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Depression during the menopause transition: impact on quality of life, social adjustment, and disability

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Abstract

The impact of depression on quality of life (QOL) and social support has neither been well characterized in clinical samples of women with perimenopausal depression (PMD) nor have the relative contributions of depression and other menopausal symptoms (e.g., hot flashes) to declining QOL been clarified. In this study, we compared QOL measures, social support, and functional disability in PMD and non-depressed perimenopausal women. We evaluated women aged 40–60 years who presented with menstrual cycle irregularity, elevated plasma FSH levels, and met criteria for perimenopause. A structured clinical interview was administered to determine the presence or absence of major and minor depression. Outcome measures included the Quality of Life Enjoyment Scale Questionnaire, the Sheehan Disability Scale, the Global Assessment of Functioning, the Social Adjustment Scale, and the Duke Social Support Index. Kruskal-Wallis tests and ANOVAs were used to compare outcome measures. Ninety women with PMD and 51 control women participated in this study. Women with PMD reported significantly decreased QOL, social support, and adjustment and increased disability compared with non-depressed perimenopausal women. Neither perimenopausal reproductive status alone nor the presence of hot flashes had a significant negative impact on QOL measures. PMD is accompanied by significant reductions in QOL, social support, and disability similar to depression in women at other stages of life. PMD may also contribute to decreased QOL in community- or clinic-based samples of perimenopausal women. It remains unclear whether the clinical characteristics we identified reflect pre-existing risk factors for depression during the perimenopause or the effects of a current depression. Future clinical and treatment studies in perimenopausal women should distinguish depressed women when outcome measures include QOL.

Keywords

Perimenopause; Depression; Quality of life; Social function; Disability

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Conflicts of interest The authors declare that they have no conflict of interest.

Introduction

The menopause transition is accompanied by a decrease in quality of life (QOL) measures for some women, and several randomized controlled trials of menopausal hormone therapy (HT) have targeted QOL as a potential indication for HT (Santen et al. 2010; Stuenkel et al. 2015). In her review of studies examining QOL during the menopause transition (Matthews and Bromberger 2005), Matthews identified several community-based studies that observed a significant reduction in QOL measures in perimenopausal women compared with women who were in the premenopause. In these studies, perimenopausal women reported more role limitations due to physical or emotional health, poorer perceived health, and more somatic symptoms (including pain) than premenopausal women. However, the presence of negative affective symptoms accounted for a high proportion of the variance in QOL measurements in the perimenopausal women (including disability related to physical symptoms). Thus, in community-based studies the presence of depression (PMD) in some perimenopausal women could be an important source of variability in measures of QOL at this stage of a woman's life. Although the majority of perimenopausal women do not develop clinically significant depression, community-based, longitudinal studies document a two- to threefold increased risk of depression during the menopause transition compared with both the premenopause and the later postmenopause (Freeman et al. 2004; 2006, 2013; Cohen et al. 2006; Bromberger et al. 2007).

Depression at any time of life is known to negatively impact QOL measures as well as social adjustment, role functioning, mobility, and health perceptions. Additionally, depression in women is frequently accompanied by somatic complaints (Halbreich and Kahn 2007; Silverstein 2002; Simon et al. 1999)—all of which will contribute to a decline in QOL measures. Thus, the prevalence of and disability accompanying depression could contribute to previous reports of declining QOL in community samples of perimenopausal women.

In addition to depression, several other factors may contribute to decreased QOL scores in perimenopausal women including physical illnesses comorbid with depression, somatic symptoms including hot flashes (Stearns et al. 2002) and the attendant sleep disruption (Ohayon 2006), and alterations in role functioning and/or social networks related to the social isolation and withdrawal accompanying depression. In particular, the impact of hot flashes on depression/depressive symptoms potentially could further contribute to the observed decline in QOL during the menopause transition (Utian 2005; Archer et al. 2011).

