

CLINICAL REVIEW

Diagnosis and management of premenstrual disorders

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Premenstrual disorders have a substantial social, occupational, academic, and psychological effect on the lives of millions of women (from menarche to menopause) and their families.¹

Published criteria for diagnosis vary greatly between authoritative bodies, so the true prevalence rates are unknown. A new classification from the International Society for Premenstrual Disorders (ISPM) will allow this to be resolved.² It will also enable clinicians to provide accurate diagnosis and effective management.² Little is known about what causes premenstrual syndromes, and the few treatments that are licensed are ineffective,³⁻⁵ although treatment can, however, be provided for most women with good effect using unlicensed approaches. In this article, we discuss the classification of premenstrual disorders, how to measure symptoms and diagnose the condition, and effective management strategies. This review is based on evidence from randomised placebo controlled trials where available, recent Cochrane reviews, Royal College of Obstetricians and Gynaecologists' evidence based guidelines and published consensus statements and textbooks by internationally recognised experts.

How should symptoms be measured?

Women usually present with their own retrospective diagnosis of premenstrual syndrome, which is based on the symptoms of previous cycles; however, a large comprehensive study that compared retrospective diagnosis with a prospective assessment of symptoms showed retrospective diagnosis to be unreliable.⁶ There is no objective diagnostic test and diagnosis depends on the woman prospectively recording symptoms over two cycles, as recommended in Royal College of Obstetricians and Gynaecologists' (RCOG) guidelines,⁷ which can delay the start of treatment. The RCOG recommends the daily record of severity of problems tool,⁷ the completion and analysis of which is laborious. More patient friendly internet based systems are now available (www.symptometrics.com). Some form of screening (patient history or structured questionnaire, such as the premenstrual syndrome screening tool⁸) would avoid patients

unnecessarily embarking on two months of data collection when diagnosis of a premenstrual disorder seems unlikely.

How are premenstrual disorders diagnosed?

The ISPM recently defined precise criteria for diagnosing the core premenstrual disorder (box 1). Symptoms occur regularly in ovulating women during the luteal phase of the cycle, resolve by the end of menstruation, and are followed by a symptom-free interval. Substantial impairment of daily activities at work or school, social activities and hobbies, and interpersonal relationships is a key feature. The criteria do not require specific symptoms to be present and, although well over 200 have been reported, some are considered key or characteristic symptoms (box 2).

Symptoms may be predominantly physical, predominantly psychological, or both. A proportion of patients with severe psychological symptoms will also fulfil American Psychiatric Association (APA) criteria for premenstrual dysphoric disorder.¹⁰ The restrictive diagnostic criteria for this disorder reduce its usefulness in clinical practice. For instance, in the United States, severely affected women who do not quite fit the specific criteria would not be eligible for treatment (and reimbursement). The American Congress of Obstetricians and Gynecologists (ACOG) and the RCOG have outlined criteria for premenstrual syndrome that are more liberal.^{7 11} The criteria for premenstrual syndrome and premenstrual dysphoric disorder fulfil the ISPM criteria for core premenstrual disorder.²

Variants of the core premenstrual disorder include premenstrual exacerbation of an underlying physiological, somatic, or medical condition¹²; premenstrual symptoms in the absence of menstruation (after hysterectomy with ovarian conservation, endometrial ablation, or with a levonorgestrel releasing intrauterine system); progestogen induced premenstrual syndrome occurring during progestogen treatment (cyclical

Summary points

- Premenstrual disorders can considerably impair functioning at work or school and affect interpersonal relationships
- The cause of premenstrual disorders is not understood but symptoms are clearly related to ovulation
- Precise diagnosis and classification are key to successful treatment of most patients
- Severity of symptoms, pregnancy and contraceptive needs, and the patient's wishes will dictate the invasiveness of treatment
- Patients may be treated effectively using non-drug based interventions, suppression of ovulation, or specific psychotropics, often in general practice
- Given the disorder's complexity, a tailored empirical approach, based on evidence and good clinical judgment, is preferable

Sources and selection criteria

We searched Medline, PubMed, evidence based specialty guidelines, and Cochrane reviews. In addition, we used the recently published consensus of the International Society for Premenstrual Disorders and a comprehensive textbook by globally recognised experts that reviewed the entire literature on premenstrual disorder. The advice also draws on the authors' 30 years of experience of research and clinical practice in gynaecology and psychiatry.

