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Lifetime History of Depression and Anxiety Disorders Predicts Low Quality-of-Life in Midlife Women in the Absence of Current Illness Episodes

Hadine Joffe, MD MSc[a], **Yuefang Chang, PhD**[b], **Sammy Dhaliwal, MS**[c], **Rachel Hess, MD**[c,d], **Rebecca Thurston, PhD**[c,d], **Ellen Gold, PhD**[e], **Karen A Matthews, PhD**[c,d], and **Joyce T Bromberger, PhD**[c,d]

[a]Center for Women's Mental Health, Department of Psychiatry, Massachusetts General Hospital, Harvard Medical School

[b]Department of Neurosurgery, University of Pittsburgh

[c]Department of Epidemiology, Graduate School of Public Health

[d]Department of Psychiatry, University of Pittsburgh

[e]Division of Epidemiology, Department of Public Health Sciences, School of Medicine, University of California at Davis

Abstract

Context—It is unknown whether a previous history of depression, anxiety disorders, or comorbid depression and anxiety influences subsequent health-related quality-of-life (HRQL) during midlife in women when vasomotor symptoms (VMS) and sleep disturbance commonly disrupt quality-of-life.

Objective—We evaluated whether prior affective illness is associated with low HRQL during midlife in the absence of current illness episodes, and whether low HRQL is explained by VMS or sleep disruption.

Design—Longitudinal, community-based.

Setting—Western Pennsylvania.

Address for correspondence/reprint requests: Hadine Joffe, MD MSc, Center for Women's Mental Health, Massachusetts General Hospital, Simches Research Building, 185 Cambridge Street, Suite 2000, Boston MA 02114, (T) 617-724-1849, (F) 617-643-3080, hjoffe@partners.org.

Clinical Centers: *University of Michigan, Ann Arbor – MaryFran Sowers, PI*; *Massachusetts General Hospital, Boston, MA – Joel Finkelstein, PI 1999 – present*; *Robert Neer, PI 1994 – 1999; Rush University, Rush University Medical Center, Chicago, IL – Howard Kravitz, PI 2009 – present*; *Lynda Powell, PI 1994 – 2009; University of California, Davis/Kaiser – Ellen Gold, PI*; *University of California, Los Angeles – Gail Greendale, PI*; *Albert Einstein College of Medicine, Bronx, NY – Rachel Wildman, PI 2010; Nanette Santoro, PI 2004 – 2010; University of Medicine and Dentistry – New Jersey Medical School, Newark – Gerson Weiss, PI 1994 – 2004;* and the *University of Pittsburgh, Pittsburgh, PA – Karen Matthews, PI.*
NIH Program Office: *National Institute on Aging, Bethesda, MD – Sherry Sherman 1994 – present; Marcia Ory 1994 – 2001; National Institute of Nursing Research, Bethesda, MD – Project Officers.*
Central Laboratory: *University of Michigan, Ann Arbor – Daniel McConnell* (Central Ligand Assay Satellite Services).
Coordinating Center: *University of Pittsburgh, Pittsburgh, PA – Kim Sutton-Tyrrell, PI 2001 – present; New England Research Institutes, Watertown, MA - Sonja McKinlay, PI 1995 – 2001.*
Steering Committee: Susan Johnson, Current Chair
Chris Gallagher, Former Chair
Dr. Joffe had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
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Participants—425 midlife women in the Study of Women's Health Across the Nation who completed the SCID and SF-36 annually during 6-years of follow-up.

Outcome Measures—SF-36 scales of social functioning (SF), role-emotional (RE), role-physical (RP), body pain (BP), and vitality.

Results—97 (22.8%) women had comorbid affective illness histories, 162 (38.1%) had prior depression only, and 21 (4.9%) had prior anxiety only. Those with comorbid illness histories and depression alone were more likely to report low HRQL on SF, RE, RP, and BP domains (ORs=2.31–3.54 and 1.59–2.28, respectively) than women with neither disorder. After adjustment for VMS and sleep disturbance, the comorbid group continued to have low HRQL on these domains (ORs=2.13–3.07), whereas the association was significant on SF and BP only for the depression-alone group (ORs= 2.08, 1.95, respectively). Compared to women with neither disorder, the anxiety-only group had low HRQL on the RP domain (OR 2.60). Sleep disturbance, but not VMS, was independently associated with low HRQL on all domains except for RE.

Conclusions—A prior history of both depression and anxiety has the most robust negative effect on HRQL in women during midlife, an association not explained by VMS or sleep disturbance. For the depression-alone group, sleep disturbance may partially explain the negative impact of prior affective illness on HRQL. Sleep disturbance remains an independent correlate of low HRQL.

Background

Depression and anxiety disorders are each associated with compromised functioning and low quality-of-life.[1] Relative to those with depression alone or an anxiety disorder alone, individuals suffering from both a depressive disorder and an anxiety disorder have the greatest risk for impaired functioning when they are in an illness episode.[2, 3] A limited literature also suggests that those with a previous history of a depression disorder subsequently have low quality-of-life, with impairment in social and interpersonal functioning, even when they are not currently depressed.[4–7] However, little is known about the long-term influence of previous depression generally, and comorbid depression and anxiety in particular,[8] on quality-of-life among midlife women.

The National Comorbidity Survey found that by the time women reach midlife, approximately 23% have experienced at least one episode of major depression and 30% have been diagnosed with an anxiety disorder.[9] Therefore, a substantial number of women may be at risk for sequellae of prior affective illness during midlife, including low health-related quality-of-life (HRQL). In the absence of an active depression episode, women ages 42−52 with prior recurrent major depression are susceptible to low HRQL before they enter the menopause transition.[4] The menopause transition is itself associated with deleterious effects on selected domains of HRQL in some studies,[10–12] while others found that the association with menopause was explained by menopausal symptoms.[10] However, to what extent prior affective illness contributes to low HRQL independent of common menopause-related symptoms is not known. No studies have examined whether midlife women with prior affective illness are at greater risk for compromised HRQL, in the absence of recurrent illness episode, than those without prior depression and/or anxiety disorders.

