# History of Postpartum Depression in a Clinic-Based Sample of Women With Premenstrual Dysphoric Disorder

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## ABSTRACT

***Objective:*** Overlapping comorbidities between premenstrual dysphoric disorder (PMDD) and postpartum depression (PPD) suggest that these disorders represent a continuum of vulnerability with shared pathophysiology. We report the past histories of PPD (and other Axis I psychiatric illnesses) in a clinic-based sample of women meeting criteria for PMDD.

***Methods:*** 215 women, ages 19 to 51 years, who attended the National Institute of Mental Health Mood Disorders Clinic between 1988 and 2013 seeking treatment for PMDD and in whom we confirmed the diagnosis of PMDD (*DSM-IV*), were identified. All were administered the Structured Clinical Interview for *DSM-III-R or -IV*. The frequency of PPD (major or minor) was established in the subgroup of women (n = 137) who had delivered at least 1 child.

***Results:*** Ninety-three women (43.3%) had a past history of a mood disorder (ie, either major [n = 67; 31.2%] or minor [n = 10; 4.7%] depression or PPD [n = 16; 7.4%; 11.7% of parous women]). Nine of the 16 women with PMDD and a past PPD had either a past major depressive episode (MDE) or subsyndromal anxiety disorder. Thirty-three women (15.3%) had a past history of an Axis I anxiety disorder. A total of 40 women (18.6%) met criteria for past alcohol or drug abuse, 3 (1.4%) met criteria for bulimia nervosa, and 2 (0.9%) met criteria for anorexia nervosa.

***Conclusions:*** Our data demonstrate that PMDD and PPD do not frequently co-occur. These data do not suggest that PMDD and PPD share similar pathophysiology beyond being ovarian-steroid–triggered mood disorders. The high comorbidity of past MDE could contribute to the increased risk both for future MDE and for PPD in some women with PMDD.


*J Clin Psychiatry 2016;77(4):e415–e420*
*dx.doi.org/10.4088/JCP.15m09779*


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Premenstrual dysphoric disorder (PMDD) and postpartum depression (PPD) are affective disorders in which changes in ovarian steroids (in the context of ostensibly normal peripheral levels) have been shown to directly trigger depression in a subset of vulnerable women.[1,2] Overlapping comorbidities between PMDD and other reproductive endocrine-related mood disorders, including postpartum[3] and perimenopausal[4] depressions, indicate that these disorders could represent a continuum of vulnerability with shared pathophysiology—both ovarian steroid triggering of and risk for these disorders.[5,6] Indeed, the results of some studies (but not all[7]) suggest that women with PMDD (as well as some women in older studies with severe premenstrual affective symptoms [ie, premenstrual dysphoria] who would also meet criteria for PMDD) are at increased risk for developing PPD.[8–11] These observations have important implications both for the clinical management of women with PMDD (specifically regarding risk counseling) and for research directions. Nonetheless, comorbidity does not necessarily indicate similar pathophysiology, and the comorbidity shared between PMDD and PPD could be uninformative about pathophysiology, analogous to the comorbidity shared between PMDD and nonreproductive depression.

In this study, we report the past histories of PPD in women who were evaluated at the National Institute of Mental Health (NIMH) Reproductive Psychiatry Clinic and who met *DSM-IV* criteria for PMDD. Additionally, we characterized the past histories of other Axis I psychiatric illnesses in those women with PMDD to determine both the comorbidity of Axis I disorders with PMDD and the possible contribution of a past Axis I disorder to the risk of PPD in this large clinic-based sample of women. Finally, we expanded the clinical characterization of the past psychiatric histories of these women with PMDD to include past episodes of subsyndromal depressive and anxiety disorders.

## METHODS

### Subject Selection

Two hundred fifteen women attended the NIMH Mood Disorders Clinic between 1988 and 2013 seeking treatment for distressing premenstrual symptoms and in whom we confirmed the diagnosis of PMDD. Women were self-referred in response to local advertisements or referred by their physician. A history, physical examination, and routine laboratory tests screened women for the absence of a current or recent (within the past 2 years) medical illness. All were medication-free except for 14 women receiving stable doses of thyroid medication. The study was approved by the NIMH Intramural Research Review Board, and written informed consent was obtained prior to participation.

