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Towards a consensus on diagnostic criteria, measurement and trial design of the premenstrual disorders: the ISPMD Montreal consensus

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Abstract

Premenstrual disorders (PMD) are characterised by a cluster of somatic and psychological symptoms of varying severity that occur during the luteal phase of the menstrual cycle and resolve during menses (Freeman and Sondheimer, Prim Care Companion J Clin Psychiatry 5:30–39, 2003; Halbreich, Gynecol Endocrinol 19:320–334, 2004). Although PMD have been widely recognised for many decades, their precise cause is still unknown and there are no definitive, universally accepted diagnostic criteria. To consider this issue, an international multidisciplinary group of experts met at a face-to-face consensus meeting to review current definitions and diagnostic criteria for PMD. This was followed by extensive correspondence. The consensus group formally became established as the International Society for Premenstrual Disorders (ISPMD). The inaugural meeting of the ISPMD was held in Montreal in September 2008. The primary aim was to provide a unified approach for the diagnostic criteria of PMD, their quantification and guidelines on clinical trial design. This report summarises their recommendations. It is hoped that the criteria proposed here will inform discussions of the next edition of the World Health Organisation's International Classification of Diseases (ICD-11), and the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-V) criteria that are currently under consideration. It is also hoped that the proposed definitions and guidelines could be used by all clinicians and investigators to provide a consistent approach to the diagnosis and treatment of PMD and to aid scientific and clinical research in this field.

Keywords

PMS; PMDD; Premenstrual disorder; Diagnostic criteria; Quantification; Trial design; International consensus

Introduction

The broad concept of premenstrual disorders (PMD) has been recognised for many decades. However, over the past 80 years, the terminology and diagnostic element of PMD has become progressively more focused. The phrase premenstrual tension (PMT) was first described in the 1930s (Frank 1931). Significantly, an association with the menstrual cycle and ovarian function was suggested, with the emphasis on the luteal phase and the activity of the corpus luteum (Horney 1931). The concept of premenstrual syndrome (PMS) was proposed in the 1950s. A severe, debilitating form of PMS was originally formalised by the American Psychiatric Association as late luteal phase dysphoric disorder (LLPDD; American Psychiatric Association 1987), and later as premenstrual dysphoric disorder (PMDD; American Psychiatric Association 1994). Less rigorous definitions of PMS were subsequently published in the American College of Obstetricians and Gynaecologists (American College of Obstetricians and Gynecologists 2000), the World Health Organisation International Classification of Diseases (ICD) 10th edition (WHO 2004), and the Royal College of Obstetricians and Gynaecologists (Royal College of Obstetricians and Gynaecologists 2007) criteria. However, it is only in the last 15 years that concerted attempts have been made to establish diagnostic criteria, definitions and classifications of premenstrual disorders (Steiner et al. 1999; Halbreich 2004). Although these endeavours have been clinically useful, they have also polarised opinions, particularly into psychiatric versus gynaecological factions. Subsequently, it has become increasingly apparent that there is a need to distinguish between the normal, relatively mild physiological symptoms of the premenstrual phase of the cycle and the severe, debilitating manifestations that comprise severe PMS and PMDD (O'Brien and Ismail 2007).

The extent to which premenstrual disorders impact on women's lives and that of their families and work colleagues is under-recognised by the majority of medical, lay people, government and health organisations. A precise, universal classification would enhance the understanding of PMD, facilitate diagnosis and enable the clinician to offer appropriate treatment. Various authoritative bodies have already attempted this but their criteria are inconsistent and disparate. Differences in the interpretation of significant premenstrual symptoms have led to marked variations in estimated prevalence; for example, 80–95% for physiological premenstrual symptoms, 30–40% for PMS and 3–8% for PMDD (Pearlstein 2007). At one end of the diagnostic spectrum, the ACOG and ICD-10 criteria are relatively liberal, allowing as few as one or two symptoms with undefined severity to constitute the disorder, although the ACOG does stipulate significant impairment. At the other extreme, the current American Psychiatric Association Diagnostic (DSM-IV) criteria for PMDD require at least five out of 11 specified symptoms (including one major mood symptom). They must occur exclusively during the luteal phase, resolve during menstruation and be sufficiently severe to interfere with work, family and social relationships. However, this

strategy can potentially exclude a severely affected patient with too few qualifying symptoms, despite severe impairment and/or distress. Furthermore, it has important negative implications for patients if effective, currently licenced PMDD treatments such as selective serotonin reuptake inhibitors (SSRIs) and specific oral contraceptives are withheld because of failure to meet these criteria (Brown et al. 2002; Yonkers et al. 2005). Inconsistencies between diagnostic criteria may also have major implications for research into both causal mechanisms and clinical trials of PMDD.

