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## Depressive Symptoms Associated with Physical Health Problems in Midlife Women: A Longitudinal Study

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### Abstract

**Background:** It is unclear if the relationship between depression and physical health problems in women is related to age, reproductive stage, obesity or socio-demographic risk factors.

**Methods:** Longitudinal data were obtained every 6 months for 36 months in 264 midlife African American, Caucasian and Latina women who began the study as healthy regularly menstruating 40 to 50-year-olds; 75 transitioned to peri- or post-menopause by 36 months. Scores of 16 or higher on the Center for Epidemiologic Studies-Depression (CES-D) scale were used to estimate depression risk.

**Results:** Depression risk was 28% at study initiation and 25% at 36 months. Significantly more women at risk for depression were unemployed, obese, or hypertensive. Women at risk were more likely to become peri- or post-menopausal during the study period. A higher percentage (38%) of overweight and obese women had CES-D scores  $\geq 16$  compared to normal weight women (23%;  $p < .001$ ). Over half (58%) of the 73 women at higher depression risk at the initial visit reported a health problem or chronic illness at 36 months, compared to only 36% of the 191 women with CES-D scores  $< 16$  ( $p = .001$ ).

**Limitations:** This was a secondary analysis of data from a relatively healthy sample of women in the decade before menopause. Chronic illness was self-reported and the CES-D is a screening tool for depressive symptoms rather than a clinical diagnostic tool.

**Conclusions:** Health care providers may be underestimating the impact of unemployment on depressive symptoms, obesity and chronic health problems in midlife women.

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Dr. Lee was the PI on the parent study and contributed significantly to the data analysis, writing, and editing. Dr. Gilliss was Co-investigator on the parent study. Drs. Gilliss, Jones, and Minarik each contributed to the development, writing, and editing of the article. All authors approved the final version of the article.

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## Keywords

depressive symptoms; CES-D; chronic illness; hypertension; midlife women; community-based cohort; premenopause; late reproductive stage

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## Introduction

Depression is the leading cause of disability in adults, costing Americans over \$210 billion per year (Greenberg et al., 2015). Most of that cost is attributed to comorbid health conditions such as sleep disorders or chronic illness, and directly associated with absenteeism or decreased work productivity rather than treatment for depression itself (Greenberg et al., 2015). Compared to men, women have twice the risk of depression, particularly as they age, leaving social and economic burden associated with depression shouldered disproportionately by women (CDC, 2010; Rai et al., 2013)

Gender disparity in depression is associated with a number of factors that include earlier onset, longer lifespan, and longer persistence after a first episode (Kessler, 2003; Barry et al., 2008). Individual-level factors such as women's race, marital status, social isolation, financial resources, and class are also linked to depression globally (Rai et al., 2013; Ruo et al., 2006; (Bromberger et al., 2004; Ohayon, 2007). Interestingly, women in higher-gross national income countries were more likely to report depressive symptoms, yet this association was not found in men (Rai et al., 2013).

Chronic physical health conditions such as obesity, heart disease, and diabetes have been associated with risk of depression (Wilson-Genderson et al., 2017). The association between depression and hypertension (HTN), however, is less clear and may differ by gender (Jackson et al., 2016; Michal et al., 2013; Shah et al., 2013). In a meta-analysis of nine cohort studies, Meng and colleagues (2012) concluded that depression was likely an independent risk factor for HTN, while other researchers posit alternative biological pathways for comorbid depression and cardiovascular disease that also involve obesity, and any one health problem might be the outcome of the other two (Tobet et al., 2013) as risk factors for both depression and cardiovascular disease are similar and include smoking, alcohol consumption, obesity, race and marital status.

Women are more likely to be diagnosed with a chronic health problem during midlife, and this often coincides with menopause, yet evidence for the association has been inconsistent (Bromberger et al., 2003, 2007; Freeman et al., 2006; Woods et al., 2002, 2006). Research with women prior to menopause transition is critical to understanding the unique biological and environmental factors that contribute not only to age and gender differences in depression, but also to understanding predictors of depression into post-menopause reproductive stage.

Longitudinal studies like the Study of Women Across the Nation (SWAN) have been instrumental in characterizing depression during menopause transition. In SWAN's multiethnic cohort, major depressive episodes were highest during perimenopause and immediate post-menopause stages compared to late pre-menopause (Bromberger et al.,

2011). They found no difference in incidence or severity of depressive symptoms between African American and Caucasian women (Brown et al., 2014). The strongest predictors of depressive symptoms in the SWAN sample were stressful life events and prior history of depression rather than menopausal status or age (Bromberger et al., 2011, 2016). Poor perceived health, one or more physical symptoms, and vasomotor symptoms were associated with higher depression scores (Bromberger et al., 2007, 2011), yet whether depression occurs prior or after onset of a chronic physical illness remains unknown.

The aim of this secondary analysis of longitudinal health data was to describe changes in health in relation to age and reproductive stage during the decade before menopause. Mental health was operationalized as depressive symptoms and physical health was operationalized as hypertension, obesity, and development of a chronic physical illness. With measures at 6-month intervals over three years, we tested three specific hypotheses: 1) Women who remain pre-menopausal will be at lower risk of depression across time compared to women transitioning to early peri-menopause and post-menopause at 30–36 months; 2) Healthy women with normal blood pressure and body weight at study initiation will have a lower risk of depression across time compared to women with HTN or obesity regardless of reproductive stage; 3) Women at high risk of depression at study initiation will be more likely to report a chronic illness at 30–36 months compared to women with low risk for depression. This study was guided by the Theory of Symptom Management, which states that any symptom experience is influenced by a variety of bio-psycho-social factors, and that health outcomes are influenced by this relationship (Dodd, et al., 2001; Bender et al., 2018).

