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Does Risk for Anxiety Increase During the Menopausal Transition? Study of Women's Health Across the Nation (SWAN)

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Abstract

Objective—Little is known about the risk of anxiety in women during midlife and the menopausal transition. We examined anxiety as a cluster of 4 symptoms and determined the association between menopausal stage and high anxiety during ten years of follow-up of 2,956 women of multiple race/ethnicities.

Methods—This study was a longitudinal analysis of data from the multi-site Study of Women's Health Across the Nation (SWAN), a study of menopause and aging. Women were 42-52 at study entry. The outcome was high anxiety, a score of 4 or greater on the sum of four anxiety symptoms rated according to frequency in the previous 2 weeks from 0 (none) to 4 (daily) (upper 20%). Covariates included sociodemographics, health factors, stressors, and vasomotor symptoms (VMS).

Results—Women with low anxiety at baseline were more likely to report high anxiety symptoms when early or late perimenopausal or postmenopausal compared to when they were premenopausal (odds ratios ranged from 1.56 to 1.61), independent of multiple risk factors, including upsetting life events, financial strain, fair/poor perceived health, and VMS. Women with high anxiety at baseline continued to have high rates of high anxiety throughout the follow-up but odds ratios did not differ by menopausal stage.

Conclusion—Women with high anxiety premenopausally may be chronically anxious and not at increased risk of high anxiety at specific stages of the menopausal transition. In contrast, women

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with low anxiety premenopausally may be more susceptible to high anxiety during and after the menopausal transition than before.

Keywords

anxiety; menopausal transition; vasomotor symptoms; longitudinal

INTRODUCTION

The prevalence of anxiety symptoms in midlife women is substantial with estimates as high as 51% of women 40-55 years old reporting any tension/nervousness or irritability in the past 2 weeks (1) or at the moment (2) and 25% reporting frequent irritability or nervousness (3). Compared with premenopausal women, perimenopausal women have a greater risk for each symptom of anxiety (3). However, studies have reported conflicting results concerning the extent to which prevalence of anxiety symptoms varies during different stages of the menopausal transition with some studies indicating no statistically significant differences by menopausal stage (4; 5) and others finding that early or late perimenopausal women have significantly higher rates of anxiety symptoms than premenopausal women (6; 7). Thus, whether the menopausal transition is a period of increased risk for anxiety is unclear.

The absence of consistent findings regarding associations between anxiety and menopausal status is likely due to assessment of different symptoms, study designs and populations studied. Anxiety is a general term that refers to varying symptoms characterizing different anxiety disorders, such as panic disorder (e.g., suddenly feeling fearful for no reason), social phobia (e.g., fear of social or performance situations), or generalized anxiety (e.g., excessive and uncontrollable worry, irritability). Such heterogeneity in anxiety symptoms and disorders is reflected in the literature, the vast majority of which includes diverse measures of individual anxiety symptoms, such as “irritability” or “feelings of panic” (8; 5), making it difficult to compare studies and draw conclusions.

Compared with depression, anxiety symptoms and disorders have generated far less attention in studies of midlife women despite the prevalence of anxiety and their association with distress, impaired quality of life, and vasomotor symptoms (VMS). Indeed, studies that focus on anxiety symptoms or syndromes usually focus on their association with VMS rather than with menopausal status per se (9-11; 12). Nevertheless, a greater understanding of the unique influence of the menopausal transition on the occurrence of anxiety symptoms and syndromes is important as anxiety is not only prevalent in community populations, but is also a problem frequently reported to health care providers by midlife women (13; 14).

An analysis of cross-sectional baseline data from the Study of Women's Health Across the Nation (SWAN) (3) found that the odds of frequent (≥ 6 days in past 2 weeks) irritability (odds ratio (OR)=1.33) and nervousness (OR=1.54), adjusted for multiple covariates, were significantly higher among early perimenopausal than premenopausal women. However, conclusions about the increase in risk of anxiety associated with the menopausal transition based on these data are limited by the cross-sectional design, the lack of late perimenopausal and postmenopausal women in the sample and the assessment of individual symptoms.

Importantly, in studies of the menopause transition (15; 9) anxiety has been consistently and significantly associated with VMS (hot flashes and/or night sweats). Because VMS are highly prevalent during the transition, it is difficult to determine if VMS underlie an observed association between anxiety and menopausal stage. Thus, it is unclear whether the transition from premenopause to postmenopause is a time of increased risk of high anxiety, independent of VMS, and if so, what are the characteristics of women at greatest risk.