Method

Review of the literature

A comprehensive review of Medline and other databases which focused on PMS, PMT, PMDD or LLPDD evaluation and diagnosis had been undertaken for previous deliberations by most members of the International Society for Premenstrual Disorders (ISPMD) group (Halbreich et al. 2007). The literature review was not repeated for this meeting. Many of the relevant studies had been published by members of the group, who were internationally recognised experts in this field.

Subsequent deliberations

The ISPMD group comprised specialists in PMS and/or PMDD and/or women's mental health, with a diversity of backgrounds that included gynaecologists, reproductive endocrinologists, psychiatrists, psychologists, a pharmacologist, a specialist nurse and an epidemiologist. A consensus was considered when there were only two (or fewer) dissident votes. Most of the issues had been resolved in the initial face-to-face discussion. The existing criteria stated in ICD-10, DSM-IV, RCOG and ACOG were considered, and conclusions were reached after formal presentations of the available research evidence at the consensus meeting. Where evidence did not exist, group consensus was achieved by a brief modified Delphi technique and through debate and discussion via email.

The first goal of the consensus group was to define premenstrual disorders. Causal mechanisms were not considered, apart from agreeing the significance of the ovarian hormone cycle and ovulation on symptom expression. It is well documented that ovarian activity and probably ovulation is required for the manifestation of premenstrual symptoms (Bäckström et al. 1983; Rubinow et al. 1988; DeVane 1991; Bäckström et al. 2003). Premenstrual disorders do not exist before puberty, during pregnancy or after the menopause, and are markedly diminished or eliminated by bilateral oophorectomy (Casson et al. 1990), suppression of the cycle with gonadotropin releasing hormone (GnRH) agonists, (Wyatt et al. 2004); danazol (Halbreich et al. 1991), and oestrogen (Magos et al. 1986; Panay and Studd 2007). Premenstrual symptoms can be mimicked as side effects of exogenous progestogens during cyclical (oestrogen/progesterone) hormone replacement therapy (Henshaw et al. 1996) and by combined oral contraceptive pills (Sveindóttir and Bäckström 2000).

It was proposed and agreed that premenstrual disorders should be divided into two categories; Core PMD which are the typical, pure or reference disorders associated with

spontaneous ovulatory menstrual cycles, and Variant PMD which are separate from Core PMD and exist where more complex features are present (Table 1).

Clinical diagnostic criteria of premenstrual disorders

Core premenstrual disorders

Core premenstrual disorders depend on the endocrine luteal phase events following ovulation. It is not necessary to confirm that ovulation has occurred. Core PMD present with typical features, although a wide range of both somatic and psychological symptoms has been reported. The key characteristic is their timing, which must occur during all or part of the 2-week premenstrual phase and resolve during or shortly after menstruation. The persistence of symptoms during menstruation does not preclude the diagnosis; however, there must be a clear, symptom-free interval between the end of menstruation and the approximate time of ovulation. This cyclical chain of events must occur in most menstrual cycles (typically two out of every three). Suppression of ovulation will result in a major reduction or elimination of symptoms. It should be noted that suppression of ovulation may cause oestrogen deficiency with symptoms or side effects similar to those of PMD, and could potentially confound diagnosis; however, they will be non-cyclical in nature. Core PMD must not be a premenstrual exacerbation of another psychiatric, physical or medical disorder. Importantly, the severity or impact of symptoms must (a) affect normal daily functioning, (b) interfere with work, school performance or interpersonal relationships or (c) cause significant distress.

The consensus group recognised that different PMD symptoms may have separate causes (albeit all triggered by ovulation and treated by its suppression) which may respond to different treatment strategies. Consideration must be given to the existence of symptom-based subcategories of PMD and whether Core PMD should be regarded as a single entity or merely an umbrella term under which different patterns or clusters of symptoms would appear. The Core premenstrual disorders were defined as PMS and PMDD.

