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Association of past and recent major depression and menstrual characteristics in midlife: Study of Women's Health Across the Nation

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Abstract

OBJECTIVE—To examine the association of a history of major depression (MD) with menstrual problems in a multi-ethnic sample of midlife women.

METHODS—Participants were 934 participants in the Study of Women's Health Across the Nation (SWAN), a multi-site study of menopause and aging. The outcomes were menstrual bleeding problems and premenstrual symptoms (PMS) in the year prior to study entry. The Structured Clinical Interview for the Diagnosis of DSM-IV Axis I Disorders (SCID) was conducted to determine recent and past psychiatric diagnoses. Covariates included socio-demographics, behavioral, and gynecological factors.

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RESULTS—One-third reported heavy bleeding, 20% other abnormal bleeding and 18% premenstrual symptoms. One-third had past; and 11% recent MD. Past MD was associated with an increased likelihood of heavy bleeding (Odds Ratio 1.89; 95% confidence interval: 1.25, 2.85) adjusting for recent MD, menopausal status and other covariates. Past MD was not associated with other abnormal bleeding or PMS in the final analysis that adjusted for recent MD.

CONCLUSIONS—Midlife women with a past history of MD are more likely to report heavy bleeding.

Keywords

major depression; bleeding; menstrual cycle; midlife

Introduction

Menstrual problems are common among premenopausal women and become more frequent with increasing reproductive age, especially just prior to and during the perimenopause. These symptoms can be bothersome, interfere with quality of life, and lead women to seek gynecologic care. Proposed as the “fifth vital sign” in women,¹ abnormal menstruation may reflect underlying pathology in the reproductive tract or hypothalamic-pituitary-gonadal (HPG) axis. Although distress is associated with menstrual problems, it is unclear whether mood problems such as depression may precede and increase susceptibility to menstrual problems, or whether they result from the menstrual difficulties. The Study of Women’s Health Across the Nation (SWAN) Mental Health Study (MHS) provided an opportunity to examine depression as a precursor to menstrual problems in a large multi-ethnic community-based cohort of midlife women. .

Prevalence estimates of menstrual problems, such as heavy bleeding, intermenstrual spotting/bleeding, long and short menstrual cycles, and premenstrual symptoms (PMS), range from 19% to 35%.^{2,3,4,5} Variation in these estimates reflects inconsistent definitions of heavy bleeding, grouping of multiple different menstrual problems together, and population differences. Nevertheless, the prevalence of heavy bleeding and short or long cycles, in particular, increases with age³ and among perimenopausal women.⁶ These conditions lead 7.2 per 100 women approaching menopause (35–44 years of age) to pursue medical attention for abnormal bleeding.⁶

The available literature indicates that menstrual problems are associated with impaired physical and social functioning,⁷ stress,^{8,9} and multiple psychological symptoms, including depressive and anxious symptoms.⁴ Most studies to date have evaluated the relationship between depressive symptoms and concurrent menstrual abnormalities^{5,10,11,12} making it difficult to assess the temporal pattern between these and the extent to which prior depression may be a risk factor for subsequent menstrual abnormalities. Although depression is often a consequence of gynecologic and menstrual morbidity, findings from a small number of studies suggest that depression may also precede and lead to alterations in menstrual function^{13,14} as well as influence women’s reporting of gynecologic morbidity.^{10,15} Strong evidence indicates that stress can result in menstrual dysfunction through interactions between the hypothalamic-pituitary-adrenal (HPA) and HPG axes.¹⁶ Similarly, depression frequently co-occurs with physical illnesses such as cardiovascular disease or diabetes,^{17,18} but can also precede the onset of or develop after a physical illness is present.^{18,19,20}

Furthermore, the existing literature about mental health precursors to menstrual dysfunction focuses largely on young, premenopausal women, with only a few addressing menstrual problems in women of older reproductive age or during the perimenopause.^{5,21,22} Studies of

menstrual problems during the perimenopause are complicated by a need to distinguish the menstrual abnormality from the menstrual changes that occur normally as part of the perimenopause itself. Given the evidence pointing to a potential role of depression as a precursor to physical illnesses and altered menstrual function, further evaluation of the linkages between history of depression and menstrual disorders is warranted, particularly during midlife when the frequency of menstrual morbidity increases.

