ORIGINAL ARTICLE

Association of Premenstrual Syndrome and Premenstrual Dysphoric Disorder with Bulimia Nervosa and Binge-Eating Disorder in a Nationally Representative Epidemiological Sample

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ABSTRACT

Objective: Bulimia nervosa (BN) and binge-eating disorder (BED) are associated with significant health impairment. Premenstrual syndrome (PMS) and premenstrual dysphoric disorder (PMDD) comprise both psychological (disturbances in mood and affect) and physiological (bloating and changes in appetite) symptoms that may trigger binge-eating and/or purging.

Method: Female participants were drawn from the Collaborative Psychiatric Epidemiological Surveys, conducted from 2001 to 2003. Weighted multivariable logistic regression modeled the association between lifetime PMS and PMDD and lifetime odds of BN or BED.

Results: Among 8,694 participants, 133 (1.0%) had BN and 185 (1.8%) BED. Additionally, 366 (4.2%) had PMDD and 3,489 (42.4%) had PMS. Prevalence of PMDD and PMS were 17.4 and 55.4% among those with BN, 10.7 and 48.9% among those with BED and 3.4 and 59.1% among those with subthreshold BED. After adjustment for age, race/ethnicity, income, education, body mass index, age at menarche, birth control use, and comorbid mental health conditions, PMDD was associated with seven times the odds of BN (OR 7.2, 95% CI 2.3, 22.4) and PMS with two times the odds of BN (OR 2.5, 95% CI 1.1, 5.7). Neither PMDD nor PMS were significantly associated with BED.

Discussion: Women with PMS and PMDD have a higher odds of BN, independent of comorbid mental health conditions. PMS and PMDD may be important comorbidities to BN to consider in clinical settings, and future research should investigate whether PMS and PMDD affect the onset and duration of bulimic symptoms as well as the potential for shared risk factors across disorders. © 2016 Wiley Periodicals, Inc.

Keywords: bulimia nervosa; binge-eating disorder; premenstrual dysphoric disorder

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Introduction

Young women are disproportionately affected by bulimia nervosa (BN) and binge-eating disorder (BED), disorders which increase the risk of chronic health problems,[1,2] reduce quality of life,[3] and increase the risk of suicide attempts,[4] and mortality.[5] BN affects approximately 1.5% of women[6] and BED approximately 3.5% of women[6] in the United States. Median duration of BN and BED have been estimated in the WHO World Mental Health Surveys as 6.5 (IQR 2.2, 15.4) years and 4.3 (IQR 1.0, 11.7) years, respectively.[2] Additionally, both have high comorbidity with mood disorders, anxiety disorders, and other mental health conditions,[2,7] which may affect the severity of both BN and BED, lengthen time to recovery,[8] and hinder treatment outcome.[9] Premenstrual syndrome (PMS) and the more severe premenstrual dysphoric disorder

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(PMDD) are potential comorbidities to BN and BED that may affect the onset, severity and duration of binge-type eating disorders among women.

PMDD and PMS affect approximately 3–8% and 20–32% of women, respectively.[10] The menstrual cycle has two phases: the follicular phase, which is marked by a surge in estrogen and begins at menstruation and ends at ovulation, and the luteal phase, which is marked by a surge in progesterone and a secondary surge in estrogen and follows ovulation.[11] PMDD and PMS are marked by changes in both psychological and physiological symptoms in the late luteal phase of the menstrual cycle.[12] Psychological symptoms, including alterations in mood and affect, and physiological symptoms, including abdominal bloating, edema and changes in appetite and cravings,[13,14] may exacerbate symptoms of binge-type eating disorders. PMDD, newly moved from the appendix to an officially recognized disorder in the *Diagnostic and Statistical Manual, Fifth Edition* (DSM-5), is a more severe form of PMS, in which symptoms lead to significant interference in usual activities or in functioning at work, school, or in interpersonal relationships.[15] To be characterized as having PMS or PMDD, symptoms must remit within a few days after the onset of menses and remain normal during the follicular phase (approximately the 2 weeks after menstruation).[5,16] If the symptoms experienced during the late-luteal phase represent worsening of an underlying mental health condition, women may be diagnosed with premenstrual exacerbation of the underlying condition (e.g., major depressive disorder),[17] rather than with PMS or PMDD.[16] Although the etiology of premenstrual conditions remains largely unknown, research has suggested that, rather than experiencing differences in menstrual function and ovarian hormone levels,[18] women with premenstrual conditions may have an increased sensitivity to the normal fluctuation of hormone levels during the menstrual cycle, particularly as relates to γ-aminobutyric acid A (GABA-A) receptor sensitivity and the serotonergic system.[19] This hypothesis is at least partly supported by the demonstrated efficacy of selective serotonin reuptake inhibitors (SSRIs) in promoting remission of PMS/PMDD symptoms in randomized clinical trials.[20]