Premenstrual syndrome—PMS is distinguished from the normal psychological and somatic premenstrual symptoms experienced by many women because of its negative influence on daily functioning and level of distress. The current ACOG and RCOG definitions of PMS exactly meet the criteria of a Core PMD. Conversely, the ICD-10 definition of PMS does not require impact or impairment, and thus fails to clearly distinguish between PMS and physiological premenstrual symptoms.

Premenstrual dysphoric disorder—The current DSM-IV definition of PMDD meets the criteria for a Core PMD, but is classified separately from PMS. The diagnosis of PMDD stipulates the number, character and severity of symptoms with particular emphasis on, and requirement for, key psychological symptoms. Physical features are not a major consideration. There are some women who experience extremely distressing premenstrual symptoms, but their number or severity does not meet the criteria for PMDD.

Variant premenstrual disorders

Variant premenstrual disorders encompass:

1. Premenstrual exacerbation
2. Symptoms that occur with non-ovulatory ovarian activity
3. Symptoms that are generated iatrogenically following hormonal therapy
4. Situations where the ovarian cycle remains intact but menstruation has been suppressed at the uterine/endometrial level.

Premenstrual exacerbation—Premenstrual exacerbation occurs when there is magnification of an underlying somatic, medical or psychiatric disorder during the luteal phase of the ovarian cycle. The profile of symptoms is similar throughout the cycle but the intensity is significantly greater in the premenstrual phase. Because the symptoms of Core PMD are non-specific, any symptom which exhibits premenstrual exacerbation (whether a common PMD symptom or not) fulfils the criteria for Variant PMD. Examples of well-recognised conditions that exhibit premenstrual exacerbation are diabetes, migraine, epilepsy, asthma and depression (Case and Reid 1998). Patients with premenstrual exacerbation are specifically excluded from the diagnosis of Core PMD.

It is important to note that a significant proportion of women will have a co-existing somatic or psychiatric condition that is not influenced by the menstrual cycle or PMD. If the menstrual cycle is suppressed, the underlying condition will not change. Such conditions are termed independent comorbidities and therefore are not Core or Variant PMD. Elimination of the ovarian cycle (e.g., with a GnRH agonist) removes the cyclical component to leave only the underlying condition. Thus, the relative contribution of the two components can be determined.

Non-ovulatory premenstrual disorders—A minority of women experience premenstrual symptoms as a result of ovarian activity which does not lead to ovulation (Schmidt et al. 1998). The mechanism underlying this phenomenon is not understood, but it may result from cyclical follicular activity that fails to culminate in normal ovulation. The principal supporting evidence is based on clinical and experimental observations in which symptoms were reproduced following reintroduction of oestrogen or progesterone after ovarian suppression (Schmidt et al. 1998). Because of limited publications documenting this event, consensus group opinion was divided regarding the strength of evidence to categorise this as a Variant PMD.

Progesterone-induced premenstrual disorders—Women receiving exogenous progestogen may develop symptoms which are similar or identical to premenstrual symptoms. This is an iatrogenic form of PMD (Henshaw et al. 1996) and is often encountered in women taking postmenopausal hormone therapy or the combined oral contraceptive pill. Symptoms occur almost exclusively during the progestogenic phase of the cycle. Although ovulation is absent or suppressed, the exogenous progestogens in the preparation are thought to introduce de novo, or re-introduce, PMD-like symptoms. Different progestogens may exert diverse effects in this respect. Women who receive continuous progestogen therapy, progestogen-only contraception or in the initial weeks, the levonorgestrel intrauterine system frequently experience symptoms similar to PMD. These

women appear to be ‘progestogen sensitive’. Although it is important to be aware of such effects, the symptoms do not constitute a Core PMD or Variant PMD because critical element of cyclicity is not present.

Premenstrual disorders without menstruation—A significant proportion of women continue to experience premenstrual disorders despite having surgically or medically induced amenorrhoea. This occurs when treatment is targeted at the endometrium but the ovarian cycle and ovulation persist. Such an effect is seen following hysterectomy with conservation of the ovaries, after endometrial ablation or when amenorrhoea follows insertion of a levonorgestrel intrauterine system for contraception or heavy menstrual bleeding.

