 11 psychosocial interventions ($n=324$) showed statistically significant beneficial effects on the severity of PMS (SMD -0.29, 95% CI -0.45 to -0.13, $I^2=27\%$). Participants who received coping skills training had significantly low severity of PMS than the control group (SMD -0.53, 95% CI -0.77 to -0.28, $p < .001$, $I^2=3\%$). There were no effects found for education program nor social support intervention.
Simsek Kucukkelepce 2021	Turkey	Randomized controlled trial	Women with premenstrual syndrome	Health belief model-based education with or without acupressure	No intervention (usual care)	163 women	Premenstrual syndrome scale (PMSS) to measure severity of premenstrual symptoms and WHO quality of life scale (WHOQOL-100)	High risk of bias in 2 domains (blinding of participants and blinding of outcome assessors)	While there was a 30.31 ± 3.5 point decrease between the pretest and posttest PMSS mean scores of the acupressure education group and a 23.78 ± 12.65 point decrease between the pretest and posttest PMSS mean scores of the education group, an increase of 3.24 ± 4.42 point was determined between the pretest and posttest PMSS mean scores of the control group ($P < .001$).

Surgical Management

<i>Author, year</i>	<i>Setting</i>	<i>Design/ approach</i>	<i>Subjects</i>	<i>Intervention</i>	<i>Comparator</i>	<i>Sample size</i>	<i>Outcomes</i>	<i>Risk of bias</i>	<i>Results</i>
Leminen 2012	Finland	Secondary analysis of a randomized controlled trial	Women aged 35-49 years	LNG-IUS	Hysterectomy	236 women	Occurrence of premenstrual symptoms evaluated by questionnaires at baseline and at follow up	High risk of bias 1 domain (selective outcome reporting)	Premenstrual symptoms decreased significantly in both groups by six months ($p \leq 0.028$) without significant differences between the groups, except that in the LNG-IUS group the decrease of breast tenderness was seen first by 12 months ($p = 0.048$). Even though 42% of the women assigned to treatment with LNG-IUS were hysterectomized during the follow-up period, the results of intention-to-treat and actual treatment analyses were comparable.
Kwan 2009	Global	Systematic review	Women with PMS	Drug treatments, hormonal treatments, psych interventions, physical therapy, dietary supplements, and surgical treatments	Placebo	56 systematic reviews, RCTs, or observational studies that met inclusion criteria	Symptom severity assessed by various questionnaires or scales	Low-quality review	Surgery is only indicated if there are coexisting gynecological problems. There is a consensus that hysterectomy with bilateral oophorectomy or laparoscopic bilateral oophorectomy almost completely eradicates the symptoms of PMS, although we found no RCTs examining this. We don't know whether endometrial ablation has the same effect.
Lukes 2011	North Carolina, USA	Prospective, single-arm cohort	Adult women with heavy menses who also reported symptoms of PMS	Endometrial ablation	N/A	36 women	Daily Symptoms Report and Daily Record of Severity of Symptoms	Moderate risk of bias in 3 domains (confounding, missing data, measurement of outcomes)	All measures of PMS showed significant improvement after endometrial ablation. Self-rating of PMS symptoms on a scale of 0 (none) to 10 (severe) improved from a baseline of 7.4 to a follow-up rating of 3.2 ($p, .05$). The vast majority of women (35/36, 97%) reported improvement in PMS after undergoing endometrial ablation. Both validated measures of PMS showed statistically significant improvement in PMS symptoms.
Nevatte 2013 (ISPMD)	Global	Guideline	Patients with premenstrual disorders	Oophorectomy	Placebo, no treatment, other treatments	Various studies on alternative therapies	Safety and efficacy of therapies on PMD symptoms	4.1 out of 7	Surgical intervention (meaning almost exclusively hysterectomy and bilateral oophorectomy), though the only permanent cure, should be the last resort and then only after detailed counselling and a trial period of a GnRH agonist.

RCOG/NICE 2017	Global	Guideline	Women with Premenstrual Disorders (PMS/PMDD)	Various interventions including CBT, CAM therapies, hormonal and nonhormonal medical management, and nutritional supplements	Different dosages and regimens for various interventions	Various studies on the efficacy and safety of PMS management options	Safety and efficacy of therapies on PMD symptoms	5.7 out of 7 on the AGREE tool	When treating women with severe PMS, hysterectomy and bilateral oophorectomy has been shown to be of benefit. When treating women with PMS, hysterectomy and bilateral oophorectomy can be considered when medical management has failed, long-term GnRH analogue treatment is required, or other gynecological conditions indicate surgery. When treating women with severe PMS, endometrial ablation and hysterectomy with conservation of the ovaries are not recommended.
Schmidt 2017	Maryland, USA	Prospective controlled crossover trial	Women aged 30-50 years meeting criteria for PMDD who experienced symptom remission after 2-3 months of GnRH agonist-induced ovarian suppression (leuprolide)	3 months estradiol/progesterone replacement	1 month of placebo	12 women	Rating for Premenstrual Tension observer and self-ratings completed every 2 weeks during clinical visits	Moderate risk of bias in 3 domains (selection, missing data, and measurement of outcomes)	Both self- and observer-rated scores on the Rating for Premenstrual Tension were significantly increased (more symptomatic) during the first month of combined estradiol/progesterone compared with the last month of leuprolide alone, the placebo month, and the second and third months of estradiol/progesterone.
Segebladh 2009	Sweden	Randomized crossover trial	Women with PMDD between 25 and 47 years of age	Add-back hormone replacement (1.5mg estradiol and 400mg progesterone or 0.5mg estradiol and 400mg progesterone)	1.5mg estradiol and placebo	27 women included in analysis	Daily symptom ratings for mood and physical symptoms	Low risk of bias	The highest dose of estradiol in combination with progesterone was associated with the most pronounced symptom recurrence, both in comparison with a lower dose of estradiol together with progesterone and estradiol-only treatment.
Wyatt 2004	Global	Systematic review and meta-analysis	Patients with a diagnosis of premenstrual syndrome	GnRHa (nasal spray, intravenous, depot)	Placebo	7 RCTs included in analysis	Reduction in overall premenstrual syndrome symptoms	Moderate-quality review	Overall standardized mean difference for all trials that assessed the efficacy of GnRHa was 1.19(95% confidence interval [CI]1.88 to 0.51). The equivalent odds ratio was 8.66 (95% CI 2.52 to 30.26) in favor of GnRHa. GnRHa were more efficacious for physical than behavioral symptoms, although the difference was not statistically significant. The addition of hormonal add-back therapy to GnRHa did not appear to reduce the efficacy