An individual symptom, while potentially distressing or bothersome, is not informative of what underlying condition or disorder it reflects and may be one of the reasons studies do not report consistent findings. Therefore, in the current report, we aimed to extend the research on anxiety in three ways: (1) assessing anxiety as a cluster of 4 symptoms (2) determining the association between menopausal stage and high anxiety during ten years of follow-up of 2956 women enrolled in SWAN, and (3) evaluating whether risk for high anxiety is different in women with and without high anxiety at study entry. We used the new measure to test the hypothesis that a cluster of anxiety symptoms, specifically, irritability, tension/nervousness, feeling fearful for no reason, and heart racing or pounding would be more likely to occur during or after the menopausal transition than before, independent of demographic, psychosocial, health factors and VMS.

METHOD

Participants and Procedures

The current report is based on data collected from participants in the Study of Women's Health Across the Nation (SWAN), a longitudinal, multiethnic, 7-site community-based study of menopause and aging among 3,302 pre- and early perimenopausal women enrolled at baseline. A description of SWAN has previously been published (16). Briefly, approximately 450 white women and a sample of a predetermined minority group were recruited at each of 7 clinical sites across the country in 1995-1997: Japanese in Los Angeles (UCLA), Chinese in Oakland, CA (Davis), African Americans in the Detroit area (University of Michigan), Chicago (Rush University), Pittsburgh (University of Pittsburgh), and Boston (Massachusetts General Hospital) and Hispanics in Newark (UMDNJ and Einstein). Eligibility criteria for SWAN included being aged 42-52, having an intact uterus, having had at least one menstrual period in the previous three months, no use of reproductive hormones in the previous three months, and self-identifying with one of the site's designated race/ethnic groups. Of the 3302 participants, the current analyses included 2,956 women who had complete anxiety data at baseline and at least one subsequent annual visit. The New Jersey site did not complete in person clinic visits after the 6th annual follow-up (completed by 25%), and resumed clinic visits at follow-up 12. Each site received Institutional Review Board approval of the study protocol. Written informed consent was obtained from all study participants.

Participants were assessed at study entry (baseline) and annually through visit 10 with a common standardized protocol that consisted of detailed questions about medical, reproductive and menstrual history; lifestyle and psychosocial factors; and physical and psychological symptoms. Measurements of height and weight were obtained using a common protocol. Interviewer- and self-administered study forms and materials were available in English, Spanish, Japanese, and Cantonese, and bilingual staff were used, as appropriate. Translations were prepared for the study (initial translation, back translation and reconciliation).

Measures

Assessment of anxiety—At each visit, women completed a symptom checklist consisting of 15 items similar to those used in numerous studies of menopause. Women were asked if they had experienced each of these symptoms in the previous two weeks and if so, how frequently: none (0), 1-2 days (1), 3-5 days (2), 6-9 days (3), daily (4). The questionnaire includes four symptoms of anxiety: irritability, nervousness or tension, feeling fearful for no reason, and heart pounding or racing. Responses to the anxiety items were summed. Due to a skewed distribution, the summed scores were dichotomized as high and low anxiety. Women with the top 20% of scores (i.e., ≥ 4) were identified as having high

anxiety. Internal consistency for the four symptoms was good based on the baseline assessment: Cronbach's alpha=.77 and the scores were highly correlated with the Generalized Anxiety Disorder-7 (GAD-7) (Spearman r=.71), a 7-item measure of generalized anxiety that was completed at the same time (visit 12) as the 4-item measure used in the current analyses. The GAD-7 has been shown to be a reliable and valid measure of anxiety in the general population and in primary care (17; 18). Furthermore, the GAD-7 means (sd) in the low and high anxiety groups were statistically different, 2.21 (sd=2.7) and 8.69 (sd=5.29), respectively ($p < .0001$) providing additional support for the validity of the cluster of symptoms.