Misattribution of psychological or physical symptoms to premenstrual disorders

Women who incorrectly attribute their somatic or psychological symptoms to a premenstrual disorder are not uncommon and many such patients attend psychiatric, gynaecology or PMD clinics. These women describe distressing symptoms and significant impairment, with features that are identical or similar to those of PMD. Characteristically, the symptoms fail to disappear by the end of menstruation and there is no symptom-free week during the menstrual cycle. In theory, if such patients were given agents to suppress ovulation (e.g., a GnRH agonist) the character and intensity of symptoms would not change. Although there is anecdotal evidence to support this hypothesis, it has never been formally evaluated as a diagnostic test. These women usually have a continuous, non-cyclical psychological disorder that has no link to the ovarian cycle. The importance of making the distinction between PMD and continuous non-cyclical psychiatric, somatic and medical disorders cannot be overstated.

Diagnosis and quantification of premenstrual disorders

In general, medical disorders are diagnosed by clinical history, examination and a combination of supplementary tests. These could include subjective/objective questionnaires, structured interviews, laboratory analyses, physical parameters, imaging techniques or interventional approaches. The ISPMD Consensus Group searched for evidence of existing techniques that could potentially identify and quantify PMD for studies of cause, diagnosis or measurement of treatment effect.

Consensus on diagnostic criteria and quantification of PMD

The following conclusions were made:

1. There is no diagnostic haematological or biochemical test for PMD. This limitation is shared with several common medical and psychiatric disorders.
2. Consistent differences in pituitary or ovarian hormone levels throughout the menstrual cycle have not been demonstrated. Measurement of mid-luteal serum progesterone to indicate ovulation may be of value when menstruation does not occur (after hysterectomy, endome-trial ablation or use of a levonorgestrel intrauterine device).

3. Changes in physical parameters such as abdominal and breast size, total body water and extracellular fluid volume are inconsistent and have no diagnostic value.

4. The use of structured interviews, questionnaires and patient self-rating scales is well established and several validated diagnostic techniques are available (Dhingra and O'Brien 2007). Most of these are cumbersome and are limited by dependence on a woman's subjective view of her symptoms. Probably the most well established and widely used system is the Daily Record of Severity of Problems (DRSP) (Endicott et al. 2006). The primary focus of the DRSP is on psychological symptoms with less attention being paid to physical symptoms.

5. Opinion was divided with regard to the most suitable patient rating technique. Many group members favoured the DRSP because it is the most commonly used technique worldwide, and it has been validated as a prospectively self-administered questionnaire (Endicott et al. 2006). Furthermore, most of the licenced treatments for PMDD in the US have used the DRSP in the relevant studies. The descriptive terms in the DRSP directly reflect PMDD. The criteria are also extensively used in research and clinical practice for all premenstrual disorders. The group acknowledged that several other validated tests exist.

6. The patient must not receive treatment during the 2-month prospective rating of symptoms. In normal clinical practice, it is recommended that whenever possible the rating technique should be completed for 2 months before the first appointment. Rarely, immediate intervention may be necessary if severe life-threatening symptoms occur.

7. Simpler methods are desirable for clinical use and for screening patients for research studies.

8. Accurate and more streamlined techniques need to be developed to avoid the delay between initial screening and start of therapy in psychiatric and gynaecology clinics and in general practice.

9. Rating techniques should receive cross-culture validation.

10. The retrospective assessment of symptoms has limited value, although the Premenstrual Symptoms Screening Tool (PSST) is potentially useful (Steiner et al. 2003). The PSST is a self-rated retrospective questionnaire that is completed during clinical consultation with the patient. However, it requires validation against an established prospective technique such as the DRSP.

11. The use of GnRH agonists as a diagnostic aid has not been scientifically validated, although its clinical use is widespread amongst gynaecologists in the UK. This strategy would be expected to completely eliminate symptoms of Core PMD (PMS and PMDD), PMD with absent menstruation and the endocrine component of premenstrual exacerbation. When such an approach is used, administration of oestrogen, continuous combined oestrogen/progestogen or tibolone add-back therapy may prevent confusion arising from induced hypo-oestrogenic effects.

Novel diagnostic techniques for premenstrual disorders

The ISPMD group also considered some new, promising areas of investigation which may elucidate causal mechanisms and eventually lead to a useful diagnostic test for PMD. The following areas reflect the interests of some of the consensus group, although this list is by no means exhaustive.