The impact of prior affective illness on HRQL during midlife may be due to the association of depression and anxiety with common menopause-associated symptoms—vasomotor symptoms (VMS; 50–85% of women) and sleep disturbances (about 50% of women)—which are each associated with low HRQL.[11] In the absence of current depression, women with a history of depression or anxiety may be at increased risk for developing sleep disturbance and VMS during midlife.[13] Although less is known about the risk for menopause-related symptoms in women with histories of both anxiety and depression, it is

expected that such a history confers greater vulnerability to these symptoms than either disorder alone. Thus, given the prevalence of VMS and sleep disturbance and their deleterious impact on HRQL, it is plausible that they may in part explain the effect of prior affective illness on HRQL during midlife.[10]

In this study, we sought to determine if, in the absence of current illness episodes, midlife women who have histories of both depression and anxiety disorders, depression alone, or an anxiety disorder alone, are more susceptible to low HRQL than those with no prior history. We hypothesized that, compared to women with no prior history of affective illness, those with prior depression and/or anxiety would be more likely to report compromised HRQL during midlife and those with histories of both depression and anxiety would be most likely to experience low HRQL. We also hypothesized that associations between prior psychiatric illness and HRQL would be in part explained by the presence of VMS and sleep disruption, given evidence that these symptoms are more common in women with prior depression and anxiety and independently contribute to poor HRQL.

Methods

Study Participants and Procedures

This study was conducted among participants in the Pittsburgh site of the Study of Women's Health Across the Nation (SWAN), a multisite community-based cohort investigation of the menopause transition and aging in midlife women. SWAN study design and sampling procedures have been described previously.[14] Each site recruited Caucasian women and a predetermined minority group. The Pittsburgh site enrolled 162 African-American and 301 Caucasian women using random digit dialing and voter registration list recruitment methods. Eligibility criteria for SWAN included age 42−52 years, an intact uterus, at least one menstrual period in the previous 3 months, no use of reproductive hormones in the previous 3 months, and for the Pittsburgh site, self-identifying as Caucasian or African American. Approximately 50% of those eligible to participate in SWAN in Pittsburgh entered the SWAN study. SWAN participants did not differ from those who were eligible but declined to participate by race, marital status, parity, quality-of-life, social support or perceived stress. Written informed consent was obtained in accordance with the University of Pittsburgh Institutional Review Board guidelines.

Of 463 women enrolled in the Pittsburgh SWAN site, 443 (95.7%) participated in the SWAN ancillary Mental Health Study (MHS), which began concurrent with the SWAN parent study. There were no significant socio-demographic differences between the SWAN participants in Pittsburgh who did and did not participate in the SWAN MHS.

The Structured Clinical Interview for DSM-IV Axis I Disorders (SCID) was conducted at the SWAN MHS study entry to obtain information on previous lifetime psychiatric history and then annually during a 6-year follow-up period to establish the presence of current and interim psychiatric disorders occurring during the previous year. The first SCID was administered 2–9 months after the SWAN baseline assessment and then annually within three months of each SWAN visit. This paper focuses on 425 women who completed at least two psychiatric interviews (baseline plus one follow-up). The mean number of annual assessments completed per subject was 6.5 ± 1.3 out of a possible 7 (Table 2). Women completing only 2 SCIDs (n=13) did not differ from those who completed all assessments (n=333).

Measures

Assessment of Psychiatric Disorders—Diagnoses of lifetime, annual and current depressive and anxiety disorders were determined from interviews conducted by trained clinicians utilizing the SCID,[15, 16] a semi-structured psychiatric interview demonstrated to have good reliability.[15] All interviewers had extensive clinical experience, a mental-health graduate degree, and were trained to administer the SCID. Qualitative procedures were used to ensure consistency of SCID administration, including centralized training, monitoring for rater drift, and inter-rater reliability testing.

Baseline SCIDs assessed lifetime and current disorders; subsequent annual SCIDs assessed current disorders and those that occurred during the previous year. Women met criteria for *current depression* if they had major or minor depression during the past month, were in partial remission of an episode of major depression that began earlier, or had a current episode of dysthymia. A previous *history of depression* was defined as an episode of major or minor depression that occurred prior to the current visit and was in full remission during the past month. Anxiety disorders (panic disorder or attacks, agoraphobia, social phobia, generalized anxiety disorder, obsessive compulsive, anxiety NOS) were defined similarly.

Health-Related Quality-of-Life (HRQL)—Health-Related Quality-of-Life (HRQL) was assessed using the SF-36, a widely used HRQL measure, scored with the original coding algorithm in which raw scores are transformed to a 0–100 range.[17] The current study used five of the eight SF-36 HRQL domains: bodily pain, vitality, role limitations as a result of physical health, role limitations as a result of emotional problems, and social functioning. The scales have been shown to have good reliability and construct validity.[18, 19] The SF-36 scales were dichotomized using the 25th percentile of the sample as the cut point between good and poor functioning as previously established [18–20] because scores were highly skewed and we were particularly interested in predictors of impaired function.

Menopause Status—Based on SWAN eligibility requirements, all women were premenopausal or early perimenopausal at baseline. Consistent with the World Health Organization classification system,[21] menopause status for the previous 12 months was assigned at each assessment based on menstrual bleeding patterns during the previous year and was categorized as: (1) *premenopausal* if menstrual periods were present in the past 3 months and there was no change in regularity in the past 12 months; (2) *menopausal transition/perimenopausal* if menstrual periods were present in the past 3 months but changed in regularity over the previous 12 months (early perimenopause) or if there was menstrual bleeding within the past 12 months but not within the past 3 months (late perimenopausal); (3) *postmenopausal* if there was no menstrual period during the past 12 months or if the woman had undergone a hysterectomy with bilateral oöphorectomy, regardless of the duration of amenorrhea, or (4) *unknown status* if women had a hysterectomy without bilateral oöphorectomy or was using hormone therapy (HT) when pre- or perimenopausal because HT can affect bleeding patterns.

Vasomotor symptoms (VMS)—At each visit, participants reported the presence of hot flashes and night sweats (termed vasomotor symptoms or VMS) in the previous two weeks. VMS were coded as present if either hot flashes or night sweats were reported, and as frequent if they occurred on 6 or more days during this interval.