## Methods

### Participants

Data were collected from a community-based sample of regularly menstruating midlife women between 40 and 50 years of age as part of the Midlife Women's Health Study, a longitudinal study that ran from 1996 to 2004 to describe changes in biopsychosocial health factors every 6 months during transition to menopause. Women with a history of major chronic health problems (e.g., heart attack, stroke, mental illness, kidney disease, cancer, diabetes mellitus, or auto-immune disease) were initially excluded, as were women regularly taking tranquilizers, antidepressants, sleeping pills, or hormone therapy that included birth control or hormone replacement. The original study was approved by the University of California, San Francisco Committee on Human Research and all participants gave written informed consent. The original sample from the San Francisco Bay Area included self-identified Caucasian (n=161), Mexican or Central Americans (Latinas) (n=95) and African Americans (n=91). Details of recruitment and retention strategies and first-year retention results are available elsewhere (Gilliss et al., 2001).

The sample includes 264 women with data over 30–36 months. There were no significant differences between this subset and the total sample except that excluded women were more likely to be 12 months post last menstrual period or hysterectomy, became pregnant, or started on hormone replacement during the first year. While women with a serious chronic illness were excluded from enrollment, most (96%) reported having a current or past health

problem at initiation, and 6% reported a hospitalization or emergency room visit during the past year.

## Measures

Questionnaires were completed during face-to-face visits at the research site or participant's home every 6 months for 3–5 years, or up to twelve months after the last menstrual period, a hysterectomy or initiating hormone therapy. Sociodemographic variables were collected with an investigator-designed demographic questionnaire that included questions about smoking and alcohol habits, nutrition, exercise, and sleep. The single-item measure of health perception from the Medical Outcomes Study Short Form was used as an indicator of general health (Stewart & Ware, 1992). This item asks about current health in general with 5 possible responses: *excellent, very good, good, fair or poor*. The number of endorsed health problems was correlated ( $r = .225, p < .001$ ) with the General Health Perception scale, and women with a health problem perceived significantly poorer health than women with no health problem (Humphreys & Lee, 2009).

Health variables were collected by trained research staff and included a first-morning urine sample for Follicle Stimulating Hormone (FSH) to indicate menopausal status, weight and height from which body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared ( $\text{kg}/\text{m}^2$ ). Systolic and diastolic blood pressure (BP) measures were taken and recorded by trained data collectors.

The Center for Epidemiologic Studies-Depression (CES-D) Scale (Radloff, 1977) was used to estimate frequency of 20 depressive symptoms in the past week from 0 (none) to 3 (5–7 days). The CES-D screens for risk of depression in the general population and has acceptable reliability and validity (Cosco et al., 2017; Radloff & Locke, 1986; Radloff & Teri, 1986; Thomas et al., 2001; Weissman et al., 1977). In this study, the CES-D score was used as a continuous variable (0–60) and as a dichotomous variable with 16 indicating high risk for depression. Cronbach alpha was .91 at study initiation.

After excluding women with a chronic illness from enrollment, health problems were assessed at study initiation and annually with an investigator-designed checklist of 15 alphabetized conditions that asked “Do you now have, or have you ever had, any of the following conditions?” with yes or no responses. There was also a fill-in space for “other” and the most frequently endorsed conditions for the entire sample at study initiation are in Table 1. Most participants had more than one health problem such as headaches, urinary tract infection, and varicose veins. At 30 months, participants were also asked chronic illness exclusion screening questions from the initial screening.

## Statistical analysis

All analyses were conducted using SPSS version 20 (SPSS, Inc., Chicago). Descriptive statistics were used to summarize demographic characteristics and frequency of health problems. The square root transformation of CES-D scores was sufficient to normalize the values. Last value carried forward from T6 (30 months) was used to replace a missing data point at T7 (36 months), and mean substitution was used to replace a single missing time point between two values during the three-year period. Groups were compared using t-tests,

one-way ANOVA, repeated measures ANOVA, and Chi-square when appropriate. All tests were 2-tailed and  $p < .05$  was considered statistically significant.

## Results

### Sample characteristics

Of the 347 women initially enrolled, 264 (77%) had data at 30–36 months for this analysis. The only significant differences between the 264 in this analysis and the 83 women who did not complete data collection at 30–36 months were age, FSH level, and post-menopausal status. These differences were expected because women who became post-menopausal, had a hysterectomy, or started hormone therapy were only followed for the subsequent year. Characteristics of the sample are in Table 2 and reflect California demographics at the time of data collection (Gilliss et al., 2001; Kennedy et al., 2005). Women self-identified as Caucasian (51%), African American (26%) or Latina (23%). Most were non-smokers, partnered, well-educated, and employed.

Women were initially screened ineligible for the study if they reported a chronic illness, had irregular menstrual cycles, planned a pregnancy, or planned to move outside the local area. However, in the first year some enrolled participants became post-menopausal, pregnant, or relocated, and were removed from this analysis. Retained in this sample were 75 (28%) women who became peri- or post-menopausal during the second or third year. Only 47% reported getting 7 hours or more sleep per night, and hours of sleep remained consistent over time. Only 41% had a BMI in normal range, and average body weight increased at the rate of 1.4 lbs per year; 91 (34%) lost weight or stayed within 1 lb, 55 (21%) gained 1–4.9 lbs, and 118 (45%) gained 5 lbs or more over time.