The goal of the current study is to evaluate the associations between a past history of depression and several types of menstrual cycle problems among middle-aged premenopausal and early perimenopausal women who are participants in the Mental Health Study (MHS) of SWAN, a multi-site longitudinal study of menopause and aging. Specifically, we sought to examine the association of a history of major depression with heavy menstrual bleeding, other abnormal bleeding symptoms, and PMS reported by a large multi-ethnic sample of women, aged 42–52. We further examined whether observed associations were independent of recent major depression, perimenopausal status and other important confounders.

METHODS

Participants and Procedures

This study was conducted among participants in the Pittsburgh, PA, Chicago, IL and Newark, NJ sites of SWAN, a multisite community-based prospective investigation of the menopause transition and aging. SWAN study design and sampling procedures have been described previously.²³ Eligibility criteria for SWAN included being aged 42–52, having an intact uterus, having had at least one menstrual period in the previous 3 months, no use of reproductive hormones in the previous 3 months, and self-identifying with one of the site's designated race/ethnic groups. Each site recruited a total of approximately 450 women, White women and a sample of a predetermined minority group. Overall, SWAN participants did not differ from those who were eligible but declined to participate by race except for Hispanics at the Newark site, marital status, parity, quality-of-life, social support or perceived stress.

The present investigation was part of a SWAN ancillary study, the Mental Health Study (MHS), in which psychiatric diagnostic data were collected from women who were available for a psychiatric interview within nine months of the baseline assessment at three of the seven SWAN sites: Chicago, IL (n=230), Newark, NJ (n=266), and Pittsburgh, PA (n=443). In addition to White women, the Pittsburgh and Chicago sites enrolled African-American women and Newark recruited Hispanic women. The MHS was restricted to these three SWAN sites because the other sites were not able to conduct an intensive mental health study. In Pittsburgh, 443 of the 463 SWAN participants invited to participate in the MHS study agreed to do so. Because of limitations at the Chicago and New Jersey sites, not all of SWAN participants were available for the MHS interview. Comparisons between MHS participants and nonparticipants at each site showed that they were similar on demographic, psychosocial, perceived health, CES-D 16, and BMI variables with the exception that in Chicago, lower proportions of African Americans (42% vs. 51% at Pittsburgh) and employed women (83% vs. 89% at both Pittsburgh and New Jersey) participated in the MHS. Each site adhered to its Institutional Review Board's guidelines for human research. At the beginning of the SWAN baseline core and psychiatric assessments written informed consent was obtained.

SWAN baseline assessments consisted of detailed questions about medical, reproductive and menstrual history; lifestyle and psychosocial factors; and physical and psychological symptoms. Interviewer- and self-administered study forms and materials were available in

English and Spanish and bilingual staff was used, as appropriate. Translations were prepared for the study (initial translation, back translation and revision). Measurements of height and weight were obtained using a common protocol. For women participating in MHS, psychiatric interviews were conducted to obtain information on previous and current psychiatric disorders in addition to the extensive data collected as part of the larger SWAN study. Specifically, the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID),²⁴ a widely used semi-structured instrument that allows interviewers to establish the presence or absence of current and past psychiatric disorders, was conducted at the start of SWAN to establish the presence of current and psychiatric disorders occurring during the previous year. Of the 939 MHS participants, the current analyses included 934 (99.5%) women who had complete depression and menstrual data.

Measures

Menstrual cycle characteristics—At baseline, we used two methods of collecting data from participants: a packet of self-administered questionnaires and a separate packet of interviewer administered questionnaires. The information collected about menstrual cycles in the previous year and between the ages 25–35, pregnancies, and medical history was obtained as part of the interviewer administered questionnaires. The information on gynecologic procedures such as dilation and curettage was provided by participants in the self report packet of questionnaires. In the current report, based on these questions and factor analyses described below, we identified three groups of menstrual problems: (a) heavy bleeding symptoms, which included passing clots larger than a dime; flooding or gushing; and on the heaviest days of menstrual flow, on average, flow was heavy or very heavy (changed protection every 1–2 hours); (b) other abnormal uterine bleeding symptoms, which included menstrual flow lasting more than 10 days; bleeding or spotting between periods more than 50% of cycles; and menstrual flow usually lasting 2 or 8 days; and (c) PMS including at least one of 2 mood symptoms (changes in mood or anxious, jittery or nervous) and one of 5 physical symptoms (abdominal pain or cramps; breast pain, tenderness or swelling; weight gain or feeling bloated; back, joint or muscle pain; or severe headaches) occurring in the week before onset of menses that interfered with work and/or home activities and ceased within a few days of menses onset. At baseline, women also completed a questionnaire asking about the occurrence of the same menstrual bleeding characteristics (with the exception of PMS) when they were between the ages 25 and 35 years.