### Inclusion Criteria

All women met study criteria for PMDD, which were based on requirements outlined in the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition

**Clinical Points**

- Some studies suggest that women with premenstrual dysphoric disorder (PMDD) (as well as women with severe premenstrual affective symptoms) are at increased risk for developing postpartum depression (PPD).
- These observations have important implications both for the risk counseling of women with PMDD and for research directions.
- Our findings demonstrate that PMDD and PPD do not frequently co-occur; PPD is experienced after childbirth in only a small minority of women with PMDD.
- These data do not suggest that PMDD and PPD share similar pathophysiology beyond both being ovarian-steroid–triggered mood disorders.

(*DSM-IV*).[12] Women reported regular menstrual cycles (ie, 21–35 days in duration) and completed 3 months of prospective daily ratings using a 3-item 100-mm visual-analog scale that confirmed the timing and severity of their menstrually related mood symptoms (depression, anxiety, and irritability) as described previously.[1,13] The mean score of at least 1 of these self-rated negative mood symptoms was at least 30% higher (relative to the range of the scale used by each woman) in the week before menstruation compared to the week after the cessation of menstruation in at least 2 of the 3 cycles assessed.

Functional impairment was assessed through self-reports of distress and functional impairment on the daily rating form.[14] The daily rating form criteria for functional impairment were as follows: a daily rating form score of 2 (minimal) or higher on 1 of 4 questions related to functional impairment (ie, stayed at home or avoided social activities, had conflicts or problems with people, symptoms interfered with relationships at work or home, or symptoms interfered with work productivity) in at least 3 of 7 days premenses. Finally, daily rating form ratings and the results of both a semistructured interview and a self-report questionnaire (ie, the Menstrual Screening Questionnaire and the Menstrual Assessment Form, respectively, both in-house tools) were employed to confirm that all women met the required number of symptoms specified in the *DSM-IV* criteria for PMDD. Additionally, women who noted on the daily rating form significant negative mood symptoms occurring during the follicular phase of the menstrual cycle were excluded. Thus, in this study, the diagnostic criteria for PMDD were augmented by the severity criterion of a 30% increase in mean negative mood during the week before menses compared with the week after menses, a more stringent criterion than that of *DSM-IV*[12] or *DSM-5*.[15] The diagnosis of PMDD was established retrospectively after reviewing daily ratings in 35 women who were admitted to the study prior to publication of *DSM-IV*.[12]

### Outcome Measures

All women were administered the Structured Clinical Interview for either *DSM-III-R*[16] or *DSM-IV-TR*[17] disorders (SCID) depending on when they entered the study (ie, before or after 1996, respectively). The results of the SCID determined the frequencies of past Axis I psychiatric disorders. The frequency of PPD (major or minor) was established in the subgroup of women (n = 137) from the original sample who had delivered at least 1 child. Postpartum depression was defined as the onset of a major depression (according to the SCID) within 4 weeks of delivery. History of minor depression was assessed with the minor depression module of the Schedule for Affective Disorders and Schizophrenia–Lifetime version (SADS-L)[18] in the earlier participants and by SCID (*DSM-IV*) criteria in the later participants. Additionally, given reports of a high rate of anxiety disorders in women with PMDD,[19–21] we determined the frequency of subsyndromal anxiety disorders in this sample, defined as follows: women did not meet full criteria for an anxiety disorder, and a criterion score of 3 coded for at least 1 core symptom, and a 2 or 3 coded for at least 1 additional symptom. Finally, one potential confound in the retrospective reports of a past Axis I condition in women with PMDD is the possibility that the presence of a woman's PMDD symptoms could be wrongly classified as meeting criteria for a major/minor depression or anxiety disorder.[22] Thus, in those women who met criteria for either a past depressive illness (ie, major or minor) or an anxiety disorder, we asked each woman if the symptoms that met criteria for these Axis I conditions were confined to the premenstrual phase of the cycle (and therefore had been mistaken for symptoms of a major depressive episode [MDE]).

### Statistical Analyses

Differences in the number of episodes of reported PPD between women with PMDD who did and did not report a past MDE were compared by $\chi^2$ (SYSTAT, Chicago, Illinois). The sample of women with PMDD was not a community-based sample and was relatively homogeneous with respect to demographic variables (eg, race, socioeconomic status, and parity), and, therefore, our sample was not sufficiently diverse to include these variables as covariates in our analyses.