Menopausal stage—Menopausal stage was based on menstrual bleeding patterns in the previous 12 months and was categorized as: a) premenopausal (menstrual period in the past 3 months with no change in regularity in the past 12 months); b) early perimenopausal (menstrual period in the past 3 months with change in regularity over the previous 12 months); c) late perimenopausal (no menstrual period within the past 3 months, but some menstrual bleeding within the past 12 months); d) post menopausal (no menstrual period within the past 12 months). The classifications are similar to those recommended by the World Health Organization (19). We also identified a separate group who were postmenopausal and using hormone therapy. Data from non-postmenopausal HT users were excluded from the visit at which HT was being used.

Covariates—Age, race/ethnicity, and education were obtained at baseline during screening for eligibility. All other variables were obtained at each follow-up examination. Women self-reported whether medication for nerves/depression was taken at least twice weekly in the month prior to interview, which was verified by examination of medication containers in the clinic or by participants reading labels to the interviewer over the telephone. Hormone therapy (HT) use was reported at each visit. Perceived health was categorized into excellent (referent category), very good, good or fair/poor. Body mass index (BMI) (kg/m^2) was calculated from measurements of weight and height, which were obtained with a calibrated scale and a stadiometer. VMS (hot flashes or night sweats) were reported on the checklist described above. Frequent VMS was defined as reporting these on six or more days in the previous two weeks. Exposure to upsetting life events in the past 12 months was determined by women's responses to a checklist of 18 possible life events that might have occurred. Women indicated whether the event occurred and if so, how upsetting it was (not at all, somewhat upsetting, very upsetting). A very upsetting life event was dichotomized as at least one versus none.

Statistical analyses

The analytic sample consisted of 2,956 women for whom we had 23,532 person years of observations over the 10 years of annual visits. We compared the baseline characteristics of women with and without high anxiety at baseline to identify factors that were significantly different between these groups. Longitudinal random effects logistic regression models were used to examine the odds of having high anxiety for each menopausal stage (premenopause, early perimenopause, late perimenopause, natural postmenopause and postmenopause with HT use) from study entry through visit 10. Women were censored at the visit when their menopausal stage was undetermined (premenopausal or perimenopausal and concurrent use of HT, which can cause bleeding), but their data were included in subsequent analyses once they ceased HT use and stage could be determined. Women who reported having a hysterectomy and/or oophorectomy were censored from that visit forward.

The initial basic model included age, race/ethnicity, education, study site, and time since baseline (as a measure of increasing age) to examine the association of menopausal stage

and anxiety without adjustment for other relevant covariates. Subsequently, based on a priori knowledge and the literature, covariates including medication use for a "nervous condition", number of medical conditions, perceived general health, difficulty paying for basics, and experiencing at least one very stressful event were added to the basic model. In the final model, we added frequent VMS to the analysis to determine whether they explained the association between menopausal stage and high anxiety. The interaction of baseline anxiety and menopausal stage was added to the random effects logistic regression fully adjusted analyses to determine if the association between stage and anxiety symptoms from visits 1 through 10 varied by whether women had high anxiety at baseline. The same set of analyses was then conducted in the two groups stratified by baseline anxiety status. Diagnostic plots and standard model fit analyses were conducted to verify model structure and assumptions. Analyses were performed with SAS version 9.3 (SAS Institute, Cary, NC).

RESULTS

Baseline characteristics of participants are described in Table 1 which shows that women with and without high anxiety at baseline differed significantly by demographics, menopausal stage and VMS, health factors and life events. Specifically, women with high anxiety were more likely to be Hispanic and less likely to be Chinese or Japanese, have a high school education or less, have difficulty paying for basics, be early perimenopausal, and report frequent VMS, worse health characteristics, and at least one very upsetting event in the previous year. Table 2 shows the number of observations over the 10 years of follow up during each menopausal stage for all women and for those with and without high baseline anxiety. Overall, women had high anxiety symptoms (i.e., score of ≥ 4 on the anxiety symptom cluster) at 15.6% of premenopausal visits, 20.7% of early perimenopausal visits, 20.2% of late perimenopausal visits, 18.1% of postmenopausal visits, and 15.5% of postmenopausal visits when using HT. Analyses stratified by baseline anxiety indicated that among women with high anxiety at baseline; the percentage of visits with high anxiety linearly decreased from premenopause (71.4%) to postmenopause (30.0%). Whereas among women with low anxiety at baseline the percentage of visits with anxiety was higher during each stage (10.7%- 13.5%) of the menopausal transition than it was during premenopause (4.4%) and peaked during late perimenopause.