### Risk of depression associated with demographic characteristics

Only 28% were at risk for depression (CES-D score  $\geq 16$ ) and the average score decreased slightly over time, but this change was not statistically significant. The risk of depression differed by ethnicity, marital status, and education (see Table 2). Women at higher risk of depression at study initiation were less likely to be college educated ( $p = .009$ ), partnered or married ( $p = .003$ ), or report getting  $\geq 7$  hours sleep at night. There was no difference in risk of depression by employment status, having children at home, income, alcohol intake or smoking status. Significantly fewer (16%) Latinas were at risk of depression (Table 2) compared to Caucasians (45%) and African Americans (38%) at study initiation ( $p = .012$ ); this ethnic difference was not present at 30–36 months.

### Risk of depression associated with age and reproductive stage

There was no relationship between CES-D scores and age or FSH level as a marker of menopause status at initial assessment or 30–36 months. There were 188 (72%) women who remained pre-menopausal throughout the study and 46 (25%) had high risk of depression; 64 began to transition into peri-menopausal and 16 (25%) had high risk of depression, while another 11 women had 12 months with no menses, hysterectomy or hormone therapy, and 5 (46%) had high risk of depression.

The first hypothesis, that pre-menopausal women would be at low risk of depression across time compared to women in early peri-menopause or post-menopause at 30–36 months was not supported: while pre-menopausal women had a lower mean CES-D score compared to peri-menopausal and post-menopausal women at 30–36 months, the difference [CES-D transformed scores] was not significant (Table 2), and differences in rates by reproductive stage were also not significant.

### **Risk of depression associated with health problems over time**

Despite excluding women with a chronic illness, 96% of the original sample reported some type of past or current health problem at study initiation (Table 1) and 20% stated the problem was current. CES-D scores were correlated with number of health problems ( $r = .199, p < .001$ ). In this longitudinal subsample, a past or current health problem was also reported by 96% at study initiation and 20% indicated that the problem was current. At 30–36 months, however, only 37% reported a health problem. Having a health problem at study initiation, or at 30–36 months, did not distinguish women at high risk of depression from women at low risk (Table 3).

As seen in Table 1, participants did not necessarily perceive obesity or HTN to be a health problem. However, at study initiation, obesity (27%) and HTN (13%) were two prevalent health problems known to be risk factors for depression. Women at higher risk of depression (CES-D  $\geq 16$ ) had a significantly worse perception of their health, higher BMI, and higher systolic blood pressure compared to women at lower risk (Table 2).

The second hypothesis, that fewer healthy women with normal weight and blood pressure at study initiation would be at risk of depression over time compared to obese or hypertensive women, was partially supported. The group of 190 healthy women had lower mean CES-D [transformed] scores at each time point, and at study initiation fewer healthy women (23%) were at high risk for depression compared to 40% of the 74 women with HTN and/or obesity ( $\chi^2 = 8.5, p = .003$ ). At 30–36 months, however, there was no significant mean difference between these two initial groups.

It should be noted that at 30–36 months, 19 healthy women became hypertensive, 16 women with a normal BMI became overweight, and 11 initially overweight women became obese. While mean CES-D scores at each time point never exceeded 16, the healthy group had CES-D mean scores ranging between 10.0 and 12.0 over time and the women with HTN and/or obesity had mean CES-D scores ranging between 14 and 16.

When BMI and blood pressure values were examined at 30–36 months, there were significant group differences in mean CES-D scores [transformed] at that time point (see Table 3) that were similar to the significant group differences at study initiation.

### **Risk of depression associated with demographics and chronic illness at 30–36 months**

At 30–36 months, the sample's risk of depression was similar (25%) to the initial score (28%) and the mean CES-D score ( $11.3 \pm 9.66$ ) was not significantly different from their initial score. However, 31% now reported a chronic illness as shown in Table 4. There was a weak association between ethnicity and chronic illness: 28 (34%) African Americans

reported a chronic illness, compared to 41 (49%) Caucasians and 14 (17%) Latinas ( $X^2_{[2]} = 5.1, p = .079$ ), but the significant association between ethnicity and risk of depression seen at study initiation was no longer present at 30–36 months ( $p = .231$ ).

In contrast to ethnicity, employment status was not a factor at study initiation but became significant for risk of depression as well as chronic illness at 30–36 months. Only 30 women (11%) were unemployed at 30–36 months, but 90% ( $n = 75$ ) of women with a chronic illness were employed. However, as a group, women unemployed at 30–36 months had a mean CES-D score 16 at each time point, including study initiation and the difference compared to employed women was significant (see Figure 1).

Women reporting a chronic illness at 30–36 months had significantly higher CES-D scores than women reporting no chronic illness, and having a chronic illness at 30–36 months was also a significant factor in risk of depression (Table 3). Women with a chronic illness had significantly higher CES-D scores over time, with only two of the seven time points having mean values above 16. The pattern of CES-D mean scores over time for participants reporting a chronic illness at 30–36 months compared to women reporting no chronic illness is seen in Figure 2. There was no significant change over time for either group, but there was a significant between-group difference in CES-D scores [transformed] ( $F = 15.4, p < .001$ ).