Sleep Disturbance—Information about sleep disturbance was collected annually using three sleep questions taken from the Women's Health Initiative scale.[22] Participants were asked how often in the past 2 weeks they experienced trouble falling asleep, waking up several times a night, and waking up earlier than planned without being able to fall asleep

again: (1) none, (2) <1 time a week, (3) 1−2 times a week, (4) 3−4 times a week, or (5) 5+ times a week. We defined sleep disturbance to be present if at least one of the three was reported to have occurred ≥3 times a week, consistent with the frequency criterion commonly used in insomnia research.[23, 24]

Covariates—Socio-demographic factors relevant to the current analyses included age, race, level of educational attainment, number of medical conditions (0, 1, or 2+), and use of mental-health treatment (psychotropic medications and/or psychotherapy/counseling). HT use at each visit was included as a separate covariate because HT users have been shown to have low HRQL relative to non-users.[25] At each visit, women indicated if they had experienced and were upset by one or more of 18 negative life events during the past year and in order to categorize women as having experienced at least one "very upsetting" event versus none/somewhat upsetting event for that interval.

Statistical analysis

Four anxiety/depression groups were defined based on the presence or absence of depression and/or anxiety disorders occurring prior to study entry or each annual visit during the 6-year prospective follow-up study period: 1) comorbid depression and anxiety, 2) depression only, 3) anxiety only, or 4) neither. Women who had lifetime histories of either disorder at baseline were always considered to have a past disorder. Women who did not have a lifetime history of either disorder at baseline, but met criteria for one or both of these between two annual visits, were considered to have a history of disorder from that visit forward. For example, a woman first diagnosed with an episode occurring between annual visits 2 and 3, would be categorized at visit 3 and thereafter as having a past disorder. If the episode occurred in the month prior to visit 3, it would be coded as current only and would not be categorized as past disorder until visit 4. Thus, at the end of 6 years, the final anxiety/depression groups reflect a cumulative indicator of prior disorders.

Initial analyses compared the characteristics at study entry of the four final groups using ANOVA and chi-square tests. Longitudinal associations between HRQL and prior lifetime history of depression and/or anxiety disorder were evaluated by separate repeated measure multi-level logistic regression models for each of the 5 HRQL outcomes. Preliminary analyses showed that 123 women met criteria for a current depression episode (new-onset or recurrent) and 85 women met criteria for a current anxiety disorder at one or more of the annual SCID assessments. Data for that study visit at which the mood or anxiety episode was present were excluded from analysis in order to ensure that HRQL measures were not influenced by current mood or anxiety episodes.

Models were first adjusted for age, race, menopause status, HT use, medical conditions, mental-health treatment, and upsetting life events. VMS and sleep disturbance were subsequently added separately and together to the models. Interactions of prior psychiatric history with VMS, sleep disturbance, and menopause status were examined. We also examined the relative influence of distant and proximal affective illness and single versus recurrent major depressive episodes on HRQL domains. Analyses were performed with SAS version 9.1.2 (SAS Institute, Cary, NC) and STATA version 9.2 (StataCorp, College Station, TX).

Results

Subject Characteristics

The mean age of participants at study entry was 46 years. One-third of the sample was African-American. The population was evenly divided between premenopausal and early

perimenopausal women. Forty percent of women reported VMS and one-third reported sleep disturbance prior to study entry (Table 1).

At the end of 6 annual follow-up visits, 97 (22.8%) subjects met lifetime criteria for both depression and anxiety disorders, 162 (38.1%) for depression disorders only, and 21 (4.9%) for anxiety disorders only. For those with depression and/or anxiety disorders recorded at any point up through the end of their study participation, the majority (82.2%) of women with a history of anxiety disorders also had a history of depression disorders, whereas only 37.5% of women with prior depression disorders also had a history of anxiety disorders.

Table 1 shows the baseline characteristics of the study population by final diagnostic group. Groups differed significantly by previous use of mental-health treatment, number of medical illnesses, and upsetting life events in the previous 12 months. There was no difference between groups in age, race, marital status, education or menopausal status. Women without a history of depression and/or anxiety disorders were less likely to have experienced VMS and sleep disturbance prior to study entry, symptoms that were reported most commonly by women who had already experienced both depression and anxiety disorders (52.6% and 43.3%, respectively).

Table 2 shows the characteristics of the study population at the end of the follow-up period by final diagnostic group. The number of annual assessments during which SCID interviews were conducted did not differ between groups (p=0.70). At their final assessment, few women (5.2%) remained premenopausal; the majority were perimenopausal or postmenopausal (41.5% and 44.4%, respectively), and the rest (9%) were of undetermined menopause status, primarily because they had started using HT prior to their final menstrual period or they had undergone a hysterectomy without bilateral oöphorectomy. The proportion that was not yet postmenopausal did not differ between groups. HT was used by 31.1% of women at some point during the study, but this proportion did not differ between groups. Overall, 81.6% of all study participants experienced VMS and 70.1% reported sleep disturbance during follow-up, with those women who had no history of affective illness least likely to report these symptoms. Women with a history of comorbid affective illness were most likely to experience at least two lifetime major depressive episodes and to seek mental-health treatment and report a medical illness during the study.

Association of Depression, Anxiety, and a Combined History of Depression and Anxiety Disorders with Quality-of-Life

Multivariate adjusted models were used to determine the associations of prior comorbid anxiety/depression disorders, depression disorders, and anxiety disorders with HRQL during follow-up. After adjusting for potential confounders (age, race, menopause status, HT use, medical conditions, mental-health treatment, and upsetting life events), there was a strong association between a comorbid history of prior depression and anxiety and of prior depression alone with low HRQL (Table 3, Model A). Women with a history of comorbid disease and depression disorders alone had worse HRQL in all SF-36 domains (ORs range 2.31–3.54 and 1.59–2.28, respectively) except for vitality. In general, the magnitude of the association between a comorbid depression/anxiety disorder history and HRQL was larger than that for depression alone. Further adjustment for a history of recurrent major depression attenuated the association between prior affective illness and low HRQL on selected domains for the comorbid group, with associations becoming trends for role-emotional (p=0.076) and role-physical (p=0.062), and losing significance for body pain, but remaining significant for social functioning. The significant association of depression alone with low HRQL was preserved for all domains except role-physical (p=0.079, trend). Recurrent depression was independently associated with low HRQL only on the role-physical and body pain domains.