Menopausal stage and anxiety

In the basic model for the entire sample (Table 3, Model A), menopausal stage was significantly associated with high anxiety over 10 years of follow-up with each stage having significantly higher odds than the premenopausal stage (odds ratios (OR) ranging from 1.41 to 1.78, overall, p<.0001. The odds of high anxiety symptoms peaked in late perimenopause, but remained elevated in postmenopause with and without HT use, compared with the premenopause. The addition of health variables and stressors did not change the overall pattern of the ORs or the significance level (p-value) of menopause stage (except for postmenopausal HT users) although the odds ratios were attenuated (Table 3, Model B). With the addition of frequent VMS to the analysis menopausal stage was no longer significant overall (Table 3, Model C). In contrast, women reporting frequent VMS had nearly triple the odds of anxiety compared with women reporting less frequent VMS, and African-American and Chinese women were significantly less likely than white women (31% and 39%, respectively) to have high anxiety symptoms even after adjusting for VMS and other covariates.

To determine whether the impact of menopausal stage on high anxiety over 10 years differed between women with and without high baseline anxiety, an interaction term of menopausal stage with presence/absence of high baseline anxiety was added to the fully adjusted model for all women. Results showed that the interaction was significant at p=.001,

indicating that the odds of high anxiety during and after the menopausal transition differed between women with and without high baseline anxiety. Therefore, final results are based on separate analyses of these groups as described below and are shown in Tables 4 and 5.

Menopausal stage and anxiety in women without high baseline anxiety—All three models (Table 4 A,B,C) for women without high baseline anxiety showed that menopausal stage was significantly associated with odds of high anxiety (p's <.05) irrespective of the addition of health and stressor related factors (Table 4, Model B) and VMS (Table 4, Model C). Specifically, among women with low anxiety at baseline, compared to when they were premenopausal, odds ratios for high anxiety were significantly greater when they were early (OR = 1.58) or late perimenopausal (OR=1.61), postmenopausal (OR=1.56) or postmenopausal and using hormone therapy (OR=1.58) adjusted for health, stressor and VMS variables. VMS were also significantly associated with high anxiety with an odds ratio of 2.43.

Menopausal stage and anxiety in women with high baseline anxiety—For women who had high anxiety at baseline menopause stage was not significantly associated with high anxiety over 10 years in the basic model (Table 5, Model A), the model including health and stressor variables (Table 5, Model B) or the model including VMS (Table 5, Model C). In the basic model, ORs were elevated in later menopause stages by 20-44%, but were not significantly different from premenopause. The addition of health, stressor, and VMS variables reduced the ORs to close to 1.0. In contrast, frequent VMS were significantly associated with high anxiety with an odds ratio of 3.56.

Covariates: As shown in Table 4 and 5, education and number of medical conditions were not associated with high anxiety in either the high or low baseline anxiety groups,. Compared to excellent perceived health, fair/poor perceived health increased the risk for high anxiety by 3.8 in the baseline high anxiety group and 6.3 times in the baseline low anxiety group, and an upsetting event more than doubled the odds of high anxiety in both groups. In the low baseline anxiety group, the odds of psychotropic drug use and a hard time paying for basics were significantly associated with high anxiety during the study, and African American and Chinese women had significantly lower odds of high anxiety than white women.

DISCUSSION

In a large sample of middle aged women, we found that over 10 years of annual assessments, women who had low anxiety at baseline were significantly more likely to meet criteria for high anxiety symptoms when perimenopausal or postmenopausal compared to when they were premenopausal, independent of multiple risk factors, including upsetting life events, financial strain, fair/poor perceived health and VMS. However, among women who started the study with high anxiety, menopausal stage was not associated with high anxiety whether or not VMS were included in the analyses. Among women with high baseline anxiety (Table 2) there was a linear reduction in the percentage of women with high anxiety across the menopausal stages (71.4% to 30.0%), suggesting regression to the mean. Among women with low baseline anxiety, the percent of those who had high anxiety peaked in the late perimenopause (13.5%), then decreased during postmenopause (12.7%), and was significantly higher compared to when these women were premenopausal (4.6%) suggesting that this may be due to the effect of menopausal stage rather than regression to the mean. To our knowledge, no other study has examined the risk of high anxiety in subgroups of women.

