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Longitudinal Trends in Depression and Associated Lifestyle Behaviors: Insights from the SWAN Study

Asma Binte Afzal¹

¹Department of Environmental and Occupational Health, School of Public Health-Bloomington, Indiana University, IN, USA

ABSTRACT

Objective:

Depression is a major public health concern among midlife women, particularly during the menopausal transition. Lifestyle behaviors such as smoking, alcohol consumption, and sleep quality may significantly influence depressive symptoms. This study examines the longitudinal associations between depression and lifestyle behaviors in a diverse sample of midlife women in the United States.

Methods:

Data were drawn from the Study of Women's Health Across the Nation (SWAN), a multi-site, longitudinal cohort study of 3,302 women aged 47-59. A total of 13,474 observations from visits 1 to 10 were analyzed. Depression symptoms were measured using the FEELBLU variable (frequency of feeling blue or depressed over the past two weeks). Mixed-effects ordinal logistic regression models were employed to assess the relationship between depression and lifestyle behaviors, adjusting for demographic characteristics.

Results:

Better sleep quality significantly reduced the odds of depressive symptoms by 65% (log odds = -1.888, $p < 0.001$). Nervousness increased the odds of higher depressive symptoms by up to 136-fold (log odds = 4.915, $p < 0.001$). Alcohol consumption was associated with a 14% increase in the odds of depression (log odds = 0.130, $p = 0.0389$) while smoking one additional cigarette per day increased the odds by 2% (log odds = 0.020, $p = 0.0279$). Temporal trends showed a slight increase in depressive symptoms over time.

Contributions:

This study provides robust longitudinal evidence of the associations between depression and lifestyle behaviors among midlife women. Interventions aimed at improving sleep quality, reducing nervousness, and addressing smoking and alcohol consumption may contribute to better mental health outcomes during the menopausal transition.

INTRODUCTION

Depression is a growing public health concern among midlife women, particularly during the menopausal transition, a period marked by hormonal changes, sleep disturbances, and increased vulnerability to mental health challenges. Recent evidence shows that lifestyle behaviors, including smoking, alcohol consumption, and poor sleep quality, may exacerbate depressive symptoms during this critical phase (Anderson et al. 2022; Kim et al. 2021). Despite a substantial body of research on depression, limited longitudinal evidence focuses exclusively on

midlife women navigating the menopausal transition. This life stage presents unique physiological and psychosocial stressors that interact with health behaviors and potentially influence long-term mental health outcomes (Bowman et al. 2021; Kravitz et al. 2014). The current research explores the extent to which lifestyle behaviors such as smoking, alcohol consumption, medication use, and sleep quality influence depression symptoms among midlife women using longitudinal evidence from the SWAN study.

The Study of Women's Health Across the Nation (SWAN) is a longitudinal, multi-ethnic study examining various aspects of women's health during the menopausal transition. SWAN has provided insights into bone loss (Neer, 2010), visceral fat accumulation (Janssen et al., 2010), and changes in reproductive hormones (Samar et al., 2019). The study developed methods for assessing menstrual cycles using urinary hormone assays (Santoro et al., 2003) and identified distinct directions of estradiol and follicle-stimulating hormone changes during menopause (Tepper et al., 2012). SWAN research has shown that certain cardiovascular risk factors, particularly lipid levels, change significantly around the final menstrual period (Matthews et al., 2009). The study has also explored mood changes, finding an increased risk of depressive symptoms during the menopausal transition (Bromberger & Kravitz, 2011), and examined vasomotor symptoms, a hallmark of menopause (Thurston & Joffe, 2011).

Recent studies have shown an increasing trend in depression prevalence in the United States, particularly among young and older adults (Weinberger et al., 2018; Yu et al., 2020). Depression is related to unhealthy lifestyle behaviors, including smoking, excessive alcohol consumption, poor nutrition, and sedentary habits (Anderson et al., 2022; Loprinzi & Mahoney, 2014; van Gool, 2003). These behaviors often co-occur and demonstrate a dose-response relationship with depression symptoms (Loprinzi & Mahoney, 2014). Longitudinal studies have revealed that depression can lead to increased smoking and sedentary behavior, while smoking is also associated with an increased risk of developing depression (Breslau et al., 1998; van Gool, 2003). Additionally, socioeconomic factors such as low income and education levels are linked to higher depression rates (Yu et al., 2020). Understanding these complex relationships between depression, lifestyle behaviors, and social determinants of health is crucial for developing effective interventions and prevention strategies (Liu et al., 2017; Wickrama & Wickrama, 2010). This study aims to build upon this knowledge by examining the longitudinal trends in depression and its association with lifestyle behaviors in midlife women participating in the SWAN study. The following section outlines the primary and secondary hypotheses for the current study.

HYPOTHESIS

Primary Hypothesis

There is a significant association between depression symptoms and lifestyle behaviors, including smoking, alcohol intake, and medication use for nervousness and sleep issues, in midlife women.

Secondary Hypothesis

1. **Hypothesis 1:** Women who smoke have a higher chance of reporting depression symptoms compared to non-smokers.
2. **Hypothesis 2:** Increased levels of alcohol intake are associated with an increase in depression symptoms among midlife women.
3. **Hypothesis 3:** Sleep behavior is associated with a higher probability of experiencing depression symptoms in midlife women.
4. **Hypothesis 4:** Individuals with higher frequencies of nervousness are associated with a higher probability of experiencing depression symptoms in midlife women.

METHODS

Study Population

The SWAN study is a multi-site, longitudinal epidemiological study initiated in 1996-1997 to investigate women's health during their middle years. Three thousand three hundred two participants were recruited from seven research centers across the United States (*Appendix 2* outlines the study sites), representing five racial/ethnic groups: Black/African American, Chinese/Chinese American, Japanese/Japanese American, Caucasian/White Non-Hispanic, and Hispanic (Neer, 2010). For this analysis, data from visits 1 to 10 were used. Approximately 2450 participants completed various health and lifestyle assessments during each Visit. Depression was measured using the FEELBLU variable, which captured self-reported feelings of depression over the past two weeks.