A lifetime history of an anxiety disorder alone was significantly associated with low HRQL on the role-physical domain, and the OR on other SF-36 domains (social functioning, body pain, and vitality) were increased, but not statistically significant. Post-hoc pairwise comparisons of the depression and anxiety groups revealed no significant differences in HRQL between groups. Menopause status was not associated with HRQL in unadjusted or adjusted models, and there were no interactions between menopause status and prior affective illness.

Impact of Adjustment for Vasomotor Symptoms and Sleep Disruption on the Association between Lifetime Histories of Depression and/or Anxiety Disorders with Quality-of-Life

VMS and sleep disruption were added separately and then jointly to the adjusted multivariate models to determine if they explained the association between prior psychiatric illness and HRQL. For women with a history of depression and anxiety, associations between psychiatric history and HRQL were not altered by further adjustment for current VMS alone (Table 3, Model B), current sleep disturbance alone (Table 3, Model C), or concurrent adjustment for both symptoms (Table 3, Model D), with associations between prior comorbid psychiatric history and low HRQL remaining statistically significant for all SF-36 scales. Adjustment for VMS alone (Table 3, Model B), sleep disturbance alone (Table 3, Model C), and both symptoms together (Table 3, Model D) attenuated the association of prior depression with several HRQL domains. Associations between prior depression alone and low HRQL remained strong for the social functioning and body pain domains, and became non-significant for the role-emotional and role-physical domains. There was no significant interaction of prior affective illness with VMS or sleep disturbance ($p \geq 0.12$ for all interactions). Results of parallel analyses examining the impact of adjusting for frequent *vs.* infrequent/no VMS were consistent with analyses adjusting for presence *vs.* absence of VMS.

For women with a history of anxiety disorders alone, adjustment for VMS and/or sleep disturbance did not alter the significant negative association between prior psychiatric illness and the role-physical domain, nor were the ORs for the associations with social functioning, body pain, and vitality substantially reduced (Table 3, Model B,C,D). As confirmation of the findings for the anxiety-alone group, models restricted to a two-group comparison between the anxiety-alone and no prior affective illness groups similarly showed an association between prior anxiety alone and the role-physical domain in the fully adjusted model (OR 2.80, 0.98–8.00, p=0.054).

The association with low HRQL during midlife was observed for all women with prior depression and/or anxiety compared to those with neither, irrespective of the timing of episodes, whether affective illness episodes occurred only before, only during, or both prior to and during the study. For example, the associations between depression and anxiety occurring only prior to midlife were significant for HRQL domains of social functioning, role-physical, and body pain (OR range 2.08–2.64; $p \leq 0.02$), and there was a statistical trend for the role-emotional domain (OR 1.74, p=0.059). Adjusting for VMS and sleep disturbance did not alter these associations.

Association of Vasomotor Symptoms and Sleep Disruption with Quality-of-Life

In unadjusted models, low HRQL was strongly associated with VMS (OR range 1.43–1.90; $p<0.05$ for all HRQL domains except role-physical) and sleep disturbance (OR range 2.04–2.96; $p<0.05$ for all HRQL domains). In models that adjusted for psychiatric illness history, VMS, sleep disturbance, and other potential confounders (age, race, menopause status, HT use, upsetting life events, medical illness, and mental-health treatment), perceived sleep

disturbance had independent associations with low HRQL across all domains except role-emotional (Table 3, Model D), whether or not VMS was included as a covariate.

In contrast to the strong independent association between sleep disturbance and low HRQL, the association between VMS and HRQL was less robust. After adjusting for prior psychiatric illness and other potential confounders, VMS was significantly associated only with low HRQL in the social functioning and role-emotional domains (Table 3, Model B). After further adjustment for sleep disturbance, the independent effect of VMS on HRQL remained only for the role-emotional domain. Results of analyses categorizing VMS into frequent *vs.* infrequent/none were consistent with those that classified VMS as present *vs.* absent. Frequent VMS was independently associated with low HRQL only on the vitality domain, while an association between sleep disturbance and low HRQL was seen for all HRQL domains (OR range 1.73–2.08), except role-emotional (p=0.096, trend).

Discussion

Results of this study show that, in the absence of a current illness episode, women with previous histories of both depression and anxiety disorders, and those with prior depression only, are at risk for compromised quality-of-life in multiple domains during midlife, whereas a previous history of anxiety disorders alone appears to have a more limited impact on HRQL. The negative impact of a combined history of depression and anxiety disorders on subsequent HRQL was not explained by the experience of VMS or sleep disturbance, which are known to reduce quality-of-life and to occur more frequently among those with prior depression and anxiety. Our findings for women with prior depression alone suggest that sleep disturbance appears to partially explain the negative effect of prior depression on selected HRQL domains. After adjusting for prior affective illness, sleep disturbance, but not VMS, was a significant and independent predictor of low HRQL in midlife women.

These study results derive from a 6-year longitudinal follow-up of 425 Caucasian and African-American women participating in the community-based SWAN study in Pittsburgh who were followed annually with SCID-rated psychiatric interviews. To our knowledge, our study is the first to examine quality-of-life longitudinally in midlife women who previously had depression and/or anxiety disorders but were not currently experiencing an episode of depression or anxiety. The magnitude and pervasive nature of the deleterious effects of prior depression on HRQL in the absence of current illness is striking. While recurrence of major depression in the comorbid disease group may explain in part the especially strong association between prior comorbid affective illness and low HRQL in midlife, the association between prior affective illness and low HRQL was observed even among women who had only experienced affective illness episodes prior to study enrollment. These findings suggest that prior depression, with or without prior anxiety, has an enduring impact on subsequent quality-of-life and/or that the constitutional make-up of those who experience mental illness confers a vulnerability to poor HRQL during midlife.

Our results also indicate that women with prior anxiety alone may not share the same broad susceptibility to poor quality-of-life during midlife, as a statistically significant association was seen only with the role-physical domain. However, the absence of statistical significance on other HRQL domains may be due to the small size of this anxiety disorder group (n=21). Future studies involving a larger number of women with histories of anxiety disorders but not depression are needed to fully examine the specific influence of previous anxiety on subsequent quality-of-life in midlife women.