Assessment of Major Depression—Diagnoses of past history and recent major depression, substance abuse and dependence, and anxiety disorders were determined from interviews conducted by trained clinicians utilizing the SCID.²⁴ Using the SCID, a diagnosis of a major depression episode is established when the response to a series of structured questions confirms that a sufficient number of depressive symptoms were present for at least 2 weeks and interfered with an individual's ability to function as specified in the Diagnostic and Statistical Manual of Axis I DSM-IV diagnosis of major depression.²⁵ Throughout this paper, the term recent major depression (MD) refers to an episode of MD that was present at the time of the baseline SWAN interview or within the previous 12 months. A past history of MD was defined as the occurrence of depression more than 12 months prior to study entry. Detailed data on depressive episodes including onset and duration relative to the SWAN baseline assessment were documented and allowed for the determination of the timing of episodes relative to the 12 months before baseline.

The SCID has been used with many different ethnic groups and extensive field-testing has demonstrated its suitability for research purposes; adequate reliability has been demonstrated in numerous studies²⁶ for both recent and lifetime diagnoses. Extensive

training and qualitative procedures were used to ensure and monitor consistency of SCID administration, symptom elicitation, and diagnostic decision-making across the sites. All interviews with study participants were audiotaped and tapes were used for supervision by senior psychiatric investigators at each site and to monitor rater drift and estimate interrater reliability. Using a systematic sampling procedure, 12 audiotapes were selected from each site and reviewed by all interviewers and supervisors to estimate interrater reliability for diagnoses of selected disorders. Interrater reliability for major depressive disorder was very good: Kappa = .81.

Menopausal status—Menopausal status was based on retrospectively-reported menstrual bleeding in the previous 12 months and was categorized as either premenopausal (menstrual period in the past 3 months with no change in cycle regularity in the past 12 months) or early perimenopausal (menstrual period in the past 3 months with change in cycle regularity over the previous 12 months).²⁷ These definitions have been widely used in menopausal studies and are similar to those recommended by the World Health Organization.²⁸

Covariates—Covariates considered include demographic and behavioral factors, such as race/ethnicity, level of educational attainment, current smoker, body mass index (BMI), and use of any prescribed medication for a “nervous condition (such as tranquilizers, sedatives, sleeping pills, anti-depressants)” in the last month. Gynecologic covariates of interest include self-reported number of pregnancies, previous diagnosis of fibroids by a doctor, nurse practitioner or other health care provider, or previous dilation and curettage “scraping of the uterus for any reason including abortion” procedure.

Statistical analyses

Sample descriptives and univariate comparisons of potential covariates and confounders with past MD and with each menstrual problem were evaluated via standard statistical methods. To statistically normalize the variability in number of pregnancies, which ranged from zero to thirteen, it was truncated at seven (i.e. 7–13 collapsed; 4% of the sample) and treated as a continuous variable. The heavy bleeding and other abnormal bleeding groups were determined via factor analyses with varimax rotation.²⁹ We identified individual menstrual problems with a factor loading of 0.40 or greater (and not loading on another factor) and factors meeting the minimum Eigenvalue criteria of 1 to create the heavy bleeding and other abnormal bleeding groups. Specifically, menstrual problems comprising ‘heavy bleeding’ were flooding/gushing, large clots, and heavy bleeding (with factor loadings of 0.79, 0.73, and 0.63, respectively); while characteristics comprising ‘other abnormal bleeding’ were flow > 10 days, spotting between periods, and bleed 2 or 8 days (with factor loadings of 0.75, 0.49, and 0.77, respectively). Three items did not load on any factors and so were dropped. Previous studies on bleeding patterns associated with heavy and other abnormal bleeding symptoms are consistent with the two types of bleeding groups that we identified.¹ For each bleeding group, a scale was computed as the sum of the three symptoms that loaded on that factor ranging from 0 to 3. In evaluating the distribution of each scale, heavy bleeding produced a 3-level outcome (no symptoms, 1 symptom, 2–3 symptoms) and Other Abnormal Bleeding produced a 2-level outcome (no symptoms vs. any, because there were too few women with 2 or 3 symptoms to consider them separately). These two bleeding groups and PMS (yes vs. no) were then investigated as our three menstrual problem outcomes.