Box 1 Criteria for diagnosing the core premenstrual disorder

- It is precipitated by ovulation
- Symptoms are not defined, although typical symptoms exist
- Any number of symptoms can be present
- Physical and psychological symptoms are important
- Symptoms recur in the luteal phase
- Symptoms disappear by the end of menstruation
- A symptom-free week occurs between menstruation and ovulation
- Symptoms must be prospectively rated
- Symptoms are not an exacerbation of an underlying psychological or physical disorder
- Symptoms cause substantial impairment

hormonal replacement therapy, hormonal contraception); and symptoms of premenstrual disorder with unspecified non-ovulatory ovarian activity. The table summarises the characteristics of the premenstrual disorders.

How are premenstrual disorders managed?**The consultation and treatment planning**

Box 3 outlines an approach to careful history taking. Bearing in mind available treatment options, it is important to review the patient's previous treatment and her future plans for pregnancy or contraception. Ask the woman whether psychotropic therapy, endocrine agents, surgery, or an intrauterine system are acceptable. The severity of symptoms and the degree of impairment will usually dictate the level of invasiveness of any intervention used. The condition can be treated by psychotropic drugs or suppression of ovulation with a hormonal agent that does not reinstitute the symptoms, and it is important to communicate this clearly to the patient.

Which treatments can be effective without suppressing ovulation?**Non-drug based treatments**

Box 4 summarises non-drug based approaches to management that are supported by some research evidence and expert consensus. These approaches may be more effective for women

with less severe symptoms. Dietary recommendations and herbal supplements have not been studied robustly. The only herbal supplement that has been shown to be effective in small placebo controlled trials is fruit extract of *Vitex agnus castus*.¹³ Placebo controlled studies show that calcium, vitamin B-6, and exercise may be superior to placebo. A programme of 10 cognitive behavioural therapy sessions that included relaxation, stress management, and assertiveness training, has been reported to be effective and comparable to treatment with fluoxetine over six months, with cognitive behavioural therapy possibly having a longer duration of effect when assessed at 12 months.¹⁴

Diuretics

Spiroonolactone 100 mg/day given in the luteal phase has been shown in randomised placebo controlled studies to reduce abdominal bloating, swelling, breast discomfort, and mood symptoms.¹⁵

Psychotropic drugs

Meta-analyses of placebo controlled trials have found that selective serotonin reuptake inhibitors (SSRIs; fluoxetine, paroxetine, citalopram, sertraline) or serotonin and noradrenaline reuptake inhibitors (SNRIs; venlafaxine) are effective in reducing mood and physical symptoms when used continuously or 14 days before menses (usually at a lower dose than that recommended to treat a mood disorder).¹⁶⁻¹⁸ Symptoms may improve within 48 hours of beginning treatment. Irritability is

Box 2 Symptoms⁹*Physical symptoms*

Joint pain, muscle pain, back pain
 Breast tenderness or pain
 Abdominal swelling or bloating
 Headaches
 Skin disorders
 Weight gain
 Swelling of extremities (hands or feet, or both)

Psychological and behavioural symptoms

Changes in appetite, overeating, or specific food cravings
 Fatigue, lethargy, or lack of energy
 Mood swings (for example, feeling suddenly sad or crying, increased sensitivity to rejection)
 Irritability
 Anger
 Sleep disturbances
 Restlessness
 Poor concentration
 Social withdrawal
 Not in control
 Lack of interest in usual activities
 Loneliness
 Anxiety
 Depressed mood
 Confusion
 Tension
 Hopelessness

Box 3 Minimum information to be obtained in first two clinic or surgery appointments