The pathways through which prior affective illness confers susceptibility to low overall HRQL in midlife women are unknown. Consistent with other studies,[10] we found that

specific stages of the menopause transition were not associated with low HRQL. Given that common menopause-related symptoms of VMS and sleep disturbance are more frequently reported in women with prior depressive or anxiety symptoms,[13] and that both symptoms correlate with low quality-of-life, we hypothesized that the experience of these symptoms would in part explain the association between prior affective illness and low HRQL during midlife. However, neither sleep disturbance nor VMS explained the robust association between prior comorbid affective illness history and poor HRQL, whereas for women with prior depression alone, our results suggest that the presence of sleep disturbance, but not VMS, may partially explain the association with poor HRQL. The absence of significant interactions between prior affective illness and sleep disturbance indicates that the effect of each predictor is independent and not increased by the presence of both.

Consistent with previous studies conducted during midlife,[10] and other life stages, we observed that sleep disturbance has a strong association with low quality-of-life. However, in contrast with other studies,[10] we did not observe a broad association between VMS and multiple domains of HRQL in adjusted models, but only an independent association between VMS and the role-emotional domain. Therefore, while VMS may be associated with compromised quality-of-life,[10] after accounting for the effect of prior depression and/or anxiety disorders, the association is substantially reduced. Taken together, these findings suggest that disturbed sleep, but not VMS or specific menopause stage status, has a robust and independent association with low quality-of-life, even in the absence of a current affective illness episode among those with and without prior affective illness.

This study has notable strengths and several limitations. Important strengths are its large size overall and that of the group with comorbid depression and anxiety, which enabled us to distinguish the HRQL burden for women who previously experienced both depression and anxiety disorders from those with prior depression alone. We were also able to determine whether prior affective illness showed an independent association with low HRQL, in the absence of a current disorder which compromises functioning. Other strengths include the long-term follow-up and racial composition of the study population, of which one-third was African-American women.

Limitations of this study include the small size of the anxiety-alone group and that, while the overwhelming majority of women had become perimenopausal, not all participants became postmenopausal before the study end. However, most women had the opportunity to develop VMS and sleep disturbance, symptoms that peak in midlife women during perimenopause,[26, 27] and the statistical approach used to analyze these data allowed women to contribute data for variable times corresponding to their menopausal stage at each assessment. Another limitation is that all SWAN and SCID data were collected annually. However, misclassification bias is unlikely to have occurred in the assessment of current illness episodes, for which data were excluded from analysis for that period of observation in order to avoid confounding of low HRQL with current or recent affective illness. Finally, while VMS frequency data were available, we do not have data describing the severity or bothersomeness of VMS, limiting our ability to discern whether severe and/or bothersome VMS contributed independently to low HRQL.

In summary, in the absence of an acute illness episode, women with a previous history of both depression and anxiety disorders have the greatest risk for low quality-of-life during midlife. This effect is not explained by an increased vulnerability to menopause-related symptoms of VMS and sleep disturbance, which are known to reduce quality-of-life. Sleep disturbance has a strong effect on reducing quality-of-life, and may in part explain why women with prior depression only are also susceptible to experiencing compromised quality-of-life during midlife. The pathways through which the prior affective illness

influences subsequent HRQL among midlife women remain largely unknown and warrant further research. Midlife women with a prior history of affective illness should be monitored during the menopause transition because of their increased risk for recurrence of depression, emergence of VMS and sleep disturbance, and, in the absence of an acute illness episode, impairment of quality-of-life.

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References

1. Bijl RV, Ravelli A. Current and residual functional disability associated with psychopathology: findings from the Netherlands Mental Health Survey and Incidence Study (NEMESIS). Psychol Med. 2000 May; 30(3):657–668. [PubMed: 10883720]
2. Frank LB, Matza LS, Revicki DA, Chung JY. Depression and health-related quality of life for low-income African-American women in the U.S. Qual Life Res. 2005 Dec; 14(10):2293–2301. [PubMed: 16328908]
3. Mittal D, Fortney JC, Pyne JM, Edlund MJ, Wetherell JL. Impact of comorbid anxiety disorders on health-related quality of life among patients with major depressive disorder. Psychiatr Serv. 2006 Dec; 57(12):1731–1737. [PubMed: 17158487]
4. Bromberger JT, Kravitz HM, Wei HL, Brown C, Youk AO, Cordal A, Powell LH, Matthews KA. History of depression and women's current health and functioning during midlife. Gen Hosp Psychiatry. May-Jun;2005 27(3):200–208. [PubMed: 15882767]
5. Coryell W, Scheftner W, Keller M, Endicott J, Maser J, Klerman GL. The enduring psychosocial consequences of mania and depression. Am J Psychiatry. 1993 May; 150(5):720–727. [PubMed: 8480816]
6. Mojtabai R. Residual Symptoms and Impairment in Major Depression in the Community. Am J Psychiatry. 2001 Oct 1; 158(10):1645–1651. 2001. [PubMed: 11578997]
7. Petty SC, Sachs-Ericsson N, Joiner TE. Interpersonal functioning deficits: temporary or stable characteristics of depressed individuals? Journal of Affective Disorders. 2004; 81(2):115–122. [PubMed: 15306136]
8. Roy-Byrne PP, Stang P, Wittchen HU, Ustun B, Walters EE, Kessler RC. Lifetime panic-depression comorbidity in the National Comorbidity Survey. Association with symptoms, impairment, course and help-seeking. Br J Psychiatry. 2000 Mar.176:229–235. [PubMed: 10755069]
9. Kessler RC, McGonagle KA, Zhao S, Nelson CB, Hughes M, Eshleman S, Wittchen H-U, Kendler KS. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States: Results from the National Comorbidity Study. Arch Gen Psychiatry. 1994; 51:8–19. [PubMed: 8279933]
10. Avis NE, Colvin A, Bromberger JT, Hess R, Matthews KA, Ory M, Schocken M. Change in health-related quality of life over the menopausal transition in a multiethnic cohort of middle-aged women: Study of Women's Health Across the Nation. Menopause. 2009 May 8; 16(5):860–869. [PubMed: 19436224]
11. Avis NEP, Ory MP, Matthews KAP, Schocken MP, Bromberger JP, Colvin AMPHp. Health-Related Quality of Life in a Multiethnic Sample of Middle-Aged Women: Study of Women's Health Across the Nation (SWAN). Medical Care. 2003; 41(11):1262–1276. [PubMed: 14583689]
12. Mishra G, Kuh D. Perceived change in quality of life during the menopause. Social Science & Medicine. 2006; 62(1):93–102. [PubMed: 15990213]

