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The Role of Family History of Depression and the Menopausal Transition in the Development of Major Depression in Midlife Women: Study of Women's Health Across the Nation Mental Health Study (SWAN MHS)

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Abstract

Background—This study evaluated whether family history of depression predicts major depression in midlife women above and beyond static risk factors (such as personal history of depression prior to midlife) and risks that may change dynamically across midlife (such as menopausal, psychosocial and health profiles).

Methods—Participants were 303 African American and Caucasian women (42–52 years at baseline) recruited into the Study of Women's Health Across the Nation (SWAN) Mental Health Study (MHS) in Pittsburgh. Major depression was assessed annually with Structured Clinical Interviews for DSM-IV. Family mental health history was collected at the ninth or tenth annual follow-up. Random effects logistic regression was used to assess the relationship between family history of depression and midlife depression, controlling for baseline sociodemographic characteristics and time-varying risk factors.

Results—Family history of depression was associated with midlife depression after adjusting for participant's history of major depression prior to midlife, trait anxiety and baseline age, and time-varying menopausal status, body mass index, very upsetting life events and chronic difficulties (OR=2.24, 95% CI=1.17–4.29, $p=.02$). Higher odds of major depression were found when women were late perimenopausal or postmenopausal relative to when they were pre- or early perimenopausal (OR=3.01, 95% CI=1.76–5.15, $p<.0001$). However, menopausal status was only associated with major depression among women without a family history.

Conclusions—Family history of depression predicts major depression in midlife women independent of the menopausal transition and other time-varying covariates. Notably, the

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menopausal transition was associated with increased risk only among women without a family history of depression.

Keywords

depression; mood disorders; epidemiology; family; life events/stress

Introduction

Depression is associated with increased morbidity and mortality and is highly prevalent, particularly in women (Cassano & Fava, 2002; Kessler et al., 2003; Kessler, Chiu, Demler, Merikangas, & Walters, 2005; Neugebauer, 1999). Studies indicate that incidence of first onset or recurrent episodes of clinical depression in women during midlife ranges from 20–30% (Cohen, Soares, Vitonis, Otto, & Harlow, 2006; Kessler et al., 1994; Kessler, McGonagle, Swartz, Blazer, & Nelson, 1993; Schmidt, Haq, & Rubinow, 2004). While recent research has examined the importance of psychosocial factors (Bromberger et al., 2007; Cohen et al., 2006; Dennerstein, Guthrie, Clark, Lehert, & Henderson, 2004; Maartens, Knottnerus, & Pop, 2002; Schmidt, Murphy, Haq, Rubinow, & Danaceau, 2004; Timur & Sahin, 2010), health profiles (Brown, Ford, Burton, Marshall, & Dobson, 2005; Dennerstein et al., 2004; Gallicchio, Schilling, Miller, Zacur, & Flaws, 2007; Krishnan et al., 2002; Lee & Kim, 2008; Simon et al., 2008), and the menopausal transition (Bromberger et al., 2011; Bromberger et al., 2007; Cohen et al., 2006; Freeman, Sammel, Lin, & Nelson, 2006; Freeman et al., 2004; Maartens et al., 2002) in the development of depression in midlife women, the role of family history of depression in this process remains largely unknown.

Numerous studies have provided evidence for the familial nature of depression (Bierut et al., 1999; Janzing et al., 2009; Kendler, Pedersen, Neale, & Mathe, 1995; Li, Sundquist, & Sundquist, 2008; Sullivan et al., 1996; Timko et al., 2008; Weissman, Kidd, & Prusoff, 1982). However, family history has been most strongly linked with early-onset depression (Janzing et al., 2009; Klein et al., 1999; Kupfer, Frank, Carpenter, & Neiswanger, 1989; Li et al., 2008; McGuffin, Katz, & Bebbington, 1987; Tozzi et al., 2008; Weissman et al., 1984). Studies of the role of family history of depression in mid- and later-life onset of depression are not as consistent, with some researchers reporting stronger associations between depression and environmental and physical health factors than between depression and family history (Tozzi et al., 2008). The role of family history in the development of depression during midlife and the menopausal transition is even less clear.