Using logistic regression models, associations between past history of MD and each type of menstrual problem were examined in unadjusted models, adjusted basic models that controlled for basic demographics (age, education level, race/ethnicity, and study site location), and fully adjusted models. In the latter, we considered as candidates for inclusion,

potential confounders that were identified in the data (i.e., related to both the independent and dependent variables) and covariates based on the literature and a priori hypotheses, including past history of anxiety disorders or substance use disorders. Appropriateness of each variable was evaluated individually for the multivariable analyses via model-building techniques, including using a cutoff of $P < 0.10$ in basic models. To explore whether BMI extremes (i.e., very high or very low BMI) were associated with any of the outcome measures, BMI-squared was tested but not statistically significant, and so only the first order BMI was entered as a covariate. Similarly, medication ‘taken for nerves / depression’ as reported by the participant, smoking, and previous dilation and curettage were tested, but lacking statistical association were not retained in the final models. Thus, for all three outcomes, the final fully-adjusted model included recent MD, age, education level, race/ethnicity, study site location, menopausal status, plus those covariates/confounders that were significant at a $P < 0.05$, which included fibroids for all three outcomes, plus BMI and number of pregnancies for the heavy bleeding model.

All analyses were implemented using SAS version 9.1 (SAS Institute, Cary, NC, USA).

RESULTS

At baseline, 633 (67.7%) reported experiencing heavy bleeding, 206 (22.1%) reported at least one symptom of other abnormal bleeding, and 164 (17.6%) met criteria for PMS. Among women reporting heavy bleeding, 288 women (45.5%) had one symptom and 345 (55%) had 2 or 3 symptoms. Women with 2–3 heavy bleeding symptoms or PMS had significantly higher rates of past (39% and 44%, respectively) and recent MD (14% and 21%, respectively) than those without any heavy bleeding or PMS (24% and 30% past MD, and 8% and 9% recent MD, respectively). Past MD and recent MD were not significantly more prevalent in women with other abnormal bleeding symptoms (37% and 14%, respectively) than those without such symptoms (30% and 10%, respectively).

Table 1 shows that women who met criteria for each of the three menstrual cycle problems were more often Hispanic, early perimenopausal and had a history of fibroids, and between ages 25–35 years, experienced multiple bleeding problems, compared to women who did not report menstrual problems at the baseline SWAN visit. Women reporting heavy bleeding and those with other abnormal bleeding symptoms were less well educated. The heavy bleeding group had higher BMI and the abnormal bleeding group had higher rates of current smokers than their counterparts without these symptoms.

Past MD was associated with an increased likelihood of having 2–3 heavy bleeding symptoms in unadjusted and adjusted models, while a recent MD diagnosis was not associated with heavy bleeding in models adjusting for past MD and other risk factors (Table 2). In the final model, women with past MD were 1.89 times as likely (95% confidence interval [CI] 1.25–2.85) to report having 2–3 heavy bleeding symptoms. Additional risk factors for 2–3 heavy bleeding symptoms included early perimenopause, more pregnancies, higher BMI and a history of fibroids. For every unit increase in BMI, there was a 5% increase in the likelihood of reporting 2–3 heavy bleeding symptoms. Consistent with findings for 2–3 heavy bleeding symptoms, women with past MD were also more likely to have 1 heavy bleeding symptom, although this association was only a statistical trend (OR 1.46, 95% CI 0.96–2.24) after adjusting for other potential risk factors, including recent MD, which was similarly not significantly associated with 1 heavy bleeding symptom after adjusting for history of MD.

In the basic model (minimally adjusted) past MD increased the odds of other abnormal bleeding. However, the lower bound of the confidence interval was nearly one. In the

unadjusted and adjusted analyses, neither a history of nor recent MD was significantly associated with symptoms of abnormal bleeding (Table 3). In the final model, a history of fibroids and being perimenopausal were significant risk factors for other abnormal bleeding.

Given the potential that menstrual problems reported currently were already present before midlife, we repeated the analyses excluding women who reported the same type of menstrual problems (heavy bleeding or other abnormal bleeding) during ages 25–35 as during the past year. Results were similar to those with the full sample for both menstrual problems. Past MD remained significantly associated with reporting 2–3 symptoms (OR=1.91, 95% CI: 1.13, 3.22) and with one symptom (OR=1.81, 95% CI: 1.06, 3.09) relative to those with no symptoms.