of GnRHa alone; standardized mean difference 0.12 (95% CI 0.35 to 0.58).

References

- Abraham S, Luscombe G, Soo I. Oral contraception and cyclic changes in premenstrual and menstrual experiences. *J Psychosom Obstet Gynaecol* 2003;24:185-93. doi: 10.3109/01674820309039672
- Alpay FB, Turhan NO. Intermittent versus continuous sertraline therapy in the treatment of premenstrual dysphoric disorders. *Int J Fertil Womens Med* 2001;46:228-31.
- Arab A, Golpour-Hamedani S, Rafie N. The association between vitamin D and premenstrual syndrome: a systematic review and meta-analysis of current literature. *J Am Coll Nutr* 2019;38:648-56. doi: 10.1080/07315724.2019.1566036
- Armour M, Ee CC, Hao J, Wilson TM, Yao SS, Smith CA. Acupuncture and acupressure for premenstrual syndrome. *Cochrane Database of Systematic Reviews* 2018, Issue 8. Art. No.: CD005290. doi: 10.1002/14651858.CD005290.pub2
- Atmaca M, Kumru S, Tezcan E. Fluoxetine versus Vitex agnus castus extract in the treatment of premenstrual dysphoric disorder. *Hum Psychopharmacol* 2003;18:191-5. doi: 10.1002/hup.470
- Ayaz-Alkaya S, Yaman-Sözbiç Ş, Terzi H. The effect of Health Belief Model-based health education programme on coping with premenstrual syndrome: a randomised controlled trial. *Int J Nurs Pract* 2020;26:e12816. doi: 10.1111/ijn.12816
- Başıoğlu C, Aydın Özkan S, Karaca T. The effects of psychoeducation based on the cognitive-behavioral approach on premenstrual syndrome symptoms: a randomized controlled trial. *Perspect Psychiatr Care* 2020;56:515-22. doi: 10.1111/ppc.12460
- Bäckström T, Ekberg K, Hirschberg AL, Bixo M, Epperson CN, Briggs P, et al. A randomized, double-blind study on efficacy and safety of sepranolone in premenstrual dysphoric disorder. *Psychoneuroendocrinology* 2021;133:105426. doi: 10.1016/j.psyneuen.2021.105426
- Berger D, Schaffner W, Schrader E, Meier B, Brattström A. Efficacy of Vitex agnus castus L. extract Ze 440 in patients with pre-menstrual syndrome (PMS). *Arch Gynecol Obstet* 2000;264:150-3. doi: 10.1007/s004040000123
- Bixo M, Ekberg K, Poromaa IS, Hirschberg AL, Jonasson AF, Andréén L, et al. Treatment of premenstrual dysphoric disorder with the GABA(A) receptor modulating steroid antagonist Sepranolone (UC1010)-a randomized controlled trial. *Psychoneuroendocrinology* 2017;80:46-55. doi: 10.1016/j.psyneuen.2017.02.031
- Borenstein J, Yu H, Wade S, Chiou C, Rapkin A. Effect of an oral contraceptive containing ethinyl estradiol and drospirenone on premenstrual symptomatology and health-related quality of life. *J Reprod Med* 2003;48:79-85.
- Bryant M, Cassidy A, Hill C, Powell J, Talbot D, Dye L. Effect of consumption of soy isoflavones on behavioural, somatic and affective symptoms in women with premenstrual syndrome. *Br J Nutr* 2005;93:731-9. doi: 10.1079/bjn20041396
- Busse JW, Montori VM, Krasnik C, Patelis-Siotis I, Guyatt GH. Psychological intervention for premenstrual syndrome: a meta-analysis of randomized controlled trials. *Psychother Psychosom* 2009;78:6-15. doi: 10.1159/000162296
- Canning S, Waterman M, Orsi N, Ayres J, Simpson N, Dye L. The efficacy of Hypericum perforatum (St John's wort) for the treatment of premenstrual syndrome: a randomized, double-blind, placebo-controlled trial. *CNS Drugs* 2010;24:207-25. doi: 10.2165/11530120-000000000-00000
- Cerqueira RO, Frey BN, Leclerc E, Brietzke E. Vitex agnus castus for premenstrual syndrome and premenstrual dysphoric disorder: a systematic review. *Arch Womens Ment Health* 2017;20:713-9. doi: 10.1007/s00737-017-0791-0