Our third and final hypothesis was that the 73 women with high risk of depression at study initiation would more likely report a chronic illness at 30–36 months compared to the 191 women with low risk for depression. As seen in Table 3, this hypothesis was supported: more women with high risk of depression at study initiation reported a chronic illness at 30–36 months (49%,  $n = 36$ ) than women with low risk of depression at study initiation (25%,  $n = 47$ ;  $X^2_{[1]} = 14.96, p < .001$ ). The group at high risk of depression at study initiation demonstrated an average reduction in CES-D scores over time (from  $24.3 \pm 7.90$  to  $17.7 \pm 11.21$ ). In contrast, the group at low risk of depression at study initiation had a slight increase (from  $7.2 \pm 4.56$  to  $9.1 \pm 7.96$ ). CES-D scores [transformed] differed significantly by time (T1, T2, T3 > T7) and group ( $p < .001$ ). While the association between risk of depression and chronic illness was significant, there was no significant association between risk of depression and report of a current or past health problem at 30–36 months ( $X^2_{[1]} = 1.68, p = .195$ ).

When the sample was categorized at 30–36 months to be either low risk ( $n=197$ ) or high risk of depression ( $n=67$ ), differences in reporting a chronic illness (28% and 40%, respectively) did not reach statistical significance ( $X^2_{[1]} = 3.3, p = .071$ ). Furthermore, these two risk groups at 30–36 months did not differ in reporting a health problem ( $X^2_{[1]} = 0.52, p = .471$ ).

## Discussion

In this study, we examined the risk of depression in relation to physical health parameters in a relatively healthy sample of late pre-menopausal women from a community-based, non-clinical population (Minarik, 2008). Risk of depression was 28% at study initiation and 25% at 30–36 months. These rates are consistent with other reports in premenopausal women (Alexander et al., 2007<sup>b</sup>), specifically 24% when the CES-D was used in ethnically diverse



women as part of the SWAN sample (Bromberger et al., 2004). However few studies have examined women over time in the decade prior to menopause or included diverse ethnic groups (Vesco et al., 2007).

Our first hypothesis that pre-menopausal women would have a lower risk of depression across time compared to early peri-menopause or post-menopause at 30–36 months was not supported and contradicted other findings (Mulhall et al., 2018). Risk of depression did not differ by reproductive stage, or by FSH level, but women who remained pre-menopausal throughout the study had a consistently lower CES-D score over time compared to either peri-menopausal or post-menopausal women at 30–36 months (Table 3). This mean difference was not significant, but the small numbers of peri- and post-menopausal women changing reproductive stage at various time points may have created more variability and limited the power to detect a statistically significant difference.

The high number of women (96%) reporting current or past health problems at study initiation was surprising, possibly indicating that women have various meanings for what they consider healthy or problematic. However, these findings are consistent with the literature on prevalence of aches and pains among midlife women (Alexander et al., 2007<sup>a</sup>; Szoeki et al., 2008). Given this high level of health issues, our second hypothesis required that we focus on health problems more common in midlife women but not necessarily endorsed as a chronic illness. Given the interrelationship between HTN and obesity, we hypothesized that fewer healthy women at study initiation would be at risk of depression compared to women with HTN and/or obesity. This hypothesis was partially supported. The healthy women had lower mean CES-D scores at each time point, and at study initiation significantly fewer (23%) healthy women had high risk for depression compared to 40% of women with HTN and/or obesity. This difference was not evident at 30–36 months, however, which could be explained by health status changes, with some healthy women becoming hypertensive or obese and others losing weight.

Given our findings, there remains a need to screen for HTN and obesity regardless of menopausal status or complaints of minor health problems to identify women at risk for depression. The difference in risk of depression by HTN and non-HTN groups, was similar for actual blood pressure, particularly systolic pressure. In contrast, others researchers report inconsistent findings (Hamer et al., 2010; Hildrum et al., 2007, 2008), positive associations (Patten et al., 2009), or weak associations (Delaney et al., 2010; Grimsrud et al., 2009) between HTN and depressive symptoms. Our finding is in contrast to a recent study in which HTN had a weaker effect on depression risk when compared to other chronic illnesses like heart disease and type 2 diabetes (Wilson-Genderson et al., 2017). By excluding women with a chronic illness from the original study design, we only had 5 women with type 2 diabetes at 30–36 months and could not analyze this small group. On the other hand, obesity, which was not considered a chronic illness when our study was initiated, was quite prevalent in our sample and there was a strong association with depressive symptoms and risk of depression.

Literature on the relationship between depression, obesity and HTN is conflicting. Some cross-sectional studies examine the relationship between depression and hypertension

concurrently, and more longitudinal studies are needed with larger sample sizes. A large population-based study suggested that multiple pathways in opposite directions may link depressive symptoms with blood pressure (Michal et al., 2013), and obesity may be a common link to both (Tobet et al., 2013). Still others note potential age and gender differences in how these comorbidities are linked (Shah et al., 2013). While our study focused only on midlife women within a narrow age range, our findings regarding systolic blood pressure and risk of depression support longitudinal findings from Shah and colleagues (2013) who examined the influence of age and gender on the relation between depressive symptoms and HTN. They found that higher CES-D scores were associated with higher systolic blood pressure in younger women.