There is reason to believe that PMS or PMDD symptoms could serve as maintenance factors for binge-type eating disorders. Similar to other eating disorder comorbidities,[2,7] the physiological and psychological symptoms associated with premenstrual conditions may serve as a trigger for binge-eating and/or purging,[21] potentially affecting the onset of binge-type eating disorders as well as serving as a maintenance factor impeding recovery. Potential triggers include physiological changes associated with PMS/PMDD, such as bloating and changes in body weight (which could be perceived as "fatness" by individuals with eating disorders) and increases in appetite and cravings (which could lead directly to binge-eating).[13,14] Studies have found that women with PMDD report significantly higher calorie intake and uncontrolled eating in the late-luteal vs. follicular phases of the menstrual cycle,[22] and greater food cravings and positive emotional response to sweet and high-fat foods in the late-luteal phase.[23] Additionally, psychological changes associated with PMS and PMDD, such as alterations in mood and affect,[13,14] may serve as triggers. Among healthy reproductive-aged women, weight preoccupation was found to be significantly higher in the premenstrual and menstrual phases of the menstrual cycle, independent of interindividual variation in estradiol and progesterone levels.[24]

Little past research has investigated the potential role of premenstrual conditions in the onset, severity and duration of binge-type eating disorders. A few studies have documented an exacerbation of bulimic symptoms during the premenstrual phase,[25–27] during which increases in the ovarian hormones progesterone and estrogen may be associated with depressed mood, irritability, and anger.[13] For example, a prospective study following eight women with BN for one menstrual cycle found that bulimic symptoms were significantly worsened in the luteal phase.[25] However, past research into this topic has been limited by small sample size, and has not explored the potential role of premenstrual conditions in the onset and duration of binge-type eating disorders.

There is also reason to believe that PMS or PMDD may have shared risk factors for binge-type eating disorders. Specifically, eating disorders typically onset during or after puberty and are more common in females, which suggests that the epigenetic changes that underlie the activation of ovarian hormones at puberty may play an etiological role.[28,29] It is also plausible that women who have increased sensitivity to fluctuations in ovarian hormones through development of PMS and PMDD are more likely to experience the symptoms of disordered eating that accompany the activation of ovarian hormones.

Although PMS and PMDD have the potential to exacerbate symptoms of binge-type eating disorders, few studies have looked at their association,

and none have quantified the degree of comorbidity. Therefore, the present study addresses these gaps in the literature by investigating the cross-sectional association between a lifetime history of PMS and PMDD, and a lifetime history of BN, BED and subthreshold BED in an ethnically diverse, nationally representative sample from the Collaborative Psychiatric Epidemiological Surveys. To address the potential for PMS and PMDD to inhibit recovery from BN and BED (e.g., by serving as a maintenance factor for disordered eating), we additionally investigated the association of PMS and PMDD with duration of lifetime binge-type eating disorder symptoms.

Method

Study Population

The Collaborative Psychiatric Epidemiological Surveys (CPES) consists of three independent surveys conducted between 2001 and 2003: The National Comorbidity Survey Replication (NCS-R); the National Survey of American Life (NSAL)-focused on African American and Afro-Caribbean populations; and the National Latino and Asian American Survey (NLAAS)—focused on Latino and Asian American populations.[30] Each survey employed a similar design, methodology, and set of assessment tools. The main aims of these surveys were to document the prevalence and correlates of mental health conditions in the United States and associated utilization of mental health services.

All three surveys used a four-stage national area probability sample, consisting of nested samples conducted in the following order: (1) US Metropolitan Statistical Areas (MSAs) and counties, (2) area segments within each selected MSA or county, (3) housing units within each selected area segment, and (4) eligible respondents in each selected housing unit. Surveys were administered by lay interviewers in the participant's home when possible, utilizing a computer-assisted personal interview (CAPI) format. Surveys included comparable content for the assessment of prevalence of mental health conditions following criteria laid out in DSM-IV.[31] All DSM-IV diagnoses were assessed using the World Health Organization's World Mental Health Survey update to the Composite International Diagnostic Interview (WMH-CIDI).[30] All participants in the Collaborative Psychiatric Epidemiological Surveys provided informed consent, and this secondary analysis was reviewed and approved by Partners Healthcare Institutional Review Board.

Binge-Type Eating Disorders

The outcomes of interest in this study were BN, BED and subthreshold BED (which is associated with similar levels of eating pathology and general psychopathology compared to full threshold BED).[32] Importantly, as data were collected before the 2013 publication of DSM-5, BN and BED were defined according to DSM-IV criteria. We excluded all participants who had a lifetime history of anorexia nervosa (AN) from analysis due to low prevalence in this dataset in addition to the low body weight associated with a diagnosis of AN, which may interfere with normal menstrual function, including inducing amenorrhea, which could affect the presence of PMDD and PMS. Therefore, participants with lifetime BN, BED and subthreshold BED in addition to lifetime AN were excluded from analysis (among the 25 participants with AN who had complete data, 8 also had a lifetime history of bulimia and 2 had a lifetime history of BED).