Menstrual history: frequency, duration, heaviness, pain, regularity, amenorrhoea, last menstrual period
 Premenstrual symptom history: character, timing, absence or presence after menstruation, symptom-free follicular phase week, when they begin, how long they have been occurring
 Has there been any suicidal ideation?
 Impairment: effect on work, school, hobbies, social activities, family, partner, work colleagues. Level of distress caused
 Is there an underlying problem (psychological, physical, medical) that worsens before menstruation? Is this reduced during the follicular phase?
 Amenorrhoea: has the patient undergone a procedure that has resulted in amenorrhoea (hysterectomy with ovarian conservation, levonorgestrel releasing intrauterine system, endometrial ablation) but symptoms persist?
 Is the patient being treated with hormones? For example, combined or progestogen-only contraception, progestogens, hormonal replacement therapy
 What are the patient's contraceptive needs and current contraception? Is her family complete, is she trying to become pregnant?
 Does she have other medical diagnoses, particularly gynaecological diagnoses like heavy menstrual bleeding, endometriosis, pelvic pain, dyspareunia, cervical smear abnormalities?
 What treatment approaches—non-medical, behavioural therapy, psychotropics, hormones, intrauterine hormones, surgical interventions—would she find acceptable?
 Is she willing to receive unlicensed drugs? Is she prepared to receive treatment that will usually prevent her getting pregnant and is she happy to use barrier methods of contraception during treatment?
 What treatments have been self administered or prescribed by doctors and what have been the positive or negative effects? Have they been used appropriately and failed or inappropriately and been unsuccessful?

particularly responsive. SSRIs are licensed in the US, but not in the United Kingdom, for the management of premenstrual dysphoric disorder.

The reversible side effects of SSRIs seem to be less common with intermittent treatment. These include fatigue, insomnia, nausea, gastrointestinal disturbance, headache, sweating, and

Box 4 Treatments

The following treatments are supported by evidence based studies and expert consensus reports. The doses that have shown efficacy in randomised trials are given in parenthesis.

*Non-drug based treatments**Lifestyle*

- Education about premenstrual syndrome
- Cognitive behavioural therapy
- Relaxation techniques
- Regular aerobic exercise (at least 20-30 minutes, three times a week)

Supplements

- Calcium carbonate
- Magnesium oxide
- Vitamin B-6 supplements (dose not to exceed 100 mg/day)
- Fruit extract of *Vitex agnus castus*

*Non-hormonal agents**Diuretics*

- Spirolactone (100 mg/day during luteal phase)

Psychotropic drugs

- Fluoxetine (selective serotonin reuptake inhibitor (SSRI); 10-20 mg/day continuously or luteal phase only; can be increased to 40 mg/day)
- Paroxetine (SSRI; 10-30 mg/day)
- Citalopram (SSRI; 10-30 mg/day)
- Sertraline (SSRI; 25-50 mg/day initially, can be increased to 150 mg/day)
- Venlafaxine (serotonin and noradrenaline reuptake inhibitor; 75-112.5 mg/day)

Anxiolytics

- Alprazolam (0.25-4.0 mg two to three times a day)
- Buspirone (10-60 mg/day)

*Hormone based treatments**Progesterone and progestogens: not recommended*

- Norethisterone
- Medroxyprogesterone acetate
- Levonorgestrel

*Ovulation suppression**Oral contraception*

- Drospirenone and lower doses of ethinylestradiol

Gonadotrophin releasing hormone agonist

- Goserelin (one off injection of 3.6 mg for one month or 10.8 mg for three months), with or without add back with gonadotrophin releasing hormone treatment (tibolone 2.5 mg/day)

Gonadotrophin inhibitor

- Danazol (200-400 mg/day)

Estradiol

- Transdermal patches (100 mg; increase to 200 mg if ovulation is not suppressed)
- Subcutaneous implants (50 mg; increase to 75 mg or 100 mg if ovulation is not suppressed)

Surgery

- Bilateral oophorectomy and hysterectomy

tremor. Continuous use has been associated with decreased libido and difficulty achieving orgasm. Dizziness, lethargy, nausea, irritability, low mood, and vivid dreams are all symptoms of serotonin withdrawal and are rarely reported with

intermittent treatment.¹⁸ SSRIs and oral contraceptives can be given concurrently without decreasing the efficacy of either class of drug. Obviously, some patients may become pregnant

while taking SSRIs and these drugs have not been shown to be teratogenic.¹⁹

Continuous treatment with SSRIs or SNRIs may be a more logical approach for patients with premenstrual exacerbation of an affective disorder.

No studies have directly compared the psychotropic agents so there is no evidence to suggest that one preparation works better than another. Moreover, the response to one SSRI does not predict the efficacy, side effects, or outcomes of another. Different drugs, doses, and timings should be tried empirically in individual patients.

Certain anxiolytics (alprazolam, buspirone) have been shown in placebo controlled studies to be superior to placebo^{18 20 21} but seem to be less effective than SSRIs. The side effect profiles of these agents and risks of dependence make them less desirable options than SSRIs.