While obesity and HTN were physical health issues associated with risk of depression more so than reproductive stage in this midlife sample, marital status and education associations with depression at study initiation were not present at 30–36 months. Most consistent and surprising was that income and employment status at study initiation was unrelated to risk of depression, yet unemployed women at 30–36 months had significantly higher CES-D scores as well as risk of depression over time compared to women employed at 30–36 months (Figure 1). While this finding needs to be replicated in other samples, it suggests that some women are experiencing depressive symptoms and risk of depression even prior to becoming unemployed and symptoms may directly or indirectly result in unemployment. Unemployment was low in this sample and stable over time, yet there were some women who changed job status during the study. It was not possible to determine whether women unemployed at study initiation desired unemployment or were already coping emotionally with not working for pay outside the home.

Although mean CES-D scores differed significantly by demographic and health risk variables such as menopausal status, sleep duration, and health perception, these differences did not distinguish high risk (CES-D > 16) women over time in the same way that unemployment and chronic illness did. Future studies should examine duration of unemployment as well as circumstances for unemployment, such as a chronic illness, when evaluating its effects on depressive symptoms and risk of depression. These findings support and extend the Theory of Symptom Management (Bender et al 2018) by highlighting how a socio-demographic factor such as employment can impact depressive symptom experience even more than a woman's biological age or reproductive stage.

Because our initial sample reported such a high rate of current or past health problems, we focused on the potentially more impactful health problem of developing a chronic illness as differentiated from more prevalent health problems. Our third hypothesis was that women with high risk of depression at study initiation would be more likely to report a chronic illness at 30–36 months compared to women with low risk for depression. In contrast with current or past health problems, this hypothesis was supported, with 49% of women at high risk of depression reporting a chronic illness at 30–36 months compared to only 25% of women at low risk. Our findings also support recent research that indicates chronic illness significantly increases a person's risk for depression (Wilson-Genderson et al., 2017).

Chronic conditions, like heart disease and arthritis, appear to have a greater impact on depression risk. This is likely because they are more debilitating and affect mobility, independence, and overall quality of life. The fact that our sample was relatively healthy at the onset of the study speaks to the significant psychological impact of chronic illness. There remains, however, the question of which comes first, depressive symptoms or chronic illness, and whether certain depressive symptoms are actually the initial experience of an as yet undiagnosed chronic illness. In our sample, women with a chronic illness at 30–36 months had significantly higher CES-D scores across time compared to women with no chronic illness (Figure 2). With measures every 6 months, the timing of a chronic illness diagnosis in relation to an increased CES-D score was not exact, and therefore whether depressive symptoms preceded, followed or developed concurrently with the diagnosis is unknown. Considering our strong findings regarding unemployment at 30–36 months, it may be that chronic illness and depressive symptoms occur prior to unemployment rather than unemployment leading to depressive symptoms.

Nevertheless, there is increasing recognition for the important role of depressive symptoms in both the etiology and outcomes related to chronic illness (Chapman et al., 2005). Consistent with current literature, our prospective data support a bi-directional relationship between depressive symptoms and chronic illness (Baewald et al., 2018; Golden et al., 2008). Chronic illnesses prevalent in older women may begin to manifest in late reproductive stages, prior to onset of menopause. Data from a subset of the SWAN sample indicates that modulation of immune function, including inflammatory cytokines, may be a common physiological pathway by which depression impacts health (Cyrankowski et al., 2007). From this perspective, recognizing and treating depressive symptoms may prevent, delay, or reduce the impact of chronic illness on women's quality of life and employment status.

Another health issue linked to depression is insomnia (Ji et al., 2019) and we found significant differences in self-reported sleep duration between women with low and high risk for depression. The CES-D includes items such as “my sleep was restless” that may be confounded by insomnia. Given our findings, depression related specifically to short sleep duration and long sleep duration as well as chronic insomnia and other sleep disorders should be explored in future research.

## Limitations

The major limitation of this study is the secondary analysis of data from 1996–2004 collected using self-report measures of health problems and chronic illness. However, there are many strengths, including the longitudinal design with minimal missing data or attrition over three years, recruiting a community sample of diverse relatively healthy, premenopausal women prior to the onset of menopause, and using objective measures of blood pressure, height, weight, and reproductive stage with urine FSH levels as well as menstrual cycle patterns.

Some weaknesses also need to be considered. The CES-D is a measure of current depressive symptoms that is useful in screening for risk of depression, and not a diagnostic measure of depressive disorder (Radloff & Teri, 1986). In addition, medical records were not used to

establish diagnosis of chronic illness. Physical health was measured using investigator-designed lists of health problems and while there was space to write in other problems, our measure did not allow for a full examination of women's health issues. Prior to enrollment, potential participants were excluded on the basis of a chronic illness by self-report. Self-report is subject to response bias and recall bias, but research has shown strong correspondence between self-reported chronic conditions and medical records (Kriegsman et al., 1996; Scott et al., 2007).

## Conclusion

Despite limitations, this study provides strong support for the association between chronic illness and risk of depression in midlife women prior to the onset of menopause and during early menopausal transition. Knowing that depression and chronic physical illnesses occur together suggests the need to assess for comorbidity of depressive symptoms during clinical health assessments regardless of menopausal status. Depressive symptoms were stable for the sample as a whole, but were higher in the presence of chronic illness, obesity, HTN, or unemployment, suggesting that these factors are highly inter-related. Determining which factor occurs first would contribute to the improvement of mental and physical health for a substantial number of midlife women.