Results for the entire sample were consistent with studies that showed individual anxiety symptoms were more strongly related to VMS than to the menopausal transition (5; 10). Other studies found that early or late perimenopausal women had significantly higher rates of anxiety symptoms than premenopausal women (6; 7) but these studies did not adjust for VMS. Of interest, the association of frequent VMS with high anxiety in the current study was significant for women with and without high anxiety at baseline but the odds were greater among the former women, 3.56 versus 2.43. For those without baseline high anxiety, both VMS and menopausal stage significantly increased the odds of high anxiety.

Given the differential impact of the menopausal transition in the two groups of women we studied, the women who entered the study with high anxiety may have had relatively chronic anxiety. We found that about 40-50% of these women had high anxiety at each annual visit and about half had three or more visits with high anxiety. In contrast, among the women with low baseline anxiety, about 11- 14% had high anxiety at each visit and 11% had three or more visits with high anxiety. As shown in Table 1 and noted above, the two groups of women were also different at baseline with the low anxiety women more likely to be Chinese or Japanese, have better socioeconomic and health characteristics, including fewer using psychotropic medications and reporting fewer frequent VMS, and less exposure to stressful events in the previous year. Thus, it appears that that the two groups of women may represent two different populations and that the menopausal transition may confer vulnerability to anxiety in women who are not typically anxious. Perhaps women who are more often or chronically anxious may be somewhat habituated to anxious feelings and less susceptible to the perturbations of the neuroactive steroids during the menopausal transition, other factors may override the effect of the transition, or there may be a ceiling effect due to measurement of anxiety, such that women with high baseline anxiety cannot become more anxious.

The current study has a number of strengths. To our knowledge, no other study has examined the risk of anxiety symptoms or syndromes during the menopausal transition separately for those who initially did and did not have high anxiety symptoms. We had 10 years of follow-up data available to evaluate changes in risk for high anxiety as women transitioned through the stages of menopause, independent of multiple menopausal, psychosocial and health factors that varied over time and were independently associated with anxiety. We used a cluster of anxiety symptoms that was highly correlated with a standard measure of Generalized Anxiety Disorder as the anxiety outcome rather than individual symptoms.

Study limitations should be considered when interpreting the results in this study. We did not have data on history of anxiety symptoms prior to study entry among the women who entered SWAN without anxiety. It is possible that they experienced such symptoms in the past and happened not to have them at the baseline assessment. However, the baseline characteristics of women with and without anxiety symptoms were significantly different, suggesting that those without symptoms represented a different population than did those with symptoms. Because the varying anxiety symptoms and full diagnostic criteria that define different anxiety disorders are not included in our measure of anxiety, caution should be taken in extrapolating the results herein to anxiety disorders themselves.

CONCLUSIONS

In conclusion, for a subset of women with low anxiety premenopausally, the risk for high anxiety was greater during or after the menopausal transition than prior to it, independent of frequent VMS and other established risk factors. However, among women with premenopausal anxiety, the risk of high anxiety remained high, irrespective of the

menopausal transition and frequent VMS with which it is consistently associated. The identification of a subgroup of women for whom the transition poses an increased risk of high anxiety points to the need for further research to determine the specific aspects of the transition that confer such vulnerability, the extent to which anxiety persists, and the history and circumstances of women who develop high anxiety. Additional research on midlife women who report high anxiety premenopausally is also warranted. The findings also have implications for clinicians, suggesting that it is useful for health care providers to obtain information from women presenting with high anxiety about its onset and duration as well as about bleeding patterns and VMS. Women with anxiety may benefit from treatment of the anxiety or referral to a mental health practitioner.

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Table 1

Baseline (BL) characteristics of all SWAN Participants and those with and without high baseline anxiety