How can we treat premenstrual disorders using hormones?

Hormonal treatment that does not suppress ovulation

Progesterone and progestogens (norethisterone, medroxyprogesterone acetate, levonorgestrel) administered in the luteal phase are the only hormonal agents licensed for managing premenstrual syndrome in the UK. However, a systematic review showed that they are ineffective and often restimulate the symptoms.⁴ These agents are useful only for endometrial protection during treatment with oestrogen to suppress ovulation.

Treatment by suppression of ovulation

Ovulation can be suppressed with oral contraceptives, gonadotrophin releasing hormone (GnRH) agonists, the gonadotrophin inhibitor danazol, oestrogen, and by removal of the ovaries (box 5).

Oral contraception

Oral contraceptive agents suppress ovulation but introduce a new exogenous endocrine cycle that can lead to progestogen induced symptoms. A newer oral contraceptive that contains drospirenone and 20 µg of ethinylestradiol, consisting of 24 active followed by four placebo pills, may counteract this effect. This regimen is not currently available in the UK. Drospirenone has antidiuretic and antiandrogenic properties, and, in combination with the lower dose of ethinylestradiol administered in the above 24/4 regimen, suppresses ovulation and treats symptoms effectively without regenerating physical or psychological symptoms, according to two randomised controlled trials.^{22 23} The 20 µg pills do have higher rates of breakthrough bleeding, as noted in a recent Cochrane review. The benefits for premenstrual disorders may still apply using a 30 µg ethinylestradiol and drospirenone oral contraceptive pill in the standard 21/7 regimen.²⁴

GnRH agonist analogues

Several randomised controlled trials have shown that GnRH agonists are effective in relieving symptoms of premenstrual disorders.²⁵ Long acting GnRH suppresses ovarian steroid production, resulting in a “medical menopause” and hence relief of premenstrual syndrome. The induced hypo-oestrogenic state can cause hot flushes and night sweats, low mood, insomnia, and eventually osteoporosis. “Add back” treatment with combinations of oestrogen and progesterone or tibolone

ameliorates side effects and prolongs treatment, without reducing efficacy. There are few long term safety data for GnRH agonists with add back treatment. GnRH agonist analogues do not prevent pregnancy, so contraception must be used. Tibolone appears less likely to reintroduce premenstrual symptoms than cyclical oestrogen and progestogen according to a recent meta-analysis.²⁵

It may be useful to consider a “trial” of GnRH agonists to establish the relative contributions of endocrine related pathology versus underlying psychopathology in patients with premenstrual exacerbation, or to mimic the effect of a bilateral oophorectomy to determine the potential benefit of surgery.

Danazol

Danazol is androgenic, and a randomised placebo controlled crossover trial found considerable benefit over placebo in the treatment of patients with premenstrual syndrome.²⁶ Administration during the luteal phase only is beneficial for cyclical mastalgia but no other symptoms of the syndrome. Its side effects are predominantly androgenic and include acne, hirsutism, weight gain, voice change and deepening, adverse lipid profile, and teratogenesis.

Estradiol

Transdermal patches and subcutaneous implants of estradiol are effective in suppressing ovulation.²⁷ The use of unopposed oestrogen may lead to endometrial hyperplasia and increases the risk of endometrial cancer. Providing endometrial protection with progestogen is important, but if administered orally progesterone may induce premenstrual symptoms. Using a levonorgestrel releasing uterine system theoretically avoids this problem because the progesterone effects of this system are intended to be local, although some women experience premenstrual symptoms and breast tenderness in the early months of treatment. The combination of oestrogen administration and the levonorgestrel releasing intrauterine system will protect the endometrium, provide contraception, and reduce menstrual flow in women who also have heavy menstrual bleeding. Although not recent, randomised controlled trials have shown the efficacy of oestrogen in suppressing ovulation and managing symptoms.^{27 28} However, the suppression of ovulation is not sufficiently assured for contraceptive purposes and patients should be advised appropriately.

Is surgery a reasonable option?