Our prior work with participants in the Study of Women's Health Across the Nation (SWAN) Mental Health Study (MHS) showed that family history of depression was a significant risk factor for experiencing a major depressive episode during midlife, above and beyond baseline health factors, psychosocial characteristics, or women's history of depression prior to entering the midlife period. (Colvin, Richardson, Cyranowski, Youk, & Bromberger, 2014). However, midlife can bring numerous and dynamic changes in social roles and circumstances, such as caring for aging parents, children leaving or returning to the home, financial strain, marital disruption, and the death of loved ones, that may lead to

depression (Rasgon, Shelton, & Halbreich, 2005). Changes in health status and health behaviors that occur over the midlife period may also contribute to depressed mood among midlife women (Alexander et al., 2007; Gallicchio et al., 2007). Finally, recent longitudinal studies have provided strong evidence of increased risk of depressed mood and major depression among women while undergoing the menopausal transition (Bromberger et al., 2011; Bromberger et al., 2007; Cohen et al., 2006; Freeman et al., 2006; Freeman et al., 2004; Maartens et al., 2002). Our prior study's focus on baseline risk factors was limited to the independent contribution of family history of depression to major depression during midlife generally and did not examine whether changes in menopausal status and health and psychosocial factors affected the relationship between family history of depression and major depression in midlife.

Thus, we extend our prior analysis to examine longitudinal follow-up data from the SWAN MHS cohort to address whether family history of depression remains a significant risk factor for major depression independent of changes in menopausal status and psychosocial and health profiles that may occur during this transitional life period. Only one other study has explored the role of family history of depression in the development of depressed mood specifically in the context of the menopausal transition (Woods et al., 2008). Woods et al. examined family history of depression and depressed mood in a population-based cohort of 302 U.S. women 35 to 55 years of age. Participants completed the Center for Epidemiologic Studies Depression Scale (CES-D) annually during the 15-year study. In bivariate longitudinal analysis, family history of depression predicted an average increase in CES-D scores of 2.05 ($p=.046$). Once the analysis was adjusted for menopausal stage, age, antidepressant use, body mass index, parity, and a history of postpartum blues, family history was no longer significantly related to depressive symptoms.

To our knowledge, the current study is the first to investigate the relationship between family history of depression and clinical depression in midlife women after taking into account the dynamic changes from the late reproductive stage through the menopausal transition to postmenopause (cessation of menses), psychosocial factors, and health profiles. Given the strong relationship between family history and major depression earlier in the lifespan, we hypothesized that family history would continue to predict depression in midlife above and beyond other static and dynamic risk factors.

The study will also examine whether the relationship between family history of depression and major depression in midlife women differs by menopausal status. The brain has numerous estrogen receptors, and changes in estrogen impact levels of serotonin, dopamine, and norepinephrine through degradation of catabolic enzymes, unblocking of binding sites, and enhancement of neurotransmitter transport (Spinelli, 2005; Studd & Panay, 2004). Despite the fact that all women undergoing menopause experience hormonal changes, not all develop depressed mood. The ability to maintain optimal psychological functioning in response to changing levels of hormones may be modified by genetic factors, thus potentially making certain subsets of women, such as those with a family history of depression, more vulnerable to depression during the menopause (Deecher, Andree, Sloan, & Schechter, 2008; Harsh, Meltzer-Brody, Rubinow, & Schmidt, 2009). Therefore, we hypothesized that we would find stronger associations between menopausal status and

midlife major depression in women with a family history of depression than in women without a family history.