Cho S, Kim J. Efficacy of acupuncture in management of premenstrual syndrome: a systematic review. *Complement Ther Med* 2010;18:104-11. doi: 10.1016/j.ctim.2009.12.001

Chou PB, Morse CA, Xu H. A controlled trial of Chinese herbal medicine for premenstrual syndrome. *J Psychosom Obstet Gynaecol* 2008;29:185-92. doi: 10.1080/01674820801893011

Coffee AL, Kuehl TJ, Willis S, Sulak PJ. Oral contraceptives and premenstrual symptoms: comparison of a 21/7 and extended regimen. *Am J Obstet Gynecol* 2006;195:1311-9. doi: 10.1016/j.ajog.2006.05.012

Cohen LS, Miner C, Brown EW, Freeman E, Halbreich U, Sundell K, et al. Premenstrual daily fluoxetine for premenstrual dysphoric disorder: a placebo-controlled, clinical trial using computerized diaries. *Obstet Gynecol* 2002;100:435-44. doi: 10.1016/s0029-7844(02)02166-x

Cohen LS, Soares CN, Yonkers KA, Bellew KM, Bridges IM, Steiner M. Paroxetine controlled release for premenstrual dysphoric disorder: a double-blind, placebo-controlled trial. *Psychosom Med* 2004;66:707-13. doi: 10.1097/01.psy.0000140005.94790.9c

Comasco E, Kopp Kallner H, Bixo M, Hirschberg AL, Nyback S, de Grauw H, et al. Ulipristal acetate for treatment of premenstrual dysphoric disorder: a proof-of-concept randomized controlled trial. *Am J Psychiatry* 2021;178:256-65. doi: 10.1176/appi.ajp.2020.20030286

Csupor D, Lantos T, Hegyi P, Benkő R, Viola R, Gyöngyi Z, et al. Vitex agnus-castus in premenstrual syndrome: meta-analysis of double-blind randomised controlled trials. *Complement Ther Med* 2019;47:102190. doi: 10.1016/j.ctim.2019.08.024

Dante G, Facchinetti F. Herbal treatments for alleviating premenstrual symptoms: a systematic review. *J Psychosom Obstet Gynaecol* 2011;32:42-51. doi: 10.3109/0167482X.2010.538102

de Wit AE, de Vries YA, de Boer MK, Scheper C, Fokkema A, Janssen CA, et al. Efficacy of combined oral contraceptives for depressive symptoms and overall symptomatology in premenstrual syndrome: pairwise and network meta-analysis of randomized trials. *Am J Obstet Gynecol* 2021;225:624-33. doi: 10.1016/j.ajog.2021.06.090

Derman O, Kanbur NO, Tokur TE, Kutluk T. Premenstrual syndrome and associated symptoms in adolescent girls. *Eur J Obstet Gynecol Reprod Biol* 2004;116:201-6. doi: 10.1016/j.ejogrb.2004.04.021

De Souza MC, Walker AF, Robinson PA, Bolland K. A synergistic effect of a daily supplement for 1 month of 200 mg magnesium plus 50 mg vitamin B6 for the relief of anxiety-related premenstrual symptoms: a randomized, double-blind, crossover study. *J Womens Health Gend Based Med* 2000;9:131-9. doi: 10.1089/152460900318623

Di Carlo C, Palomba S, Tommaselli GA, Guida M, Di Spiezio Sardo A, Nappi C. Use of leuprolide acetate plus tibolone in the treatment of severe premenstrual syndrome. *Fertil Steril* 2001;75:380-4. doi: 10.1016/s0015-0282(00)01707-6

Dimmock PW, Wyatt KM, Jones PW, O'Brien PM. Efficacy of selective serotonin-reuptake inhibitors in premenstrual syndrome: a systematic review. *Lancet* 2000;356:1131-6. doi: 10.1016/s0140-6736(00)02754-9

Eisenlohr-Moul TA, Girdler SS, Johnson JL, Schmidt PJ, Rubinow DR. Treatment of premenstrual dysphoria with continuous versus intermittent dosing of oral contraceptives: results of a three-arm randomized controlled trial. *Depress Anxiety* 2017;34:908-17. doi: 10.1002/da.22673

Eriksson E, Ekman A, Sinclair S, Sörvik K, Ysander C, Mattson U, et al. Escitalopram administered in the luteal phase exerts a marked and dose-dependent effect in premenstrual dysphoric disorder. *J Clin Psychopharmacol* 2008;28:195-202. doi: 10.1097/JCP.0b013e3181678a28