Saccadic Eye Velocity (SEV) is considered to be a measure of GABA receptor sensitivity, and appears to vary across the menstrual cycle in a pattern that may distinguish between women with severe PMS or PMDD and healthy controls (Andréen et al. 2009). This technique warrants further exploration and may ultimately prove to be useful for clarifying pathophysiological mechanisms. However, SEV may not be sufficiently specific for identifying PMD patients for the purposes of research to investigate aetiology or treatment.

It is likely that there is a genetic component to PMD, and studies of sex steroid and neurotransmitter gene polymorphisms are potential areas for continued investigation. However, preliminary data do not indicate that the genetic approach provides a robust diagnostic tool for PMD or potential treatment response (Magnay and Ismail 2007).

Brain imaging using positron emission tomography, proton magnetic resonance spectroscopy, and functional magnetic resonance imaging has shown promising initial results but there remains insufficient evidence for its use in the clinical or research setting (Epperson et al. 2007).

The consensus group concluded that there is currently no objective parameter to measure or diagnose PMD. Clinicians and researchers must continue to depend on validated, subjective self-rated paper-based quantification techniques to which PMD research has been limited for many years (Epperson et al. 2007).

Requirements of quantification techniques for premenstrual disorders

Quantification techniques must specifically identify Core and Variant PMD and be capable of distinguishing these disorders from co-morbidity and misattributed symptoms. In Variant PMD they should distinguish the relative contributions of menstrual and non-menstrual components.

Such techniques must demonstrate:

1. Character and timing of the specific symptoms
2. Cyclicity and recurrence in the premenstrual phase
3. Resolution of symptoms by the end of menstruation
4. Impact of symptoms, impairment and distress
5. The presence/magnitude of background, non-PMD symptoms

Specific symptoms—Although precise symptoms are not specified in the consensus definition of PMD, they are characterised for PMDD. Furthermore, knowledge of symptom type may influence treatment choice, particularly if symptom-based subtypes of PMD are

subsequently demonstrated. Prospectively administered rating techniques are crucial to this approach. The DRSP is based on the diagnostic features of PMDD, but it is also relevant for all PMD. The single 'physical' symptom question addressed in the DRSP does not allow patients to distinguish between the many somatic manifestations that can be experienced. Alternative rating techniques exist or are currently being developed to achieve these aims, and may ultimately prove to be more appropriate in this respect.

Cyclicity of symptoms—Most of the available rating techniques will clearly demonstrate cyclicity of symptoms. It is crucial to demonstrate that symptoms are specific to the premenstrual phase of the cycle.

Resolution of symptoms—The available rating techniques will demonstrate the disappearance of symptoms with menstruation. If manifestations persist beyond this time, an alternative diagnosis should be considered. The demonstration of the characteristic 'on/offness' between luteal and follicular phases is an important diagnostic concept.

Impact, impairment and distress—The impact of symptoms must be determined to distinguish PMD from normal or physiological premenstrual symptoms. Numerous diagnostic tools are available that include some relatively complex psychiatric or quality of life questionnaires. The DRSP requires patients to rate three relatively simple questions to achieve this aim, in common with other existing methods.

Magnitude of background symptoms—It is important to quantify the degree and relative contribution of background symptomatology to PMD symptoms. Complex structured interview and rating techniques are available and may be necessary for specific patients or research trials. For clinical purposes, current rating techniques including the DRSP follicular phase scores will identify the magnitude of symptoms that persist following menstruation. Thus, a differential diagnosis can be made between premenstrual exacerbation and PMD. The use of other rating techniques can provide comparable information. When symptom scores remain high throughout the menstrual cycle, it may indicate a non-cyclical psychiatric diagnosis.

Clinical trial design

There are numerous publications of clinical trials that use a range of diagnostic terminologies and study designs. This makes it difficult to directly compare and meaningfully interpret data between different reports. Clearly, there is a need to improve and standardise methodology in investigations of PMD.

Consensus group recommendations on clinical trial design

1. The PSST is potentially a valuable retrospective screening mechanism for entry into clinical trials but is not yet considered a sufficiently robust diagnostic tool for inclusion criteria or for outcome measures.