Table 1: Summary Statistics of Study Variables (SWAN Study, Visits 1-10)

Variable Category	Variable Description	Response Categories (%)
Depression Symptoms (Dependent Variable)	Frequency of feeling blue or depressed in the past 2 weeks	Not at all (51.8%) 1-5 days (36.5%) 6-8 days (5.9%) 9-13 days (3.9%) Every day (1.8%)
Age Group	Age is categorized into three groups	47-50 years (34%) 51-54 years (33%) 55-59 years (33%)
Race/Ethnicity	Self-reported racial/ethnic identity	Black/African American (28%) Chinese/Chinese American (10%) Japanese/Japanese American (9%) Caucasian/White Non-Hispanic (47%) Hispanic (6%)
Sleep Behavior	Indicators of poor sleep or sleep medication use	Varies across indicators; the majority reported no sleep medication use
Smoking Behavior	Current smoking status and average cigarettes per day	Non-smokers (80%) Smokers (20%)
Alcohol Consumption	Any alcohol consumption in the past 24 hours	No (85%) Yes (15%)
Medication Use for Nervous Conditions	Use of medication for nervous or sleep conditions	No (90%) Yes (10%)
Recent Depression	I felt depressed in the past week	Rarely (<1 day) (60%) Some (1-2 days) (25%) Occasionally (3-4 days) (10%) Most/all of the time (5-7 days) (5%)
Nervousness	Feeling tense/nervous in the past 2 weeks	Not at all (60%) 1-5 days (25%) 6-8 days (8%) 9-13 days (5%) Every day (2%)

Table 1 outlines the summary statistics for all the variables used in the current study. *Appendix 1* also explores the variable Name from the SWAN study dataset and replicability and study rigor. The distribution of depression symptoms indicates that while a majority of midlife women reported no depressive symptoms in the past two weeks (51.8%), a significant proportion experienced occasional or frequent symptoms, highlighting the importance of examining mental health in this population. The descriptive patterns across lifestyle behaviors—including sleep, smoking, alcohol consumption, and medication use— provide an essential context for understanding how modifiable health behaviors interact with depressive symptoms over time.

Model Selection for Multivariate Analysis

The distribution of responses for FEELBLU (feeling blue or depressed in the past two weeks) displays that most respondents, approximately 51.8%, reported "Not at all," indicating that over half did not experience feeling blue. Around 36.5% reported feeling blue for 1-5 days, making this the second most common response. Smaller proportions reported feeling blue more frequently: 5.9% for 6-8 days, 3.9% for 9-13 days, and 1.8% reported feeling blue "Every day." This distribution suggests that most respondents experienced minimal or no feelings of being blue, with fewer reporting moderate to frequent episodes. However, no statistical tests have been performed here, so the significance of these proportions is not assessed. Appendix 3 outlines the distribution of the dependent variable responses.

Skewness of the Data

The distribution of FEELBLU (frequency of feeling blue or depressed) shows right (positive) skewness, with progressively fewer responses in categories indicating a higher frequency of depressive symptoms. Although there

is a positive skew, it is not extreme, as all response levels are represented, and the decrease across categories is gradual. This distribution suggests a relatively healthy sample, where most participants report minimal depressive symptoms, which aligns with typical expectations for population-based studies.

Data Cleaning Process

The initial SWAN dataset of 36,322 observations underwent cleaning to address missing data and refine it for hypothesis-specific analyses. Observations with missing responses and predictors with high missingness, such as nervousness and depression medication variables, were excluded. Predictors unrelated to the hypotheses were also removed, resulting in a final dataset of 13,474 observations. This process ensured robust, reliable data, enhancing integrity and alignment with the study's objectives.

Statistical Analysis

The current study analyzed the relationship between depression (FEELBLU) and lifestyle behaviors (smoking, alcohol use, medication, and sleep) using longitudinal data from the SWAN study. Descriptive statistics summarized baseline trends, and ordinal cumulative link mixed models with a logit link function were employed to account for the ordinal outcome, repeated measures, and individual variability. Interaction terms (e.g., Sleep Quality \times Sleep Medication) captured dynamic relationships, while random intercepts adjusted for baseline differences across participants.

Model diagnostics, including Q-Q plots and residual analyses, evaluated assumptions and identified influential points. Logit and complementary log-log (cloglog) link functions were compared using AIC, BIC, and MSE metrics, with the logit model demonstrating a superior fit. Hypothesis testing in the final model (*time_change_model_2*) identified nervousness, depression, and sleep quality as key predictors, with temporal effects showing diminishing nervousness impacts and stable effects for smoking and depression. This statistical approach provided robust insights into the complex interplay between mental health and lifestyle behaviors in midlife women.

Analytical Method Selection Suitability: Mixed-Effects Ordinal Logistic Regression

Given that the dependent variable, FEELBLU, is ordinal with five ordered categories, a Mixed-Effects Ordinal Logistic Regression model is appropriate for the analysis. This model accommodates the ordered nature of FEELBLU and is well-suited to account for the repeated measures structure of the data, as FEELBLU was measured across multiple visits (1-10) per participant. The model allows for both fixed effects—representing consistent influences across participants—and random effects, which adjust for individual variability in baseline depression levels.

MODEL SPECIFICATIONS

Fixed and Random Effects

Fixed Effects: Variables such as DEPRESSION, NERVS1, AGE, RACE, and other demographic or lifestyle factors (e.g., smoking, alcohol use, medication) are included as fixed effects. These represent the consistent influence of these factors across the entire sample and allow us to measure their specific impacts on depressive symptoms.