Methods

Participants and Procedures

Study data were collected from women participating in the SWAN MHS at the Pittsburgh site. SWAN is a multi-center longitudinal study of the natural history of the menopausal transition. The SWAN MHS is an ancillary project designed to obtain diagnostic psychiatric interview data from SWAN Pittsburgh participants. Eligible women were aged 42–52 years, had an intact uterus, were not using hormones, had at least one menstrual period in the last 3 months, and self-identified as non-Hispanic White or African American. A total of 463 women were recruited into the Pittsburgh SWAN sample through random digit dialing and voter registration lists. Of these, 443 (95.7%) SWAN Pittsburgh women participated in the SWAN MHS. There were no significant differences between the MHS participants and non-participants with respect to sociodemographic factors and CES-D scores. Family history of depression was obtained from 303 women still participating in the SWAN MHS during annual visits 9 and 10 (September 2005–November 2007); these women comprise the sample for the current study. Reasons for nonparticipation in the family history assessment were as follows: withdrew from SWAN before visit 9 ($n=78$), missed the visit ($n=30$), completed the visit but not the assessment of family history of depression ($n=25$), and deceased ($n=7$). Compared to women who completed the family history assessment, non-completers ($N=140$) were younger ($p=.007$), more likely to be African American ($p=.02$), less educated ($p=.01$), more likely to be experiencing financial strain ($p<.0001$), and less likely to be married ($p=.03$).

The University of Pittsburgh Institutional Review Board approved this study, and all participants provided informed consent. Participants have been followed annually since 1996 with a protocol that includes biological, medical, and psychosocial measures. Psychiatric interviews were conducted at baseline and annually from January of 1996 through December of 2007 using the Structured Clinical Interview for DSM-IV (SCID) (Spitzer, Williams, Gibbon, & First, 1992). Non-time-varying independent variables analyzed in the current study were collected at baseline unless otherwise indicated, while time-varying independent variables were collected annually from baseline through visit 10.

Measures

Assessment of Major Depression—History of major depression prior to midlife was assessed at baseline by trained SCID interviewers and defined as the occurrence of a major depressive episode prior to enrollment in the SWAN. Participants were assessed for current or past-year major depression annually through visit 10. Interviewers were required to hold a Masters or a PhD in a mental health field and to have prior clinical experience. Participant interviews were audiotaped for assessment of interviewing skills and inter-rater reliability. Within SWAN, reliability was good for lifetime ($k=0.81$) and past year major depression ($k=0.76–0.89$).

Family History of Depression—Trained interviewers obtained family history of depression in first degree relatives using the family history method and a modified version of the depression module from the Family Interview for Genetic Studies (FIGS) (Maxwell ME, 1992; Nurnberger et al., 1994). The family history method, in which an informant is queried about the history of mental illness in relatives, has been used in numerous studies with acceptable reliability and validity (Andreasen, Endicott, Spitzer, & Winokur, 1977; Weissman et al., 2000). In brief, the modified FIGS consisted of three interviewer administered questionnaires. Participants were first screened with a Family Mental Health History form. Those who endorsed a relative with depression and/or attempted/completed suicide then completed a questionnaire to collect more detailed information about their relative's symptoms, followed by a Depression Symptoms Checklist, which confirmed whether or not their relative met the DSM-IV criteria for major depression.

Menopause—Menopausal status was based on self-reported menstrual bleeding patterns. Women were classified as: premenopausal (menstrual bleeding in the past 3 months with no change in cycle regularity in the past 12 months), early perimenopausal (menstrual bleeding in the past 3 months accompanied by changes in cycle regularity), late perimenopausal (menstrual bleeding within the past 12 months but not the past 3), postmenopausal (no menstrual bleeding within the past 12 months). We censored women who underwent a hysterectomy from the time of surgery forward, and hormone therapy users were excluded for the duration of their hormone use. If a pre- or perimenopausal participant stopped hormone therapy during the study, her data were included from the time her menopausal status could again be reliably determined forward. Menopausal status was combined into pre-/early perimenopause and late perimenopause/postmenopause as there were few late perimenopausal observations overall and few premenopausal women at visits 5 through 10.

Socioeconomic Indicators—Data from baseline for difficulty paying for basic necessities and educational attainment were included in analyses as indicators of socioeconomic status. Sociodemographic variables included age, ethnicity, and marital status.

