

## NIH Public Access

Author Manuscript

Arch Gen Psychiatry. Author manuscript; available in PMC 2012 June 08.

#### Published in final edited form as:

Arch Gen Psychiatry. 2012 March ; 69(3): 300–305. doi:10.1001/archgenpsychiatry.2011.1368.

### **Criteria for Premenstrual Dysphoric Disorder:**

#### Secondary Analyses of Relevant Data Sets

S. Ann Hartlage, PhD, Sally Freels, PhD, Nathan Gotman, MS, and Kimberly Yonkers, MD Departments of Psychiatry and Behavioral Sciences, Rush University Medical Center and Rush Medical College (Dr Hartlage) and Division of Epidemiology and Biostatistics, School of Public Health, University of Illinois at Chicago (Dr Freels), Chicago; and Departments of Psychiatry (Mr Gotman and Dr Yonkers) and Obstetrics, Gynecology, and Reproductive Sciences (Dr Yonkers), Yale University School of Medicine, New Haven, Connecticut.

### Abstract

**Context**—There is substantial information that premenstrual dysphoric disorder(PMDD) is a clinically significant disorder with biological underpinnings that differ from other psychiatric disorders. However, data regarding the symptoms noted in *DSM-IV* and timing of their expression in the menstrual cycle have had little empirical support.

**Objective**—To provide evidence informing the definitional criteria for PMDD.

Design—Prospective surveys.

Setting—General community and clinical settings.

**Participants**—Two cohorts that included a representative sample and a self-identified treatment-seeking cohort.

Main Outcome Measure—Daily ratings of perimenstrual symptoms and functioning.

**Results**—Mood and physical symptoms were most severe and were accompanied by impairment in the 4 days before through the first 2 days of menses for the self-identified group and in the 3 days before through the first 3 days of menses in the community sample. The most problematic symptoms endorsed were those listed in *DSM-IV*, but depressed mood was less frequent than other affective symptoms. In the combined sample, 4 or more symptoms was the optimal cutoff point for maximizing both sensitivity and specificity when predicting impairment.

**Conclusions**—This is informative for *DSM-5* in that the most symptomatic period typically includes the few days before through the first 3 days of menses rather than only the premenstrual phase. Further, we validated the salience of PMDD symptoms included in *DSM-IV*. Although the number of symptoms most associated with distress and impairment differed between the 2 cohorts, results from the combined cohort suggest that 4 symptoms are linked with impairment from PMDD symptoms.

There is substantial information from biological investigations that premenstrual dysphoric disorder (PMDD) is a clinically significant psychiatric disorder with unique biological

Financial Disclosure: None reported.

<sup>© 2012</sup> American Medical Association. All rights reserved.

Correspondence: S. Ann Hartlage, PhD, Department of Psychiatry, Rush University Medical Center, Rush West Campus, 2150 W Harrison St, Chicago, IL 60612 (ann\_hartlage@rush.edu)..

Author Contributions: Dr Hartlage had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

underpinnings.<sup>1</sup> The condition is responsive to treatments that are useful for other mood and anxiety disorders<sup>2,3</sup> and also to unique, hormonal treatments.<sup>4-6</sup>

Previous iterations of the *DSM* outlined draft criteria for PMDD that included proposed symptoms as well as the stipulation that prospective daily ratings should be used to confirm a retrospective report of PMDD. In work commissioned by the American Psychiatric Association to inform *DSM-IV*,<sup>7</sup> consultants reanalyzed a large clinical cohort of women who endorsed PMDD and completed daily ratings.<sup>8</sup> The report explored the optimal method for defining a meaningful change between the follicular and luteal phases of the menstrual cycle and identified mood, behavioral, and physical symptoms commonly endorsed by women with PMDD. The results were notable in that they established the salience of a number of symptoms and showed that women could be symptomatic during the premenstrual phase of the cycle independent of another psychiatric condition.

However, the work was limited in several ways. First, the large data set analyzed was not from a community cohort but from women who were provisionally determined to have a premenstrual disorder. Moreover, the cohort was built on the assumption that symptoms occur premenstrually and offset at the start of menstruation. However, work published by several groups<sup>9-11</sup> suggests that perimenstrual symptoms peak on the day before or the first day of menses and often linger several days into the follicular phase of the menstrual cycle rather than cease as soon as the menstrual period begins.