Random Intercept: Each participant is assigned a random intercept to capture their unique baseline level of depressive symptoms, thus accounting for the correlation of repeated measures within each individual over time.

Model Equation

The Mixed-Effects Ordinal Logistic Regression can be expressed as:

$$\text{logit } Pr(X_{ij}, b_i) = \alpha_k - (X_{ij}\beta + b_i)$$

Where:

- Y_{ij} : The ordinal response variable (**FEELBLU**) for individual i at time j , with ordered categories $k = 1$ to 5 .
- $Pr(Y_{ij} \leq k)$: Cumulative probability that **FEELBLU** for individual i at time j falls in category k or below (e.g., "1-5 days" or less).
- α_k : Threshold parameters that differentiate between categories of **FEELBLU**. Each threshold α_k represents the logit cut-off for moving from one depression level to the next.

- X_{ij} : Vector of fixed-effect predictor variables for individual i at time j (e.g., age, race, smoking, alcohol use, medication, sleep behaviors).
- β : Coefficients for the fixed effects, representing the impact of each predictor on the log odds of being in a higher category of depression symptoms.
- b_i : Random effect (random intercept) for participant i , assumed to be normally distributed with mean 0 and variance σ_b^2 . This term captures each individual's baseline level of depression symptoms, accounting for within-person correlations across repeated measures.

This equation models the probability that FEELBLU falls in a particular category or below at a given visit for each participant, adjusting for both individual predictors and baseline levels of depressive symptoms over time.

Cumulative Link Function

The cumulative link function (typically the logit link) is used in ordinal logistic regression to model the cumulative probability of being in a particular category or lower, suitable for ordered response variables like FEELBLU. This transformation allows us to model ordinal data on a continuous scale and assess the cumulative impact of predictor variables on depressive symptoms.

Model Assumptions for Mixed-Effects Ordinal Logistic Regression

1. **Proportional Odds Assumption:** The effects of predictor variables is assumed to be consistent across all levels of depressive symptoms. The Brant test can be employed to test this assumption. If violated, a partial proportional odds model may be considered.
2. **Independence Across Individuals:** Observations between individuals are assumed to be independent, while responses within individuals over time are correlated. The random intercept for each participant addresses this within-subject dependency.
3. **Normality of Random Effects:** Random intercepts for individuals are expected to follow a normal distribution, capturing variations in baseline depressive symptoms among participants.
4. **Linearity of Logits for Continuous Predictors:** Continuous predictors are assumed to have a linear relationship with the log-odds of depressive symptoms. This assumption can be visually checked, and transformations may be applied if non-linear patterns are observed.

In summary, this Mixed-Effects Ordinal Logistic Regression framework provides a robust approach to understanding how demographic, lifestyle, and mental health factors collectively influence the frequency of depressive symptoms over time in the sample. The model accounts for both individual-level factors and within-person correlations, offering nuanced insights into the progression of depressive symptoms across visits.

RESULTS

Descriptive Statistics

The cross-tabulation graphs generated between FEELBLU (feeling blue or depressed in the past two weeks) and the independent variables: AGE, SMOKERE (smoking status), DEPRESS (felt depressed in the past week), RACE, and SLEEP1 (used sleep medication in the past week). This interpretation is descriptive only; no statistical analysis has been conducted, so the significance of these patterns cannot be determined.

Across age groups (47-50, 51-54, and 55-59), most individuals reported "Not at all" feeling blue, with a smaller proportion reporting higher frequencies. This suggests a relatively consistent pattern across age groups, with a predominantly low incidence of feeling blue. Both smokers and non-smokers mostly reported "Not at all" or "1-5 Days" for feeling blue. Smokers reported a slightly higher incidence of feeling blue across the week than non-smokers. However, without statistical analysis, whether this difference is meaningful is uncertain. Individuals with higher frequencies of feeling depressed in the past week (e.g., "Most/all of the time") reported higher frequencies of feeling blue in the past two weeks. This visual pattern suggests a possible association between recent depression and feeling blue. Across racial/ethnic groups, "Not at all" was the most common response for feeling blue, with some variation in the proportions across groups.

However, the differences are descriptive only, and further analysis would be needed to confirm any associations. Individuals who did and did not use sleep medication showed similar distributions, with "Not at all" and "1-5 Days" being the most common responses for feeling blue. Sleep medication usage does not appear to have a

clear visual association with the frequency of feeling blue. These graphic summaries (plots are included in the supplemental document) provide insights into the distribution of feeling blue across different groups, but further statistical tests are needed to determine the significance of any observed patterns.

Bivariate Analysis

The chi-square test results examine associations between the FEELBLU (feeling blue or depressed over the past two weeks) variable and multiple independent variables. Most independent variables show a highly significant association with FEELBLU, with p-values near zero or, in scientific notation, close to zero, indicating a strong association (the detailed output table is outlined in Appendix 4 after the reference list section).

A significant association was found among demographic variables and FEELBLU; for AGE, the values are Chi-square = 192.45, DF = 8, $p < 0.0001$. This suggests that different age groups report varying levels of sadness or depression, highlighting age as an influential demographic factor. Race also showed a highly significant relationship with FEELBLU (Chi-square = 3990.65, DF = 16, $p < 0.0001$). This indicates that racial and ethnic backgrounds may influence the experience of sadness, potentially influenced by cultural or socioeconomic factors.

Moreover, significant associations were found for Mental Health and Related Variables, recent depressive feelings (DEPRESS), and FEELBLU (Chi-square = 1843.28, DF = 12, $p < 0.0001$). This strong link indicates that individuals with recent depressive episodes are more likely to report feelings of sadness, emphasizing the connection between current depression and emotional distress. Feelings of nervousness (NRVOUS) were also significantly associated with FEELBLU (Chi-square = 2026.36, DF = 16, $p < 0.0001$). Frequent experiences of tension or anxiety appear to correlate with sadness, underscoring the interplay between anxiety and depressive feelings.