Prior to completing the diagnostic module for BN and BED, participants were assessed with a screening question asking whether they had ever in their lifetime engaged in a period of eating binges which occurred at least twice per week for several months. Among those that answered that they had engaged in a period of binge-eating, participants met DSM-IV criteria for lifetime BN if, in the absence of AN, they reported a period of binge-eating (i.e., consuming a large amount of food while feeling a loss of control) at least twice per week for 3 months or longer that was accompanied by inappropriate compensatory behavior. Participants met criteria for lifetime BED if, in the absence of AN and BN, they reported a period of binge-eating at least twice per week for 6 months or longer that was associated with at least three of the five DSM-IV binge features. Participants were classified as having lifetime subthreshold BED if, in the absence of AN, BN, or BED, they reported a period of binge-eating at least twice per week for three months or longer.[33] Of note, a subset of individuals defined in our study as having DSM-IV sub-threshold BED may also have met criteria for full-threshold BED under DSM-5 if they reported duration of 3 months or longer (but not 6 months or longer) and met all other criteria for binge-eating disorder, including at least 3 of 5 binge features. For the purpose of analysis, participants were classified according to their most severe lifetime eating disorder (exclusive of AN), in the order of BN, BED, subthreshold BED and no lifetime history of a DSM-IV eating disorder. For example, women with a lifetime history of both BN and BED would be classified as having a lifetime history of BN. For BN, the CIDI has moderate to good reliability (test–retest kappa = 0.64 and interrater kappa = 0.78)[34] and validity[35] as compared to clinician diagnoses.

Premenstrual Syndrome and Premenstrual Dysphoric Disorder

To screen women for the premenstrual syndrome module, participants were first asked whether they ever

had a time in their life when their mood became worse in the week before their menstrual period and returned to normal within a few days of the start of their menstrual period. Because standard diagnostic criteria for PMS requires remission of PMS-related symptoms during the follicular phase of the menstrual cycles cycle,[16] the measure employed in the Collaborative Psychiatric Epidemiological Surveys included mood-related symptoms of both PMS and premenstrual exacerbation of existing mental health conditions, and therefore our analyses included women with either PMS or premenstrual exacerbation not associated with significant interference in daily functioning.

PMDD was defined in this study according to DSM-IV criteria[31] (also consistent with DSM-5 criteria), and endorsed when participants met all of the following criteria: (1) presence of PMS as defined above, (2) worsening of mood occurring in at least 7 months/year, (3) worsening of mood occurring most or all of the time in the week prior to menstruation, (4) mood symptoms accompanied by physiological symptoms, including difficulty concentrating, tiredness or appetite or sleep changes, and (5) worsening of mood leading to interference in work, social life, or personal relationships some, most or all of the time. Similar to the classification of PMS using the CIDI, PMDD as measured by the CIDI included both PMDD as defined by DSM-IV and premenstrual exacerbation of existing mental health conditions leading to significant interference in daily functioning, and therefore our analyses included women with either PMDD or premenstrual exacerbation associated with significant interference in daily functioning.

Covariates

Demographic factors assessed include age (years), race/ethnicity (Latino, non-Latino black, non-Latino white, another race/ethnicity), educational attainment (less than high school, high school, at least some college), annual household income (<$15,000, $15,000 to <$35,000, $35,000 to <$75,000, ≥$75,000), partner status (married/cohabitating, divorced/separated/widowed, never married), and occupational status (employed, unemployed, not in the workforce). Reproductive factors assessed include age at menarche (years), having ever used hormonal birth control and having ever given birth. Weight status was assessed using body mass index (BMI) (<18.5, 18.5 to <25, 25 to <30, ≥30 kg/m^2). Comorbid mental health conditions were defined according to DSM-IV criteria and include lifetime history of major depressive disorder (MDD), dysthymia, bipolar disorder, agoraphobia, panic disorder, generalized anxiety disorder, social phobia, substance use disorders (defined as having at least one of the following: alcohol abuse, alcohol dependence, substance abuse, or substance dependence), and post-traumatic stress disorder.