Second, the analyses found that a number of symptoms were expressed in the premenstrual phase, but they did not address the minimum number of symptoms that should be required for a premenstrual disorder diagnosis. This is important because some research finds that functional impairment can occur in women who have fewer than the 5 symptoms stipulated by *DSM-IV*.<sup>12</sup>

In recognition of this and in preparation for *DSM-5*, the American Psychiatric Association commissioned a secondary analysis of 2 data sets to study the symptoms associated with the PMDD diagnosis, determine the timing of perimenstrual symptoms, and estimate the number of symptoms associated with distress or functional impairment.

This study reanalyzes data from 2 cohorts: a large community cohort of women who were recruited blind of a perceived diagnosis of PMDD<sup>13</sup> and a cohort of women who retrospectively reported PMDD and prospectively monitored symptoms for at least 1 but ideally 2 menstrual cycles. The community cohort is notable because the women who participated were not identified as treatment seeking, were representative of their Midwestern geographic area, and kept daily ratings of symptoms for at least 2 menstrual cycles. The treatment-seeking cohort was notable for the large number of perimenstru-ally symptomatic women who also kept up to 2 cycles of daily ratings.

For this work, we had an initial hypothesis that menstrual-related symptoms would not be limited to the premenstrual period but would continue into the menstrual period (hypothesis 1). We further postulated that symptoms previously associated with PMDD would show the greatest change and severity from the perimenstrual to the postmenstrual phase of the cycle (hypothesis 2). We did not have an a priori hypothesis about the number of symptoms that should be required for *DSM-5*, but since *DSM-IV* did not empirically evaluate this, we explored the optimal number of symptoms that would be associated with symptom expression and functional impairment.

#### METHODS

We conducted post hoc analyses in the 2 data sets and did not limit our analyses to females who met *DSM-IV* criteria for PMDD because that would have been circular. Institutional review boards at Rush University Medical Center and Yale University School of Medicine approved the studies. All respondents gave written informed consent and rated symptoms on a 6-point scale ranging from not at all to extreme.

#### DATA SETS

The community data set was from an area probability sample of 864 females with no missing data (mean age, 31.8 years) not identified via treatment-seeking behavior who lived in urban (Chicago) or rural (DeKalb County) Illinois. Participants completed daily ratings of 50 items (see Table 1 for all negative symptom items), including all symptoms listed for PMDD in *DSM-IV*, and questions regarding impairment. The interview provided demographic data to weight the sample, including whether the respondent was Hispanic or Latina. A second question was whether she would describe herself as American Indian or Alaskan native; Asian; native Hawaiian or Pacific Islander; black or African American; white; more than 1 race; or other. Participants were paid \$80 for 2 complete menstrual cycles of data.

The clinical data set included 193 women who responded to an advertisement for those with PMDD or severe premenstrual syndrome who were interested in participating in a National Institute of Mental Health–funded clinical trial that took place in New York, Connecticut, and Virginia. The advertisement did not stipulate number of symptoms. Respondents retrospectively endorsed problems with PMDD and went on to prospectively rate symptoms (Table 2) for typically 1 to 2 complete menstrual cycles to assess eligibility for participation. Potentially qualifying (nontreatment) cycles were used for this analysis. Symptoms were collected via the Daily Rating of Severity of Problems, which includes all *DSM-IV* symptoms of PMDD as well as other symptoms. Seven additional symptoms (eg, diarrhea, dreams, ringing in ears) were monitored to assess withdrawal in later treatment phases of the clinical study. Demographic data also were available.

#### STATISTICAL ANALYSIS

Statistical analyses were performed under the direction of a bio-statistician (S.F.). Because our charge was to evaluate the current diagnostic criteria for PMDD taking into consideration the previous work done by the *DSM-IV* Work Group, we began with an exploration of what would constitute a menstrual-related symptom. In accord with the *DSM-IV* Work Group, we adapted the effect size method as illustrated by Hurt et al,<sup>8</sup> which could measure the change between the postmenstrual and perimenstrual periods, yet retain a measure of background variability across the menstrual cycle. Hence, for each symptom, we computed an effect size as follows. We subtracted the postmenstrual follicular score (average ratings on days 7-12 after menses) from the perimenstrual score (average ratings during various 6-day intervals near menses) and divided the difference by the standard deviation of ratings during the entire cycle.

To test hypothesis 1 and identify the maximum follicular to perimenstrual phase change, we computed change scores using different permutations of the frame for perimenstrual symptoms. Specifically, we calculated effect sizes for various perimenstrual intervals: 6 days through 1 day before the onset of menses (days –6 through –1), 5 days before through the first day of menses (days –5 through 1), days –4 through 2, and days –3 through 3. To further assess the optimal time frame for perimenstrual symptoms, we tabulated functional impairment scores (eg, symptom effects on productivity and on relationships) during various

days of the cycle to determine when functioning was most impaired. These items also were computed as effect sizes relative to follicular scores. For women with multiple cycles, cycles were averaged for this and other subsequent analyses.