## RESULTS

The ages of the women ranged from 19 to 51 years, and the mean ± SD age was 38.0 ± 6.0 years. One hundred thirty-seven women (63.7%) had given birth to at least 1 child. Ninety-eight women (45.6%) did not meet criteria for any past Axis I disorder (Table 1).

Ninety-three women (43.3%) had a past history of a mood disorder (ie, either major [n = 67; 31.2%] or minor [n = 10; 4.7%] depression or PPD [n = 16; 7.4%; 11.7% of parous women]). Twenty-one women (9.8%) reported experiencing more than 1 episode of depression in the past (Table 1).

Nine of the 16 women with PMDD and a past PPD had either a past MDE or a past subsyndromal anxiety disorder. Six (37.5%) of the 16 women with PPD reported that the onset of their PMDD preceded the onset of PPD by several

**Table 1. Demographic Characteristics and Frequencies of Past Axis I Psychiatric Illness in Women With PMDD (N = 215)[a]**

| Variable | Value |
|---|---|
| Demographic characteristics | |
| Age (whole sample), mean (SD), y | 38.0 (6.0) |
| Parity, mean (SD) | 1.3 (1.3) |
| No. of parous women, n (%) | 137 (63.7) |
| Age (parous women), mean (SD), y | 39.5 (5.4) |
| History of Axis I psychiatric disorders, n (%) | |
| Major depression | 67 (31.2) |
| Minor depression | 10 (4.7) |
| Postpartum onset (with parity > 0)[b] | 16 (11.7) |
| Anxiety disorders, n (%) | |
| Panic disorder | 13 (6.0) |
| Posttraumatic stress disorder | 10 (4.7) |
| Agoraphobia without panic disorder | 2 (0.9) |
| Obsessive-compulsive disorder | 1 (0.5) |
| Generalized anxiety disorder | 4 (1.9) |
| Simple phobia | 3 (1.4) |
| Social phobia | 0 |
| Any Axis I anxiety disorder | 33 (15.3) |
| Multiple Axis I anxiety disorders | 3 (1.4) |
| Other disorders, n (%) | |
| Substance abuse/dependence | 40 (18.6) |
| Bulimia nervosa | 3 (1.4) |
| Anorexia nervosa | 2 (0.9) |
| No. of past Axis I diagnoses, n (%) | |
| No diagnosis | 98 (45.6) |
| 1 diagnosis | 72 (33.5) |
| 2 diagnoses | 34 (15.8) |
| 3 diagnoses | 10 (4.7) |
| 4 diagnoses | 1 (0.5) |

[a]All women met study criteria for PMDD, which are based on requirements outlined in the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (*DSM-IV*). Functional impairment was assessed through self-reports of distress and functional impairment on the daily rating form. The daily rating form criteria for functional impairment were as follows: a daily rating form score of 2 (minimal) or higher on 1 of 4 questions related to functional impairment (ie, stayed at home or avoided social activities, had conflicts or problems with people, symptoms interfered with relationships at work or home, or symptoms interfered with work productivity) in at least 3 days out of 7 days premenses. Finally, daily rating form ratings and the results of both a semistructured interview and a self-report questionnaire (ie, the Menstrual Screening Questionnaire and the Menstrual Assessment Form, respectively) were employed to confirm that all women met the required number of symptoms specified in the *DSM* criteria for PMDD.

[b]In the 16 women with PMDD and a past postpartum depression, 6 also had a history of MDE (unrelated to pregnancy, postpartum, or the luteal phase of their menstrual cycle); none had a separate past minor depression, 2 women met criteria for an Axis I anxiety disorder (both of whom also met criteria for a past MDE), and 4 women met criteria for a subsyndromal anxiety disorder (1 of whom also met criteria for a past MDE). Percentage listed reflects number of women who met criteria for postpartum depression relative to the 137 women with parity > 0.

Abbreviations: MDE = major depressive episode, PMDD = premenstrual dysphoric disorder.

years. In the numbers of women with PMDD who met criteria for a past PPD, there was no significant difference between those with a past MDE (n = 6) and those with no past MDE (n = 10) ($\chi^2 = 0.2$, $P = .67$).