Endometrial ablation or hysterectomy will eliminate menstruation but not premenstrual symptoms because ovarian function is conserved. Women with severe and debilitating symptoms may request bilateral oophorectomy. This may be considered, but we recommend careful counselling of the woman to outline the drawbacks and consequences of a premature surgical menopause. It is important to replace oestrogen until the age of the natural menopause. Removing the uterus when oophorectomy is performed allows women to receive unopposed oestrogen replacement and avoid recurrent progestogen induced premenstrual symptoms. A trial of GnRH is advisable before deciding to perform bilateral oophorectomy and hysterectomy.

Women with severe premenstrual syndrome who are undergoing hysterectomy for another gynaecological indication may also elect to have their ovaries removed to avoid ongoing premenstrual symptoms.

Box 5 Suppression of ovulation

- Oral contraceptives containing ethinylestradiol and drospirenone
- Estradiol patch or implant with cyclical oral or intrauterine progestogen
- Gonadotrophin releasing hormone agonist with or without oestrogen and progestogen or tibolone add back treatment
- Danazol continuously (luteal phase for breast symptoms)
- Bilateral salpingo-oophorectomy and hysterectomy with unopposed oestrogen replacement

A patient's perspective

I have always had severe mood swings, but over the past few years they got worse. They lasted for days and left me physically and emotionally exhausted. I was verbally aggressive and so nasty that when the mood had passed I would be devastated by my actions. This had a huge effect on my relationship with my son; I couldn't book holidays or outings because I would spoil them. I became a hermit for a couple of years.

I tried many prescription drugs including citalopram, over the counter remedies, and I trawled the internet but nothing came close to working. At this point I was desperate.

My general practitioner referred me to a consultant gynaecologist who gave me mood diaries to fill in. These showed that my symptoms occurred before menstruation and got better during my period—I had typical premenstrual syndrome. I received injections of a gonadotrophin releasing hormone agonist (Prostap) and later a levonorgestrel releasing intrauterine system and oestrogen patches. Initially, my moods were very up and down, then one day I suddenly realised that I hadn't had a symptom for a while. Now I can't remember when I had my last one.

Recently, I was talking to my son who gave me the biggest hug going and said "I've got my mum back."

Managing premenstrual disorders in general practice

The figure shows how different premenstrual disorders may be presented on the daily record of severity of problems chart. The diagnosis of a premenstrual disorder should be based on two months of recording using a paper or electronic based system of rating symptoms, and this is easily done in primary care. It is of course difficult to send away a severely affected patient without treatment but this initial process is essential. No woman should wait to be seen in secondary care only to be sent away for two months of chart recording because this can easily take place between referral and consultation. The prospective record of symptoms will give the clinician an idea of whether there is a positive diagnosis and how severely the woman is affected.

Women who have premenstrual symptoms that are debilitating but who are symptom free for at least one week after menstruation have core premenstrual disorder. Their symptoms may or may not fit the diagnostic criteria for premenstrual dysphoric disorder. Treat these women as outlined above according to their wishes after all information is presented. A hierarchical approach that takes into account the severity of symptoms, previous treatment, and background characteristics (table) is preferable.

Women with mild physiological premenstrual symptoms that have no substantial impact on their functioning may need no more than support and reassurance of normality. Advise good nutrition, exercise, and stress reduction, which are realistic and healthful, albeit unproved, non-medical approaches.

A patient who has debilitating symptoms but no symptom-free week may have an underlying psychological, psychiatric, or physical condition that is not related to the ovarian cycle and which is unlikely to be a premenstrual disorder. Explore alternative diagnoses and refer to psychiatric services if necessary. Symptoms of the perimenopause can be similar to the premenstrual syndrome but are also non-cyclical.

Women with a premenstrual syndrome-like cycle associated with progestogen treatment may be managed easily by changing type, dose, or duration of the treatment. Consider administration

of progesterone via a levonorgestrel releasing intrauterine system. In women whose symptoms are caused by the oral contraceptive, consider changing the pill or changing to an intrauterine system.

Women who have substantial premenstrual impairment with only partial relief after menstruation could have an underlying psychological or physical condition with exacerbations related to ovarian function. In such cases consider one of the following approaches. Either treat the underlying condition adequately, in which case the premenstrual phase may become tolerable, or suppress ovulation to reduce luteal phase symptoms to the level of the follicular phase. Psychological interventions and psychotropic agents may achieve both aims simultaneously in these patients or in those with both a psychiatric disorder and premenstrual syndrome.