- Facchinetti F, Fioroni L, Sances G, Romano G, Nappi G, Genazzani AR. Naproxen sodium in the treatment of premenstrual symptoms. A placebo-controlled study. *Gynecol Obstet Invest* 1989;28:205-8. doi: 10.1159/000293579
- Ford O, Lethaby A, Roberts H, Mol BW. Progesterone for premenstrual syndrome. *Cochrane Database of Systematic Reviews* 2012, Issue 3. Art. No.: CD003415. doi: 10.1002/14651858.CD003415.pub4
- Freeman EW, Sondheimer SJ, Polansky M, Garcia-Espagna B. Predictors of response to sertraline treatment of severe premenstrual syndromes. *J Clin Psychiatry* 2000;61:579-84. doi: 10.4088/jcp.v61n0807
- Freeman EW, Rickels K, Yonkers KA, Kunz NR, McPherson M, Upton GV. Venlafaxine in the treatment of premenstrual dysphoric disorder. *Obstet Gynecol* 2001;98:737-44. doi: 10.1016/s0029-7844(01)01530-7
- Freeman EW, Rickels K, Sondheimer SJ, Polansky M, Xiao S. Continuous or intermittent dosing with sertraline for patients with severe premenstrual syndrome or premenstrual dysphoric disorder. *Am J Psychiatry* 2004;161:343-51. doi: 10.1176/appi.ajp.161.2.343
- Freeman EW, Sondheimer SJ, Sammel MD, Ferdousi T, Lin H. A preliminary study of luteal phase versus symptom-onset dosing with escitalopram for premenstrual dysphoric disorder. *J Clin Psychiatry* 2005;66:769-73. doi: 10.4088/jcp.v66n0616
- Freeman EW, Rickels K, Sammel MD, Lin H, Sondheimer SJ. Time to relapse after short- or long-term treatment of severe premenstrual syndrome with sertraline. *Arch Gen Psychiatry* 2009;66:537-44. doi: 10.1001/archgenpsychiatry.2008.547
- Freeman EW, Sammel MD, Lin H, Rickels K, Sondheimer SJ. Clinical subtypes of premenstrual syndrome and responses to sertraline treatment. *Obstet Gynecol* 2011;118:1293-300. doi: 10.1097/AOG.0b013e318236edf2
- Gianfranco C, Vittorio U, Silvia B, Francesco D. Myo-inositol in the treatment of premenstrual dysphoric disorder. *Hum Psychopharmacol* 2011;26:526-30. doi: 10.1002/hup.1241
- Halbreich U, Bergeron R, Yonkers KA, Freeman E, Stout AL, Cohen L. Efficacy of intermittent, luteal phase sertraline treatment of premenstrual dysphoric disorder. *Obstet Gynecol* 2002;100:1219-29. doi: 10.1016/s0029-7844(02)02326-8
- Halbreich U, Freeman EW, Rapkin AJ, Cohen LS, Grubb GS, Bergeron R, et al. Continuous oral levonorgestrel/ethinyl estradiol for treating premenstrual dysphoric disorder. *Contraception* 2012;85:19-27. doi: 10.1016/j.contraception.2011.05.008
- Han J, Cha Y, Kim S. Effect of psychosocial interventions on the severity of premenstrual syndrome: a meta-analysis. *J Psychosom Obstet Gynaecol* 2019;40:176-84. doi: 10.1080/0167482X.2018.1480606
- Hernandez-Reif M, Martinez A, Field T, Quintero O, Hart S, Burman I. Premenstrual symptoms are relieved by massage therapy. *J Psychosom Obstet Gynaecol* 2000;21:9-15. doi: 10.3109/01674820009075603
- Hofmeister S, Bodden S. Premenstrual syndrome and premenstrual dysphoric disorder. *Am Fam Physician* 2016;94:236-40.
- Hunter MS, Ussher JM, Browne SJ, Cariss M, Jelley R, Katz M. A randomized comparison of psychological (cognitive behavior therapy), medical (fluoxetine) and combined treatment for women with premenstrual dysphoric disorder. *J Psychosom Obstet Gynaecol* 2002;23:193-9. doi: 10.3109/01674820209074672
- Ismaili E, Walsh S, O'Brien PM, Bäckström T, Brown C, Dennerstein L, et al. Fourth consensus of the International Society for Premenstrual Disorders (ISPM): auditable standards for diagnosis and management of premenstrual disorder. Consensus Group of the International Society for Premenstrual Disorders. *Arch Womens Ment Health* 2016;19:953-8. doi: 10.1007/s00737-016-0631-7