Thirty-three women (15.3%) had a past history of an Axis I anxiety disorder (including panic disorder [6.0%], posttraumatic stress disorder [4.7%], simple phobia [1.3%], and generalized anxiety disorder [1.9%]), and 5 of these women reported that symptoms occurred only during the premenstrual phase of their cycle. An additional 35 women met criteria for past subsyndromal anxiety disorder (Table 2).

A total of 40 women (18.6%) met criteria for past alcohol or drug abuse, 3 (1.4%) met criteria for bulimia nervosa,

**Table 2. Frequency of Past Subsyndromal Anxiety Disorders in Women With PMDD (N = 215)[a]**

| Subsyndromal Anxiety | n | % |
|---|---|---|
| Panic disorder | 11 | 6.0 |
| Posttraumatic stress disorder | 10 | 5.5 |
| Specific phobia | 7 | 3.8 |
| Generalized anxiety disorder | 4 | 2.2 |
| Agoraphobia without panic disorder | 1 | 0.5 |
| Obsessive-compulsive disorder | 10 | 5.5 |
| Social phobia | 6 | 3.3 |

[a]Several women had multiple diagnoses (see Table 1).

Abbreviation: PMDD = premenstrual dysphoric disorder.

and 2 (0.9%) met criteria for anorexia nervosa. None of the women with PMDD who reported a past PPD, and 5 women with PMDD who met criteria for a past MDE, reported episodes of either alcohol (n = 4) or substance (n = 1) abuse concurrent with their episodes of PPD or MDE, respectively. Forty-five (38.5%) of the 117 women with a SCID diagnosis met criteria for 2 or more Axis I disorders. The majority of these women (n = 37) were diagnosed with a past episode of major depression and at least 1 or 2 other disorders (Table 1).

## DISCUSSION

We found little evidence to support the claim that PMDD and PPD are associated disorders or two expressions of a similar underlying pathophysiology defined by a behavioral sensitivity to changes in ovarian steroids. Only 11.7% of the 137 childbearing women with prospectively confirmed PMDD met criteria for a past PPD, not substantially different from the reported incidence of PPD in the general population of women.[23] Second, albeit a small sample of only 16 parous women with PMDD and a past PPD, 9 of these women reported a past episode of an affective or anxiety disorder, suggestive that a past MDE or anxiety disorder could contribute to the risk of PPD as much as the presence of PMDD. Third, almost half of the women with PMDD had no past Axis I psychiatric illness, and, therefore, PMDD can occur in many women independent of other Axis I comorbidity. We did confirm the previously reported high percentage of women with PMDD with single or multiple episodes of past mood disorders (43.2%) but observed a surprisingly low percentage of women with other Axis I conditions including past anxiety disorders (15.3%). Thus, our findings suggest that PMDD has a more specific relationship with mood disorders, primarily major depression, compared with other Axis I conditions. Finally, a relatively high rate of substance abuse was identified in these women, whereas eating disorders were rarely reported.

The prevalence of a past PPD in parous women with PMDD in our sample is comparable to the Agency for Healthcare Research and Quality incidence rates for postpartum major depression, reported to occur after 7% of deliveries.[23] Thus, the relatively small numbers of women with PMDD reporting a past PPD suggests that the majority of women with PMDD are not at greater risk for PPD than women without PMDD. Past MDE is an established risk factor for

PPD, and due to the high comorbidity of PPD and past MDE, it is difficult to disentangle the effects of PMDD from those of past MDE in women with PMDD. Studies observe a higher than expected rate of reported premenstrual dysphoria and PMDD in women who developed PPD. All of these studies employed retrospective interviews to diagnose premenstrual dysphoria/PMDD and, therefore, could have overestimated the likely frequency of premenstrual dysphoria/PMDD. Nonetheless, in the study by Buttner et al,[8] a retrospective screening form with reported reliability in defining PMDD[24] was employed, and a tentative diagnosis of PMDD increased the risk of subsequent PPD by approximately 2-fold. Moreover, Buttner et al[8] found that the effect of PMDD to increase the risk of PPD was independent of that for past MDE. Our observation of a relatively lower frequency of past PPD than that described by Buttner et al[8] could reflect our use of a clinic-based rather than community-based sample, our smaller sample size of women with PPD, or our use of strict prospectively confirmed diagnostic criteria for PMDD.