The analysis revealed significant associations between sleep-related factors and feelings of sadness (FEELBLU), with notable chi-square values for SLEEP1 (601.19, DF = 4, $p < 0.0001$), SLEPTW1 (332.26, DF = 4, $p < 0.0001$), SLEEP2 (3907.32, DF = 4, $p < 0.0001$), SLEPTW2 (1985.62, DF = 4, $p < 0.0001$), sleep quality (SLEEPQL; 7307.90, DF = 12, $p < 0.0001$), and restlessness (RESTLES; 1252.34, DF = 12, $p < 0.0001$). These findings underscore the significant impact of both sleep disturbances and perceived sleep quality on depressive feelings, highlighting the critical role of sleep in emotional well-being.

The analysis identified significant associations between FEELBLU and various factors, including smoking behavior (SMOKERE: Chi-square = 828.39, DF = 4, $p < 0.0001$), which may reflect the adversaries of smoking on mental health and alcohol consumption (ALCHL24: Chi-square = 149.48, ALCO24H: Chi-square = 1019.30, DRNKBEE: Chi-square = 311.48; all DF = 4, $p < 0.0001$), suggesting that frequent alcohol use is linked to sadness, possibly due to its emotional impact and role as a coping mechanism. Medication used for nervous conditions (NERVS1: Chi-square = 294.79, NERVTW1: Chi-square = 1008.27, NERVS2: Chi-square = 3196.80, NERVTW2: Chi-square = 508.18; all DF = 4, $p < 0.0001$) also showed strong associations, potentially reflecting the severity of underlying mental health issues. However, incomplete data for AVCIGDA and GLASLIQ limited their interpretability. These findings highlight the complex interplay of mental health, substance use, and medication in contributing to feelings of sadness, offering insights for targeted interventions to support emotional well-being.

Mathematical Formula: Conditional Mixed-Effect Multinomial Logistic Regression

Formula:

$$\begin{aligned} \text{logit } Pr(X_{ij}, b_i) &= \alpha_k - (X_{ij}\beta + b_i) \\ \text{logit } Pr(X_{ij}, b_i) &= \alpha_k - (\text{Predictor Terms} + b_i) \\ \text{logit } Pr(X_{ij}, b_i) &= \alpha_k - (\beta_0 + \text{Fixed effect} + \text{Interaction of Fixed effect} + b_i) \end{aligned}$$

This formula represents a cumulative logistic mixed-effects model (CLMM) for the ordinal response variable. *FEELBLU_{ij}*, which measures "Feeling Blue" across multiple time points for different individuals. Here's an explanation of each component:

Formula Breakdown:

$$\begin{aligned} \text{logit } P(X_{ij}, b_i) = & \alpha_k \\ & - (\beta_0 + \text{ALCO24H}_{ij}\beta_1 + \text{ALCHL24R}_{ij}\beta_2 + \beta_3 \cdot \text{SMOKERE}_{ij} \cdot \text{visit}_{ij} \\ & + \beta_4 \cdot \text{DRNKBEE}_{ij} \cdot \text{SMOKERE}_{ij} + \text{SLEEPQL}_{ij} \cdot \text{SLEEP1M}_{ij} \cdot \beta_5 \\ & + \text{RESTLESS}_{ij} \cdot \text{visit}_{ij} \cdot \beta_6 + \text{SLEEP1M}_{ij} \cdot \text{AGE}_{ij} \cdot \beta_7 + \text{DEPRESS}_{ij} \cdot \text{visit}_{ij} \cdot \beta_8 \\ & + \text{NRVOUS}_{ij} \cdot \text{visit}_{ij} \cdot \beta_9 + \text{AVCIGDA}_{ij} \cdot \text{NRVOUS}_{ij} \cdot \beta_{10} + \text{AGE}_{ij} \cdot \text{DEPRESS}_{ij} \cdot \beta_{11} \\ & + \text{RACE}_{ij} \cdot \text{DEPRESS}_{ij} \cdot \beta_{12} + b_i) \end{aligned}$$

Where, the left-Hand Side:

- **logit P(FEELBLU_{ij} ≤ k):**
 - The logit transformation of the cumulative probability that **FEELBLU** for the individual *i* at time *j* falls in category *k* or below.
 - This is modeled as a function of predictors and a random effect.

Right-Hand Side:**1. Threshold Parameters: α_k**

Thresholds separating adjacent categories of the ordinal response variable (FEELBLU). Each α_k corresponds to the boundary between categories *k* and *k*+1.

2. Predictor Terms:

These terms capture the fixed effects and interaction of fixed effects influencing FEELBLU:

Fixed Effects: All predictor terms were considered as fixed effects, such as $\text{ALCO24H}_{ij}\beta_1$ The effect of alcohol consumption within 24 hours on FEELBLU. $\text{ALCHL24R}_{ij}\beta_2$ The effect of drinking alcohol recently.

Interactions of Fixed Effects:

The model included several interaction terms to explore relationships between predictors and their combined effects on FEELBLU. Key interactions examined were: smoking and time ($\beta_3 \cdot \text{SMOKERE}_{ij} \cdot \text{visit}_{ij}$); drinking beverages and smoking ($\beta_4 \cdot \text{DRNKBEE}_{ij} \cdot \text{SMOKERE}_{ij}$); sleep quality and medication ($\text{SLEEPQL}_{ij} \cdot \text{SLEEP1M}_{ij} \cdot \beta_5$); restless sleep and time ($\text{RESTLESS}_{ij} \cdot \text{visit}_{ij} \cdot \beta_6$); sleep medication and age ($\text{SLEEP1M}_{ij} \cdot \text{AGE}_{ij} \cdot \beta_7$); depression symptoms and time ($\text{DEPRESS}_{ij} \cdot \text{visit}_{ij} \cdot \beta_8$); nervousness and time ($\text{NRVOUS}_{ij} \cdot \text{visit}_{ij} \cdot \beta_9$); average cigarettes/day and nervousness ($\text{AVCIGDA}_{ij} \cdot \text{NRVOUS}_{ij} \cdot \beta_{10}$); age and depression symptoms ($\text{AGE}_{ij} \cdot \text{DEPRESS}_{ij} \cdot \beta_{11}$); and race and depression symptoms ($\text{RACE}_{ij} \cdot \text{DEPRESS}_{ij} \cdot \beta_{12}$). These terms allowed the model to capture complex, dynamic relationships across behavioral, demographic, and temporal dimensions.