No study has characterized the range of dysfunctions and personal disability associated with PMD in otherwise healthy women, and therefore, the impact of PMD can only be inferred from studies of depression occurring at other stages of life. The goals of this study were as follows: (1) to evaluate the QOL, social adjustment, and personal disability in women with PMD and non-depressed perimenopausal control women and (2) to examine the effects of hot flashes on QOL in women with and without perimenopausal depression. We selected a broad range of measures not only to both characterize several dimensions of QOL and disability in PMD but also to permit comparisons with published studies of major depression occurring at different stages of life. Finally, we also examined the effects on outcome

measures associated with perimenopausal major compared with minor depression and first-onset PMD compared with recurrent PMD.

Methods

Participant selection

Perimenopausal women between the ages of 40 and 60 who reported the onset of depression and who presented to the NIMH midlife clinic between 1999 and 2014 participated in this study. Women reported the onset of depressive symptoms associated with personal distress or occupational impairment in the context of menstrual irregularity of at least 6 months but not more than 1 year of amenorrhea. All women were either self-referred in response to local advertisements or referred by their physicians. All depressed women entering this study met the following criteria: (1) a current episode of major or minor depression as determined by the Structured Clinical Interview for DSM-IV (SCID) (First et al. 2002) or Primary Care Evaluation of Mental Disorders (PRIME-MD) (Spitzer et al. 2000; Spitzer et al. 1999) (in four women [see below]) supplemented with a past history form (Hirschfeld 2002) to characterize past history of Axis I psychiatric illness and to distinguish first-onset and recurrent PMD (i.e., those women with no past Axis I affective or anxiety disorder and those with at least one past episode of Axis I affective or anxiety disorder unrelated to the perimenopause); and (2) at least one elevated plasma follicle-stimulating hormone (FSH) level > 14 IU/L obtained during a screening phase [plasma FSH levels of 14 IU/L represent two standard deviations above the mean values for the early follicular phase FSH levels in women of reproductive age, consistent with the Stages of Reproductive Aging Workshop (STRAW) criteria (Soules et al. 2001)]. Women were excluded if they had a medical illness (current or recent medical illness confirmed by medical history and physical examination in addition to laboratory tests), were taking medication (with the exception of long term stable doses of thyroid replacement), had an abnormal gynecologic exam or mammogram, or had a history of psychiatric illness during the 2 years prior to the reported onset of their current episode of depression. All women were free of any menopausal hormonal therapy or psychoactive medications (other than thyroid hormone). The PRIME-MD was substituted for the SCID in only four women (PMD $n = 1$ and non-depressed perimenopausal women $n = 3$) who did not attend all visits but who attended sufficient visits to complete the measures employed in this study except for the full SCID interview which was performed during the last clinic visit in many women. Each woman completed a semi-structured interview during the first visit that detailed presenting symptoms, the duration and level of functional impairment associated with the depression, the presence of hot flushes, and the characteristics of the menstrual cycle irregularity or amenorrhea.

Non-depressed perimenopausal women between the ages of 40 and 60 were recruited to participate as a control group in this study and were matched on the basis of reproductive status and age. These control women participated in a screening procedure similar to the women with PMD. All women met clinical and endocrine research criteria for the perimenopause (as described above) in the absence of any significant current episodes of depression as determined by SCID interview (First et al. 2002) or the PRIME-MD (Spitzer et al. 2000; Spitzer et al. 1999). Additionally, all control women were subject to the same exclusion

criteria as the women with PMD. Upon completion of this study, asymptomatic participants received compensation for their time as determined by the NIH Office of Healthy Volunteers.

This protocol was approved by the Central Neuroscience Intramural Research Board, and written informed consent was obtained from each woman prior to entering the study.