To test hypothesis 2, the perimenstrual interval was days –4 through 2. A symptom was considered present if the effect size was 1.0 or greater.

To explore the optimal number of symptoms associated with distress and impairment for a premenstrual condition, symptoms were grouped into the following 11 *DSM-IV* categories: depressed mood, anxiety, mood swings/rejection, irritability/ anger, interest, concentration, lethargy, appetite, sleep, overwhelmed/out of control, and physical symptoms. Each of the 11 symptom groups (eg, sleep) was considered present if any of the constituent symptoms (eg, difficulty sleeping, slept more) had an effect size of 1.0 or greater. There were some symptoms (eg, chills) that we did not use. Criterion A of *DSM-IV* stipulates that at least 1 symptom must be a mood symptom (markedly depressed mood, feelings of hopelessness, or self-deprecating thoughts; marked anxiety, tension, feeling "keyed up," or feeling "on edge"; marked affective lability; persistent and marked anger or irritability or increased interpersonal conflicts). Thus, if any of the first 4 symptoms in criterion A was present, then the number of PMDD symptoms was defined as the total across the 11 items. If none of the first 4 symptoms was defined as 0 because the subject could not have functional impairment due to PMDD.

A woman was considered to have functional impairment if symptoms interfered with her ability to get things done at home, school, or work, with hobbies or social activities, or with her relationships with others. Impairment was considered present if any of the effect sizes was 1.0 or greater.

Cross-tabulations between the number of PMDD symptoms and functional impairment were generated and analyzed for the clinical sample, the community sample, and a combined sample with both samples weighted equally.

For each of the samples, sensitivity and specificity were computed corresponding to each potential cutoff point in the number of PMDD symptoms as a predictor of functional impairment. A suggested method for determination of the optimal cutoff point is to find the point with the maximum sum of sensitivity and specificity, or equivalently the maximum of Youden J statistic (sensitivity+specificity-1).<sup>14</sup> Hosmer and Lemeshow<sup>15</sup> suggest plotting sensitivity and specificity on the same graph and using the point where the curves cross as the optimal cutoff point, which tends to be consistent with using the Youden J statistic. Receiver operating characteristic curves were calculated as an overall measure of association between the number of PMDD symptoms and functional impairment.

#### RESULTS

Of the weighted community sample, 15.2% were Hispanic regardless of race, 65.2% were white, 14.3% were black, and 5.3% were other. The median education was some college or technical school. Of those reporting employment status, 69.1% were employed, 16.4% were students regardless of employment, 8.7% were homemakers, and 2.3% were unemployed. The mean household income was \$30 000 to \$39 999.

Of the clinical sample, 33.3% were in their 20s, 37.1% were in their 30s, and 29.6% were in their 40s; 12.6% were Hispanic, 65.2% were white, 17.4% were black, and 4.7% were other. For marital status, 46.0% were married or

livingtogetherand53.0% were single, divorced, or separated.

Mean effect sizes by PMDD symptom or functioning measure and perimenstrual interval in the community and clinical samples are presented in Table 1 and Table 2, respectively. Visual inspection of the community data (Table 1) indicates that, consistent with hypothesis 1, symptoms most often occurred 3 days before the onset of menses through the first 3 days into the menstrual period. In the clinical sample (Table 2), symptoms most often occurred 4 days before the onset of menses through the first 2 days of the menstrual period. Severe symptoms occurred in tandem with functional impairment in both samples.

To assess hypothesis 2, symptoms in Table 1 and Table 2 were ranked in descending order of change and severity for the 4 days prior to and first 2 days of menses. Physical symptoms (eg, bloating, breast tenderness) showed the greatest change in both samples regardless of the perimenstrual interval. It is especially apparent from Table 2 that symptoms previously associated with PMDD (eg, mood swings and irritability vs diarrhea and sweating) show the greatest change and severity from the perimenstrual phase to the postmenstrual phase of the cycle. Of note, the most common affective symptom was mood swings. Affective lability, irritability, and feeling anxious/tense/on edge were more frequent than depressed mood in both samples.