Our findings also have implications for healthcare providers. When women are diagnosed with a chronic condition, assessing depressive symptoms, obesity, and employment status is warranted. If a woman with a chronic illness desires to continue employment, strategies to continue working should be explored from the perspective of minimizing other health problems such as obesity and depression. Women who present with depression are at greater risk for physical health problems such as obesity and HTN, and may be at greater risk for disability and unemployment. General medical services cannot be separate from mental health services, and these comorbidities require more focused attention (Scott et al., 2007). This study adds to literature on temporal relationships between depression symptoms and chronic illness in midlife women to more effectively understand this type of mental-physical comorbidity issue and consequences for the health of women after menopause.

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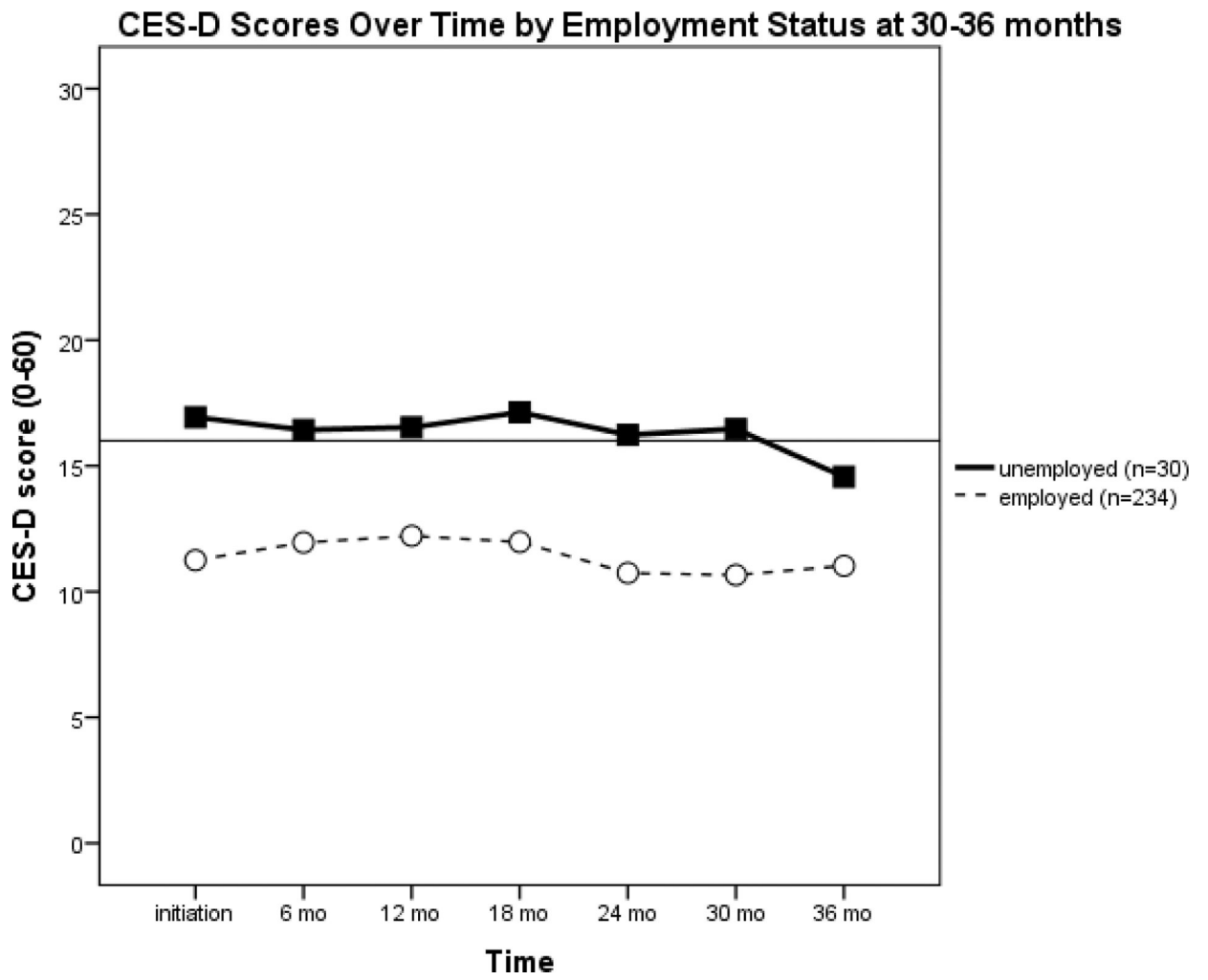
### Highlights

- Depression symptoms in late premenopause, prior to the onset of menopause, were higher in the presence of chronic illness.
- The temporal relationship between depression symptoms and chronic illness in midlife women has implications for healthcare providers caring for midlife women.
- Significant differences were noted in self-reported sleep duration between women at low and high risk for depression.
- Chronic illnesses prevalent in older women may begin to manifest in late reproductive stages, prior to onset of menopause.