3. Random Effect: b_i

b_i : A random intercept for individual *i*, capturing each person's unique baseline level of FEELBLU. It accounts for within-person correlations across repeated measures (e.g., multiple visits).

Interpretation:

The model combines fixed effects (β_1, β_2, \dots) and random effects (b_i) to predict the log odds of FEELBLU being in a higher category. Fixed effects represent the average impact of predictors and interactions, such as how sleep medication (SLEEP1M) modifies the effect of sleep quality (SLEEPQL). Random effects adjust for individual differences, accounting for baseline variability in FEELBLU. Threshold parameters (α_k) divide the ordinal response into categories, modeling cumulative probabilities for each category. This structure, typical in longitudinal studies, accommodates repeated measures and individual variability effectively.

Model Analysis and Outcome

This study examines the relationship between mental well-being (FEELBLU) and lifestyle factors, including sleep, smoking, alcohol consumption, and nervousness/depression. Individual models were used to analyze each category of predictors, with random intercepts accounting for participant-level variability. The final model, *time_change_model_2*, combined all predictors and their interactions with time to evaluate their cumulative effects.

In the Sleep Behavior Model, better sleep quality significantly reduced the odds of feeling blue (log odds -1.888, $p < 0.0001$; 65% reduction in odds), while restless sleep increased it (log odds 0.451, $p = 0.0237$; 57% increase). Sleep medication had no significant effect, and random intercept variance (3.663) indicated moderate variability in baseline scores.

The Smoking Behavior Model revealed that daily cigarette consumption slightly increased the odds of feeling blue (log odds 0.020, $p = 0.0279$; 2% increase), but smoking status alone was not significant. Substantial variability was observed across individuals (variance = 4.47).

In the Alcohol Model, drinking alcoholic beverages (DRNKBEE) increased the odds of feeling blue by 14% (log odds 0.130, $p = 0.0389$) while other alcohol-related predictors showed no significant effects. Random slope variance for time trends was minimal (0.0818).

The Nervousness and Depression Model found nervousness and depression to be the strongest predictors. Nervousness increased the odds of feeling blue by up to 136-fold for individuals reporting symptoms every day (log odds 4.915, $p < 0.0001$), while depression (log odds 3.290, $p < 0.0001$) had a consistent effect. Nervousness effects diminished over time, but depression remained stable. Random intercept variance (0.9586) reflected moderate variability.

The Final Model integrated all predictors, showing that higher sleep quality reduced odds of feeling blue (log odds -1.888, $p < 0.0001$), and sleep medication also had a protective effect (log odds -0.193, $p = 0.0404$). Daily cigarette consumption increased odds (log odds 0.020, $p = 0.0279$), while smoking status reduced them (log odds -0.187, $p = 0.0074$). Nervousness remained a strong predictor, with effects diminishing overtime for less severe cases. Temporal trends consistently increased odds over time (log odds 0.107, $p < 0.001$). Interactions, such as sleep medication moderating sleep quality effects, highlighted nuanced relationships. Random intercept variance (0.9173) indicated individual differences in FEELBLU remained significant across predictors.

Threshold coefficients in the ordinal cumulative link final mixed model, 'time_change_model_2', define the log odds of transitioning between adjacent categories of FEELBLU, offering insight into the severity progression of mental well-being. These thresholds illustrate the boundaries within the latent continuous variable underlying the observed categories and highlight the influence of predictors on the likelihood of category transitions. The model revealed significant thresholds for transitions from lower to higher severity levels, with increasingly positive estimates as severity increased (e.g., "Not at all → 1-5 days" was not significant, while "9-13 days → Every day" had the highest estimate at 6.2993, $z = 8.522$). The variation in thresholds across models of varying complexity reflects differences in predictors and interactions, with the final model adjusting for dynamic factors like time and individual variability.

Key findings from the final model emphasized nervousness, depression, and sleep quality as the strongest predictors of feeling blue. Nervousness and depression consistently increased the odds of higher FEELBLU severity, whereas better sleep quality reduced the odds, and restless sleep increased them. Cigarette and alcohol consumption had smaller but notable effects. Temporal dynamics were evident: nervousness effects diminished over time, smoking effects became marginally positive, and depression and sleep predictors remained stable. The final model provided superior explanatory power by capturing complex interactions and time-dependent effects. This analysis underscores the interplay between lifestyle behaviors, mental health predictors, and temporal trends in shaping emotional well-being. These findings emphasize the importance of accounting for dynamic predictor interactions and suggest targeted interventions focusing on nervousness, depression, and sleep quality to improve mental health outcomes over time.