Prospective studies in sufficiently large samples of women who develop PPD would need to be performed to determine whether prospectively confirmed PMDD increases an individual woman's risk for PPD beyond other established risks. However, only 6 of the 16 women with PPD in our sample reported that the onset of their PMDD preceded the onset of PPD, and, therefore, even within this small sample, the presence of PMDD did not uniformly precede PPD. Our finding that only 11.7% of the 137 childbearing women with PMDD met criteria for a past PPD is consistent with some,[7,26] but not all,[3,25] reports. Pearlstein et al[3] and Critchlow et al[25] reported higher percentages of women with comorbid premenstrual dysphoria and PPD in 15 of 51 women with late luteal phase dysphoric disorder (ie, 29%) and 10 of 15 women with PMDD (ie, 67%), respectively. In contrast, our finding is comparable to the percentages reported by Harrison et al[26] and Haywood et al[7] (6 of 86 women with late luteal phase dysphoric disorder [ie, 7%] and 1 of 7 women with clinically significant premenstrual dysphoria [ie, 14%], respectively). Differences in these studies could reflect the smaller sample sizes of women with PMDD, use of different diagnostic criteria, inclusion of minor depression during the postpartum,[3,7] and differences in the duration of time between birth and the onset of depression, which in the SCID is relatively narrow (ie, 4 weeks) and was not specified in some[3,25,26] studies. Thus, it is possible that had we employed a wider window of time postpartum, we would have identified more women with a past PPD, although none of the nonpostpartum MDEs in our sample occurred with any proximity to the reported date of childbirth. In a previous study[27] of 116 women with perimenopause-related depression, we observed that 6% met SCID criteria for a past PPD. Although the percentage of women with PMDD and a past PPD is higher than in perimenopausal depression (ie, 11.7% vs 6%, respectively), neither finding supports suggestions that these reproductive-related mood disorders cluster within individual women.[5,6,27–31] Nor do these findings suggest that these 3 reproductive endocrine-related disorders represent a continuum of vulnerability; although some overlap may exist, they are clearly not the same disorder.

There is only limited evidence in women with PMDD that the presence of a past Axis I condition influences specific clinical characteristics, although few studies are sufficiently powered to adequately examine this question. Warner et al[32] and Bancroft et al[33] observed that a past MDE was associated with several distinct clinical characteristics in premenstrual dysphoria, including an early onset of premenstrual dysphoria symptoms during the luteal phase, a longer persistence of premenstrual dysphoria symptoms after the onset of menses, and more severe premenstrual dysphoria symptoms. Soares et al[34] found a lower education level in women with PMDD with a past MDE compared with those without past MDE, potentially supporting the suggestion by Bancroft[33] and Warner[32] that the comorbidity of PMDD and MDE leads to more severe premenstrual dysphoria symptoms, more functional impairment, and, therefore, lower achievement. However, lower achievement also could be secondary to the disabling effects of an episode of MDE at an early age independent of PMDD. Thus, only limited data suggest that a past MDE conveys specific clinical features to PMDD.

Similar rates of past depression have been reported in other studies of both clinic- and community-based samples of women with premenstrual dysphoria/PMDD,[3,19,25,35–40] and the current study confirms these findings in a large, well-characterized, clinic-based sample of PMDD. We did not find an elevated rate of comorbid minor depression or dysthymia in these women, in contrast to the study by Pearlstein et al[3] in which higher rates of minor depression were observed in women with late luteal phase dysphoric disorder. Finally, none of the past episodes of depression were confined to the premenstrual phase, and therefore, to the extent possible with historically obtained data, the diagnoses of major depression did not appear to be cases of PMDD mistaken for MDE. The high prevalence of past MDE in women with premenstrual dysphoria/PMDD has led some investigators to suggest that MDE is a risk factor for PMDD.[41] However, 46% of our sample did not meet criteria for any past Axis I psychiatric illness. The ages of the women who met a past Axis I illness did not differ from those of women with no past Axis I condition. Thus, it is unlikely that a greater number of years at risk in the women with past depression explain the absence of psychiatric comorbidity. Although this study cannot directly address the risk of PMDD in women with a past MDE, comorbidity with MDE is not exclusive to PMDD. Indeed, DeJong and colleagues[35] observed an increased rate of past MDE in women with recurrent brief depressions (who did not meet criteria for premenstrual dysphoria) compared with women with prospectively confirmed premenstrual dysphoria.