Health-related Factors—Chronic medical conditions were assessed annually by asking participants whether a medical professional had ever told them that they had any of the following: diabetes, hypertension, arthritis/osteoarthritis, under/overactive thyroid, cardiovascular disease, or cancer. The total number of chronic medical conditions reported was categorized into none vs. one or more conditions. Perceived overall health was assessed by asking participants to rate their overall health as excellent, very good, good, fair, or poor, which was dichotomized into excellent/very good/good vs. fair/poor. Vasomotor symptoms data were collected as part of a symptom checklist that has been used in several menopause studies (Matthews et al., 1990; Neugarten & Kraines, 1965). Women indicated how often they had experienced hot flashes and night sweats in the past two weeks. Those who reported experiencing hot flashes and/or night sweats at least 6 out of 14 days were classified as having frequent vasomotor symptoms.

Lifestyle—Height and weight were measured annually by trained staff according to a standard protocol and were used to calculate body mass index (BMI) as weight (kg)/height (m)². A modified version of the Baecke (Baecke, Burema, & Frijters, 1982) physical activity questionnaire was administered to obtain information on the intensity, duration, and frequency of activity related to the domains of daily living, exercise/sports, and home/child care at baseline. A total physical activity score was calculated to reflect activity across all domains.

Psychosocial Variables—Life stress was assessed using an 18-item version of the Psychiatric Epidemiology Research Interview Life Events Scale (PERI) (Dohrenwend et al., 1987). Women were asked whether they had 1) experienced any of 18 negative life events across eight domains (school, work, romantic relationships, children, family, criminal/legal matters, finances, and health) in the past year and 2) how upsetting each of the events was for them (not at all upsetting, somewhat upsetting, very upsetting, very upsetting and still upsetting) Women were categorized as having experienced at least one very upsetting life event in the past year or having experienced no such event. Women also reported whether they had experienced any of the following nine chronic difficulties for 12 months or longer: own health problems, health problems with partner or child, substance abuse in a family member, work difficulties, financial strain, housing problems, problem with a close relationship, helping sick family member or friend on a regular basis, any other ongoing problem (Bromberger & Matthews, 1996). Women rated how upsetting each chronic difficulty was for them on a three-point scale (not upsetting, somewhat upsetting, or very upsetting). Women were categorized as having experienced at least one very upsetting chronic difficulty in the past year or having experienced no such difficulty. Responses from the 4-item Medical Outcomes Study Social Support Survey (Sherbourne & Stewart, 1991) were summed to create a social support score, with higher scores indicating more social support.

Optimism was measured at follow-up visit 1 with the six-item Life Orientation Test. Items were scored and summed to create a total optimism score as per Scheier and Carver (1985). Higher scores indicate greater optimism. Trait anxiety was also assessed at visit 1 with a 10-item version of the Spielberger Trait Anxiety Inventory (Spielberger C, Gorsuch R, & Lushene R, 1970); higher scores reflect higher levels of trait anxiety.

Statistical Methods

The STATA system version 12 was used for statistical analyses. Differences in baseline characteristics between women with and without a family history of depression were assessed using chi square tests for comparison of categorical variables and t-tests or Wilcoxon rank-sum tests for unadjusted comparisons of continuous variables.

To address the question of whether family history of depression is associated with major depression in midlife women after adjusting for changes in menopausal status and other time-varying covariates, multivariable repeated measures random effects logistic regression models were constructed (xtlogit procedure). This modeling approach accounts for the

correlation of repeated observations from each woman resulting from the longitudinal design. Women were treated as the random effect (i.e. woman-specific intercept).

Time-invariant covariates included baseline age, ethnicity, education, financial strain, optimism, trait anxiety, and history of major depression prior to midlife. Time-varying covariates included marital status, menopausal status, vasomotor symptoms, chronic medical conditions, overall health, physical activity, body mass index, stressful life events, chronic difficulties, and social support. Potential covariates were assessed in bivariate repeated measures random effects logistic regression analyses, and results from these analyses, as well as results from prior literature, informed which variables were included in the multivariable model building process. Covariates identified in bivariate analyses at $p < .15$ were entered into the logistic regression model, and manual backwards elimination was used (retaining variables significant at $p < .10$) to obtain a final parsimonious multivariable model. To explore whether the relationship between family history of depression and major depression during midlife differed by menopausal status, an interaction term was added to the final multivariable model.