Diagnostic evaluation and group assignments

During the screening phase, all participants completed the midlife Daily Rating Form (DRF) (Endicott et al. 1986), a six-point Likert-type scale modified to measure nighttime and daytime hot flushes. The DRF was completed nightly to reflect a composite rating for the previous 24 h; DRF scores range from 1 (symptoms not present) to 6 (symptoms present in the extreme). This form was used to confirm the presence or absence of clinically significant daytime and nighttime hot flushes, operationally defined by a 2-week minimum average score >2 (2 = minimal). Additionally, the Center for Epidemiologic Studies Depression Scale (CES-D) was administered at each clinic visit. CES-D scores >16 are consistent with clinically significant depressive symptoms of at least moderate severity (Freeman et al. 2004; Roberts and Vernon 1983). Women meeting study criteria for perimenopausal depression as well as non-depressed perimenopausal women were further classified into subgroups based on the presence or absence of hot flushes.

FSH plasma levels were measured by microparticle enzyme immunoassay AxSYM radioimmunoassay (Abbott Laboratories, Abbot Park, Ill), the low end of sensitivity for this assay was 0.1 IU/L, results above 170 IU/L require repeat assay with a diluted sample, and intra- and inter-assay percent CVs (i.e., average of low, mid, and high concentrations of standard) were 3.3 and 8.6, respectively.

Outcome measures

1. Quality of Life Enjoyment Satisfaction Questionnaire (QLESQ) (Endicott and Harrison 1990)—a self-report scale used to measure the enjoyment and quality of life as well as overall life satisfaction. We employed the QLESQ (SF) which includes 16 items that assess domains related to physical health, subjective feelings, leisure time activities, social relationships, general activities, work, household duties, and school/course work (Endicott et al. 1993). This 16-item short form of the questionnaire constitutes the general activities domain of the long form 93-item version of the QLESQ. A total score on the QLESQ (SF) is derived from the sum of scores for items 1–14, where each item is scored from very poor (1) to very good (5) based on the patient's experience during the week prior to scale completion. The sums of scores for item 1–14 can range from 14 (i.e., minimum possible score) to 70 (i.e., maximum possible score) and are expressed as a percentage (1–100) of the maximum total score that is achievable. Specifically, we calculated the percent score by using the following formula: $(\text{total raw score} - \text{minimum possible score}) / (\text{maximum possible score} - \text{minimum possible score})$. Both the total score and the individual item score for overall satisfaction were compared across groups of women.

2. Global Assessment of Functioning (GAF) (Hilsenroth et al. 2000)— an assessment administered with the SCID interview by a clinician in order to assess overall psychosocial/somatic disturbance and impairment related to the woman's PMD. This rating scale is measured from 0 to 100 (0 = low function/ suicidality, 100 = high function/asymptomatic). GAF scores between 51 and 60 are consistent with moderately severe symptoms or moderate functional impairment (Hilsenroth et al. 2000).
3. Sheehan Disability Scale (SDS) (Sheehan 2002)—a self-report measure of disability in the performance of social, work, and family life activities during the week prior to completion of the scale. We employed the SDS which includes three items that assess domains related to disease-related disability and have scores which range from 0 (no disability) to 10 (significant disability) based on the woman's current experience. The sum of scores for items 1–3 can range from 3 (i.e., minimum possible score) to 30 (i.e., maximum possible score) with higher scores reflecting greater severity of impairment.
4. Social Adjustment Scale (SAS) (Weissman 1976)—a self-report measure of functioning in the woman's daily roles including paid employee, homemaker, student, parent, and spouse/partner, as well as additional questions about social and leisure behaviors. We employed the SAS-SR which includes 54 possible items that are completed by each woman if applicable. A total score on the SAS-SR is derived from the average scores for each item which are scored from 1 (i.e., minimal adjustment) to 5 (i.e., maximal adjustment) based on the woman's experience during the 2 weeks prior to scale completion. Scoring procedure for this rating scale consisted of calculating the total scores for each item and adjusting it based on the number of applicable questions to obtain an overall adjusted score.
5. Duke Social Support Index (DSSI) (Landerman et al. 1989)—a self-report measure of perceived social support and social satisfaction. We used the satisfaction subscale score in our analysis and did not include scores responsive to questions about marital status. We employed the ten-item abbreviated version of the DSSI. Of these ten items, seven items were used to calculate the total score. Scores for each item on the DSSI range from 1 (i.e., low perceived social support) to 3 (i.e., high perceived social support). The maximum total score for this rating scale is 21.