13. Freeman EW, Sammel MD, Lin H. Temporal associations of hot flashes and depression in the transition to menopause. Menopause. 2009 Jul-Aug;16(4):728–734. [PubMed: 19188849]

14. Sowers, MF.; Crawford, SL.; Sternfeld, B.; Morgenstein, D.; Gold, EB.; Greendale, GA.; Evans, D.; Neer, R.; Matthews, K.; Sherman, S.; Lo, A.; Weiss, G.; Kelsey, J. SWAN: a multi-center, multi-ethnic, community-based cohort study of women and the menopause. In: Lobo, R.; Kelsey, J.; Marcus, R.; Kelsey, J., editors. Menopause: Biology and Pathobiology. San Diego, CA: Academic Press; 2000. p. 175-178.

15. Spitzer RL, Williams JB, Gibbon M, First MB. The Structured Clinical Interview for DSM-III-R (SCID). I: History, rationale, and description. Arch Gen Psychiatry. 1992 Aug; 49(8):624–629. [PubMed: 1637252]

16. Williams JB, Gibbon M, First MB, Spitzer RL, Davies M, Borus J, Howes MJ, Kane J, Pope HG Jr, Rounsaville B. The Structured Clinical Interview for DSM-III-R (SCID). II Multisite test-retest reliability. Arch Gen Psychiatry. 1992; 49(8):630–636. [PubMed: 1637253]

17. Ware JE, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care. 1992; 30(6):473–483. [PubMed: 1593914]

18. Brazier JE, Harper R, Jones NM, O'Cathain A, Thomas KJ, Usherwood T, Westlake L. Validating the SF-36 health survey questionnaire: new outcome measure for primary care. BMJ. 1992 Jul 18; 305(6846):160–164. [PubMed: 1285753]

19. McHorney CA, Ware JE Jr, Lu JF, Sherbourne CD. The MOS 36-item Short-Form Health Survey (SF-36): III. Tests of data quality, scaling assumptions, and reliability across diverse patient groups. Med Care. 1994 Jan; 32(1):40–66. [PubMed: 8277801]

20. Rose MS, Koshman ML, Spreng S, Sheldon R. Statistical issues encountered in the comparison of health-related quality of life in diseased patients to published general population norms: problems and solutions. J Clin Epidemiol. 1999 May; 52(5):405–412. [PubMed: 10360335]

21. Group WHOS. Research on the Menopause in the 1990's. Vol WHO Technical Report Series 866. Geneva, Switzerland: World Health Organization; 1996.

22. Levine DW, Kaplan RM, Kripke DF, Bowen DJ, Naughton MJ, Shumaker SA. Factor structure and measurement invariance of the Women's Health Initiative Insomnia Rating Scale. Psychol Assess. 2003 Jun; 15(2):123–136. [PubMed: 12847773]

23. Edinger JD, Bonnet MH, Bootzin RR, Doghramji K, Dorsey CM, Espie CA, Jamieson AO, McCall WV, Morin CM, Stepanski EJ. Derivation of research diagnostic criteria for insomnia: report of an American Academy of Sleep Medicine Work Group. Sleep. 2004 Dec 15; 27(8):1567–1596. [PubMed: 15683149]

24. Lichstein KL, Durrence HH, Taylor DJ, Bush AJ, Riedel BW. Quantitative criteria for insomnia. Behav Res Ther. 2003 Apr; 41(4):427–445. [PubMed: 12643966]

25. Hess R, Colvin A, Avis NE, Bromberger JT, Schocken M, Johnston JM, Matthews KA. The impact of hormone therapy on health-related quality of life: longitudinal results from the Study of Women's Health Across the Nation. Menopause. May-Jun;2008 15(3):422–428. [PubMed: 18467950]

26. Gold EB, Colvin A, Avis N, Bromberger J, Greendale GA, Powell L, Sternfeld B, Matthews K. Longitudinal analysis of the association between vasomotor symptoms and race/ethnicity across the menopausal transition: Study of women's health across the nation. Am J Public Health. 2006 Jul; 96(7):1226–1235. [PubMed: 16735636]

27. Kravitz HM, Zhao X, Bromberger JT, Gold EB, Hall MH, Matthews KA, Sowers MR. Sleep disturbance during the menopausal transition in a multi-ethnic community sample of women. Sleep. 2008 Jul 1; 31(7):979–990. [PubMed: 18652093]

Table 1

Characteristics at baseline for 425 midlife women participating in SWAN Pittsburgh Mental Health Study according to cumulative depression and anxiety disorder status at final annual study visit