- Jackson C, Pearson B, Girdler S, Johnson J, Hamer RM, Killenberg S, et al. Double-blind, placebo-controlled pilot study of adjunctive quetiapine SR in the treatment of PMS/PMDD. *Hum Psychopharmacol* 2015;30:425-34. doi: 10.1002/hup.2494
- Jang H, Lee MS. Effects of qi therapy (external qigong) on premenstrual syndrome: a randomized placebo-controlled study. *J Altern Complement Med* 2004;10:456-62. doi: 10.1089/1075553041323902
- Jang SH, Kim DI, Choi M. Effects and treatment methods of acupuncture and herbal medicine for premenstrual syndrome/premenstrual dysphoric disorder: systematic review. *BMC Complement Altern Med* 2014;14:11-. doi: 10.1186/1472-6882-14-11
- Jarvis CI, Lynch AM, Morin AK. Management strategies for premenstrual syndrome/premenstrual dysphoric disorder. *Ann Pharmacother* 2008;42:967-78. doi: 10.17226/13050
- Jing Z, Yang X, Ismail KM, Chen XY, Wu T. Chinese herbal medicine for premenstrual syndrome. *Cochrane Database of Systematic Reviews* 2009, Issue 1. Art. No.: CD006414. doi: 10.1002/14651858.CD006414.pub2
- Kim S, Park H, Lee H, Lee H. Acupuncture for premenstrual syndrome: a systematic review and meta-analysis of randomised controlled trials. *BJOG* 2011;118:899-915. doi: 10.1111/j.1471-0528.2011.02994.x
- Kleinstäuber M, Witthöft M, Hiller W. Cognitive-behavioral and pharmacological interventions for premenstrual syndrome or premenstrual dysphoric disorder: a meta-analysis. *J Clin Psychol Med Settings* 2012;19:308-19. doi: 10.1007/s10880-012-9299-y
- Kornstein SG, Pearlstein TB, Fayyad R, Farfel GM, Gillespie JA. Low-dose sertraline in the treatment of moderate-to-severe premenstrual syndrome: efficacy of 3 dosing strategies. *J Clin Psychiatry* 2006;67:1624-32. doi: 10.4088/jcp.v67n1020
- Krasnik C, Montori VM, Guyatt GH, Heels-Ansdell D, Busse JW. The effect of bright light therapy on depression associated with premenstrual dysphoric disorder. Medically Unexplained Syndromes Study Group. *Am J Obstet Gynecol* 2005;193:658-61. doi: 10.1016/j.ajog.2005.01.055
- Kwan I, Onwude JL. Premenstrual syndrome. *BMJ Clin Evid* 2009;2009:0806.
- Kwan I, Onwude JL. Premenstrual syndrome. *BMJ Clin Evid* 2015;2015:0806.
- Landén M, Eriksson O, Sundblad C, Andersch B, Naessén T, Eriksson E. Compounds with affinity for serotonergic receptors in the treatment of premenstrual dysphoria: a comparison of buspirone, nefazodone and placebo. *Psychopharmacology (Berl)* 2001;155:292-8. doi: 10.1007/s002130100718
- Landén M, Nissbrandt H, Allgulander C, Sörvik K, Ysander C, Eriksson E. Placebo-controlled trial comparing intermittent and continuous paroxetine in premenstrual dysphoric disorder. *Neuropsychopharmacology* 2007;32:153-61. doi: 10.1038/sj.npp.1301216
- Landén M, Erlandsson H, Bengtsson F, Andersch B, Eriksson E. Short onset of action of a serotonin reuptake inhibitor when used to reduce premenstrual irritability. *Neuropsychopharmacology* 2009;34:585-92. doi: 10.1038/npp.2008.86
- Le Mellédo JM, Van Driel M, Coupland NJ, Lott P, Jhangri GS. Response to flumazenil in women with premenstrual dysphoric disorder. *Am J Psychiatry* 2000;157:821-3. doi: 10.1176/appi.ajp.157.5.821
- Leminen H, Heliövaara-Peippo S, Halmesmäki K, Teperi J, Grenman S, Kivelä A, et al. The effect of hysterectomy or levonorgestrel-releasing intrauterine system on premenstrual symptoms in women treated for menorrhagia: secondary analysis of a randomized controlled trial. *Acta Obstet Gynecol Scand* 2012;91:318-25. doi: 10.1111/j.1600-0412.2011.01340.x