Results

Descriptive data for the study participants are presented in Table 1. At baseline, participants were 42–52 years of age with a mean age of 46. Thirty-one percent of the participants were African American and 34% had a family history of depression. Participants with a family history of depression were more educated ($\chi^2_{(2, N=303)} = 7.01, p = 0.03$), more likely to have experienced a very upsetting chronic difficulty in the past year ($\chi^2_{(1, N=284)} = 5.61, p < 0.01$), and more likely to have a history of major depression prior to midlife ($\chi^2_{(1, N=303)} = 14.00, p < 0.001$) compared to those with no family history.

Out of the total 2,574 observations, 241 major depressive episodes were diagnosed during the study (Table 2). Major depressive episodes were identified during 115 (8.1%) of the 1,412 pre-/early perimenopause observations and 126 (10.8%) of the 1,162 late perimenopause/postmenopause observations.

Table 3 shows the association of family history of depression and major depression during the study adjusted for menopausal status and other covariates. The odds of major depression were approximately 2.2 times greater for those with a family history of depression than for those without a family history (OR=2.24, 95% CI=1.17–4.29, $p = 0.02$). Menopausal status was also significantly associated with major depression in midlife women, with higher odds of major depression found when women were late perimenopausal or postmenopausal relative to when they were pre- or early perimenopausal (OR=3.01, 95% CI=1.76–5.15, $p < 0.0001$). Baseline age, trait anxiety, history of major depression prior to midlife, body mass index, and very upsetting chronic difficulties were significantly related with major depression. The adjusted relationship between major depression and very upsetting life events was marginally statistically significant (OR=1.71, 95% CI=0.98–2.98, $p = 0.06$). Major depression was not significantly associated with parity (OR=1.24, 95% CI=0.52–2.94, $p = 0.63$) or history of postpartum depression (OR=0.98, 95% CI=0.25–3.84, $p = 0.98$) in

bivariate analyses in our cohort of women, and they were therefore not included in the final multivariate models.

To determine whether the relationship between family history of depression and major depression during midlife differed by menopausal status, an interaction term was added to the model presented in Table 3. A statistically significant interaction between family history of depression and menopausal status was observed ($p=0.04$). To illustrate this interaction, adjusted models stratified by family history of depression are presented in Table 4. Menopausal status was not significantly associated with major depression in midlife among women with a family history of depression ($OR=1.36$, 95% $CI=0.84-2.20$, $p=0.21$). However, for women without a family history, the odds of reporting major depression during the study were higher when they were late perimenopausal or postmenopausal compared to when they were pre- or early perimenopausal ($OR=3.36$, 95% $CI=1.79-6.32$, $p<0.0001$).

When antidepressant use was added to the final model, family history of depression remained a significant predictor of major depression in women during midlife ($OR=1.90$, 95% $CI=1.10-3.62$, $p=0.03$). These results are presented in Table 5.

Discussion

This is the first prospective study to evaluate whether family history of depression is a risk factor for major depression in midlife women after taking dynamic changes in menopausal status and other important time-varying covariates, such as health and psychosocial factors, into account. Specifically, the odds of experiencing a major depressive episode were approximately 2.2 times greater for those with a family history of depression than for those without a family history even after adjusting for menopausal status, age, BMI, trait anxiety, very upsetting chronic difficulties and stressful events, and history of depression prior to midlife.

While the results confirm our primary hypothesis regarding the impact of family history on midlife depression risk, they are not consistent with findings from Woods et al. (2008). Woods et al. did not find a significant association between depressive symptoms and family history of depression after they adjusted for antidepressant use, stress, BMI, age, menopausal stage, history of postpartum depression, and parity. The inconsistency in results may be due to differences in the method of ascertaining family history, the evaluation of depressive symptoms vs. clinical depression, and the inclusion of different variables in the final multivariable models. We explored the effects of parity and history of postpartum depression but neither variable was significantly related to major depression in our cohort of midlife women. The addition of antidepressant use to the final models also did not significantly alter our results.