	All (N=425)	Ever lifetime depressive and anxiety disorder (N=97, 22.8%)	Ever lifetime depressive disorder (N=162, 38.1%)	Ever lifetime anxiety disorder (N=21, 4.9%)	Never lifetime depressive or anxiety disorder (N=145, 34.1%)
Age (mean, SD)	45.6 (2.5)	45.0 (2.4)	45.8 (2.4)	45.2 (2.2)	45.7 (2.7)
Race, N (%)					
Caucasian	278 (65.4)	66 (68.0)	107 (66.0)	15 (71.4)	90 (62.1)
African-American	147 (34.6)	31 (32.0)	55 (34.0)	6 (28.6)	55 (37.9)
Marital status, N (%)					
Married	281 (66.1)	66 (68.0)	96 (59.3)	14 (66.7)	105 (72.4)
Never married	54 (12.7)	9 (9.3)	22 (13.6)	3 (14.3)	20 (13.8)
Separated/widowed/Divorced	90 (21.2)	22 (22.7)	44 (27.1)	4 (19.0)	20 (13.8)
Employed, N (%)	364 (85.6)	78 (80.4)	139 (85.8)	19 (90.5)	128 (88.3)
Education status, N (%)					
High school or less	100 (23.5)	18 (18.5)	30 (18.5)	9 (42.9)	43 (29.7)
Some college	158 (37.2)	35 (36.1)	69 (42.6)	7 (33.3)	47 (32.4)
College graduate	72 (16.9)	21 (21.7)	27 (16.7)	2 (9.5)	22 (15.2)
More than college	95 (22.4)	23 (23.7)	36 (22.2)	3 (14.3)	33 (22.8)
Menopause status, N (%)					
Premenopausal	224 (52.7)	50 (51.6)	82 (50.6)	10 (47.6)	82 (56.6)
Early perimenopausal	201 (47.3)	47 (48.4)	80 (49.4)	11 (52.4)	63 (43.4)
Lifetime history of depression or anxiety prior to study entry, N (%) **	220 (51.8)	88 (90.7)	121 (74.7)	11 (52.4)	N/A
Upsetting life event, N (%) ≠	222 (52.4)	62 (63.9)	95 (58.6)	7 (33.3)	58 (40.3)
Medical illness prior to study entry, N (%) €					
None	136 (32.0)	22 (22.7)	47 (29.0)	8 (38.1)	59 (40.7)
One	143 (33.6)	32 (33.0)	53 (32.7)	7 (33.3)	51 (35.2)
Two or more	146 (34.4)	43 (44.3)	62 (38.3)	6 (28.6)	35 (24.1)
Mental health treatment prior to study entry, N (%) **a	187 (44.0)	68 (70.1)	89 (54.9)	4 (19.1)	26 (17.9)

	All (N=425)	Ever lifetime depressive and anxiety disorder (N=97, 22.8%)	Ever lifetime depressive disorder (N=162, 38.1%)	Ever lifetime anxiety disorder (N=21, 4.9%)	Never lifetime depressive or anxiety disorder (N=145, 34.1%)
VMS at study entry, N (%) *	172 (40.6)	51 (52.6)	69 (42.6)	8 (38.1)	44 (30.6)
Sleep disturbance at study entry, N (%) †	132 (31.1)	42 (43.3)	50 (30.9)	6 (28.6)	34 (23.4)

VMS = vasomotor symptoms, defined as report of hot flashes and/or night sweats during the previous 2 weeks.

Sleep disturbance is defined categorically as trouble falling asleep, waking up several times at night, and/or waking up earlier than planned and unable to fall asleep again for ≥3 nights per week during previous 2 weeks

*p=0.007,

†p=0.013,

‡p=0.0002,

**p<0.0001,

€p=0.02 between-group differences.

[a]Mental health treatment includes use of psychotropic medications and/or psychotherapy/counseling.

Table 2

Characteristics at final annual study visit for 425 midlife women participating in SWAN Pittsburgh Mental Health Study according to cumulative depression and anxiety disorder status

	All (N=425)	Ever lifetime depressive and anxiety disorder (N=97, 22.8%)	Ever lifetime depressive disorder (N=162, 38.1%)	Ever lifetime anxiety disorder (N=21, 4.9%)	Never lifetime depressive or anxiety disorder (N=145, 34.1%)
Age (mean, SD)	51.3 (2.8)	50.6 (2.7)	51.4 (2.6)	50.8 (3.4)	51.6 (3.0)
Number of SCID assessments/annual visits (mean, SD)	6.5 (1.3)	6.5 (1.2)	6.5 (1.2)	5.9 (1.9)	6.5 (1.3)
Menopause status, N (%)					
Premenopausal	22 (5.2)	6 (6.2)	6 (3.7)	1 (4.8)	9 (6.2)
Early perimenopausal	129 (30.4)	33 (34.0)	52 (32.1)	6 (28.6)	38 (26.2)
Late perimenopausal	47(11.1)	10 (10.3)	15 (9.3)	3 (14.3)	19 (13.1)
Natural postmenopause	151(35.5)	27 (27.8)	64 (39.5)	5 (23.8)	55 (37.9)
Surgical postmenopause	38 (8.9)	11 (11.3)	12 (7.4)	6 (28.6)	9 (6.2)
Cannot determine	38 (8.9)	10 (10.3)	13 (8.0)	0	15 (10.3)
Episode of depression and/or anxiety during study, N (%) †	160 (37.6)	82 (84.5)	61 (37.7)	11 (52.4)	N/A *b*
Lifetime number of episodes of major depression, N (%) €					
One	71 (27.4)	19 (19.6)	52 (32.1)		
Two or more	121 (46.7)	58 (59.8)	63 (38.9)	N/A	N/A
Minor depression only	67 (25.9)	20 (20.6)	47 (29.0)		
Mental health treatment during study, N (%) † *a*	155 (36.5)	63 (65.0)	65 (40.1)	5 (23.8)	22 (15.2)
Upsetting life event during study, N (%) †	376 (88.5)	92 (94.9)	151 (93.2)	19 (90.5)	114 (78.6)
Medical illness during study, N (%) ‡					
None	118 (27.8)	20 (20.6)	41 (25.3)	7 (33.3)	50 (34.5)
One	135 (31.8)	28 (28.9)	51 (31.5)	5 (23.8)	51 (35.2)
Two or more	172 (40.5)	49 (50.5)	70 (43.2)	9 (42.9)	44 (30.3)
VMS during study, N (%) *	347 (81.6)	87 (89.7)	135 (83.3)	14 (66.7)	111 (76.6)
Sleep disturbance during study, N (%) **	298 (70.1)	77 (79.4)	120 (74.1)	16 (76.2)	85 (58.6)

VMS = vasomotor symptoms, defined as report of hot flashes and/or night sweats during the previous 2 weeks.

Sleep disturbance is defined categorically as trouble falling asleep, waking up several times at night, and/or waking up earlier than planned and unable to fall asleep again for ≥3 nights per week during previous 2 weeks

[a] Mental health treatment includes use of psychotropic medications and/or psychotherapy/counseling.

[b] 6 women had a single episode of a depressive or anxiety disorder during the 6-year follow-up and no prior history of depression or anxiety episodes before study entry. Because data from visits during an active illness episode were not included in the model, these women contributed data only for visits when they did not have a depression/anxiety episode and they are therefore included in the group that never had a lifetime episode of a depressive or anxiety disorder.