		All Women n = 2956		Women with low BL anxiety n = 2304		Women with high BL anxiety n = 652	
BL variable		***n***	***col %***	***n***	***col %***	***n***	***col %***
Race/Ethnicity	*White*	*1407*	*(47.60)*	*1094*	*(47.48)*	*313*	*(48.01)*
	African American	*818*	*(27.67)*	*626*	*(27.17)*	*192*	*(29.45)*
	Chinese	*237*	*(8.02)*	*203*	*(8.81)*	*34*	*(5.21)*
	Hispanic	*221*	*(7.48)*	*144*	*(6.25)*	*77*	*(11.81)*
	Japanese	*273*	*(9.24)*	*237*	*(10.29)*	*36*	*(5.52)*
Education	*<=HS*	*694*	*(23.69)*	*505*	*(22.12)*	*189*	*(29.21)*
	Some college	*951*	*(32.46)*	*739*	*(32.37)*	*212*	*(32.77)*
	>= College	*1285*	*(43.86)*	*1039*	*(45.51)*	*246*	*(38.02)*
Paying for basics	*very hard*	*247*	*(8.41)*	*156*	*(6.82)*	*91*	*(14.02)*
	somewhat hard	*882*	*(30.02)*	*624*	*(27.26)*	*258*	*(39.75)*
	not hard at all	*1809*	*(61.57)*	*1509*	*(65.92)*	*300*	*(46.22)*
Vasomotor symptoms (Hot flash/night sweats)	*<6 days/past 2 weeks*	*2639*	*(89.28)*	*2147*	*(93.19)*	*492*	*(75.46)*
	6+ days/past 2 weeks	*317*	*(10.72)*	*157*	*(6.81)*	*160*	*(24.54)*
Menopausal Stage	*early*						
	perimenopause	*1325*	*(45.88)*	*977*	*(43.38)*	*348*	*(54.72)*
	premenopause	*1563*	*(54.12)*	*1275*	*(56.62)*	*288*	*(45.28)*
Psychotropic medication use	*no*	*2654*	*(90 06)*	*2141*	*(93.29)*	*513*	*(78.68)*
	yes	*293*	*(9.94)*	*154*	*(6.71)*	*139*	*(21.32)*
Perceived health	*excellent*	*649*	*(22.29)*	*564*	*(24.87)*	*85*	*(13.22)*
	very good	*1073*	*(36.86)*	*883*	*(38.93)*	*190*	*(29.55)*
	good	*822*	*(28.24)*	*599*	*(26.41)*	*223*	*(34.68)*
	fair/poor	*367*	*(12.61)*	*222*	*(9.79)*	*145*	*(22.55)*
Number of medical conditions							

		All Women n = 2956		Women with low BL anxiety n = 2304		Women with high BL anxiety n = 652	
BL variable		***n***	***col %***	***n***	***col %***	***n***	***col %***
	0	*1681*	*(60.62)*	*1383*	*(63.56)*	*298*	*(49.92)*
	1	*690*	*(24.88)*	*524*	*(24.08)*	*166*	*(27.81)*
	2+	*402*	*(14.50)*	*269*	*(12.36)*	*133*	*22.28*
At least 1 upsetting event in the past year							
	no	*1492*	*(50.68)*	*1284*	*(55.90)*	*208*	*(32.15)*
	yes	*1452*	*(49.32)*	*1013*	*(44.10)*	*439*	*(67.85)*
		mean	*SD*	*mean*	*SD*	*mean*	*SD*
Age		*46.33*	*2.69*	*46.38*	*2 69*	*46.18*	*2.68*

Except for age (p=.08), all ps <.0001

Note: All characteristics do not sum to total N in each of their respective columns (all, low baseline anxiety, high baseline anxiety) due to missing values. Percentages were calculated after excluding participants with missing data for each individual characteristic

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Table 2

Number (%) of visits with high anxiety at each menopausal stage for the total sample of women and separately for women with low and high baseline anxiety across ten years of follow up.

	Total	**Low anxiety at baseline**	**High anxiety at baseline**
	N (%) 23,532 visits	N (%) 18,744 visits	N (%) 4,788 visits
Premenopause	557 (15.6)	130 (4.4)	427 (71.4)
Early perimenopause	2073 (20.7)	834 (10.7)	1239 (56.3)
Late perimenopause	397 (20.2)	211 (13.5)	186 (46.4)
Postmenopause	1241 (18.1)	695 (12.7)	546 (39.4)
Postmenopause + hormone therapy	173 (15.5)	112 (12.3)	61(30.0)

Table 3

Results of Random Effect Logistic Regression Analyses for Odds of Anxiety from Baseline to Visit 10 for all Women (n=2956)