In the total sample, higher odds of major depression were found when women were late perimenopausal or postmenopausal relative to when they were pre- or early perimenopausal. This is consistent with recent longitudinal studies, including the Woods et al. study, which have provided strong evidence of increased risk of depressed mood among women undergoing the menopausal transition. Freeman et al. (2004) showed that reporting of high

depressive symptoms (CES-D 16) increased significantly during the transition (OR=2.89, 95% CI: 1.29–6.45) and decreased during the postmenopausal period (OR=0.78, 95% CI: 0.10–6.17) in an urban community sample of US women, and Bromberger et al. (2011) reported that women were two to four times more likely to have a major depressive episode when they were perimenopausal (OR=1.98, 95% CI: 1.00–3.92) or early postmenopausal (OR=3.86, 95% CI: 1.36–10.92) compared to when they were premenopausal.

We hypothesized that the relationship between menopausal status and midlife major depression would be stronger in women with a family history of depression compared to women without a family history. In contrast, we found that menopausal status was significantly associated with major depression in those without a family history of depression, but not in those with a family history. Twin studies have reported that familiarity of depression is mostly a result of genetic and individual environmental influences (Sullivan, Neale, & Kendler, 2000) and, therefore, women with a family history of depression may be more vulnerable to depression across the lifespan and less affected by factors specific to midlife, such as the menopausal transition.

In terms of the health and psychosocial factors we examined, we found that BMI was significantly associated with major depression in women during midlife. Several cross-sectional and prospective general population studies suggest a significant relationship between obesity and depression in adults (Faith et al., 2011; Luppino et al., 2010), particularly in women (Bjerkset, Romundstad, Evans, & Gunnell, 2008; Herva et al., 2006; Kasen, Cohen, Chen, & Must, 2008; Roberts, Deleger, Strawbridge, & Kaplan, 2003). Multiple biological mechanisms have been proposed to explain observed obesity and depression associations, such as inflammation, altered cortisol secretion, poor health behaviors, and obesity-related health conditions (Faith, Matz, & Jorge, 2002; Jorm et al., 2003; Stunkard, Faith, & Allison, 2003). We also found that stressful life events and chronic difficulties were related with depression among midlife women, as has been shown in other studies (Amore et al., 2004; Bromberger et al., 2007; Bromberger et al., 2010; Cohen et al., 2006; Dennerstein et al., 2004; Kaufert, Gilbert, & Tate, 1992; Maartens et al., 2002; Schmidt, Murphy, et al., 2004; Timur & Sahin, 2010). Trait anxiety was associated with midlife depression in the current study as well. Cross-sectional and prospective studies have reported that higher levels of neuroticism are strongly associated with depression (De Graaf, Bijl, Ravelli, Smit, & Vollebergh, 2002; Fanous, Neale, Aggen, & Kendler, 2007; Kendler, Gatz, Gardner, & Pedersen, 2006; Kendler, Neale, Kessler, Heath, & Eaves, 1993; Kotov, Gamez, Schmidt, & Watson, 2010). However, some research has shown that neuroticism is only a risk factor for early-onset major depression (Korten, Comijs, Lamers, & Penninx, 2012; Sneed, Kasen, & Cohen, 2007), while others have found that neuroticism is also an important risk factor for depression in mid- and later life (Steunenberg, Beekman, Deeg, & Kerkhof, 2006; Steunenberg, Braam, Beekman, Deeg, & Kerkhof, 2009). The current study supports the enduring role of trait anxiety on midlife depression risk, while also identifying the role of changing health and psychosocial risks that occur across the midlife years.

The main limitation of the current study is the method used to ascertain family history of depression. Due to time and financial constraints, direct family interviews were not conducted, and family history was instead collected through participant self-report.