Statistical analyses

Baseline characteristics (age, BMI, and CES-D scores) of PMD and controls were compared using the Pearson chi-square and Student's *t* tests. Differences between diagnostic groups in the scores of each rating scale were analyzed using Kruskal-Wallis tests (SYSTAT version 13). We also evaluated the effects of the presence or absence of either daytime or nighttime hot flushes on rating scale scores using ANOVA with diagnosis (i.e., depressed or controls) and hot flushes (i.e., presence or absence) as between group factors to examine both main effects as well as possible diagnosis by hot flush interactions. Similarly, analyses were performed to examine possible effects of self-reported PMS and STRAW stage on QOL

measures. Finally, we employed Kruskal-Wallis tests to evaluate differences in rating scale scores between perimenopausal women with major depression and those with minor depression, and those women with PMD with and without a past episode of Axis I affective or anxiety disorder (i.e., first-onset PMD versus recurrent PMD).

Finally, Pearson correlations were performed to examine the relationship between CES-D scores and QOL measures in depressed perimenopausal women. *P* values (two-tailed) less than 0.05 reflect a significant difference between comparison groups.

Results

Participant characteristics

Ninety women with PMD and 51 control women participated in this study. There were no significant differences between depressed perimenopausal women and control women in either age (50.2 ± 3.5 years, 51.1 ± 2.9 years, respectively) or BMI (26.9 ± 5.9 kg/m², 27.0 ± 6.7 kg/m², respectively) (Table 1). CES-D scores showed a significant difference (as expected) between depressed women and non-depressed women (32.8 ± 8.2 , 3.2 ± 3.3 , respectively), and race and ethnicity were comparable between groups. Ten women (depressed perimenopausal women $n = 6$, control women $n = 4$) were taking thyroid replacement.

We observed a significant difference between women with PMD and controls in all outcome measures (Table 2). Depressed women had significantly lower scores than non-depressed control women on both the subscales and overall satisfaction item of the QLESQ scale ($P < 0.001$ both comparisons), the GAF ($P < 0.001$), and the DSSI ($P < 0.001$) reflecting decreased quality of life, decreased perceived social support, and increased disability in the depressed perimenopausal women. Similarly, depressed women had significantly higher scores than control women on the SDS ($P < 0.001$) and the SAS ($P < 0.001$) reflecting increased disability and poorer social adjustment when compared with non-depressed control women.

Effect of hot flushes, type of depression, self-reports of PMS, and STRAW stage

Comparisons of the effects of hot flushes and depression on scores from the QLESQ, GAF, SDS, SAS, and DSSI showed a similar pattern of significant main effects related to the presence of PMD; however, ANOVA identified no main or interactive effects of hot flushes on any measures (Table 3). There were no significant differences in any outcome measure between the PMD women with major depression and those with minor depression. Nonetheless, there were trends for significance in scores of the QLESQ ($P = 0.08$), SDS ($P = 0.06$), and SAS ($P = 0.08$), reflecting lower QOL, higher disability, and lower social adjustment in the women with major depression compared with those with minor depression. There also were no significant differences in any outcome measure ($P = \text{ns}$, all comparisons) between those women with first-onset PMD and those women with PMD who met SCID criteria for a past Axis I affective or anxiety disorder (unrelated to the perimenopause). Finally, neither self-reports of PMS nor STRAW stage of each woman impacted on the observed effects of PMD on QOL measures.

Correlation between rating scale scores and CES-D scores

We observed significant positive correlations between CES-D scale scores and both the SDS ($P < 0.001$) and the SAS ($P < 0.001$), reflecting higher depression severity scores associated with higher disability and poorer social adjustment. In contrast, there were no significant correlations between CESD scores and scores on the QLESQ ($P = 0.2$), overall satisfaction QLESQ ($P = 0.08$), GAF ($P = 1.00$), and DSSI ($P = 0.13$) scales.