	OR (95% CI)		
	Model A	**Model B**	**Model C**
Age at baseline- m(sd)	0.95 (0.92-0.99)**	0.96 (0.93-1.00)*	0.96 (0.93-0.99)*
Menopause Stage (referent category: pre-menopause)	***	***	
early peri-menopause	1.41 (1.20-1.66)	1.33 (1.13-1.57)	1.22 (1.03-1.44)
late peri-menopause	1.78 (1.42-2.25)	1.66 (1.31-2.10)	1.19 (0.94-1.52)
Post menopause	1.64 (1.30-2.08)	1.48 (1.16-1.89)	1.18 (0.92-1.51)
Post menopause + Hormone Therapy	1.38 (1.01-1.88)	1.18 (0.86-1.62)	1.06 (0.77-1.46)
Race/Ethnicity (referent category: Caucasians)	*	**	**
African American	1.02 (0.80-1.29)	0.74 (0.59-0.93)	0.69 (0.55-0.86)
Chinese	0.54 (0.34-0.84)	0.56 (0.37-0.86)	0.61 (0.40-0.93)
Hispanic	1.64 (0.91-2.94)	1.11 (0.64-1.94)	1.18 (0.68-2.05)
Japanese	0.74 (0.48-1.15)	0.67 (0.44-1.01)	0.71 (0.47-1.07)
Education (referent category: < or = high school)	*		
some college	0.83 (0.65-1.06)	0.98 (0.78-1.24)	0.98 (0.78-1.23)
>=college	0.70 (0.55-0.89)	1.04 (0.82-1.32)	1.10 (0.87-1.39)
Psychotropic medication use		1.45 (1.23-1.70)***	1.39 (1.18-1.64)***
Perceived Health (referent category: excellent)		***	***
Very good		1.42 (1.18-1.71)	1.39 (1.16-1.67)
Good		2.43 (1.99-2.96)	2.36 (1.93-2.89)
Fair/poor		5.46 (4.32-6.89)	5.29 (4.18-6.68)
Number of Medical Conditions (referent category: no medical conditions)		*	*
1		1.15 (1.01-1.30)	1.12 (0.98-1.27)
2+		1.24 (1.07-1.44)	1.21 (1.04-1.40)
At least 1 upsetting event in past year		2.62 (2.36-2.90)***	2.56 (2.31-2.84)***
Paying for basics (referent category: not hard at all)		***	***
somewhat hard		1.81 (1.49-2.19)	1.81 (1.50-2.19)
very hard		2.56 (1.87-3.49)	2.44 (1.79-3.32)
VMS/Hot Flashes/night sweats			

	OR (95% CI)		
	Model A	**Model B**	**Model C**
6+ days/past 2 weeks			2.95 (2.62-3.31)***

All analyses adjusted for site and time.

Model A = Basic Model includes sociodemographic variables

Model B = Model includes health and stress related variables

Model C = Fully adjusted model includes VMS

* ps ≤ .05

** ps ≤ .008

*** ps < .0001

Table 4

Results of Random Effects Logistic Regression Models for Visits 1-10 for Women with Low Anxiety at Baseline (n=2304)

	OR (95% CI)		
	Model A	**Model B**	**Model C**
Age at baseline	0.93 (0.90-0.97)***	0.95 (0.91-0.99)**	0.95 (0.91-0.99)***
Menopause Stage (referent category: pre-menopause)	***	***	*
early peri-menopause	1.69 (1.29-2.23)	1.70 (1.29-2.25)	1.58 (1.19-2.09)
late peri-menopause	2.28 (1.63-3.19)	2.13 (1.51-3.00)	1.61 (1.14-2.28)
Post menopause	2.05 (1.45-2.90)	1.91 (1.35-2.72)	1.56 (1.09-2.22)
Post menopause + Hormone Therapy	1.97 (1.29-3.01)	1.76 (1.14-2.70)	1.58 (1.03-2.42)
Race/Ethnicity (referent category: Caucasians)		**	***
African American	0.91 (0.69-1.21)	0.68 (0.52-0.89)	0.65 (0.49-0.85)
Chinese	0.59 (0.35-0.98)	0.59 (0.36-0.97)	0.64 (0.40-1.05)
Hispanic	1.76 (0.82-3.81)	1.24 (0.59-2.60)	1.33 (0.64-2.77)
Japanese	0.90 (0.54-1.48)	0.73 (0.45-1.18)	0.75 (0.46-1.20)
Education (referent category: < or = high school)	**		
Some college	0.89 (0.66-1.19)	1.05 (0.79-1.38)	1.02 (0.77-1.35)
≥ college	0.68 (0.51-0.91)	0.96 (0.72-1.28)	1.00 (0.75-1.33)
Psychotropic medication use		1.35 (1.07-1.70)**	1.32 (1.04-1.66)**
Perceived health (referent category: excellent)		***	***
very good		1.37 (1.08-1.75)	1.35 (1.07-1.72)
good		2.61 (2.02-3.39)	2.56 (1.97-3.31)
fair/poor		6.33 (4.67-8.58)	6.09 (4.49-8.26)
Number of medical conditions (referent category: no medical conditions)			
1		1.00 (0.85-1.18)	0.98 (0.83-1.15)
2+		1.05 (0.86-1.27)	1.04 (0.85-1.26)
At least 1 upsetting event in the past year		2.76 (2.41-3.17)***	2.70 (2.36-3.10)***
Paying for basics at baseline (referent category: not hard at all)		***	***
somewhat hard		1.41 (1.12-1.77)	1.41 (1.13-1.78)
very hard		2.05 (1.39-3.02)	1.98 (1.34-2.91)
VMS/Hot flashes/night sweats			