Participants may have incorrectly reported the psychopathology of their relatives, and it is possible that women who have experienced depression may be more likely to remember their relatives as being depressed than women without a history of depression. Thus, the results may have been affected by both limited knowledge of relatives' emotional health and recall bias. However, the family history method has established validity and reliability and has often been used in studies of psychiatric disorders. In addition, rather than relying on a simple yes/no question to obtain family history information, the assessment used in the current study was based on DSM-IV criteria, which may have helped to limit the amount of misclassification.

Because there were few late perimenopausal observations overall and very few premenopausal observations at visits 5 through 10, we combined the pre- and early perimenopause categories and the late perimenopause and postmenopause categories for our analyses. A larger sample would have allowed us to better characterize the relationship between depression and the menopause at each of the stages of the transition. The study has a number of strengths. While most epidemiologic studies of depression in midlife women have examined depressive symptoms, we had 11 years of clinical depression data collected with a semi-structured diagnostic interview, which allowed for a more accurate classification and examination of depression. In addition, SWAN has collected a wealth of longitudinal data from one of the few community cohorts of menopausal women, and we were able to use these data to determine the importance of the relationship between family history of depression and major depression during midlife in the context of other risk factors, including the menopausal transition, and changes in biological and psychosocial factors.

In conclusion, our results indicate that family history of depression is a risk factor for major depression in midlife women independent of the menopausal transition and dynamic changes in psychosocial and health profiles that occur during the midlife period. This suggests that clinicians should be aware that family history continues to play an important role in the development of depression in women during midlife. On the other hand, it is also important to recognize that women without a family history of depression may be more vulnerable to the effects of the menopausal transition than women with such a history and that this group of women may benefit from increased monitoring for signs of depression during midlife. Such monitoring could lead to earlier interventions, including behavioral, pharmacological or psychological therapy that could interrupt the progression from depressive mood to minor or major depression and are efficacious at other times in the life cycle. During the menopausal transition, interventions can also include brief counseling on coping with changes in mood and symptoms associated with perimenopause, targeting symptoms that may exacerbate or be associated with depression and are unique to this period in a woman's life, such as vasomotor and genitourinary symptoms and sleep difficulties (Frey, Lord, & Soares, 2008; Stewart DE & Khalid MJ, 2006).

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Table 1

Baseline characteristics by family history of major depression (MD)

	Total N=303	No family history of MD n=199 (65.7%)	Family history of MD n=104 (34.3%)	p value
Age (years), mean (SD)	46.3 (2.6)	46.4 (2.6)	46.1 (2.4)	0.51
African American, n (%)	95 (31.3)	62 (31.2)	33 (31.7)	0.91
Education, n (%)				
Less than high school	70 (23.1)	55 (27.6)	15 (14.4)	0.03
High school/some college	102 (33.7)	65 (32.7)	37 (35.6)	
College/more than college	131 (43.2)	79 (39.7)	52 (50.0)	
Marital status, n (%)				
Married	208 (69.1)	141 (70.8)	67 (65.7)	0.45
Never married	37 (12.3)	25 (12.6)	12 (11.8)	
Separated/widowed/divorced	56 (18.6)	33 (16.6)	23 (22.5)	
Somewhat/very hard to pay for basics, n (%)	84 (27.8)	55 (27.8)	29 (27.9)	0.98
Menopausal status, n (%)				
Premenopausal	165 (54.5)	114 (57.3)	51 (49.0)	0.17
Early perimenopausal	138 (45.5)	85 (42.7)	53 (51.0)	
Vasomotor symptoms: at least 6/14 days, n (%)	28 (9.3)	14 (7.1)	14 (13.5)	0.07
Any chronic medical condition, n (%)	110 (36.3)	68 (34.2)	42 (40.4)	0.28
Overall health, n (%)				
Good/very good/excellent	258 (85.7)	171 (86.4)	87 (84.5)	0.66
Poor/fair	43 (14.3)	27 (13.6)	16 (15.5)	
Body mass index (kg/m ²), mean (SD)	28.6 (6.6)	28.3 (6.5)	29.2 (6.9)	0.25
Physical activity score (range, 0–14), mean (SD)	7.9 (1.7)	7.9 (1.7)	7.8 (1.7)	0.65
Very upsetting life event in past year, n (%)	157 (52.0)	98 (49.5)	59 (56.7)	0.23
Very upsetting chronic difficulty in past year, n (%)	72 (25.4)	40 (21.0)	32 (34.0)	<0.01
Social support (range, 0–16), mean (SD)	12.9 (2.8)	13.0 (2.8)	12.8 (2.7)	0.27
Optimism (range, 0–18), mean (SD)	13.0 (3.8)	13.0 (3.7)	13.1 (4.0)	0.63
Trait anxiety (range, 10–40), mean (SD)	15.9 (4.7)	15.6 (4.6)	16.5 (5.0)	0.12
History of MD prior to midlife, n (%)	103 (34.0)	53 (26.6)	50 (48.1)	<0.001