Statistical Analysis

All analyses were weighted to account for sampling probabilities inherent in the survey design. Numbers and frequencies or means and standard deviations were calculated for descriptive statistics, with distributional differences between groups assessed using Rao–Scott χ^2 tests or weighted least-squares linear regression. Lifetime history of an eating disorder was modeled as a series of dummy variables, including (1) lifetime BN, (2) lifetime BED in the absence of BN, (3) subthreshold BED (lifetime history of a period of binge-eating with episodes at least twice per week for 3 months or longer, in the absence of BN and BED), and (4) no history of a DSM-IV eating disorder. Bivariate multinomial logistic regression was used to model the unadjusted association between lifetime history of PMS and PMDD and BN, BED and subthreshold BED. Two adjusted models were run: an *a priori* model and a full model. For the *a priori* model, we identified potential confounders from the literature[2,36] including age, race/ethnicity, income, education, age at menarche, lifetime use of hormonal birth control and lifetime diagnosis of major depressive disorder. For the full model, we retained all *a priori* covariates. Additional potential confounders, including demographic factors, menstrual cycle characteristics, and comorbid mental health conditions other than major depressive disorder, were assessed by adding each independently into the *a priori* model, and retaining them if their addition to the *a priori* resulted in a 10% or greater change in one of the main effect estimates. Confounders identified using this method include a lifetime diagnosis of dysthymia, bipolar disorder, social phobia, and substance use disorder. In separate subsets of participants with a lifetime history of BN, BED, and subthreshold BED, respectively, we used linear regression to model the association of PMS and PMDD with duration of each condition, similarly by first using bivariate linear regression to model the duration of each condition in relation to lifetime history of PMS and PMDD, next using an *a priori* model, and finally using a full model, both adjusting for the covariates identified above. All analyses were conducted in SAS 9.3 (SAS Institute Inc., Cary, NC).

Results

Of 20,013 total Collaborative Psychiatric Epidemiological Surveys participants, 11,463 (51.9%) were female and eligible for inclusion in this study. Of these, 9,111 (94.8%) were asked questions about both eating disorders and PMS/PMDD (519 non-Latina white participants in National Survey of

American Life were not assessed for eating disorders or PMS/PMDD[37] and 1,833 of participants in National Comorbidity Survey Replication did not complete the long-form survey which included questions on PMS/PMDD). Furthermore, 392 (3.6%) were missing data on PMS/PMDD and 146 (0.9%) were missing data on eating disorders, resulting in a final study population of 8,694 participants. Women who were excluded from analysis were more likely to be older (mean 49.6 vs. 43.4 years, $P < 0.001$), be non-Latina white (86.8 vs. 62.4%), have a lower household income (13.3 vs. 23.8% with income $\geq$\$75,000), have completed high school or at least some college (84.7% vs. 81.4%), be divorced, separated, or widowed (28.3 vs. 24.5%) and not have children in the household (74.3 vs. 65.3%). Among women included in the analysis, mean age at menarche was 12.7 (SEM 0.03) years. A total of 5,607 (65.3%) had ever used hormonal birth control, and 6,669 (74.7%) had given birth. A total of 1,749 (19.9%) had a lifetime history of major depressive disorder.

Table 1 presents study population characteristics by eating disorder. In total, 133 (1.0%) participants had a lifetime history of BN, 185 (1.8%) had a lifetime history of BED, 106 (0.6%) had a lifetime history of subthreshold BED, and 8,270 (96.6%) had no history of an eating disorder. Average duration of each condition was 13.0 (SEM 1.5, range 0–49) years for BN, 13.7 (SEM 1.8, range 0–56) years for BED and 6.4 (SEM 1.6, range 0–63) years for subthreshold BED. Women with a lifetime history of BN or subthreshold BED were younger, less likely to be non-Latina white, and had lower educational attainment compared to women without a history of an eating disorder. Women with BED and subthreshold BED were less likely to be married, and women with BN and BED were more likely to smoke, than women without a history of an eating disorder. Women with BN and BED additionally had a significantly lower age at menarche, and were significantly more likely than women without a history of an eating disorder to have ever used hormonal birth control. All comorbid mental health conditions assessed were more common among women with an eating disorder than among those without, with particularly high prevalence among those with BN. The most common comorbidities of BN were major depressive disorder (38.2%), post-traumatic stress disorder (34.9%), social phobia (33.5%) and dysthymia (27.4%). Finally, 366 (4.2%) met criteria for PMDD, 3,489 (42.4%) met criteria for PMS in the absence of PMDD, and 4,839 (53.4%) did not meet criteria for PMS or PMDD.

PMS, PMDD, and Prevalence of Eating Disorders

In unadjusted analysis, the prevalence of both PMDD and PMS were greater among those with BN, BED or subthreshold BED as compared to those without BN, BED or subthreshold BED. Among those without BN, BED, or subthreshold BED, prevalence of PMDD was 3.9% and PMS was 42.0%. Comparatively, among those with BN, 17.4% had PMDD and 55.4% had PMS; among those with BED, 10.7% had PMDD and 48.9% had PMS; and, among those with subthreshold BED, 3.4% had PMDD and 59.1% had PMS. **Table 2** presents the results of the multinomial logistic regression models for lifetime prevalence of PMS and PMDD and lifetime prevalence of binge-type eating disorders. In bivariate models, PMDD was associated with almost 9-times the odds of BN (OR 8.7, 95% CI 4.0, 19.1) and PMS was associated with 2.6 times the odds of BN (OR 2.6, 95% CI 1.5, 4.6). Additionally, PMDD was significantly associated with >3 times the odds of BED (OR 3.6, 95% CI 1.8, 7.4) and PMS was associated with two times the odds of subthreshold BED (OR 2.0, 95% CI 1.2, 3.5). Results were largely unchanged in the *a priori* adjusted model, with PMDD associated with 9 times the odds of BN (9.4, 95% CI 3.9, 22.5) and PMS associated with 2.7 times the odds of BN (OR 2.7, 95% CI 1.4, 5.2). In the *a priori* model, PMDD was significantly associated with >3 times the odds of BED (OR 3.6, 95% CI 1.7, 7.6) and PMS was associated with two times the odds of subthreshold BED (OR 2.1, 05% CI 1.2, 3.7). After combining participants with full BED and subthreshold BED into one group, both PMDD and PMS were associated with a greater odds of combined full and subthreshold BED in both the unadjusted and *a priori* adjusted models.