Past MD was a significant risk factor for PMS in midlife in the unadjusted and basic models (OR 1.81, 95% CI 1.27–2.58), but the association between prior MD and PMS was no longer statistically significant (OR 1.29, 95% CI 0.84–1.98) in the final model that adjusted for other potential risk factors for PMS, including recent MD (Table 4). In the final adjusted model, recent MD (OR 2.59, 95% CI 1.49–4.50) and a history of fibroids (OR 1.59, 95% CI 1.04, 2.42) were significantly associated with an increased likelihood of PMS.

Neither anxiety disorders nor substance use disorders influenced the association between past MD and menstrual problems in any models.

DISCUSSION

This study examined the association of a past major depression with three separate, common types of menstrual problems occurring in a large multi-ethnic cohort of 42–52-year-old premenopausal and early perimenopausal women. Menstrual problems studied included symptoms of heavy bleeding, other abnormal bleeding symptoms and PMS. Results showed that women with past MD were more likely to report heavy bleeding symptoms, independent of known risk factors for heavy bleeding, such as high BMI, fibroids, being early perimenopausal and MD occurring concurrently with heavy bleeding. The association between past MD and heavy bleeding showed a dose-effect, with a stronger association observed between past MD and 2–3 out of 3 heavy bleeding symptoms than with 1 out of 3 symptoms. In contrast to heavy bleeding, neither a history of nor recent MD was associated with other abnormal bleeding symptoms. An association between past MD and PMS symptoms was observed, but, after adjustment for other potential predictors of PMS, including recent MD, the association of past MD with PMS was no longer statistically significant.

Several studies have reported an association between psychiatric illness and menstrual problems, although the nature of the mental illness, the specific type of menstrual problem, and the timing of the mental illness (recent or past) are not always specified.^{4,11,20} Results of the 2002 National Health Interview Survey suggest that the likelihood of menstrual-related problems of heavy bleeding, bothersome cramping, or premenstrual syndrome doubled among women aged 18–55 years who were likely to have a serious mental illness compared to those without psychiatric symptoms or illness.⁴ Two other studies also reported that women ages 40–55¹¹ and 35–59²⁰ who were psychiatric “cases” were more likely to report heavier bleeding relative to psychiatric “non-cases” (49% versus 23%).

MD has been shown to be a risk factor for the subsequent development of important health conditions, such as diabetes, cardiovascular disease, pain, backache, and dizziness.^{30,31} Behavioral and biological theories suggest several mechanisms that may explain the link between depression and health problems. These include behavioral changes associated with MD (e.g., smoking, diet, physical inactivity, non-compliance with medical regimens),

specific personality traits (e.g., somatic sensitivity, neuroticism), and physiologic dysregulation or arousal involving neuroendocrine, autonomic, and immune/ inflammatory systems,³² including the inflammatory markers CRP³³ and procytokine IL-6.³⁴ It is also possible that behavioral and personality characteristics, or a negative view of one's bodily experiences associated with a history of MD, may play important roles in explaining the associations we observed between past MD and heavy bleeding. Dysregulated physiologic systems in MD, perhaps through the relationship of the hypothalamic-pituitary-adrenal and the hypothalamic-pituitary-ovarian axes, could play a role although the exact mechanisms through which MD may exert its effects on menstrual bleeding problems are not understood. It may be that irregular fluctuations in estrogen levels are responsible for both abnormal menstrual bleeding as well as dysregulation of neurotransmitter systems (particularly serotonergic and noradrenergic) within circuits in the brain that mediate depressive symptoms.