Discussion

Our findings are relevant for both interpreting the results of epidemiologic studies of the menopause transition and future clinical trials of HT. Additionally, these data provide important and clinically relevant information for clinicians working with perimenopausal depressed women. This study is the first clinic-based study to examine quality of life, social support, and disability in a well-characterized sample of both clinically depressed and non-depressed perimenopausal women. First, we observed that decreased QOL and social support and increased complaints of disability characterize PMD but are not common in non-depressed perimenopausal women. These findings confirm the proposal by Matthews et al. (Matthews and Bromberger 2005) and suggest that epidemiologic studies of community samples of perimenopausal women need to distinguish between those women with PMD and non-depressed women to avoid attribution of decreased QOL to the menopause transition alone. Similarly, trials of HT in perimenopausal women should clearly distinguish between women with PMD and non-depressed women, since one would predict the baseline level of QOL and the subsequent response to treatment would differ between depressed and non-depressed perimenopausal women, as suggested by Rubinow et al. (Rubinow et al. 2015). Finally, our findings characterize the extent and severity of the negative impact of PMD on measures of QOL, disability, social adjustment, and role functioning previously documented in depressive disorders occurring independent of the menopause transition. Importantly, we observed similar levels of disability in perimenopausal women with major depressive episode (MDE) compared with those who met criteria for minor depression and in those with a past Axis I affective or anxiety disorder compared with those without a past Axis I affective or anxiety disorder. The presence of hot flushes did not significantly impact any measure in either the women with PMD or the control women.

These findings confirm previous suggestions that PMD could account for the majority of the variance in QOL measures observed in community-based studies of the menopause transition. Thus, these data are consistent with findings by Matthews (Matthews and Bromberger 2005) and others (Bromberger and di Scalea 2009) and suggest that the menopause transition alone is not uniformly accompanied by declining levels of QOL, role functioning, or social adjustment. Similarly, depressive symptoms and depression not only contribute to the significant reductions in QOL observed in perimenopausal women participating in epidemiologic studies but also to the outcomes of some clinical trials evaluating the effects of hormone therapies on quality of life in peri- and postmenopausal women. The study by Hlatky et al. (Hlatky et al. 2002) suggested that the beneficial effects of HT on QOL were associated primarily with improvement in depressive symptoms. Thus, the presence or absence of depressed women in clinical trials of menopausal hormone

therapies also could influence the observed outcomes after hormone therapy (Rubinow et al. 2015). In contrast, the inclusion of relatively asymptomatic women in two previous studies that examined the impact of HT on QOL measurements likely confounded observed results (Hlatky et al. 2002; Hays et al. 2003). The potential confound of depression in the interpretation of QOL outcomes in HT trials in heterogeneous groups of perimenopausal women is further suggested by reports of the short-term efficacy of estradiol in PMD (Schmidt et al. 2000; Soares et al. 2001; Joffe et al. 2011; Rubinow et al. 2015) and the emergence of depressive symptoms after the discontinuation of HT (Ockene et al. 2005; Grady et al. 2003; Ness et al. 2006; Schmidt et al. 2015).

Our study also informs our understanding of PMD in the context of depression experienced outside of the menopause transition. QLESQ scores in our sample of women with PMD were comparable to other cohorts reported in the literature. Average percent scores on the QLESQ SF in women with PMD were 56.5%, whereas previous studies in men and women with depression or anxiety disorders report average scores ranging from approximately 38 to 51% (Endicott et al. 2014; Ishak et al. 2013; Pearlstein et al. 2000; Pollack et al. 2008; Wyrwich et al. 2009). Similarly, QLESQ scores from healthy asymptomatic community-dwelling men and women are observed to be generally over 70% and frequently in the 80% range, (Schechter et al. 2007; Swan et al. 2009) comparable to those control women in our sample (i.e., 88%). (Rapaport et al. 2005). Thus, QOL is reduced in PMD and the reductions in both major and minor PMD are comparable to those observed in clinically significant depressions during other times in a woman's life. Similarly, a past Axis I affective or anxiety disorder did not impact the severity of QOL measures (nor measures of disability, social adjustment, and support). These findings are consistent with a previous publication from our group in which we reported several clinical characteristics in PMD that did not differ between women with first-onset PMD and those with recurrent PMD (as well as those with major versus minor PMD) (Steinberg et al. 2008).