	OR (95% CI)		
	Model A	**Model B**	**Model C**
6+ days/past 2 weeks			2.43 (2.09-2.84)***

All analyses adjusted for time and site.

* ps ≤ .05

** ps < .02

*** ps ≤ .008

Table 5

Results of Random Effects Logistic Regression Models for Visits 1-10 for Women with High Anxiety at Baseline (n=652)

	OR (95% CI)		
	Model A	**Model B**	**Model C**
Age at baseline	1.01 (0.94-1.07)	1.01 (0.94-1.07)	1.00 (0.93-1.07)
Menopause Stage (referent category: pre-menopause)			
early peri-menopause	1.24 (0.81-1.90)	1.13 (0.74-1.74)	0.99 (0.64-1.54)
late peri-menopause	1.44 (0.85-2.42)	1.39 (0.82-2.36)	0.93 (0.54-1.61)
Post menopause	1.20 (0.70-2.06)	1.08 (0.63-1.86)	0.80 (0.46-1.40)
Post menopause + Hormone Therapy	0.85 (0.44-1.65)	0.76 (0.39-1.48)	0.64 (0.32-1.26)
Race/Ethnicity (referent category: Caucasians)			
African American	1.10 (0.71-1.72)	0.90 (0.59-1.38)	0.75 (0.49-1.16)
Chinese	1.61 (0.62-4.21)	1.48 (0.59-3.74)	1.59 (0.62-4.08)
Hispanic	1.85 (0.70-4.88)	1.35 (0.53-3.48)	1.39 (0.53-3.61)
Japanese	1.19 (0.46-3.09)	1.13 (0.45-2.81)	1.26 (0.50-3.17)
Education (referent category: < or = high school)			
Some college	0.95 (0.61-1.50)	0.99 (0.64-1.53)	1.07 (0.69-1.66)
≥ college	1.11 (0.70-1.76)	1.25 (0.80-1.97)	1.39 (0.88-2.19)
Psychotropic medication use		1.11 (0.84-1.46)	1.05 (0.79-1.39)
Perceived health (referent category: excellent)		***	***
very good		1.51 (0.98-2.30)	1.45 (0.94-2.22)
good		1.94 (1.24-3.03)	1.88 (1.20-2.97)
fair/poor		3.81 (2.32-6.25)	3.76 (2.27-6.22)
Number of medical conditions (referent category: no medical conditions)			
1		1.33 (1.05-1.69)	1.28 (1.00-1.64)
2+		1.26 (0.96-1.65)	1.19 (0.91-1.57)
At least 1 upsetting event in the past year		2.29 (1.87-2.79)***	2.21 (1.80-2.71)***
Paying for basics at baseline (referent category: not hard at all)			
somewhat hard		1.24 (0.86-1.79)	1.26 (0.87-1.82)
very hard		1.49 (0.87-2.55)	1.47 (0.85-2.52)
VMS/Hot flashes/night sweats			

	OR (95% CI)		
	Model A	**Model B**	**Model C**
6+ days/past 2 weeks			3.56 (2.85-4.44)***

All analyses adjusted for time and site.

* ps ≤ .05

** ps < .02

*** ps ≤ .008