In the full adjusted model, the association between PMDD and BN was attenuated but remained significant (OR 7.2, 95% CI 2.3, 22.4), as was the association between PMS and BN (OR 2.5, 95% CI 1.1, 5.7). The association between PMDD and BED and PMS and subthreshold BED were no longer significant. After combining participants with full and subthreshold BED into one group, both PMDD and PMS were no longer significantly associated with combined full and subthreshold BED. Among the five comorbid mental health conditions adjusted for in the full model, all of which were significantly associated with eating disorders in bivariate analyses (**Table 1**), only dysthymia (OR 4.9, 95% CI 1.9, 12.7) remained significantly associated with BN.

TABLE 1. Study population characteristics by eating disorder diagnosis (n = 8,694)

	BN (n = 133)		BED (n = 185)		Subthreshold BED (n = 106)		No Binge-Eating (n = 8270)		
	n	%	n	%	n	%	n	%	P
Age (weighted mean, SEM)	35.6	1.3	41.6	1.9	38.0	2.3	45.5	0.4	<0.001
Race/ethnicity									
Asian	12	5.9	15	3.8	17	12.8	1067	4.7	<0.001
Latina	32	18.7	53	15.1	26	22.8	1684	11.6	
Non-Latina black	62	21.5	67	13.4	51	31.0	3220	12.2	
Non-Latina white	24	45.3	49	65.0	10	29.3	2197	69.3	
Other race/ethnicity	3	8.6	1	2.8	2	4.2	102	2.3	
Income									
<$15,000	47	32.2	56	19.2	39	34.0	1991	19.7	0.16
$15,000 to <$35,000	42	26.8	55	28.3	26	24.7	2322	24.0	
$35,000 to <$75,000	27	23.3	40	27.7	25	24.1	2341	32.2	
$75,000+	17	17.8	34	24.8	16	17.1	1616	24.1	
Education (years)									
0–11	32	30.6	61	26.8	33	33.6	1756	17.1	<0.001
12	48	26.2	47	20.5	25	26.8	2426	31.3	
13+	53	43.3	77	52.7	48	39.6	4088	51.6	
Marital status									
Married/cohabitating	55	52.8	80	49.1	45	43.9	4040	54.8	0.008
Divorced/separated/widowed	37	27.7	48	17.1	29	25.5	2205	25.4	
Never married	41	19.4	57	33.8	32	30.6	2025	19.8	
Work status									
Employed	85	65.3	107	65.2	54	54.3	5114	59.2	0.14
Unemployed	15	8.6	18	8.1	19	17.5	691	7.2	
Not in labor force	33	26.1	60	26.7	33	28.1	2456	33.5	
Ever smoke (yes vs. no)	59	52.0	89	54.6	44	37.3	2885	42.2	0.032
Body mass index (kg/m2)									
<18.5	3	4.1	8	3.7	3	2.4	318	5.7	<0.001
18.5 to <25	33	26.1	34	18.4	41	42.8	3208	42.5	
25 to <30	28	22.7	50	31.2	27	25.0	2296	27.6	
≥30	64	47.2	88	46.7	33	29.7	2243	24.2	
Reproductive factors									
Age at menarche (weighted mean, SEM)	12.4	0.2	12.2	0.2	12.7	0.2	12.7	0.04	0.004
Ever use birth control (yes vs. no)	100	77.4	122	77.2	64	60.9	5321	67.3	0.029
Given birth (yes vs. no)	98	70.3	138	73.1	87	75.3	6346	74.7	0.88
Lifetime mental health comorbidities (yes vs. no)									
Major depression	50	38.2	65	30.2	23	33.9	1659	19.3	<0.001
Dysthymia	27	27.4	29	13.4	10	12.1	395	4.7	<0.001
Bipolar disorder	17	11.8	11	7.4	2	1.6	149	1.9	<0.001
Agoraphobia	24	13.8	21	7.9	6	2.9	279	2.6	<0.001
Generalized anxiety disorder	26	17.4	28	12.6	8	5.8	751	9.3	0.042
Panic disorder	26	13.6	29	13.4	9	11.6	470	5.6	<0.001
Social phobia	41	33.5	50	27.2	20	25.4	967	11.3	<0.001
Substance abuse	23	21.1	38	20.9	10	10.9	613	7.9	<0.001
Post-traumatic stress disorder	41	34.9	36	21.3	14	12.0	822	9.0	<0.001
Premenstrual conditions									
PMS/PMDD									
PMDD	23	17.4	25	10.7	6	3.4	312	3.9	<0.001
PMS, no PMDD	72	55.4	93	48.9	53	59.1	3271	42.0	
No PMDD or PMS	38	27.3	67	40.4	47	37.4	4687	54.0	