The GAF scores in PMD were in the moderate range of dysfunction and similar to scores reported in several studies of men and women with anxiety and depressive disorders (Grootenboer et al. 2012; Hilsenroth et al. 2000). The corresponding scores in the SDS also are consistent with those reported in the literature from clinic-based studies of men and women with anxiety disorders (Sheehan and Sheehan 2008) and in one prior report of peri- and postmenopausal women with depression who participated in a trial of the antidepressant desvenlafaxine (Kornstein et al. 2014), but lower than two studies employing the SDS in clinic-based samples of men and women with major depression (Lai 2011; Pollack et al. 2008) in which scores were in the low twenties. Similar patterns of scores were observed between our sample and those reported in the literature for the DSSI, although our sample rated relatively more social support than some studies in depressed patients (Koenig et al. 1993; Hays et al. 1997; Stanaway et al. 2011; Goodger et al. 1999; Pachana et al. 2008) (albeit with different forms of the scale employed across studies). Finally, the average (SD) SAS score in our sample of women with PMD was 2.2 (0.5), which is comparable to reports in the literature of men and women with major depression (Bothwell and Weissman 1977) (albeit slightly lower than some studies (Weissman et al. 1978)). Thus, although epidemiologic studies have frequently been unclear about the clinical relevance of depressive symptoms during the menopause transition, the results of our studies in

perimenopausal women with major and minor depression document that women presenting to clinic for this condition experience similar levels of disability, poor QOL, social mal-adjustment, and role dysfunction as women with traditional (non-reproductive) anxiety and depressive disorders.

We found no significant main or interactive effects of the presence of hot flushes on any of the outcome measures. Thus, in our sample of PMD (and control women), hot flushes did not have a negative impact on QOL or other related measures. Although these findings are potentially consistent with studies observing that hot flushes are not significant contributors to the severity of depressive symptoms, it would seem possible that hot flushes could become sufficiently severe in some women that either the sleep disturbance or direct distress of hot flushes in a woman's life could negatively impact QOL. Indeed, reviews of the impact of hot flushes on QOL measures have reported mixed results (Zollner et al. 2005; Archer et al. 2011; Utian 2005). Additionally, the QOL scales that we employed in this study do not include specific symptom severity scores for hot flushes in the overall score, whereas alternate scales (e.g., the Menopause-specific Quality of Life scale (Hilditch et al. 1996)) include symptom severity measures of hot flushes within the scale's overall score. Thus, it is possible that had we recruited a more symptomatic group of control women or employed a different QOL measure, a larger impact of hot flushes would have been observed.

Finally, although no significant differences between major and minor depression were observed, our data showed that the severity of CES-D scores positively correlated with the Sheehan Disability Scale and the Social Adjustment Scale. In these rating scales, higher scores are represented by higher levels of functional impairment. Thus, the severity of depressive symptoms (independent of the diagnosis of major or minor depression) impacted women's scoring and their perceptions of disability and social function.