There appears to be little evidence that PMDD is comorbid to a notable degree (ie, in excess of that reported in community-based studies) with Axis I disorders other than major depression. The prevalence rate of 38.6% of

women with PMDD meeting criteria for a past MDE (when postpartum major depression was included) is considerably larger than the 20% lifetime prevalence rates reported in community samples.[42] In contrast to the frequency of past MDE, only 15.3% of women with PMDD met criteria for any anxiety disorder compared to lifetime prevalence rates of 36% in community-based samples of women.[42] When we included those women who met criteria for a subsyndromal anxiety disorder, the percentage (31.6%) did approach but did not exceed rates of even Axis I anxiety disorders observed in the community. Our data are consistent with the results of Pearlstein et al,[3] who reported a similarly low frequency of past anxiety disorders in their sample of women with late luteal phase dysphoric disorder but not those of Wittchen et al,[43] who observed a rate of 47% for any Axis I anxiety disorder in their sample of women with premenstrual dysphoria. Thus, *DSM* anxiety disorders do not appear to share the same comorbidity with PMDD as does MDE (at least in this clinic-based sample). Similarly, the rates of individual anxiety disorders were also comparable to those of community-based studies and those of other studies in women with PMDD.[3,26,38,44–46]

The observed rate of substance abuse in our sample of women with PMDD (18.6%) is higher than the lifetime rates reported in women from community-based samples (ie, 14.1%[42]), notwithstanding our failure to specifically include nicotine dependence as a diagnostic category. Our finding emphasizes the clinical reports that some women with PMDD will self-medicate and, as reported by Tobin et al,[47] self-medication could contribute to dysphoric symptoms during the luteal phase. Finally, although women with PMDD frequently experience changes in appetite and uncontrollable cravings for certain foods during the luteal phase, we found that few women also met criteria for a past eating disorder, although our findings were similar to rates in community-based samples.[48] Comparatively few studies in women with premenstrual dysphoria/PMDD have documented comorbidity with eating disorders, although Wittchen and others[43] reported rates of any eating disorder of 5.2% in women with premenstrual dysphoria, considerably higher than the rate of 2.3% that we observed.

Our use of a clinic-based sample of women with PMDD limits our ability to generalize our findings to women with PMDD in the community, since treatment-seeking women could report higher rates of past psychiatric disorders. Thus, our results could overestimate the prevalence of psychiatric comorbidity. Additionally, it is possible that past use of oral contraceptive medications could alter menstrual cycle symptoms sufficiently to interfere with a woman's memory of the timing of the onset of their PMDD prior to an episode of PPD or the recall of the timing of MDE symptoms in relation to menses. Indeed, in the absence of prospectively acquired data, the possibility that recall bias influenced the retrospective reports of past medical or psychiatric illness in these women cannot be excluded.

Overall, our data demonstrate that PMDD and PPD do not frequently co-occur. Although PMDD could increase the risk for PPD in some women, PPD is experienced after childbirth in only a small minority of women with PMDD. Thus, these data do not suggest that PMDD and PPD share similar pathophysiology beyond both being ovarian-steroid–triggered mood disorders (by increasing levels of ovarian steroids in PMDD[1] and by putative withdrawal of ovarian steroids in PPD[2]). The high comorbidity of past MDE could contribute to the increased risk both for future MDE and for PPD in some women with PMDD.

***Submitted:*** January 6, 2015; accepted May 7, 2015.

***Online first:*** March 15, 2016.

***Potential conflicts of interest:*** None of the authors have potential conflicts of interest to report.

***Funding/support:*** This research was supported by the Intramural Research Program of the National Institute of Mental Health (NIMH; NIMH protocol 81-M-0126; project MH002865).

***Role of the sponsor:*** The funding agency had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; or preparation and review of the manuscript.

***Disclaimer:*** This work was written as part of Dr Schmidt's official duties as a US Government employee. The views expressed in this article do not necessarily represent the views of the NIMH, National Institutes of Health, US Department of Health and Human Services, or the US Government.

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*Editor's Note:* We encourage authors to submit papers for consideration as a part of our Focus on Women's Mental Health section. Please contact Marlene P. Freeman, MD, at mfreeman@psychiatrist.com.