Total percentages may not equal to 100 due to rounding

Table 2

Number of women with major depression (MD) by visit and menopausal status

Total	Pre-/Early Perimenopause			Late Peri-/Postmenopause	
	No. of observations	No. with MD	No. of observations	No. with MD	No. with MD
Baseline	303	9	303	9	0
01	256	22	243	19	3
02	240	23	211	20	3
03	226	16	178	13	3
04	208	20	142	13	7
05	207	24	107	14	10
06	202	25	83	10	15
07	216	17	59	3	14
08	240	24	43	7	17
09	244	31	30	5	26
10	232	30	13	2	28
<i>Total</i>	<i>2,574</i>	<i>241 (9.4%)</i>	<i>1,412</i>	<i>115 (8.1%)</i>	<i>126 (10.8%)</i>

Table 3

Random effects logistic regression analyses for odds of major depression (MD) among 285 women (1,513 observations)

	OR	95% CI	p value
Family history of MD	2.24	1.17–4.29	0.02
Age at baseline (years)	0.80	0.69–0.92	0.003
Menopausal status			
Pre-/early perimenopausal (REF)	REF	REF	<0.0001
Late perimenopausal/post	3.01	1.76–5.15	
BMI (kg/m ²)	1.07	1.03–1.11	0.001
Trait anxiety	1.14	1.07–1.20	<0.0001
History of MD prior to midlife	2.92	1.50–5.66	0.002
Very upsetting life event in past year	1.71	0.98–2.98	0.06
Very upsetting chronic difficulty in past year	1.85	1.08–3.15	0.02

BMI, body mass index; OR, odds ratio; CI, confidence interval; REF, reference category.

Table 4

Random effects logistic regression for odds of major depression (MD) by family history

	No family history of MD n=199		Family history of MD n=104	
	OR (95% CI)	p value	OR (95% CI)	p value
Menopausal status				
Pre-/early perimenopausal (REF)	REF	<0.0001	REF	0.21
Late perimenopausal/post	3.36 (1.79–6.32)		1.36 (0.84–2.20)	

OR, odds ratio; CI, confidence interval; REF, reference category. Model adjusted for baseline age, trait anxiety, history of MD prior to midlife, body mass index, very upsetting chronic difficulty, and very upsetting life event

Table 5

Random effects logistic regression analyses for odds of major depression (MD) among 285 women (1,513 observations), antidepressant use included

	OR	95% CI	p value
Family history of MD	1.90	1.10–3.62	0.03
Age at baseline (years)	0.82	0.71–0.95	0.009
Menopausal status			
Pre-/early perimenopausal (REF)	REF	REF	<0.0001
Late perimenopausal/post	2.61	1.53–4.48	
BMI (kg/m ²)	1.07	1.02–1.11	0.002
Trait anxiety	1.11	1.05–1.18	<0.0001
History of MD prior to midlife	2.64	1.37–5.08	0.004
Very upsetting life event in past year	1.79	1.03–3.10	0.04
Very upsetting chronic difficulty in past year	1.66	1.00–2.84	0.05
Antidepressant use	3.42	1.92–6.10	0.001

BMI, body mass index; OR, odds ratio; CI, confidence interval; REF, reference category.