This study has several limitations that should be discussed. First, our findings are relevant to a sample of women with well-characterized PMD all of whom presented for evaluation and/or treatment of their symptoms. Thus, our finding cannot be readily generalized to community-dwelling women experiencing depression or those non-depressed women transitioning through the menopause. Indeed, epidemiologic studies of men and women with depression document the delay (up to 8 years) before the majority of depressed men and women present for treatment, and therefore, our sample of women who presented for evaluation at our clinic may differ in several clinical characteristics from those women in the community. Nonetheless, health care providers should be alerted by the presence of decreased QOL or disability in perimenopausal women, since epidemiologic studies also document that a large proportion of depressed men and women with major depression receive neither prompt nor adequate diagnostic evaluations and treatment recommendations (Sherbourne et al. 1994; Spitzer et al. 1995; Wang et al. 2000; Spitzer et al. 2000; Greden 2001; Kessler et al. 2003). Second, our sample was medically screened for the absence of significant medical illness and, therefore, the QOL scores could be substantially higher than those observed in community-based studies, since depression is frequently co-morbid with a range of medical conditions, which in themselves could negatively impact QOL. The focus of this study was to characterize QOL, social adjustment, disability, and role functioning in a clinic-based sample of women with PMD. Clearly, there is considerable overlap in many of

the items listed in these scales, and although differences between PMD and controls were consistent across scales, we cannot distinguish the specific factors (e.g., social support or work performance) that had the largest impact on QOL measures. Similarly, since this was a cross-sectional study, we also cannot address whether the decreases in QOL, social support, or social adjustment appeared prior to the onset of depression in the women with PMD and, therefore, whether these factors contributed to the risk of PMD or were reflections of the impact of PMD on a woman's functioning. Clearly, longitudinal studies following women as they transition through the perimenopause could answer the relative impact of QOL measures on the risks for PMD.

The recent community-based studies estimate that 20–40% of women will develop an episode of depression during the menopause transition. (Cohen et al. 2006; Freeman et al. 2006) The 2012 U.S. Census recorded 22+ million women in the 45–54-year-old age range. Thus, the impact of depression on measurements of quality of life in women during the menopause transition is of both epidemiologic and clinical significance. Because the presence or absence of depressed perimenopausal women in the sample studied could represent a significant confound to the interpretation of quality of life data, studies of quality of life during the menopause transition must identify the presence and evaluate the severity of depression in the women studied.

Future studies of the association between depression, the menopause transition, and quality of life should consider several caveats. First, in depression, it is not clear whether quality of life measures will provide additional information beyond that obtained from standardized depression rating scales. Second, the use of a multidimensional quality of life scale will not adequately evaluate the impact of other symptoms of the menopause transition (such as hot flashes, sleep disturbance, or musculoskeletal pain) unless the quality of life measures control for the presence of depression. Finally, the presence or absence of depression in the samples of perimenopausal women will substantially affect evaluations of the impact of HT on QOL measurements.

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Table 1
Demographic characteristics of depressed ($n = 90$) and non-depressed ($n = 51$) perimenopausal women

	Perimenopausal depressed women	Perimenopausal non-depressed women
Age (years)		
Mean (SD)	50.2 (3.4)	51.0 (3.0)
BMI (kg/m ²)		
Mean (SD)	26.8 (5.8)	27.0 (6.7)
Thyroid medication # of women (%)	6 (7%)	4 (8%)
Current depression history # of women (%)		
Major depression	75 (83%)	-
Minor depression	15 (17%)	-
CES-D		
Mean (SD)	32.5 (9.3)	3.3 (3.4)
STRAW stage # of women (%)		
-3	1 (1%)	-
-2	9 (10%)	7 (14%)
-1	61 (68%)	40 (78%)
0	2 (2%)	-
+1	17 (19%)	4 (8%)
HF presence in women ^a (%)	60 (67%)	19 (37%)
Marital status # of women (%)		
Married	53 (58%)	28 (55%)
Divorced/separated	24 (27%)	12 (24%)
Single	15 (17%)	11 (22%)
Past depression history # of women (%)		
Major depression	43 (48%)	2 (4%)
Minor depression	15 (17%)	2 (4%)
PPD Hx	9 (10%)	1 (2%)
PMS Hx ^b # of women (%)	48 (53%)	20 (39%)
Smoking Hx # of women (%)	8 (9%)	3 (6%)