While our findings show that the onset of MD preceded the onset of heavy bleeding, the time interval between the two conditions is unknown and likely variable for our participants. The potential contribution of inflammation, neuroendocrine, or other physiologic perturbations is more easily explained when the interval between the two conditions is shorter, unless prior MD has a more persistent and prolonged effect on these physiologic processes. Also, the absence of data on prior or current treatment of bleeding symptoms makes it difficult to identify hypothesized physiologic mechanisms. It is possible that the prior MD is a marker of an underlying predisposition to MD exacerbated by the normal changes of the transition, perhaps because of increasing variability in hormone levels. An alternative explanation is via increased awareness of bodily function leading to an over-reporting bias of bothersome symptoms, as suggested in previous studies of gynecologic symptoms.¹⁰

To our knowledge, no studies have examined the relationship between past MD and abnormal menstrual bleeding symptoms, and relatively few studies have evaluated the association between past MD and premenstrual dysphoric disorder (PMDD)²² or PMS in older menstruating women. In a community sample of 513 women, aged 36 – 44 years, without recent MD, past MD was strongly associated with current, prospectively confirmed PMDD after adjusting for other important predictors of PMDD.²² Our results, however, are not entirely consistent with these findings. In SWAN, the association of past MD with PMS was not evident when recent MD was accounted for in the analysis. The differences in the results are likely due to the different outcome criteria. While the previous study used the diagnostic criteria to determine PMDD,²² we used a retrospective proxy for symptoms occurring cyclically prior to menses onset. Numerous studies have shown that women who report PMS to clinicians based on past symptoms and then complete prospective daily diaries are found to have current MD rather than premenstrual-related symptoms.³⁵ Thus, it is not surprising that the association between past MD and PMS was no longer apparent after adjusting for recent MD. Indeed, we found that recent MD and PMS were strongly associated, similar to other studies of middle-aged women.⁵

Several limitations of this study should be noted. These include the absence of prospective diaries to document whether symptoms reported to be premenstrual were exclusively premenstrual in their timing. Like PMS, other symptoms were also captured retrospectively including bleeding patterns over the past year and menstrual characteristics during ages 25–35. It is possible that women's observation of the characteristics of their menstrual flow may be inaccurate as some women with normal menses, for example, may think their menses are heavy and vice versa. One way we addressed this issue was by providing descriptive criteria for heavy bleeding (changed protection every 1–2 hours on average) and clots (passed clots larger than a dime). However, in the case of characteristics recalled at ages 25–35, it is

difficult to rely on recollections of events that occurred 10–20 years earlier. Furthermore, we did not have objective measures of blood loss or anemia. It is the case that self reports of heavy bleeding are not consistent with the clinical definition of menorrhagia, which is defined as blood loss of >80 mL per period.³⁶ However, it is very difficult to obtain objective measures of menstrual blood loss in both research studies and clinical practice, which commonly use self-reports. Studies find that only about 30–35% of women who report heavy or very heavy bleeding actually meet the clinical level.^{6,36} Thus, we can only generalize our findings to perception of heavy bleeding as is the standard approach in large epidemiologic observational studies and not to objective excessive bleeding.^{36,37}

Retrospective lifetime reports of major depression are also subject to recall biases. However, the standard way of obtaining lifetime psychiatric diagnoses is through a semi-structured interview such as the SCID, which has been used in numerous psychiatric and epidemiologic studies of women's health. Importantly, the SCID was used as the core of the clinical validation study of the Composite International Diagnostic Interview (CIDI), the interview used by the WHO and the National Comorbidity Survey of mental disorders³⁸ to diagnose lifetime psychiatric disorders.

Despite the limitations, the study has several important strengths. It is the first to examine the relationship between past MD and menstrual problems in a large cohort of women in their late reproductive and early perimenopausal years. We were able to distinguish past depression from recent depression, and accounted for perimenopausal status, which overlaps with menstrual cycle bleeding symptoms, and we were also able to determine that the association of past MD with menstrual bleeding problems in midlife was present even among those who did not have similar menstrual symptoms at a younger age. Furthermore, we adjusted for self-reported history of fibroids, a major risk factor for heavy bleeding.

CONCLUSIONS

This study indicates that MD is not only a correlate of menstrual problems, but can precede the onset of heavy bleeding, reported by midlife women. Future longitudinal and mechanistic studies are needed to evaluate why past MD increases the likelihood of subsequent heavy menstrual bleeding in midlife women. Importantly, menstrual problems can have a substantial negative effect on quality of life. The evidence that heavy bleeding may be associated with past MD as well as recent experiences of significant depression suggests the importance of physicians or their staff obtaining assessments of current as well as past depression, particularly in patients with no underlying pathology. Such assessments can be conducted with brief self-report instruments or interviews^{39,40} in the healthcare setting and may help health care providers to identify midlife women with heavy bleeding problems who may benefit from attention to the emotional and functional sequelae of depression.