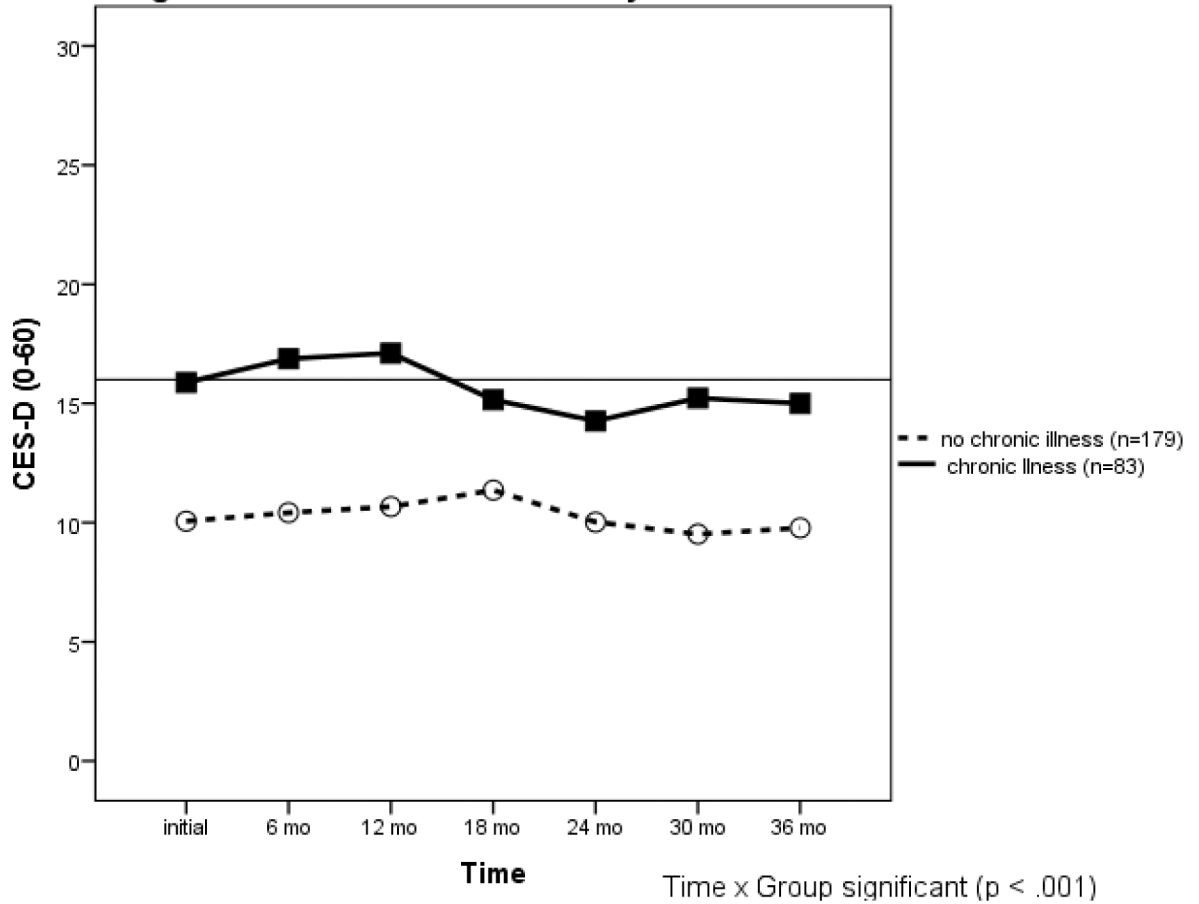
**Limitations:**

- This is a secondary analysis of data collected at intervals of 6 months and self-report measures of health problems and chronic illness.
- The CES-D, used in this study to assess depressive symptoms, is not a diagnostic measure of depressive disorder.
- Medical records were not used to establish diagnosis of chronic illness.
- The investigator-designed physical health measure did not allow for a full examination of women's health issues.
- Self-report is subject to response bias and recall bias.



**Fig. 1.** Within-subjects effects (NS); between-subjects effects ( $F_{[1,262]} = 11.5, p = .001$ )  
 CES-D = Center for Epidemiologic Studies-Depression scale

**Change in CES-D Scores Over Time by Chronic Illness at 30-36 months**



**Figure 2. Depressive Symptoms Scores over Time by Chronic Illness Group**  
 Within-subjects effects ( $F= 2.6, p= .02$ ); Between-subjects effects ( $F= 31.4, p < .001$ )  
 CES-D = Center for Epidemiologic Studies-Depression scale

**Table 1.**

Ten Most Frequent Current or Past Health Problems at Study Initiation (N = 347)

Current or Past Health Problem	<i>n</i>	%
Allergies (including hay fever)	207	60
Headaches or migraines	192	55
Back problems	181	52
Hemorrhoids	136	39
Skin problems, psoriasis, eczema or dermatitis	127	37
Kidney, bladder or urinary problems	91	26
Varicose veins	83	24
Irritable bowel problems	71	21
Asthma	55	16
Arthritis	54	16
One or more health problems in the past	330	96
One or more health problems currently	68	20
Hospitalized or emergency room visit (past year)	21	6