^a Presence or absence of clinically significant daytime and nighttime hot flushes, operationally defined by a 2-week minimum average score greater than 2 on the DRF (2 = minimal)

q Self-reported PMS and therefore not confirmed prospectively

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Outcome measures in depressed ($n = 90$) and non-depressed ($n = 51$) perimenopausal women

Table 2

Rating scale	Perimenopausal depressed women mean (SD)	Perimenopausal non-depressed women mean (SD)	<i>R</i> value ^a	<i>P</i> value
Quality of Life Enjoyment and Satisfaction Scale: overall satisfaction ^{b,c} (17 PMD and 1 HC missing)	3.1 (0.8)	4.8 (0.4)	0.59	$P < 0.001$
Quality of Life Enjoyment and Satisfaction Scale: percent score ^{b,d} (17 PMD and 1 HC missing)	56.5 (14.8)	88.7 (9.6)	0.59	$P < 0.001$
Global Assessment of Functioning ^b (15 PMD missing)	64.5 (7.0)	91.1 (4.2)	0.79	$P < 0.001$
Sheehan Disability Scale ^b (6 PMD and 4 HC missing)	14.6 (6.2)	1.2 (3.9)	0.60	$P < 0.001$
Social Adjustment Scale—self-report ^b (8 PMD and 8 HC missing)	2.2 (0.5)	1.5 (0.3)	0.38	$P < 0.001$
Duke Social Support Index ^b (14 PMD and 1 HC missing)	16.3 (3.5)	19.9 (1.5)	0.26	$P < 0.001$

^aThese *R* values are from Kruskal-Wallis analysis. All *P* values have $df = 1$ ^bResults showed a significant difference ($P < 0.001$) in values scored by perimenopausal depressed women compared to perimenopausal non-depressed women in each rating scale^cQLESQ item 16 is a global rating of overall life satisfaction and contentment^dQLESQ item 15 queries patients on their satisfaction with the medication they are receiving which was not relevant to this study, and item 16 of the QLESQ is also not included in this measure

Table 3

Results of ANOVA for each outcome measure in depressed ($n = 90$) and non-depressed ($n = 51$) perimenopausal women: interaction with presence or absence of hot flushes (HF)

Rating scale	Perimenopausal depressed women mean (SD)		Perimenopausal non-depressed women mean (SD)		<i>P</i> value main effect of HF	<i>P</i> value interaction (HF $\times$ diagnosis)
	HF+	HF-	HF+	HF-		
Quality of Life Enjoyment and Satisfaction Scale: overall satisfaction	3.1 (0.9)	3.0 (0.6)	4.8 (0.4)	4.8 (0.4)	$P = 0.802$	$P = 0.782$
Quality of Life Enjoyment and Satisfaction Scale: percent score	57.0 (16.2)	55.7 (12.5)	88.1 (8.2)	89.1 (10.4)	$P = 0.954$	$P = 0.628$
Global Assessment of Functioning	65.1 (7.9)	63.6 (5.8)	92.2 (3.3)	90.5 (4.6)	$P = 0.150$	$P = 0.919$
Sheehan Disability Scale	15.1 (6.4)	14.5 (5.9)	1.3 (3.8)	1.2 (4.0)	$P = 0.718$	$P = 0.811$
Social Adjustment Scale—self-report	2.2 (0.5)	2.2 (0.5)	1.5 (0.2)	1.5 (0.3)	$P = 0.718$	$P = 0.870$
Duke Social Support Index	16.3 (3.5)	16.1 (3.5)	19.8 (1.7)	20.0 (1.4)	$P = 0.971$	$P = 0.667$

During the screening phase, all participants completed the midlife Daily Rating Form (DRF) (Endicott et al. 1986), a six-point Likert-type scale modified to measure nighttime and daytime hot flushes. The DRF was completed nightly to reflect a composite rating for the previous 24 h; DRF scores range from 1 (symptoms not present) to 6 (symptoms present in the extreme). This form was used to confirm the presence (HF+) or absence (HF-) of clinically significant daytime and nighttime hot flushes, operationally defined by a 2-week minimum average score >2 (2 = minimal)