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Table 1

Description of Sample by Outcome

Characteristic	Heavy Bleeding Pattern ¹			Abnormal Bleeding Pattern ²		PMS-Like Syndrome ³	
	None n=301(32%)	1 Symptom n=288(31%)	2-3 Symptom n=345(37%)	None n=728(78%)	Any Symptom n=206(22%)	No n=750(80%)	Yes n=164(20%)
Age, Mean±SD	46.2 ± 2.6 *	46.0 ± 2.8	46.2 ± 2.6	46.0 ± 2.6 *	46.6 ± 2.7	46.2 ± 2.7 †	45.9 ± 2.4
Race/ethnicity							
African American	86 (29)	66 (23)	95 (28)	205 (28)	42 (20)	201 (27)	40 (24)
Caucasian	175 (58)	156 (54)	183 (53)	416 (57)	98 (48)	432 (58)	72 (44)
Hispanic	40 (13) *	66 (23)	67 (19)	107 (15) †	66 (32)	117 (16)	52 (32)
Education							
High school	75 (26)	85 (30)	109 (33)	191 (27)	78 (39)	206 (28)	60 (37)
Post high school	83 (28)	86 (31)	114 (34)	222 (31)	61 (31)	225 (31)	50 (31)
College degree	56 (19)	45 (16)	55 (17)	123 (17)	33 (17)	125 (17)	26 (16)
Post college	80 (27)	64 (23)	55 (17)	172 (24)	27 (14)	169 (23)	27 (17)
Body mass index, Mean±SD	27.9 ± 6.1 †	28.8 ± 6.6	29.6 ± 6.6	28.7 ± 6.2	29.0 ± 7.3	28.7 ± 6.3	29.2 ± 7.2
Early perimenopausal	115 (40) †	127 (47)	172 (52)	291 (42) †	123 (64)	322 (45) *	86 (54)
Current smoker	60 (20)	50 (18)	68 (20)	128 (18) *	50 (25)	136 (18)	38 (23)
Past history MD	72 (24) †	92 (32)	135 (39)	222 (30)	77 (37)	223 (30) †	72 (44)
Recent MD	23 (8) *	31 (11)	50 (14)	75 (10)	29 (14)	65 (9) †	35 (21)
Medication for nerves last month	25 (8)	26 (9)	41 (12)	67 (9)	25 (12)	67 (9)	22(13)
Reproductive History							
Dilation & curettage procedure (ever)	136 (45)	124 (43)	179 (52)	344(48)	95 (46)	350 (47)	82 (50)
Fibroids (ever)	44 (15) †	56 (20)	92 (28)	137 (20) *	55 (28)	142 (20) †	46 (29)
No. of pregnancies(0-7), Mean±SD	2.8 ± 1.8	2.9 ± 1.8	3.3 ± 1.7	3.0 ± 1.7	3.2 ± 1.9	3.0 ± 1.8	3.1 ± 1.8
Menstrual cycle characteristic age 25-35							
Menstrual flow > 10days	9 (3) †	13 (5)	28 (9)	29 (4) †	21 (11)	42 (6)	7 (5)
Bleeding/spotting between periods	17 (6)	15 (6)	26 (8)	27 (4) †	31 (16)	41 (6) *	17 (11)
Flooding or gushing	38 (14) †	67 (25)	145 (47)	187 (28)	63 (34)	190 (28) †	57 (39)

Characteristic	Heavy Bleeding Pattern ¹			Abnormal Bleeding Pattern ²		PMS-Like Syndrome ³	
	None n=301(32%)	1 Symptom n=288(31%)	2-3 Symptom n=345(37%)	None n=728(78%)	Any Symptom n=206(22 %)	No n=750(80%)	Yes n=164(20%)
Pass large clots	55 (20) [‡]	126 (49)	169 (55)	261 (40) [*]	89 (48)	274 (40)	72 (48)

^{*} p 0.05,

[‡] p 0.01,

[‡] p 0.001 comparing the no symptom group with the symptom group(s) individually for each menstrual cycle measure

MD=major depressive disorder occurring currently/within the past year ("recent MD") or prior to the past year ("past history MD") Listed in table is number (percentage) unless otherwise noted.

Twenty women were missing PMS-like syndrome data so total sample for this outcome is 914 instead of 934. Similarly, smaller N's for individual characteristics reflect specific missingness.