- Lombardi I, Luisi S, Quirici B, Monteleone P, Bernardi F, Liut M, et al. Adrenal response to adrenocorticotrophic hormone stimulation in patients with premenstrual syndrome. *Gynecol Endocrinol* 2004;18:79-87. doi: 10.1080/09513590310001652955
- Lopez LM, Kaptein AA, Helmerhorst FM. Oral contraceptives containing drospirenone for premenstrual syndrome. *Cochrane Database of Systematic Reviews* 2012, Issue 2. Art. No.: CD006586. doi: 10.1002/14651858.CD006586.pub4
- Lukes AS, McBride RJ, Herring AH, Fried M, Sherwani A, Dell D. Improved premenstrual syndrome symptoms after NovaSure endometrial ablation. *J Minim Invasive Gynecol* 2011;18:607-11. doi: 10.1016/j.jmig.2011.06.001
- Lustyk MK, Gerrish WG, Shaver S, Keys SL. Cognitive-behavioral therapy for premenstrual syndrome and premenstrual dysphoric disorder: a systematic review. *Arch Womens Ment Health* 2009;12:85-96. doi: 10.1007/s00737-009-0052-y
- Ma S, Song SJ. Oral contraceptives containing drospirenone for premenstrual syndrome. *Cochrane Database of Systematic Reviews* 2023, Issue 6. Art. No.: CD006586. doi: 10.1002/14651858.CD006586.pub5
- Management of premenstrual syndrome: Green-top Guideline No. 48. *BJOG* 2017;124:e73-105. doi: 10.1111/1471-0528.14260
- Marjoribanks J, Brown J, O'Brien PM, Wyatt K. Selective serotonin reuptake inhibitors for premenstrual syndrome. *Cochrane Database of Systematic Reviews* 2013, Issue 6. Art. No.: CD001396. doi: 10.1002/14651858.CD001396.pub3
- Marr J, Niknian M, Shulman LP, Lynen R. Premenstrual dysphoric disorder symptom cluster improvement by cycle with the combined oral contraceptive ethinylestradiol 20 mcg plus drospirenone 3 mg administered in a 24/4 regimen. *Contraception* 2011;84:81-6. doi: 10.1016/j.contraception.2010.10.010
- Marr J, Heinemann K, Kunz M, Rapkin A. Ethinyl estradiol 20µg/drospirenone 3mg 24/4 oral contraceptive for the treatment of functional impairment in women with premenstrual dysphoric disorder. *Int J Gynaecol Obstet* 2011;113:103-7. doi: 10.1016/j.ijgo.2010.10.029
- Martinez PE, Rubinow DR, Nieman LK, Koziol DE, Morrow AL, Schiller CE, et al. 5α-reductase inhibition prevents the luteal phase increase in plasma allopregnanolone levels and mitigates symptoms in women with premenstrual dysphoric disorder. *Neuropsychopharmacology* 2016;41:1093-102. doi: 10.1038/npp.2015.246
- Miner C, Brown E, McCray S, Gonzales J, Wohlreich M. Weekly luteal-phase dosing with enteric-coated fluoxetine 90 mg in premenstrual dysphoric disorder: a randomized, double-blind, placebo-controlled clinical trial. *Clin Ther* 2002;24:417-33. doi: 10.1016/s0149-2918(02)85043-3
- Mira M, McNeil D, Fraser IS, Vizzard J, Abraham S. Mefenamic acid in the treatment of premenstrual syndrome. *Obstet Gynecol* 1986;68:395-8. doi: 10.1097/00006250-198609000-00022
- Momoeda M, Sasaki H, Tagashira E, Ogishima M, Takano Y, Ochiai K. Efficacy and safety of Vitex agnus-castus extract for treatment of premenstrual syndrome in Japanese patients: a prospective, open-label study. *Adv Ther* 2014;31:362-73. doi: 10.1007/s12325-014-0106-z
- Naheed B, Kuiper JH, Uthman OA, O'Mahony F, O'Brien PMS. Non-contraceptive oestrogen-containing preparations for controlling symptoms of premenstrual syndrome. *Cochrane Database of Systematic Reviews* 2017, Issue 3. Art. No.: CD010503. doi: 10.1002/14651858.CD010503.pub2
- Nemets B, Talesnick B, Belmaker RH, Levine J. Myo-inositol has no beneficial effect on premenstrual dysphoric disorder. *World J Biol Psychiatry* 2002;3:147-9. doi: 10.3109/15622970209150615
- Nevatte T, O'Brien PM, Bäckström T, Brown C, Dennerstein L, Endicott J, et al. ISPMDS consensus on the management of premenstrual disorders. *Arch Womens Ment Health* 2013;16:279-91. doi: 10.1007/s00737-013-0346-y

- Nguyen TV, Reuter JM, Gaikwad NW, Rotroff DM, Kucera HR, Motsinger-Reif A, et al. The steroid metabolome in women with premenstrual dysphoric disorder during GnRH agonist-induced ovarian suppression: effects of estradiol and progesterone addback. *Transl Psychiatry* 2017;7:e1193. doi: 10.1038/tp.2017.146
- Ooi SL, Watts S, McClean R, Pak SC. Vitex agnus-castus for the treatment of cyclic mastalgia: a systematic review and meta-analysis. *J Womens Health (Larchmt)* 2020;29:262-78. doi: 10.1089/jwh.2019.7770
- Pal A, Nath B, Paul S, Meena S. Evaluation of the effectiveness of yoga in management of premenstrual syndrome: a systematic review and meta-analysis. *J Psychosom Obstet Gynaecol* 2022;43:517-25. doi: 10.1080/0167482X.2022.2086457
- Pearlstein TB, Halbreich U, Batzar ED, Brown CS, Endicott J, Frank E, et al. Psychosocial functioning in women with premenstrual dysphoric disorder before and after treatment with sertraline or placebo. *J Clin Psychiatry* 2000;61:101-9. doi: 10.4088/jcp.v61n0205
- Pearlstein T, Joliat MJ, Brown EB, Miner CM. Recurrence of symptoms of premenstrual dysphoric disorder after the cessation of luteal-phase fluoxetine treatment. *Am J Obstet Gynecol* 2003;188:887-95. doi: 10.1067/mob.2003.207
- Pearlstein TB, Bachmann GA, Zacur HA, Yonkers KA. Treatment of premenstrual dysphoric disorder with a new drospirenone-containing oral contraceptive formulation. *Contraception* 2005;72:414-21. doi: 10.1016/j.contraception.2005.08.021
- Quaranta S, Buscaglia MA, Meroni MG, Colombo E, Cella S. Pilot study of the efficacy and safety of a modified-release magnesium 250 mg tablet (Sincromag) for the treatment of premenstrual syndrome. *Clin Drug Investig* 2007;27:51-8. doi: 10.2165/00044011-200727010-00004
- Reilly TJ, Wallman P, Clark I, Knox C, Craig MC, Taylor D. Intermittent selective serotonin reuptake inhibitors for premenstrual syndromes: a systematic review and meta-analysis of randomised trials. *J Psychopharmacol* 2023;37:261-7. doi: 10.1177/02698811221099645
- Retallick-Brown H, Blampied N, Rucklidge JJ. A pilot randomized treatment-controlled trial comparing vitamin B6 with broad-spectrum micronutrients for premenstrual syndrome. *J Altern Complement Med* 2020;26:88-97. doi: 10.1089/acm.2019.0305
- Roca CA, Schmidt PJ, Smith MJ, Danaceau MA, Murphy DL, Rubinow DR. Effects of metergoline on symptoms in women with premenstrual dysphoric disorder. *Am J Psychiatry* 2002;159:1876-81. doi: 10.1176/appi.ajp.159.11.1876
- Ross C, Coleman G, Stojanovska C. Prospectively reported symptom change across the menstrual cycle in users and non-users of oral contraceptives. *J Psychosom Obstet Gynaecol* 2003;24:15-29. doi: 10.3109/01674820309042797
- Sadler C, Smith H, Hammond J, Bayly R, Borland S, Panay N, et al. Lifestyle factors, hormonal contraception, and premenstrual symptoms: the United Kingdom Southampton Women's Survey. *J Womens Health (Larchmt)* 2010;19:391-6. doi: 10.1089/jwh.2008.1210
- Schellenberg R. Treatment for the premenstrual syndrome with agnus castus fruit extract: prospective, randomised, placebo controlled study. *BMJ* 2001;322:134-7. doi: 10.1136/bmj.322.7279.134
- Schellenberg R, Zimmermann C, Drewe J, Hoexter G, Zahner C. Dose-dependent efficacy of the Vitex agnus castus extract Ze 440 in patients suffering from premenstrual syndrome. *Phytomedicine* 2012;19:1325-31. doi: 10.1016/j.phymed.2012.08.006
- Schmidt PJ, Martinez PE, Nieman LK, Koziol DE, Thompson KD, Schenkel L, et al. Premenstrual dysphoric disorder symptoms following ovarian suppression: triggered by change in ovarian steroid levels but not continuous stable levels. *Am J Psychiatry* 2017;174:980-9. doi: 10.1176/appi.ajp.2017.16101113
- Segebladh B, Borgström A, Nyberg S, Bixo M, Sundström-Poromaa I. Evaluation of different add-back estradiol and progesterone treatments to gonadotropin-releasing hormone agonist treatment in patients with premenstrual dysphoric disorder. *Am J Obstet Gynecol* 2009;201:139.e1-8. doi: 10.1016/j.ajog.2009.03.016