Results of the exploration of the number of symptoms as related to impairment are presented in Table 3. The optimal cutoff point for the number of symptoms is chosen to maximize the sum of sensitivity and specificity for prediction of impairment. The optimal number of symptoms associated with impairment in the community cohort was 2, while in the clinical cohort it was 7. After combining the 2 cohorts and weighting them equally, the optimal cutoff point was 4 symptoms.

#### COMMENT

We examined data from a community sample and a clinical cohort to generate empirical evidence that would inform the DSM-5 sub-Work Group regarding criteria for PMDD. Hypothesis 1 was supported by both samples in that the peak of symptoms included premenstrual and menstrual days, although the frame differed by 1 day in the respective cohorts. These findings held for physical symptoms, affective symptoms, and functional impairment. Our results are in accord with findings from a large health maintenance organization population,<sup>9</sup> where women showed a peak of symptom severity either the day before or the first day of menses. Interestingly, women with the most severe symptoms were most likely to reach a zenith the day before menses, while women with less severe symptoms had the worst symptoms on the first day of menses. If women in our clinical cohort have more severe symptoms than those in the community, which is a reasonable assumption, our results would have great consistency with this prior study. Notably, the criteria for PMDD outlined in DSM-IV accommodate this interval because DSM-IV stipulates that symptoms occur in the "last week of the luteal phase and remit within a few days of the onset of the follicular phase."<sup>7</sup> The implication of this analysis is that clinicians and researchers may consider the measurement of symptoms from 4 days before through the first 3 days of menses rather than the traditional method of measuring symptoms of PMDD during the premenstrual week only.

We also found that our second hypothesis, that *DSM-IV* includes symptoms highly associated with a premenstrual disorder, was supported. Regardless of the data set and perimenstrual interval selected, the symptom of mood swings was among the most severe of the 4 affective symptoms listed in *DSM-IV*, 1 of which is required for a diagnosis of PMDD. Depressed mood was the least severe in this group. This introduces the possibility of listing mood swings first among the symptom criteria rather than depressed mood, because the latter implies that depressed mood is the most common symptom of the

Hartlage et al.

disorder. However, our study did not determine whether mood swings are a symptom specifically associated with PMDD or a symptom more commonly experienced by women in general when they are premenstrual. If future analyses are able to confirm that this symptom is highly associated with PMDD, it may warrant higher listing among the possible symptoms. It should be noted, however, that breast tenderness and bloating were highly related to the menstrual cycle in both cohorts. Given that the *DSM* focus is on emotional conditions, the Work Group may prefer to not indicate this as the first symptom in the criteria list.

In our exploration of the optimal number of symptoms that reflect functional impairment, results differed greatly according to the cohort. An optimal cutoff of 2 was found for the community cohort, while a cutoff of 7 was suggested for the clinical cohort. Differences in the characteristics of subjects likely contributed to this in that the women in the clinical cohort were treatment seeking and were more likely to have had severe symptoms. Our method of choosing an optimal cutoff point for the number of symptoms places equal consideration on sensitivity and specificity. Sensitivity, the probability of symptoms above the cutoff given impairment, is very low at higher scores in the community sample because there are few women in this sample with many symptoms. In the clinical sample, however, there are more symptoms generally and more symptoms in the impaired group, so sensitivity remains strong at higher cutoff points. Specificity, the probability of staying below the cutoff in patients without impairment, is sufficiently high for low cutoff points in the epidemiologic sample because of low numbers of symptoms in the group without impairment. The clinical sample has more symptoms in the group without impairment, and a higher cutoff is required to achieve high specificity. We think that weighing these 2 estimates equally is a compromise suitable for future use with a wider group of patients who may be less symptomatic than our clinical sample but more symptomatic than the overall population.

Our best estimate after combining the 2 cohorts was an optimal cutoff of 4 symptoms.

The American College of Obstetricians and Gynecologists definition of premenstrual syndrome requires only 1 symptom that is present within 5 days of the onset of menses and ends within 4 days of the menstrual flow, causes functional impairment, and is documented in 3 menstrual cycles. This definition may be more in line with what we found in our community sample. This issue requires greater exploration because if the *DSM-IV* requirement for 5 symptoms is retained, many women may not be diagnosed as having PMDD if they have 3 or 4 symptoms perimenstrually, even if they have impairment.