PMS, PMDD, and Duration of Eating Disorders

Table 3 presents the results of the linear regression models for duration of each eating disorder in the presence of PMS and PMDD. In bivariate models, lifetime history of PMDD versus no PMS or PMDD was associated with a significant 11-year greater duration of BN (mean duration of BN 20.5, 95% CI 12.6, 28.4 years among those with PMDD; mean duration of BN 9.4, 95% CI 4.1, 14.7 years among those without PMDD, $P < 0.01$). In contrast, PMS was not significantly associated with duration of BN, and neither PMDD nor PMS were significantly associated with duration of BED or subthreshold BED. In multivariable models, the duration of BN for women with PMDD as compared to those without PMS remained significant in the *a priori* model (MD 6.6, 95% CI 0.4, 12.8), but was no longer significant in the full model (MD 6.6, 95% CI −0.2, 13.3).

TABLE 2. Association of premenstrual syndrome and premenstrual dysphoric disorder with bulimia nervosa and binge-eating disorders; multinomial logistic regression analyses

	BN (n = 133)			BED (n = 185)			Subthreshold BED (n = 106)		
	OR	95% CI	*P*	OR	95% CI	*P*	OR	95% CI	*P*
Bivariate									
PMS/PMDD									
PMDD	8.72	(3.98, 19.14)	<0.001	3.64	(1.79, 7.41)	<0.001	1.26	(0.50, 3.15)	0.63
PMS, no PMDD	2.61	(1.47, 4.62)	0.001	1.55	(0.94, 2.57)	0.087	2.03	(1.17, 3.53)	0.012
No PMDD or PMS		Ref			Ref			Ref	
a priori ***multivariable model***[a]									
PMS/PMDD									
PMDD	9.35	(3.89, 22.49)	<0.001	3.55	(1.67, 7.55)	0.001	1.50	(0.56, 4.03)	0.42
PMS, no PMDD	2.72	(1.44, 5.15)	0.002	1.63	(0.95, 2.79)	0.08	2.10	(1.18, 3.73)	0.011
No PMDD or PMS		Ref			Ref			Ref	
MDD	2.00	(1.13, 3.56)	0.018	1.49	(0.91, 2.44)	0.12	2.77	(1.48, 5.17)	0.001
Full multivariable model[a]									
PMS/PMDD									
PMDD	7.17	(2.30, 22.42)	0.001	2.29	(0.90, 5.80)	0.08	1.65	(0.48, 5.63)	0.43
PMS, no PMDD	2.51	(1.11, 5.67)	0.027	1.27	(0.68, 2.39)	0.45	1.82	(0.80, 4.18)	0.16
No PMDD or PMS		Ref			Ref			Ref	
MDD	1.28	(0.52, 3.16)	0.59	1.23	(0.66, 2.26)	0.52	3.14	(1.28, 7.71)	0.012
Dysthymia	4.88	(1.87, 12.72)	0.001	1.44	(0.65, 3.19)	0.37	2.21	(0.70, 7.03)	0.18
Bipolar	2.27	(0.76, 6.76)	0.14	1.73	(0.61, 4.90)	0.30	0.80	(0.15, 4.14)	0.79
Social phobia	2.31	(0.98, 5.42)	0.055	1.77	(0.93, 3.38)	0.09	1.88	(0.74, 4.80)	0.19
Substance abuse	0.93	(0.43, 2.00)	0.85	1.83	(0.98, 3.41)	0.059	1.03	(0.30, 3.59)	0.96

[a]*A priori* model adjusted for age, race/ethnicity, income, education, body mass index, age at menarche, lifetime use of birth control, and lifetime history of major depressive disorder (MDD). Full model adjusted for *a priori* covariates and additionally for dysthymia, bipolar disorder, social phobia, and substance use disorder.