- Shah NR, Jones JB, Aperi J, Shemtov R, Karne A, Borenstein J. Selective serotonin reuptake inhibitors for premenstrual syndrome and premenstrual dysphoric disorder: a meta-analysis. *Obstet Gynecol* 2008;111:1175-82. doi: 10.1097/AOG.0b013e31816fd73b
- Simsek Küçükkelepçe D, Timur Tashan S. The effects of health belief model-based education and acupressure for coping with premenstrual syndrome on premenstrual symptoms and quality of life: a randomized-controlled trial. *Perspect Psychiatr Care* 2021;57:189-97. doi: 10.1111/ppc.12546
- Solt Kırca A, Kızılkaya T. Effects of music medicine on premenstrual symptoms levels and quality of life: a randomized controlled trial. *Complement Ther Clin Pract* 2022;46:101542. doi: 10.1016/j.ctcp.2022.101542
- Steinberg EM, Cardoso GM, Martinez PE, Rubinow DR, Schmidt PJ. Rapid response to fluoxetine in women with premenstrual dysphoric disorder. *Depress Anxiety* 2012;29:531-40. doi: 10.1002/da.21959
- Steiner M, Romano SJ, Babcock S, Dillon J, Shuler C, Berger C, et al. The efficacy of fluoxetine in improving physical symptoms associated with premenstrual dysphoric disorder. *BJOG* 2001;108:462-8. doi: 10.1111/j.1471-0528.2001.00120.x
- Steiner M, Brown E, Trzepacz P, Dillon J, Berger C, Carter D, et al. Fluoxetine improves functional work capacity in women with premenstrual dysphoric disorder. *Arch Womens Ment Health* 2003;6:71-7. doi: 10.1007/s00737-002-0162-2
- Steiner M, Hirschberg AL, Bergeron R, Holland F, Gee MD, Van Erp E. Luteal phase dosing with paroxetine controlled release (CR) in the treatment of premenstrual dysphoric disorder. *Am J Obstet Gynecol* 2005;193:352-60. doi: 10.1016/j.ajog.2005.01.021
- Steiner M, Ravindran AV, LeMelledo J, Carter D, Huang JO, Anonychuk AM, et al. Luteal phase administration of paroxetine for the treatment of premenstrual dysphoric disorder: a randomized, double-blind, placebo-controlled trial in Canadian women. *J Clin Psychiatry* 2008;69:991-8. doi: 10.4088/jcp.v69n0616
- Stevinson C, Ernst E. A pilot study of Hypericum perforatum for the treatment of premenstrual syndrome. *BJOG* 2000;107:870-6. doi: 10.1111/j.1471-0528.2000.tb11085.x
- Stoddard JL, Dent CW, Shames L, Bernstein L. Exercise training effects on premenstrual distress and ovarian steroid hormones. *Eur J Appl Physiol* 2007;99:27-37. doi: 10.1007/s00421-006-0313-7
- Sveindóttir H, Bäckström T. Prevalence of menstrual cycle symptom cyclicity and premenstrual dysphoric disorder in a random sample of women using and not using oral contraceptives. *Acta Obstet Gynecol Scand* 2000;79:405-13. doi: 10.1080/j.1600-0412.2000.079005405.x
- Tamayo JM, Gómez G, Barrios R, Holguín J, Adrianzén C. Differential time course efficacy on dysphoric and physical symptoms of the intermittent dosing of fluoxetine in the premenstrual dysphoric disorder. *J Clin Psychopharmacol* 2004;24:469-71. doi: 10.1097/01.jcp.0000132445.20230.7e
- Thys-Jacobs S, Ceccarelli S, Bierman A, Weisman H, Cohen MA, Alvir J. Calcium supplementation in premenstrual syndrome: a randomized crossover trial. *J Gen Intern Med* 1989;4:183-9. doi: 10.1007/BF02599520
- Thys-Jacobs S, Starkey P, Bernstein D, Tian J. Calcium carbonate and the premenstrual syndrome: effects on premenstrual and menstrual symptoms. *Premenstrual Syndrome Study Group. Am J Obstet Gynecol* 1998;179:444-52. doi: 10.1016/s0002-9378(98)70377-1
- Tommaselli GA, Di Carlo C, Bifulco G, Di Spiezio Sardo A, Pellicano M, Nappi C. Serum leptin levels in patients with premenstrual syndrome treated with GnRH analogues alone and in association with tibolone. *Clin Endocrinol (Oxf)* 2003;59:716-22. doi: 10.1046/j.1365-2265.2003.01911.x
- Ussher JM, Perz J. Evaluation of the relative efficacy of a couple cognitive-behaviour therapy (CBT) for premenstrual disorders (PMDs), in comparison to one-to-one CBT and a wait list control: a randomized controlled trial. *PLoS One* 2017;12:e0175068. doi: 10.1371/journal.pone.0175068