Between-group differences:

[*] p=0.017,

[**] p=0.002,

[†] p<0.0001,

[‡] p=0.054,

[€] p=0.005 (depression and anxiety group *vs.* depression-alone group; data available for the number of discrete episodes of major depressive disorder, but not minor depression or anxiety disorders).

Table 3

Effect of cumulative lifetime history of depression and/or anxiety disorders, depression only, anxiety only on quality-of-life, as measured by SF-36 outcomes for repeated measured analysis during a 6-year follow-up of 425 midlife women participating in the SWAN Pittsburgh ancillary Mental Health Study.

	Social Functioning		Role-Emotional		Role-Physical		Body Pain		Vitality	
	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI
A) Basic model[a]										
No depression or anxiety	1.0		1.0		1.0		1.0		1.0	
Both depression and anxiety	3.54	(1.85, 6.77) ≠	2.48	(1.32, 4.67) ¥	2.35	(1.18, 4.67) *	2.31	(1.21, 4.40) *	1.27	(0.66, 2.45)
Depression only Anxiety only	2.28	(1.40, 3.71) ≠	1.59	(0.99, 2.56)*	1.71	(1.03, 2.82) *	2.03	(1.27, 3.24) ¥	1.45	(0.89, 2.34)
Anxiety only	2.26	(0.90, 5.66)	1.02	(0.37, 2.81)	2.72	(1.08, 6.83) *	2.05	(0.82, 5.12)	2.01	(0.82, 4.93)
B) Basic model[a] + VMS										
No depression or anxiety	1.0		1.0		1.0		1.0		1.0	
Both depression and anxiety	3.29	(1.72, 6.29) ≠	2.22	(1.20, 4.10) †	2.27	(1.14, 4.53) *	2.24	(1.18, 4.26) *	1.21	(0.62, 2.33)
Depression only	2.20	(1.35, 3.59) ¥	1.51	(0.95, 2.39)	1.68	(1.02, 2.78) *	2.01	(1.26, 3.20) ¥	1.42	(0.88, 2.30)
Anxiety only	2.27	(0.91, 5.67)	1.00	(0.37, 2.71)	2.71	(1.08, 6.83) *	2.04	(0.82, 5.09)	2.00	(0.82, 4.92)
VMS (yes/no)	1.47	(1.00, 2.17) *	1.66	(1.12, 2.44) †	1.2	(0.81, 1.77)	1.21	(0.86, 1.71)	1.39	(0.99, 1.94)
C) Basic model[a]+ sleep disturbance										
No depression or anxiety	1.0		1.0		1.0		1.0		1.0	
Both depression and anxiety	3.24	(1.70, 6.20) ≠	2.37	(1.26, 4.47) †	2.17	(1.08, 4.33) *	2.21	(1.16, 4.19) *	1.17	(0.61, 2.27)
Depression only	2.13	(1.31, 3.47 ¥	1.55	(0.96, 2.48)	1.61	(0.97, 2.65)	1.96	(1.23, 3.13) ¥	1.36	(0.84, 2.20)
Anxiety only	2.15	(0.86, 5.38)	0.99	(0.36, 2.72)	2.6	(1.03, 6.56) *	1.97	(0.79, 4.90)	1.94	(0.79, 4.75)
Sleep disturbance	1.98	(1.33, 2.93) ≠	1.42	(0.95, 2.12)	1.88	(1.27, 2.81) ¥	1.76	(1.24, 2.50) ¥	2.23	(1.56, 3.13) ≠
D) Basic model[a]+ VMS + sleep disturbance										
No depression or anxiety	1.0		1.0		1.0		1.0		1.0	
Both depression and anxiety	3.07	(1.60, 5.88) ≠	2.14	(1.16, 3.98)*	2.13	(1.06, 4.26) *	2.17	(1.14, 4.12) *	1.14	(0.59, 2.20)
Depression only	2.08	(1.28, 3.40 ¥	1.48	(0.93, 2.34)	1.59	(0.96, 2.64)	1.95	(1.22, 3.11) ¥	1.34	(0.83, 2.17)
Anxiety only	2.16	(0.86, 5.40)	0.98	(0.36, 2.63)	2.6	(1.03, 6.55) *	1.96	(0.79, 4.89)	1.93	(0.79, 4.76)
VMS (yes/no)	1.36	(0.92, 2.02)	1.6	(1.08, 2.36)*	1.1	(0.74, 1.64)	1.12	(0.79, 1.58)	1.24	(0.89, 1.75)

	Social Functioning		Role-Emotional		Role-Physical		Body Pain		Vitality	
	OR	**95%CI**	**OR**	**95%CI**	**OR**	**95%CI**	**OR**	**95%CI**	**OR**	**95%CI**
Sleep disturbance	1.9	(1.28, 2.83) ≠	1.33	(0.90, 1.98)	1.86	(1.25, 2.79) ¥	1.73	(1.21, 2.47) ¥	2.17	(1.54, 3.06) ≠

*indicates p ≤ 0.05

†indicates p ≤ 0.01

≠indicates p ≤ 0.001

¥indicates p ≤ 0.005

[a]Model is adjusted for age, race (White vs. African-American), menopause status (perimenopausal, postmenopausal/surgical menopause, unknown vs. premenopausal/reference), hormone therapy use (current use vs. not current use), medical conditions (0, 1, 2+), mental health treatment, and upsetting life events

Model compares the groups with (1) a cumulative lifetime history of a depressive and an anxiety disorder, (2) cumulative lifetime history of an anxiety disorder, and (3) a cumulative lifetime history of an anxiety disorder, against a reference group of women who have no cumulative lifetime history of depression or anxiety.

All categorical SF-36 outcomes are dichotomized as ≤25%ile vs >25%ile and presented as odds ratio (95% confidence intervals).

VMS: vasomotor symptoms, coded as yes/no during 2 weeks prior to study visit

Sleep disturbance is defined categorically as trouble falling asleep, waking up several times at night, and/or waking up earlier than planned and unable to fall asleep again for ≥3 nights per week during previous 2 weeks