TABLE 3. Association of premenstrual syndrome and premenstrual dysphoric disorder with duration of bulimia nervosa and binge-eating disorder symptoms; linear regression analyses

	BN (n = 133)			BED (n = 185)			Subthreshold BED (n = 106)		
	Mean Difference	95% CI	*P*	Mean Difference	95% CI	*P*	Mean Difference	95% CI	*P*
Bivariate									
PMS/PMDD									
PMDD	11.1	(1.5, 20.8)	0.024	−5.3	(−15.4, 4.7)	0.29	−0.6	(−11.4, 10.2)	0.91
PMS, no PMDD	2.7	(−3.5, 8.8)	0.39	−5.2	(−13.3, 2.9)	0.21	−3.9	(−11.6, 3.8)	0.32
No PMDD or PMS		Ref			Ref			Ref	
a priori ***multivariable model***[a]									
PMS/PMDD									
PMDD	6.6	(0.4, 12.8)	0.038	0.2	(−9.2, 9.6)	0.96	0.2	(−8.0, 8.4)	0.96
PMS, no PMDD	−2.5	(−6.9, 2.0)	0.28	−2.7	(−8.2, 2.8)	0.33	−3.9	(−9.1, 1.4)	0.15
No PMDD or PMS		Ref			Ref			Ref	
MDD	−1.5	(−4.9, 1.8)	0.37	−2.4	(−7.6, 2.8)	0.36	−4.5	(−10.7, 1.8)	0.16
Full multivariable model[a]									
PMS/PMDD									
PMDD	6.6	(−0.2, 13.3)	0.057	2.4	(−8.0, 12.8)	0.65	−6.9	(−15.7, 2.0)	0.13
PMS, no PMDD	−2.6	(−8.0, 2.9)	0.36	−2.5	(−9.2, 4.3)	0.47	−8.4	(−15.5, −1.3)	0.022
No PMDD or PMS		Ref			Ref			Ref	
MDD	−4.0	(−8.9, 0.9)	0.11	−1.5	(−8.1, 5.1)	0.65	−2.5	(−14.1, 9.0)	0.66
Dysthymia	5.9	(1.2, 10.6)	0.015	5.0	(−3.8, 13.7)	0.26	−0.9	(−12.6, 10.8)	0.88
Bipolar	−3.6	(−11.7, 4.5)	0.39	3.6	(−7.7, 14.9)	0.53	3.0	(−21.3, 27.3)	0.80
Social phobia	0.6	(−3.2, 4.4)	0.75	1.5	(−6.5, 9.5)	0.71	3.7	(−5.2, 12.6)	0.41
Substance abuse	−1.3	(−5.8, 3.2)	0.57	4.5	(−1.3, 10.2)	0.13	14.6	(4.0, 25.2)	0.008

[a]*A priori* model adjusted for age, race/ethnicity, income, education, body mass index, age at menarche, lifetime use of birth control and lifetime history of major depressive disorder. Full model adjusted for *a priori* covariates and additionally for dysthymia, bipolar disorder, social phobia, and substance use disorder.

Discussion

In this cross-sectional study drawn from a large, nationally representative, ethnically diverse epidemiological survey, we found that both PMS and PMDD were significantly associated with a higher odds of BN in multivariable models adjusting for age, race/ethnicity, household income, education, age at menarche, lifetime use of birth control, and major depressive disorder. These associations remained significant after adjusting for lifetime history of other comorbid mental health conditions (dysthymia, bipolar disorder, social phobia, and substance use disorder). Additionally, PMDD was significantly positively associated with BED and PMS with subthreshold BED in models adjusting for sociodemographic factors, reproductive health factors and major depressive disorder, although these associations were attenuated and no longer significant when adjusting for other comorbid mental health conditions. Finally, PMDD was significantly associated with a longer reported duration of BN in bivariate models and models adjusting for sociodemographic factors, reproductive health factors and major depressive disorder, but not in models adjusting for other comorbid mental health conditions.

This is the first study to evaluate the association between PMS, PMDD, and eating disorders in a nationally representative epidemiological sample. Our findings of an association between lifetime PMDD and lifetime BN adds to previous research that has reported an exacerbation of bulimic symptoms during the late luteal phase among women with and without premenstrual symptoms[25–27,38,39] and evaluating eating- and body image-related symptoms among women with PMDD but who do not have diagnosed eating disorders.[22–24] As these studies suggest, it is possible that women with PMDD are at greater risk for developing binge-eating because they experience greater premenstrual negative affect and appetite for high-calorie foods, which, in turn, leads to binge-eating.[22,39,40] Alternatively, it is possible that some women are particularly vulnerable to the impact of ovarian hormones, and that variations in ovarian hormones may increase risk for both binge-eating and negative effect, thereby increasing risk of both disorders simultaneously. The high degree of comorbidity found in this study for both PMDD and PMS with BN suggests that PMS and PMDD may be important conditions to screen for and take into consideration in treatment of BN. While we found a significantly longer duration of bulimic symptoms among women with PMDD in the *a priori* adjusted models (mean difference 6.6, 95% CI 0.4, 12.8), prospective studies are needed to evaluate whether women with BN and concurrent comorbid PMDD have a longer time to recovery than women with BN who do not have comorbid PMDD.