- Uzunçakmak T, Ayaz Alkaya S. Effect of aromatherapy on coping with premenstrual syndrome: a randomized controlled trial. *Complement Ther Med* 2018;36:63-7. doi: 10.1016/j.ctim.2017.11.022
- van Die MD, Burger HG, Teede HJ, Bone KM. Vitex agnus-castus extracts for female reproductive disorders: a systematic review of clinical trials. *Planta Med* 2013;79:562-75. doi: 10.1055/s-0032-1327831
- Verkaik S, Kamperman AM, van Westrhenen R, Schulte PF. The treatment of premenstrual syndrome with preparations of Vitex agnus castus: a systematic review and meta-analysis. *Am J Obstet Gynecol* 2017;217:150-66. doi: 10.1016/j.ajog.2017.02.028
- Weise C, Kaiser G, Janda C, Kues JN, Andersson G, Strahler J, et al. Internet-based cognitive-behavioural intervention for women with premenstrual dysphoric disorder: a randomized controlled trial. *Psychother Psychosom* 2019;88:16-29. doi: 10.1159/000496237
- Whelan AM, Jurgens TM, Naylor H. Herbs, vitamins and minerals in the treatment of premenstrual syndrome: a systematic review. *Can J Clin Pharmacol* 2009;16:e407-29.
- Wyatt K, Dimmock P, Jones P, Obhrai M, O'Brien S. Efficacy of progesterone and progestogens in management of premenstrual syndrome: systematic review. *BMJ* 2001;323:776-80. doi: 10.1136/bmj.323.7316.776
- Wyatt KM, Dimmock PW, Ismail KM, Jones PW, O'Brien PM. The effectiveness of GnRHa with and without 'add-back' therapy in treating premenstrual syndrome: a meta analysis. *BJOG* 2004;111:585-93. doi: 10.1111/j.1471-0528.2004.00135.x
- Yesildere Saglam H, Orsal O. Effect of exercise on premenstrual symptoms: a systematic review. *Complement Ther Med* 2020;48:102272. doi: 10.1016/j.ctim.2019.102272
- Yonkers KA, Pearlstein T, Fayyad R, Gillespie JA. Luteal phase treatment of premenstrual dysphoric disorder improves symptoms that continue into the postmenstrual phase. *J Affect Disord* 2005;85:317-21. doi: 10.1016/j.jad.2004.10.006
- Yonkers KA, Brown C, Pearlstein TB, Foegh M, Sampson-Landers C, Rapkin A. Efficacy of a new low-dose oral contraceptive with drospirenone in premenstrual dysphoric disorder. *Obstet Gynecol* 2005;106:492-501. doi: 10.1097/01.AOG.0000175834.77215.2e
- Yonkers KA, Holthausen GA, Poschman K, Howell HB. Symptom-onset treatment for women with premenstrual dysphoric disorder. *J Clin Psychopharmacol* 2006;26:198-202. doi: 10.1097/01.jcp.0000203197.03829.ae
- Yonkers KA, Pearlstein TB, Gotman N. A pilot study to compare fluoxetine, calcium, and placebo in the treatment of premenstrual syndrome. *J Clin Psychopharmacol* 2013;33:614-20. doi: 10.1097/JCP.0b013e31829c7697
- Yonkers KA, Kornstein SG, Gueorguieva R, Merry B, Van Steenburgh K, Altemus M. Symptom-onset dosing of sertraline for the treatment of premenstrual dysphoric disorder: a randomized clinical trial. *JAMA Psychiatry* 2015;72:1037-44. doi: 10.1001/jamapsychiatry.2015.1472
- Yonkers KA, Cameron B, Gueorguieva R, Altemus M, Kornstein SG. The influence of cyclic hormonal contraception on expression of premenstrual syndrome. *J Womens Health (Larchmt)* 2017;26:321-8. doi: 10.1089/jwh.2016.5941