It is easy to overlook cyclical symptoms in the absence of a reference menstrual bleed. In women who do not menstruate (as a result of hysterectomy, endometrial ablation, or a levonorgestrel releasing intrauterine system) but report a regular pattern of symptoms, measuring progesterone blood concentrations and noting a peak of symptoms will help to show the association between symptoms and ovulation. Manage as for core premenstrual disorder. It will be more difficult to use luteal phase-only treatment without a menstrual cycle as a guide.

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Areas for future research

- To develop a simple one stop diagnostic test so that patients don't have to record symptoms for two months before they can start treatment
- To replace paper based rating techniques with electronic symptom recording using the internet from a computer, laptop, tablet, or mobile phone
- To develop a neuroimaging technique (such as functional magnetic resonance imaging) that can be conducted across menstrual cycles to distinguish patients with and without premenstrual disorders. This could provide the pathway to objective diagnosis and determination of the aetiology of premenstrual disorders
- To develop an agent that provides endometrial protection without regenerating premenstrual symptoms
- To validate a "GnRH test" that would enable us to identify the contributing component symptoms in patients with premenstrual exacerbation and predict the likely effect of removing the ovaries (GnRH would stop the menstrual cycle, removing all symptoms caused by it, so for premenstrual exacerbation it would show the level of the underlying condition and whether removing the ovaries during a hysterectomy would be beneficial)
- To develop a method of ovulation suppression that avoids hypo-oestrogenic side effects and does not reintroduce premenstrual symptoms

Tips for non-specialists

- Diagnosis can be achieved only by the use of prospectively administered charts. The daily record of severity of problems is ideal for this. If a patient is referred to secondary care the charts must be completed while she is waiting for the appointment
- Careful diagnosis and classification of the disorder will limit the likelihood of treatment failure
- When patient led or non-drug based approaches fail, selective serotonin reuptake inhibitors or oral contraceptives may be considered. Identify a progestogen (oral or intrauterine) that does not reintroduce premenstrual symptoms—this may need to be done empirically on an individual basis
- Many patients will benefit from suppression of ovulation, which can be achieved in several ways; in primary care this is most easily achieved by use of transdermal estradiol and levonorgestrel releasing intrauterine systems

Additional educational resources*Resources for patients*

- National Association for Premenstrual Syndrome (www.pms.org.uk)—Information and support for women with premenstrual syndrome
- Royal College of Obstetricians and Gynaecologists (www.rcog.org.uk/files/rcog-corp/ManagingPremenstrualSyndromePMSInformationForYou.pdf)—Patient information leaflet on managing premenstrual syndrome
- Medline Plus (www.nlm.nih.gov/medlineplus/premenstrualsyndrome.html)—Health information on premenstrual syndrome from the US National Library of Medicine
- American Congress of Obstetricians and Gynecologists (www.acog.org/publications/patient_education/bp057.cfm)—Patient education leaflet on premenstrual syndrome
- NHS choices (www.nhs.uk/conditions/premenstrual-syndrome)—Information on premenstrual syndrome

Resources for healthcare professionals

- Royal College of Obstetricians and Gynaecologists. Management of premenstrual syndrome. 2007. www.rcog.org.uk/files/rcog-corp/uploaded-files/GT48ManagementPremenstrualSyndrome.pdf
- Map of medicine (http://eng.mapofmedicine.com/evidence/map/menstrual_cycle_irregularities_and_post_menopausal_bleeding_pmb_7.html)—Evidence-based, practice-informed care maps for the management of PMS
- Symptometrics (www.symptometrics.com/Information/MenstrualSymptometrics/PremenstrualDisorders.aspx)—Information about premenstrual disorders and prospective recording of data
- Medscape (<http://emedicine.medscape.com/article/293257-overview>)—Overview of premenstrual dysphoric disorder