Our analyses have several limitations that should be considered. The most obvious is that the 2 cohorts used in this secondary analysis are different in a variety of ways. While we did not combine them when we tested hypotheses 1 and 2, we did for our exploratory analysis. A second consideration is that we used a statistical parameter, the effect size, to derive what we would consider a meaningful symptom. However, symptoms are subjective and this parameter, in particular the cutoff of 1, may not reflect a clinically significant difference. On the other hand, the fact that the application of an effect size of 1.0 for symptoms correlated with an effect size of 1.0 for functional impairment suggests that this cutoff is reasonable. Finally, our exploration of perimenstrual dates meant that we needed data from the first few days of a third menstrual cycle for subjects and we only had 1 or 2 cycles that included the first few days of menses for some subjects. Thus, we did not require that changes be shown across several menstrual cycles, which would have been a very rigorous test of PMDD criteria and is stipulated by *DSM-IV*. The need for 2 or more menstrual cycles to further validate the criteria for PMDD should be assessed in future work.

#### Acknowledgments

**Funding/Support:** This study was supported by grants from the American Psychiatric Association (Drs Hart-lage and Yonkers) and by grants MH055221 (Dr Hart-lage) and MH072955 (Mr Gotman and Dr Yonkers) from the National Institute of Mental Health.

#### REFERENCES

- Yonkers KA, O'Brien PM, Eriksson E. Premenstrual syndrome. Lancet. 2008; 371(9619):1200– 1210. [PubMed: 18395582]
- Steiner M, Steinberg S, Stewart D, Carter D, Berger C, Reid R, Grover D, Streiner D, Canadian Fluoxetine/Premenstrual Dysphoria Collaborative Study Group. Fluoxetine in the treatment of premenstrual dysphoria. N Engl J Med. 1995; 332(23):1529–1534. [PubMed: 7739706]
- Yonkers KA, Halbreich U, Freeman E, Brown C, Endicott J, Frank E, Parry B, Pearlstein T, Severino S, Stout A, Stone A, Harrison W, Sertraline Premenstrual Dysphoric Collaborative Study Group. Symptomatic improvement of premenstrual dysphoric disorder with sertraline treatment: a randomized controlled trial. JAMA. 1997; 278(12):983–988. [PubMed: 9307345]
- O'Brien PM, Craven D, Selby C, Symonds EM. Treatment of premenstrual syndrome by spironolactone. Br J Obstet Gynaecol. 1979; 86(2):142–147. [PubMed: 371663]
- Watson NR, Studd JW, Savvas M, Garnett T, Baber RJ. Treatment of severe premenstrual syndrome with oestradiol patches and cyclical oral norethisterone. Lancet. 1989; 2(8665):730–732. [PubMed: 2570971]
- 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(3):492–501. [PubMed: 16135578]
- 7. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 4th ed.. American Psychiatric Association; Washington, DC: 1994.
- Hurt SW, Schnurr PP, Severino SK, Freeman EW, Gise LH, Rivera-Tovar A, Steege JF. Late luteal phase dysphoric disorder in 670 women evaluated for premenstrual complaints. Am J Psychiatry. 1992; 149(4):525–530. [PubMed: 1554039]
- Sternfeld B, Swindle R, Chawla A, Long S, Kennedy S. Severity of premenstrual symptoms in a health maintenance organization population. Obstet Gynecol. 2002; 99(6):1014–1024. [PubMed: 12052592]
- Meaden PM, Hartlage SA, Cook-Karr J. Timing and severity of symptoms associated with the menstrual cycle in a community-based sample in the Midwestern United States. Psychiatry Res. 2005; 134(1):27–36. [PubMed: 15808287]
- Pearlstein TB, Bellew KM, Endicott J, Steiner M. Paroxetine controlled release for premenstrual dysphoric disorder: remission analysis following a randomized, double-blind, placebo-controlled trial. Prim Care Companion J Clin Psychiatry. 2005; 7(2):53–60. [PubMed: 15841196]
- Halbreich U, Borenstein J, Pearlstein T, Kahn LS. The prevalence, impairment, impact, and burden of premenstrual dysphoric disorder (PMS/PMDD). Psychoneuroendocrinology. 2003; 28(suppl 3): 1–23.
- Gehlert S, Song IH, Chang C-H, Hartlage SA. The prevalence of premenstrual dysphoric disorder in a randomly selected group of urban and rural women. Psychol Med. 2009; 39(1):129–136. [PubMed: 18366818]
- Szklo, M.; Nieto, J. Epidemiology: Beyond the Basics. 2nd ed.. Jones & Bartlett; Sudbury, MA: 2007.
- Hosmer, DW.; Lemeshow, S. Applied Logistic Regression. 2nd ed.. Wiley-Interscience; New York, NY: 2000.