¹ Heavy bleeding pattern = heavy bleeding, flooding/gushing, and/or large clots

² Other abnormal bleeding pattern = flow > 10 days, spotting between periods, and/or bleed 2 or 8 days

³ PMS-like syndrome = changes in at least one mood symptoms (mood suddenly sad or anxious, jittery, nervous) and at least one physical symptom (abdominal pain, cramps, breast pain, breast tenderness, breast swelling, weight gain, feeling bloated, increased appetite, food cravings, pain in back, joints, or muscles, or severe headaches) occurring prior to the menstrual bleed and resolving with onset of menses.

Table 2Multinomial Logistic Regression Models for **Heavy Bleeding Pattern** (reference = no symptoms)^{*}

	2–3 Heavy Bleeding Symptoms vs. None		1 Heavy Bleeding Symptom vs. None	
	Odds Ratio	Confidence Interval	Odds Ratio	Confidence Interval
Unadjusted Model (n=934)				
Past history MD	2.04	1.45, 2.88	1.49	1.04, 2.15
Basic Model ¹ (n=907)				
Past history MD	2.13	1.50, 3.03	1.51	1.04, 2.18
Final Model ² (n=870)				
Past history MD	1.89	1.25, 2.85	1.46	0.96, 2.24
Age	0.98	0.92, 1.05	0.95	0.89, 1.02
Fibroids	2.37	1.53, 3.68	1.59	1.00, 2.53
Body mass index	1.05	1.02, 1.07	1.03	1.003, 1.06
Number of pregnancies	1.15	1.04, 1.27	1.01	0.91, 1.12
Recent MD	1.16	0.61, 2.19	1.09	0.56, 2.13
Early Perimenopausal (reference pre)	1.55	1.10, 2.18	1.32	0.93, 1.88

^{*} Heavy Bleeding Pattern = heavy bleeding, flooding/gushing, and/or large clots

MD=major depressive disorder occurring currently/within the past year (“recent/ MD”) or prior to the past year (“past history MD”)

¹ Basic Model: Past history MD, site, race, age, education

² Final Model: Past history MD, site, race, age, education, recent MD, menopausal status, fibroids, body mass index, and number of pregnancies

Table 3

Logistic Regression Models for Other Abnormal Bleeding Pattern *

	Odds Ratio	Confidence Interval
Unadjusted Model (n=934)		
Past history MD	1.36	0.99, 1.88
Basic Model ¹ (n=907)		
Past history MD	1.41	1.003, 1.98
Final Model ² (n=882)		
Past History MD	1.20	0.80, 1.79
Age	1.07	1.003, 1.14
Fibroids	1.64	1.10, 2.46
Recent MD	1.14	0.64, 2.03
Early Perimenopausal (reference pre)	2.56	1.80, 3.64

* Other abnormal bleeding pattern = menstrual flow > 10 days, spotting between periods, and/or bleed 2 or 8 days;

MD=major depressive disorder occurring currently/within the past year ("recent MD") or prior to the past year ("past history MD")

¹ Basic Model: Past history MD, site, race, age, education

² Final Model: Past history MD, site, race, age, education, recent MD, menopausal status and fibroids

Table 4Logistic Regression Models for PMS-like Syndrome ^{*}

	Odds Ratio	Confidence Interval
Unadjusted Model (n=914)		
Past history MD	1.85	1.31, 2.61
Basic Model ¹ (n=888)		
Past history MD	1.81	1.27, 2.58
Final Model ² (n=863)		
Past history MD	1.29	0.84, 1.98
Age	0.96	0.89, 1.03
Fibroids	1.59	1.04, 2.42
Recent MD	2.59	1.49, 4.50
Early Perimenopausal (reference pre)	1.37	0.95, 1.98

^{*} PMS-like syndrome = changes in at least one mood symptoms (mood suddenly sad or anxious, jittery, nervous) and at least one physical symptom (abdominal pain, cramps, breast pain, breast tenderness, breast swelling, weight gain, feeling bloated, increased appetite, food cravings, pain in back, joints, or muscles, or severe headaches) occurring prior to the menstrual bleed that interfered with work and ceased within a few days of menses onset.

MD=major depressive disorder occurring currently/within the past year ("recent MD") or prior to the past year ("past history MD")

¹ Basic Model: Past history MD, site, race, age, education

² Final Model: Past history MD, site, race, age, education, recent MD, menopausal status, and fibroids