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Table

Table 1 | Possible diagnoses in women presenting with premenstrual symptoms

Diagnosis	Cyclical symptoms	Symptoms in luteal phase	Symptoms in follicular phase	Impairment	Comment
Physiological premenstrual symptoms*	Present	Present	Absent	None	Although symptoms are cyclical and there is a symptom-free week, they are of insufficient severity to cause serious impairment
Core premenstrual disorder*	Present	Present	Absent	Present	This is the typical or core premenstrual disorder: symptoms are cyclical, relieved by the end of menstruation with a follicular phase symptom-free week; they cause serious impairment
Premenstrual exacerbation	Present	Present	Remain high but reduced compared with luteal phase	Present	Symptoms are cyclical, cause serious impairment but are only partially alleviated by menstruation because of an underlying psychological, physical, or medical condition
Premenstrual disorder, menstruation absent*	Present	Present	Absent	Present	Essentially the same as core premenstrual disorder but without menstruation as a reference event as a result of iatrogenic amenorrhoea (hysterectomy with ovarian conservation, endometrial ablation, levonorgestrel intrauterine system)
Progestogen induced premenstrual disorder†	Present	Present during progestogen treatment	Absent during progestogen-free phase of HRT or variably during exposure to hormonal contraceptives	Present	Symptoms are generated without ovulation by the cyclical administration of progestogen for therapeutic (HRT) or contraception purposes
Mis-attribution	Absent	Present	Present	Present	Although symptoms may be severe they are non-cyclical; this suggests the presence of a continuous and serious psychological disorder

*Symptoms probably result from ovulation and endogenous progesterone or its metabolites.

†Symptoms are iatrogenic and result from treatment with exogenous progestogens.

HRT=hormone replacement therapy.

Figure

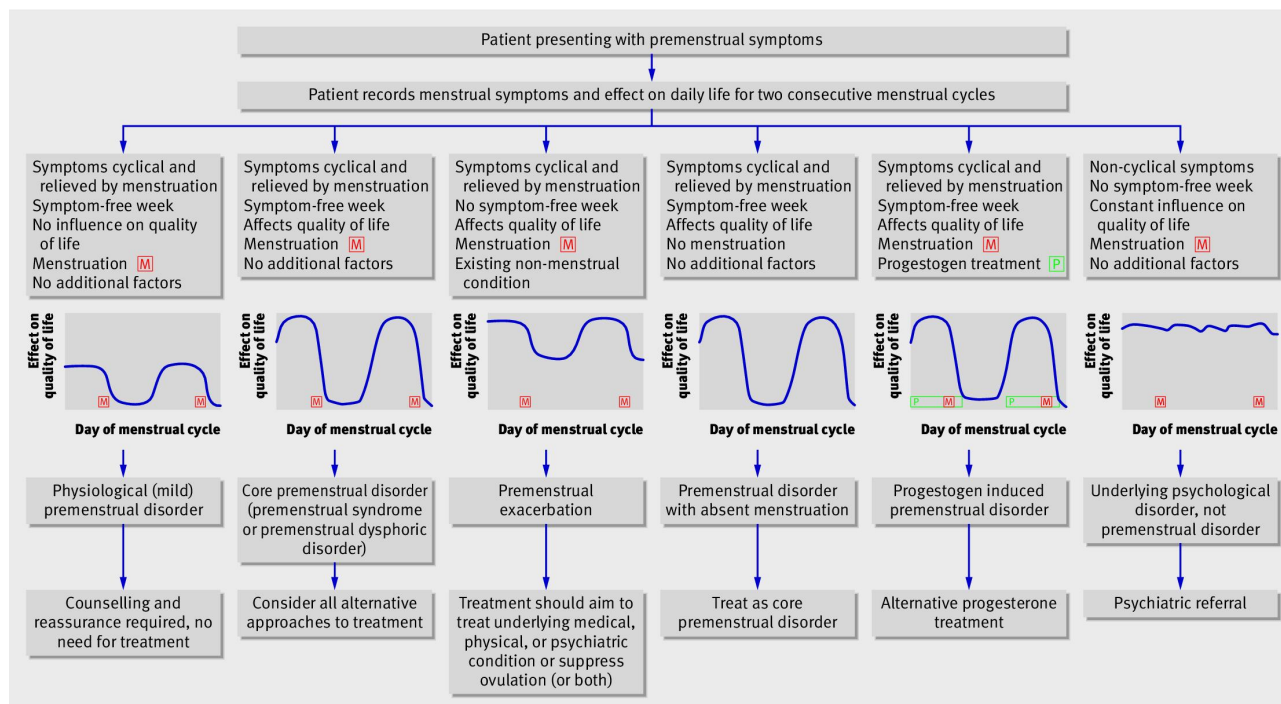


Fig 1 Schematic representation of daily record of severity of problems charts obtained on patients presenting with a presumed diagnosis of premenstrual disorder