# Table 1

Mean Effect Sizes and Symptom Ratings by Premenstrual Dysphoric Disorder Symptom or Functioning Measure and Perimenstrual Interval in 864 Participants in the Community Sample

|  | Sym         | ptom Rating <sup>b</sup> |          | Effect | Size <sup>c</sup> |         |
|--|-------------|--------------------------|----------|--------|-------------------|---------|
| Symptom <sup>a</sup>                                 | Day of Peak | Mean Rating at Peak      | (-6, -1) | (-5,1) | (-4,2)            | (-3, 3) |
| Physical symptoms, eg, bloating                      | 1           | 2.87                     | 0.33     | 0.49   | 0.58              | 0.62    |
| Food cravings  | 1           | 1.84                     | 0.24     | 0.27   | 0.29              | 0.31    |
| Low sex drive  | 1           | 1.90                     | 0.21     | 0.27   | 0.29              | 0.29    |
| Mood swings  | 1           | 1.83                     | 0.20     | 0.26   | 0.28              | 0.29    |
| Change in appetite                                   | 1           | 1.85                     | 0.15     | 0.20   | 0.23              | 0.24    |
| Suddenly sad or tearful                              | 2           | 1.70                     | 0.13     | 0.18   | 0.22              | 0.23    |
| Suddenly irritable                                   | 1           | 1.93                     | 0.15     | 0.20   | 0.21              | 0.22    |
| Sensitive to rejection                               | 1           | 1.74                     | 0.15     | 0.18   | 0.20              | 0.20    |
| Irritability that stayed with me                     | 1           | 1.72                     | 0.16     | 0.20   | 0.19              | 0.18    |
| Easily upset   | 1           | 1.86                     | 0.13     | 0.17   | 0.18              | 0.18    |
| Symptoms interfered with getting things done at work | 1           | 1.66                     | 0.14     | 0.16   | 0.18              | 0.20    |
| Felt "on edge"                                       | 1           | 1.73                     | 0.12     | 0.16   | 0.17              | 0.17    |
| Depressed mood                                       | 1           | 1.72                     | 0.10     | 0.14   | 0.16              | 0.18    |
| Symptoms interfered with relationships at home       | 1           | 1.60                     | 0.09     | 0.15   | 0.16              | 0.17    |
| Wanted to be alone                                   | 1           | 1.86                     | 0.12     | 0.15   | 0.16              | 0.16    |
| Felt distractible                                    | 1           | 1.62                     | 0.10     | 0.15   | 0.15              | 0.17    |
| Symptoms interfered with relationships at work       | 1           | 1.63                     | 0.14     | 0.15   | 0.15              | 0.16    |
| Felt "out of control"                                | 1           | 1.41                     | 0.11     | 0.14   | 0.15              | 0.16    |
| Increased interpersonal conflict                     |             | 1.61                     | 0.13     | 0.15   | 0.15              | 0.13    |
| Feelings of tension                                  | 1           | 2.12                     | 0.10     | 0.14   | 0.15              | 0.15    |
| No energy  | 1           | 2.25                     | 0.05     | 0.10   | 0.14              | 0.18    |
| Easily fatigued                                      | 1           | 2.18                     | 0.04     | 0.10   | 0.14              | 0.17    |
| Agitated   | 1           | 1.92                     | 0.11     | 0.13   | 0.14              | 0.14    |
| Negative thoughts about myself                       | 1           | 1.61                     | 0.10     | 0.15   | 0.14              | 0.14    |
| Time missed from work                                | 1           | NA                       | 0.06     | 0.10   | 0.14              | 0.13    |
| Overeating   | 1           | 1.71                     | 0.15     | 0.15   | 0.14              | 0.14    |