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**Table 2.**

## Participant Characteristics at Study Initiation (Time 1)

Characteristic	Total N = 264	*CES-D < 16 n = 191 (72%)	*CES-D ≥ 16 n = 73 (28%)	Test statistic, p value
	mean ± SD	mean ± SD	mean ± SD	
CES-D (0–60) *	11.9 ± 9.50	7.2 ± 4.55	24.2 ± 7.88	$t = 17.4, p < .001$
Age (years)	43.4 ± 2.3	43.4 ± 2.4	43.3 ± 2.2	$t = 0.15, p = NS$
FSH (IU/dL)	1.03 ± 1.50	0.91 ± 1.21 (median=0.40)	1.18 ± 1.89 (median=0.50)	$t = 1.27, p = NS$ $MWU = NS$
General health perception	2.3 ± 0.91	2.1 ± 0.86	2.7 ± 0.88	$t = 5.2, p < .001$
Body mass index (BMI; kg/m <sup>2</sup> )	27.5 ± 6.47	26.6 ± 5.74	29.7 ± 7.67	$t = 3.6, p < .001$
Blood Pressure				
Systolic	116 ± 12.5	115 ± 12.6	119 ± 11.9	$t = 2.2, p = .027$
Diastolic	76 ± 9.5	75 ± 9.9	77 ± 9.9	$t = 1.3, p = NS$
Self-reported sleep time (hrs)	6.8 ± 1.04	7.0 ± 0.86	6.2 ± 1.23	$t = 5.2, p < .001$
< 7 hrs per night	124 (47%)	74 (39%)	50 (69%)	$\chi^2 = 18.8, p < .001$
	%	%	%	
Race/Ethnicity				$\chi^2 = 8.9, p = .012$
African American (n=68)	26%	21%	38%	
Latina (n=61)	23%	26%	16%	
Caucasian (n=135)	51%	53%	45%	
Education				$\chi^2 = 6.9, p = .009$
High school graduate or less	38%	33%	51%	
College graduate or more	62%	67%	49%	
Marital status				$\chi^2 = 8.5, p = .003$
Married/partnered	52%	57%	37%	
Single/divorced/widowed	48%	43%	63%	
Household gross income				$\chi^2 = 0.42, p = NS$
< \$31,000	16%	16%	18%	
\$31,000-\$80,999	54%	58%	59%	
>\$81, 000	24%	26%	23%	
Not reported	6%			
Employed				$\chi^2 = 0.26, p = NS$
Yes	86%	87%	84%	
No	14%	13%	16%	
Children				$\chi^2 = 2.10, p = NS$
Yes	66%	64%	73%	
No	34%	36%	27%	
Current Smoker				$\chi^2 = 0.49, p = NS$
Yes	10%	9%	12%	
No	90%	91%	88%	

SD = standard deviation; NS = not significant ( $p > .05$ ); FSH = Follicle Stimulating Hormone; MWU = Mann-Whitney U non-parametric test for median difference between groups.

\* CES-D = Center for Epidemiologic Studies-Depression scale (square root transformations not shown)

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**Table 3.**

Group Differences in Depressive Symptom Scores by Physical Health Problems at Time 1 (study initiation) and Time 6 (36 months)

Physical Health	N (%)	CES-D score* (mean ± SD)	Test statistic, p value
<b>Time 1 Current or past health problem</b>			$t = 0.24$
None	13 (4%)	13.3 ± 11.58	$p = \text{NS}$
One or more	251 (96%)	11.9 ± 9.49	
<b>Time 6 Current or past health problem</b>			$t = 0.11$
None	165 (63%)	11.5 ± 9.55	$p = \text{NS}$
One or more	99 (37%)	11.3 ± 9.97	
<b>Time 1 Body Mass Index</b>			$F_{[2,261]} = 10.4$
Normal weight (BMI < 25.0)	109 (41%)	9.0 ± 7.71	$P < .001$
Overweight (BMI 25.0 – 29.9)	85 (32%)	12.9 ± 9.80	
Obese (BMI ≥ 30)	70 (27%)	15.2 ± 10.41	
<b>Time 6 Body Mass Index</b>			$F_{[2,261]} = 6.3$
Normal weight (BMI < 25.0)	107 (41%)	10.5 ± 8.99	$P = .002$
Overweight (BMI 25.0 – 29.9)	74 (28%)	9.1 ± 7.56	
Obese (BMI ≥ 30)	83 (31%)	14.1 ± 10.90	
<b>Time 1 Measured Blood Pressure</b>			$t = 2.7$
<b>Hypertension &gt; 140/90</b>			$p = .007$
No hypertension	250 (95%)	11.5 ± 9.17	
Hypertension	14 (5%)	18.6 ± 12.76	
<b>Time 6 Measured Blood Pressure</b>			$t = 2.1$
<b>Hypertension &gt; 140/90</b>			$p = .037$
No hypertension	231 (87%)	10.7 ± 8.89	
Hypertension	33 (13%)	14.1 ± 11.65	
<b>Time 6 menopausal status</b>			$F_{[2,261]} = 1.4$
Pre-menopausal	189 (72%)	10.9 ± 9.14	$P = \text{NS}$
Peri-menopausal	64 (24%)	12.6 ± 11.30	
Post-menopausal	11 (4%)	13.9 ± 11.18	
<b>Time 6 Chronic illness</b>			$t = 4.38$
No	181 (69%)	9.4 ± 8.18	$p < .001$
Yes	83 (31%)	15.2 ± 10.70	

\*CES-D = Center for Epidemiologic Studies-Depression scale (square root transformation values not shown)

**Table 4.**

Chronic Illness Health Problems Self-Reported at Time 6 (n = 264)

Chronic Illness or Health Problem	<i>n</i>	%
High blood pressure	34	12.9
Thyroid disorder	25	9.5
Psychiatric illness	14	5.3
Gall bladder disease	10	3.8
Stomach ulcer	7	2.7
Cancer	7	2.7
Type 2 diabetes	5	1.9
Diabetes while pregnant	5	1.9
Stroke	4	1.5
Pain	4	1.5
Muscle or joint problems	4	1.5
Asthma	4	1.5
Fibroids	4	1.5
Eye problems	3	1.1
Headache or migraine	3	1.1
Kidney disease or renal dialysis	2	0.8
Type 1 Diabetes	0	0

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