2. Prior to randomisation, 2-months prospective charting of symptoms is required. The DRSP is the most widely used and accepted tool both for this purpose and to quantify outcome, although many other techniques have been validated.
3. Such techniques have the flexibility to provide not only the total scores for each diagnostic symptom, but also their detailed daily scores, including timing and severity.
4. PMD do not occur in every cycle. Therefore, if only one of the two monitored cycles is diagnostic, a third cycle should be recorded and two of three positive cycles should be deemed a positive diagnosis.
5. Studies should ideally be randomised, parallel, double-blind and placebo controlled.
6. A single-blind initial placebo lead-in study design is not mandatory. However, it may reduce the placebo response rate in ensuing clinical trials and has been used in several recent studies.
7. The minimum duration of the treatment and placebo arms should each be 3 months.
8. Longer studies are desirable to determine the duration of treatment and placebo effects. Six months is considered acceptable, but 50% of the consensus group were concerned by the fact that patients in the placebo arm of the trial would receive no treatment for 8 or 9 months. This can be overcome by adopting a relapse prevention design.
9. Although there is no ‘gold standard’ therapeutic comparator by which new therapies can be judged, both SSRI treatment and GnRH agonists do have the potential to fulfil such a role.
10. Research studies on causal mechanisms and clinical trials of effectiveness should make a clear distinction between those which assess Core PMD and Variant PMD. This will enable unambiguous interpretation of outcome data.

Conclusion

The consensus process represents the first attempt to develop an international universally acceptable multidisciplinary agreement regarding specific aspects of PMD; namely definition, quantification and clinical trial design. The ISPMD ultimately aims to construct consensus statements on all aspects of premenstrual disorders, including aetiology and management. The progress of views from relative disparity at the start of the process to almost complete unanimity is extremely encouraging. The ISPMD Criteria for the Classification of Premenstrual Disorders was supported by 100% of the consensus group.

There remain several areas of continued debate:

1. Ten percent of the group thought there was sufficient evidence to propose that anovulatory ovarian activity could be responsible for PMD symptoms in certain women. This was addressed by designating this patient subgroup under Variant PMD, thereby retaining ovulation as a key factor in Core PMD.

2. For clinical trial design, 100% of the group considered the ideal trial design to be a 3 month minimum, randomised, double-blind, placebo-controlled, parallel group study preceded by 2-months symptom documentation. Ten percent of the group considered that a 1-month single-blind placebo lead-in should be included. Consequently, a total of 3 months without therapy would be required before randomisation. This minimises the otherwise high placebo effect encountered in all PMD research into treatment strategies.

3. In the absence of an objective test, the whole consensus group agreed that prospective, daily, patient-recorded symptom rating is currently the only reliable and validated method to diagnose and quantify PMD. Ninety per cent of the group favoured the DRSP to be the accepted quantification technique of the ISPMD; the remainder wished to consider the use of other well-validated techniques. This was accepted by the whole group.

4. All discussants agreed that simpler validated objective or ‘one-stop’ techniques such as the PSST should be sought and/or validated to avoid delaying treatment for 2 months during the diagnostic phase of care.

This document represents the majority opinion of the multi-professional ISPMD consensus group. It is anticipated, or at least hoped, that such an authoritative reference document will be considered by WHO and the American Psychiatric Association during the development of respectively, the 11th International statistical classification of diseases and related health problems (ICD-11) and The Diagnostic and Statistical Manual of Mental Disorders fifth edition (DSM-V). Most previous research has been published without reference to the categories of PMD described in this document. We would also wish that the new classification of PMD forms the basis for future scientific study, clinical trials and for clinical guidance developed by specialty colleges and other authoritative bodies.

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Table 1
Classification of premenstrual disorders (PMD)

PMD category	Characteristics
Core PMD	Symptoms occur in ovulatory cycles
	Symptoms are not specified—they may be somatic and/or psychological
	The number of symptoms is not specified
	Symptoms are absent after menstruation and before ovulation
	They must recur in luteal phase
	They must be prospectively rated (two cycles minimum)
	Symptoms must cause significant impairment[a]
Variants of PMD	
Premenstrual exacerbation	Symptoms of an underlying psychological or somatic disorder significantly worsen premenstrually
PMD due to non-ovulatory ovarian activity	Symptoms arise from continued ovarian activity even though menstruation has been suppressed
Progestogen induced PMD	Symptoms result (rarely) from ovarian activity other than those of ovulation
PMD with absent menstruation	Symptoms result from exogenous progestogen administration

[a] Work, school, social activities, hobbies, interpersonal relationships, distress