|  | Sym         | ptom Rating <sup>b</sup> |          | Effect | Size <sup>c</sup> |         |
|--|-------------|--------------------------|----------|--------|-------------------|---------|
| Symptom <sup>a</sup>                                   | Day of Peak | Mean Rating at Peak      | (-6, -1) | (-5,1) | (-4,2)            | (-3, 3) |
| Symptoms interfered with social activities             | 1           | 1.62                     | 0.07     | 0.11   | 0.14              | 0.15    |
| Felt restless  | 1           | 1.74                     | 0.09     | 0.12   | 0.14              | 0.14    |
| Felt suddenly angry                                    | 1           | 1.68                     | 0.09     | 0.12   | 0.13              | 0.11    |
| Arguments with people                                  | 1           | 1.36                     | 0.11     | 0.13   | 0.13              | 0.12    |
| Felt "keyed up"  | 1           | 1.59                     | 0.09     | 0.12   | 0.13              | 0.11    |
| Decreased interest in usual activities                 | 1           | 1.63                     | 0.07     | 0.11   | 0.12              | 0.14    |
| Symptoms interfered with getting things done at home   | 1           | 1.75                     | 0.06     | 0.11   | 0.12              | 0.14    |
| Trouble sleeping                                       | 1           | 1.87                     | 0.08     | 0.11   | 0.11              | 0.13    |
| Less productive at home                                | 1           | 1.89                     | 0.05     | 0.09   | 0.11              | 0.13    |
| Difficulty concentrating                               | 1           | 1.81                     | 0.05     | 0.08   | 0.11              | 0.13    |
| Less productive at work                                | 1           | 1.12                     | 0.05     | 0.08   | 0.11              | 0.14    |
| Symptoms interfered with getting things done at school | 1           | 1.52                     | -0.04    | 0.06   | 0.10              | 0.14    |
| Avoided social activities                              | 1           | 1.53                     | 0.04     | 0.07   | 0.09              | 0.10    |
| Anger that stayed with me                              | 1           | 1.51                     | 0.09     | 0.09   | 0.09              | 0.08    |
| Felt hopeless  | 1           | 1.48                     | 0.05     | 0.07   | 0.08              | 0.09    |
| Slept too much   | 1           | 1.49                     | 0.05     | 0.07   | 0.08              | 0.08    |
| Felt lonely  | 1           | 1.62                     | 0.04     | 0.07   | 0.07              | 0.08    |
| Felt anxious   | 1           | 1.97                     | 0.02     | 0.05   | 0.07              | 0.08    |
| Felt guilty  | 1           | 1.48                     | 0.03     | 0.04   | 0.05              | 0.04    |
| Felt overwhelmed                                       | 1           | 1.91                     | 0.01     | 0.04   | 0.04              | 0.05    |
| Time missed from class                                 | 1           | NA                       | 0.11     | -1.01  | 0.03              | 0.06    |
| Symptoms interfered with relationships at school       | 1           | 1.64                     | 0.09     | -1.02  | -0.05             | 0.01    |

Arch Gen Psychiatry. Author manuscript; available in PMC 2012 June 08.

Abbreviation: NA, not applicable.

 $a^{3}$  Symptoms are presented in descending order of severity and change during the last 4 days before and the first 2 days of the menstrual period.

 $b_{\rm c}$  Ratings are on a 6-point scale: 1 indicates not at all; 2, minimal; 3, mild; 4, moderate; 5, severe; and 6, extreme.

<sup>C</sup>Effect size measures the increase in symptom endorsement during the perimenstrual interval compared with a nonmenstrual interval adjusted for the standard deviation of symptom endorsement during the entire cycle. The interval (-6, -1) indicates 6 days before through 1 day before menses; (-5,1), 5 days before through the first day of menses; (-4, 2), 4 days before through the first 2 days of menses; and (-3, 3), 3 days before through the first 3 days of menses.

# Table 2

Mean Effect Sizes and Symptom Ratings by Premenstrual Dysphoric Disorder Symptom or Functioning Measure and Perimenstrual Interval in 193 Participants in the Clinical Sample

Hartlage et al.