Although our data suggest comorbidity between premenstrual conditions and BN, future research is needed to indicate whether onset of premenstrual conditions precede onset of BN, and therefore may plausibly contribute to risk of BN. Experience of premenstrual symptoms after puberty may directly contribute to risk of BN through regular exacerbation of subclinical disordered eating, increasing the likelihood of development of full-blown BN. Early identification and treatment of PMDD and PMS among young women with subclinical binge-eating could therefore be an important step in preventing development of full-blown BN. It is also possible that the sensitivity to fluctuations in ovarian hormones indicated by PMS and PMDD may indicate a shared genetic risk with BN, and that women who experience one or both may share a similar genetic vulnerability to the presence of ovarian hormones.[28] Future research identifying the mechanisms underlying this vulnerability may suggest therapeutic approaches that are beneficial to women with both bulimia nervosa and premenstrual conditions.

Given the greater prevalence of BED versus BN in our sample, it seems unlikely that the lack of association between BED and premenstrual dysphoria was a result of lower statistical power in the BED group. Indeed, when we combined participants with full and subthreshold BED into one group, the results remained nonsignificant in the fully adjusted model. One possible reason for this differential finding is a higher level of dietary restraint in the BN group. Specifically, a previous study identifying hormonal predictors of eating disorder symptoms across the menstrual cycle among community women highlighted a trend-level interaction between estradiol and dietary restraint, in which emotional eating was elevated in the premenstrual phase among individuals with high restraint scores only.[39] It is therefore possible that the individuals with BN (who typically exhibit high levels of dietary restraint) are more vulnerable than those with BED (who may or may not exhibit high levels of dietary restraint) to the impact of ovarian hormones, putting them at greater risk for both emotional eating in the premenstrual phase and for premenstrual dysphoria.

Although our study is unique in its description of the comorbidity of PMS and PMDD with eating

disorders, our data must be interpreted in the context of certain limitations. Potential confounding of the relationship between premenstrual conditions and BN by other mental health comorbidities is a potential concern, although the Collaborative Psychiatric Epidemiological Surveys are uniquely suited to evaluate this confounding, as they include validated DSM-IV diagnoses of a broad range of mood, anxiety and other mental health conditions. In our analyses, after assessing a range of mental health conditions as confounders, we found that major depressive disorder, dysthymia, bipolar disorder, social phobia, and substance abuse disorder appeared to partially explain the association between premenstrual conditions and bulimia by attenuating the effect estimates, although the association between premenstrual conditions and bulimia remained statistically significant. A second potential limitation is the use of the WMH-CIDI for assessing eating disorders. Specifically, our assessment of BN, BED, and subthreshold BED was specific to DSM-IV and would therefore have missed clinically significant presentations that now appear in DSM-5, including DSM-5 BED with binge-eating less than twice per week, or BN/BED of limited frequency or duration (now examples of Other Specified Feeding or Eating Disorder). Additionally, the CIDI has been shown to underdiagnose AN and BN,[35] both of which may be reflected in the low prevalence of eating disorders in our sample.

A third limitation is the exclusion of 2,744 potentially eligible women, who differed significantly from the included participants on several demographic characteristics, due to missing data. Although 1,833 of these participants completed the short-form for the National Comorbidity Survey Replication, and weights were incorporated to account for missing data, the additional 911 missing participants could have introduced a selection bias. A fourth limitation of our study was the cross-sectional design, restricting the ability to demonstrate a temporal relationship between premenstrual conditions and BN and BED. Finally, accuracy of recall is a concern in this study due to the survey design, as participants may have difficulty remembering past symptoms and their age at onset. For the analysis of BN and BED duration, misclassification of age at onset could have led to attenuation of the effect estimates. Recall bias is possible as participants with premenstrual conditions, BN or BED may be more likely to recall other psychological symptoms, which could exaggerate the effect estimates. This potential bias is partially addressed by adjusting for additional psychological comorbidities, such as major depressive disorder, which may serve as a partial indicator of this form of recall bias. Our findings are likely generalizable to all women at risk for premenstrual conditions and without a lifetime history of AN, due to the use of a nationally-representative survey.

Our finding of a significant association between lifetime PMDD and PMS and lifetime BN, independent of comorbid mental health conditions, in a nationally-representative survey suggests that women with BN are more likely to experience the cyclical physiological and psychological effects of PMDD than women who have no history of a DSM-IV eating disorder. Given past research highlighting a predictable exacerbation of bulimic symptoms in the late-luteal phase of the menstrual cycle, comorbid premenstrual conditions may be an important consideration in the course of treatment for binge-type eating disorders. Future research incorporating a longitudinal design would help to better elucidate the potential for premenstrual conditions to affect the onset and duration of BN and other eating disorders. Additionally, the high degree of comorbidity between PMDD and BN found in this study suggests that evaluating the presence of and potential exacerbation of binge-type eating disorder symptoms by PMDD may be important in clinical practice.

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