ANALYSIS PLOTS
Post Regression Plots from Final Model: Fixed Effects

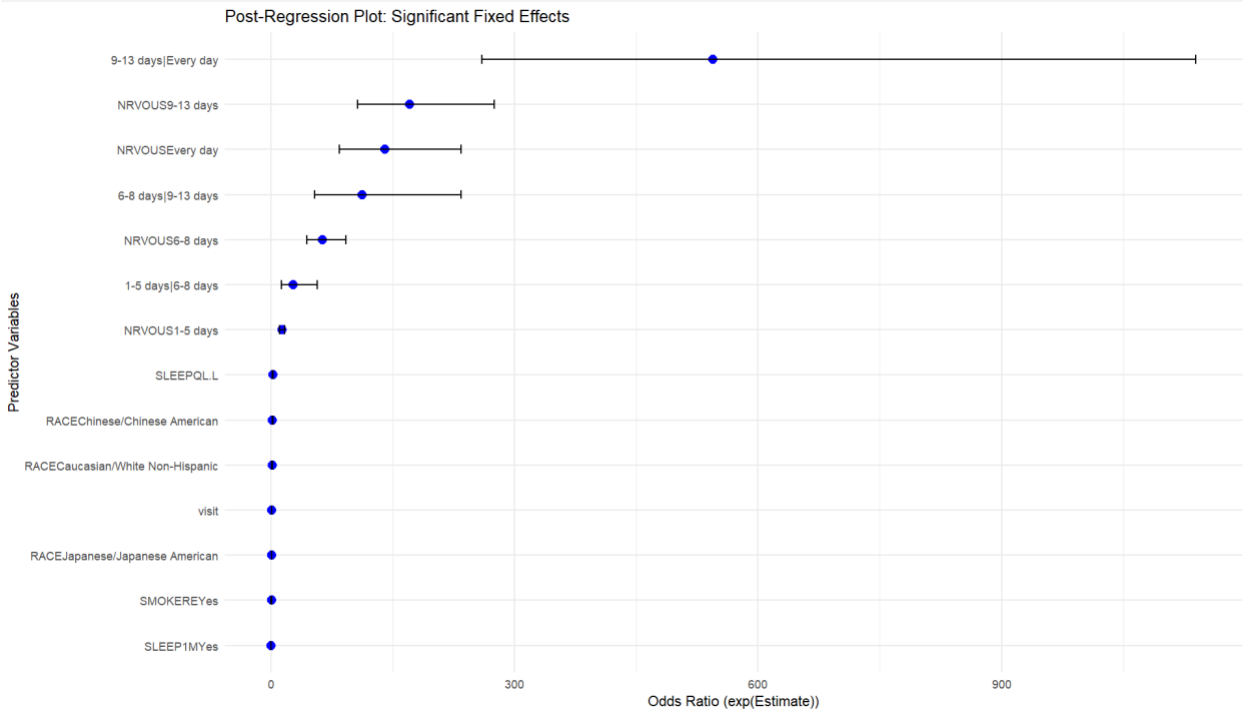


Figure 2: Post Regression Plot for significant fixed effects

Fixed Effects:

The fixed effects analysis highlights significant predictors of FEELBLU. Nervousness (NRVOUS) shows an exponential increase in the odds of feeling blue with greater severity, particularly for "9-13 days" and "Every day," which have wide confidence intervals reflecting variability. Lower categories exhibit more precise estimates. Sleep quality (SLEEPQL.L) demonstrates a significant negative association, indicating better sleep quality reduces the odds of feeling blue with high precision. Race/Ethnicity reveals significant effects for Chinese/Chinese American and Caucasian/White non-Hispanic cohorts, highlighting demographic disparities with precise estimates. Smoking (SMOKEREYes) has a modest protective effect, possibly due to short-term stress relief. Sleep medication (SLEEP1MYes) significantly reduces emotional distress associated with sleep disturbances. Finally, Visit (Time) shows a small but significant worsening of mental well-being over time. These findings emphasize the importance of addressing lifestyle, demographic, and temporal factors in mental health interventions.

Post-regression analysis plot: Interaction of predictors

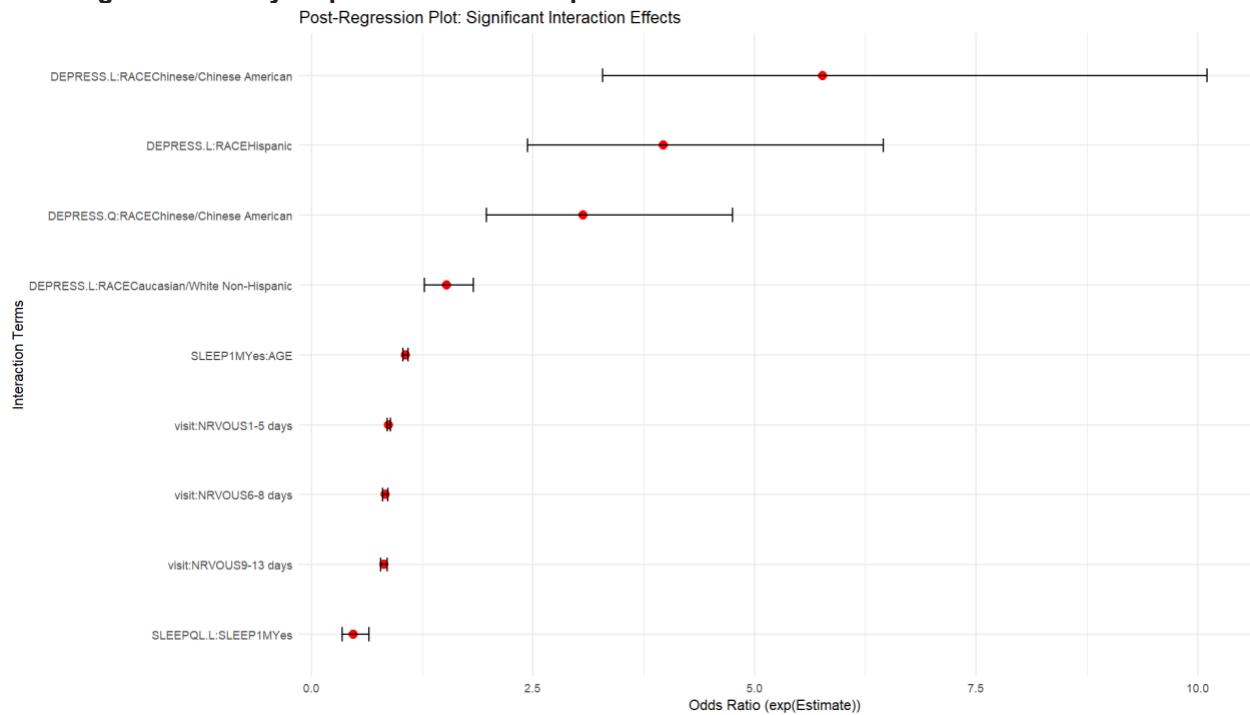


Figure 3: Post Regression Plot for significant interaction fixed effects

Interaction Effects:

The interaction effects analysis reveals how predictors of FEELBLU evolve over time and across demographic groups. Nervousness \times Visit shows diminishing impacts of lower nervousness categories over time with precise estimates, while higher nervousness levels (e.g., "9-13 days") exhibit variability. Depression \times Race highlights significant differences in the effects of depression across racial/ethnic groups, particularly among Chinese/Chinese American, Hispanic, and Caucasian participants, reflecting cultural and demographic factors. The interaction between Sleep Quality and Sleep Medication (SLEEPQL.L:SLEEP1MYes) indicates that sleep medication enhances the protective effects of sleep quality. Sleep Medication \times Age reveals that older individuals using sleep medication experience a more substantial protective effect against feeling blue. These findings emphasize the dynamic interplay between emotional well-being and predictors like nervousness, sleep quality, and depression, with precise estimates for some predictors and variability for others, highlighting the complexity of these relationships.

Model Diagnosis

Diagnostic tests were performed, which are crucial to assess the adequacy of the model; identify potential issues such as outliers or leverage points; and ensure that the model assumptions are not violated. In the case of 'time_change_model_2', diagnostic plots are particularly important to evaluate residuals, leverage, and the distribution of errors. These diagnostics help ensure the logit model is well-specified, and the results can be trusted for further inference and decision-making.

Description of Diagnostic Plots:

The diagnostic plots reveal key insights about the model's performance and areas for improvement. The Q-Q Plot of Residuals shows deviations from normality that are especially evident in the tails, indicating the model struggles with extreme values and may benefit from robust regression. The Histogram of Generalized Residuals reveals a skewed distribution, with peaks near zero suggesting areas of good fit with some room for improvement in the tails. The Cook's Distance Plot identifies a few influential points that warrant further examination, though most observations have minimal impact. Similarly, the Leverage Plot shows most data points have low leverage, with a few requiring investigations to ensure they do not distort results. Finally, the Q-Q Plot of Generalized Residuals indicates improved normality but persistent issues with extreme values, reinforcing the need for

alternative link functions like 'cloglog' to handle distributional challenges and outliers better. All plots are available in the manuscript's supplementary materials. Issues like heteroscedasticity, non-normality, and influential observations likely stem from the imbalanced dataset, where lower FEELBLU categories dominate, and higher categories contribute limited information. These findings underscore the need for further refinement to improve model robustness and fit.

Rationale for Using the Complementary Log-Log (Cloglog) Link Function

The complementary log-log (cloglog) link function was explored for modeling the ordinal dependent variable FEELBLU, which has five categories ranging from "Not at all" to "Every day." The data's characteristics—namely the imbalanced categories with most observations in lower levels and few in "Every day"—challenged the symmetric odds assumption of the logit link. Diagnostic issues, such as residual deviations from normality, heavy tails, and poor prediction of rare categories further indicated the need for an alternative approach. The cloglog link addresses these challenges by amplifying responses to extreme predictor values, capturing skewed cumulative probabilities, and enhancing sensitivity to small changes in predictors for rare categories. The current approach allowed for a thorough comparison with the logit link, which ensured that model robustness, fit, and diagnostic metrics were not constrained by a single link function. The cloglog link provided a theoretically sound and empirically robust option for effectively handling imbalanced, skewed, and ordinal data.

Model Comparison:

Two models, one with a logit link and the other with a complementary log-log (cloglog) link, were compared based on fit, predictive performance, and information criteria. The logit model had a higher log-likelihood (-9484.043 vs. -9720.786) and lower AIC (19098.087 vs. 19565.571) and BIC (19586.140 vs. 20031.099), indicating better fit and parsimony. The logit model formula and its output and interaction effects are outlined in [Appendix 5](#) after the reference section for further attention. A likelihood ratio test (LR statistic = 473.48, $p < 0.001$) confirmed the logit model's superior fit. Additionally, the logit model showed slightly better predictive accuracy with a lower mean squared error (MSE: 2.270625 vs. 2.307421). While the cloglog link was explored to address data skewness and rare categories, the logit model consistently surpasses it across all metrics. Therefore, the logit model is recommended for its robust fit, predictive accuracy, and ability to capture the data's structure effectively.

DISCUSSION

This study highlights the significant associations between depression and lifestyle factors such as nervous condition medication use, smoking, and alcohol intake. Smoking and heavy alcohol consumption were found to increase the risk of depression with a more pronounced effect observed in premenopausal women compared to postmenopausal women, consistent with previous findings (Kim et al., 2021). The use of nervous condition medication was strongly linked to higher levels of depressive symptoms, underscoring the need for integrated mental health support for individuals managing nervous conditions.