|                      | Sym         | ptom Rating <sup>b</sup> |          | Effect | Size <sup>c</sup> |         |
|----------------------|-------------|--------------------------|----------|--------|-------------------|---------|
| Symptom <sup>a</sup> | Day of Peak | Mean Rating at Peak      | (-6, -1) | (-5,1) | (-4,2)            | (-3, 3) |
| Bloated              | -1          | 3.29                     | 1.16     | 1.32   | 1.38              | 1.33    |
| Mood swings          | -           | 3.42                     | 1.03     | 1.14   | 1.19              | 1.16    |
| Irritable            | -1          | 3.46                     | 1.03     | 1.13   | 1.16              | 1.12    |
| Lethargic            | 1           | 3.47                     | 0.97     | 1.10   | 1.15              | 1.13    |
| Tender breast        | -2          | 2.70                     | 1.04     | 1.13   | 1.15              | 1.07    |
| Anxious/tense        | -1          | 3.30                     | 0.97     | 1.06   | 1.09              | 1.05    |
| Rejection            | -1          | 3.07                     | 0.95     | 1.03   | 1.07              | 1.05    |
| Depressed/sad        | -1          | 2.92                     | 0.87     | 0.98   | 1.03              | 1.01    |
| Overeating           | -           | 2.85                     | 0.92     | 1.01   | 1.03              | 0.99    |
| Less interest        | -           | 2.96                     | 0.83     | 0.93   | 0.98              | 0.97    |
| Cravings             | -           | 2.65                     | 0.85     | 0.93   | 0.96              | 0.92    |
| Concentration        | -2          | 2.86                     | 0.81     | 0.89   | 0.93              | 0.91    |
| Conflicts            | -           | 2.82                     | 0.83     | 0.89   | 0.92              | 06.0    |
| Slept more           | -           | 2.87                     | 0.79     | 0.87   | 0.92              | 06.0    |
| Overwhelmed          | -           | 2.76                     | 0.86     | 06.0   | 06.0              | 0.84    |
| Out of control       | -2          | 2.56                     | 0.78     | 0.82   | 0.83              | 0.79    |
| Physically agitated  | -           | 2.49                     | 0.72     | 0.79   | 0.82              | 0.78    |
| Muscle pain          | 1           | 2.49                     | 0.67     | 0.78   | 0.80              | 0.80    |
| Difficulty sleeping  | -           | 2.59                     | 0.65     | 0.74   | 0.76              | 0.71    |
| Hopeless             | -           | 2.40                     | 0.63     | 0.71   | 0.75              | 0.73    |
| Worthless/guilty     | -           | 2.27                     | 0.62     | 0.70   | 0.73              | 0.71    |
| Headache             | -           | 2.24                     | 0.48     | 0.57   | 0.62              | 0.63    |
| Diarrhea             | 1           | 2.04                     | 0.37     | 0.51   | 0.57              | 0.57    |
| Sweating             | -           | 1.88                     | 0.45     | 0.53   | 0.52              | 0.50    |
| Dreams               | -2          | 1.95                     | 0.49     | 0.51   | 0.49              | 0.44    |
| Nausea               | 7-          | 1 52                     | 030      | 035    | 036               | 0 33    |

Г

Hartlage et al.

|                      | Sym         | otom Rating <sup>b</sup> |          | Effect | Size <sup>c</sup> |         |
|----------------------|-------------|--------------------------|----------|--------|-------------------|---------|
| Symptom <sup>a</sup> | Day of Peak | Mean Rating at Peak      | (-6, -1) | (-5,1) | (-4,2)            | (-3, 3) |
| Chills               | -2          | 1.42                     | 0.25     | 0.28   | 0.28              | 0.28    |
| Dizzy                | -           | 1.44                     | 0.21     | 0.24   | 0.27              | 0.26    |
| Ringing in ears      | -1          | 1.21                     | 0.16     | 0.17   | 0.17              | 0.17    |

 $a^{3}$  Symptoms are sorted by mean effect size in the last 4 days before and the first 2 days of the menstrual period (the -4, 2 interval).

b Ratings are on a 6-point scale: 1 indicates not at all; 2, minimal; 3, mild; 4, moderate; 5, severe; and 6, extreme.

 $c^{c}$  Effect size measures the increase in symptom endorsement during the perimenstrual interval compared with a nonmenstrual interval adjusted for the standard deviation of symptom endorsement during the entire cycle. The interval (-6, -1) indicates 6 days before through 1 day before meases; (-5,1), 5 days before through the first day of meases; (-4, 2), 4 days before through the first 2 days of meases; and (-3, 3), 3 days before through the first 3 days of menses.

#### Table 3

#### Functional Impairment and Number of Symptoms of Premenstrual Dysphoric Disorder

| Outcome                               | Clinical Sample (n = 193) | Community Sample (n = 864) | Combined Clinical and<br>Community Sample (N = 1057) <sup><i>a</i></sup> |
|---------------------------------------|---------------------------|----------------------------|--|
| Prevalence of impairment, %           | 67.9                      | 25.3                       | 46.6   |
| PMDD symptoms, mean, No.              | 6.96                      | 0.81                       | 3.89   |
| Optimal cutoff point, No. of symptoms | 7                         | 2                          | 4  |
| Sensitivity for optimal cutoff        | 0.80                      | 0.39                       | 0.74   |
| Specificity for optimal cutoff        | 0.82                      | 0.87                       | 0.86   |
| Youden J statistic for optimal cutoff | 0.62                      | 0.26                       | 0.60   |
| Area under ROC curve                  | 0.89                      | 0.65                       | 0.76   |

Abbreviations: PMDD, premenstrual dysphoric disorder; ROC, receiver operating characteristic.

<sup>a</sup>Combined samples are weighted to place equal weight on each of the 2 samples.