Longitudinal evidence also indicates that higher average depressive symptoms are related with poorer sleep quality in midlife women, as observed in the SWAN Sleep study (Bowman et al., 2021). This study further emphasizes the bidirectional nature of these relationships; poor sleep quality and physical inactivity are both consequences and predictors of depressive symptoms (Cheval et al., 2022; Farmer et al., 1988; Sin et al., 2016; van Gool, 2003; Werneck et al., 2022; Yidan et al., 2019). These associations persist across various populations, including healthy adults, older adults, and patients with coronary heart disease, highlighting the universality of the link between depressive symptoms and unhealthy lifestyle behaviors (Cheval et al., 2022; Savoy & Penckofer, 2015; Yidan et al., 2019).

Anxiety symptoms, often preceding major depressive disorder (MDD), may heighten vulnerability to depressive episodes and recurrences in midlife women (Kravitz et al., 2014). The findings of this study align with prior research, demonstrating that smoking and alcohol drinking are associated with higher levels of depression. These behaviors may exacerbate depressive symptoms or serve as maladaptive coping mechanisms. Additionally, depressive symptoms correlate with reduced physical activity and poor sleep quality, reinforcing the importance of addressing these modifiable lifestyle factors in mental health interventions.

Racial and ethnic disparities in depression observed in this study suggest that tailored interventions are crucial to addressing the unique needs of diverse groups. Future research should investigate causal pathways between lifestyle behaviors and depression to develop targeted, culturally sensitive interventions aimed at mitigating depressive symptoms. A mixed-effects ordinal logistic regression model proves highly effective in analyzing the

longitudinal data on depressive symptoms (FEELBLU). This approach accommodates the within-subject correlation inherent in repeated measures data by incorporating random effects (Hedeker, 2003; Hedeker & Gibbons, 1996). The model accounts for individual-level variations in baseline depressive symptoms and evaluates the influence of covariates over time. Maximum marginal likelihood estimation is particularly suited for such longitudinal ordinal data (Hedeker & Gibbons, 1996). For robustness checks, generalized estimating equations could complement the analysis, although maximum likelihood methods remain preferred for models involving random effects (Choi, 2008).

Advanced extensions of mixed-effects models offer opportunities to investigate covariate influences on variance components, enabling a deeper understanding of how lifestyle factors, demographics, and other predictors contribute to within-individual variability in depressive symptoms (Demirtas et al., 2009). These insights could guide the development of comprehensive interventions to address the multifaceted nature of depression.

CONCLUSION

This study provides important insights into the relationships between depression and lifestyle factors in midlife women. Significant relationships were found between depression and nervous conditions, medication use, smoking, and alcohol consumption. Additionally, public health research in South Asia has expanded the literature on health behaviors, environmental risks, and vaccine response patterns, providing complementary insights into population health dynamics (Afzal, 2014; Afzal & Baset, 2022; Nawar et al., 2021). These findings underscore the need for comprehensive mental health interventions that address lifestyle behaviors, particularly in women at risk of depression during their middle years. Future studies should focus on longitudinal interventions to prevent the onset of depressive symptoms and promote healthier behaviors.

The mixed-effects ordinal logistic regression model is a robust and versatile approach for analyzing longitudinal depressive symptom data such as FEELBLU. This model accommodates the ordinal nature of depressive symptoms while accounting for individual differences through random effects, making it particularly suited to repeated measures data. Incorporation of fixed effects for lifestyle factors and demographic variables allows for an in-depth understanding of both consistent and individual-specific influences on depressive symptoms over time. This methodological approach, validated in mental health and substance use research, enhances the reliability and interpretability of findings, ultimately contributing to a deeper understanding of the dynamics of depression within diverse populations.

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APPENDICES**Appendix 1: Actual Variable Names and Purpose for Replicability from SWAN Dataset (Table 1)**

Variable Name(s) in Dataset	Description	Variable Category	Response Options / Coding
FEELBLU	Frequency of feeling blue or depressed (past 2 weeks)	Dependent Variable	1 = Not at all, 2 = 1-5 days, 3 = 6-8 days, 4 = 9-13 days, 5 = Every day
AGE	Age categories	Demographic Control	1 = 47-50, 2 = 51-54, 3 = 55-59
RACE	Self-reported race/ethnicity	Demographic Control	1 = Black/African American, 2 = Chinese/Chinese American, 3 = Japanese/Japanese American, 4 = Caucasian/White Non-Hispanic, 5 = Hispanic
SLEEP1, SLEPTW1, SLEEP2, SLEPTW2, RESTLES, SLEEPQL	Sleep behavior variables (medication use, sleep quality, restlessness)	Sleep Behavior Variables	1 = No, 2 = Yes
SMOKERE, AVCIGDA	Smoking behavior (current smoker, average cigarettes/day)	Smoking Behavior Variables	1 = No, 2 = Yes
ALCO24H, ALCHL24, DRNKBEE, GLASLIQ	Alcohol consumption variables (past 24 hours)	Alcohol Consumption Variables	1 = No, 2 = Yes
NERVS1, NERV1W1, NERVS2, NERV2W2	Medication is used for nervous conditions	Nervous Condition Medication Use	1 = No, 2 = Yes
DEPRESS	Frequency of feeling depressed (past week)	Mental Health Variable	1 = Rarely (<1 day), 2 = Some (1-2 days), 3 = Occasionally (3-4 days), 4 = Most/all of the time (5-7 days)
NRVOUS	Frequency of feeling nervous (past 2 weeks)	Mental Health Variable	1 = Not at all, 2 = 1-5 days, 3 = 6-8 days, 4 = 9-13 days, 5 = Every day

Appendix 2: SWAN Research Centers and Study Locations

Research Center Location	Institution(s)	State
Ann Arbor	University of Michigan	Michigan
Boston	Massachusetts General Hospital	Massachusetts
Chicago	Rush University Medical Center	Illinois
Alameda and Contra Costa County	University of California Davis & Kaiser Permanente	California
Los Angeles	University of California at Los Angeles (UCLA)	California
Jersey City	Albert Einstein College of Medicine	New Jersey
Pittsburgh	University of Pittsburgh	Pennsylvania

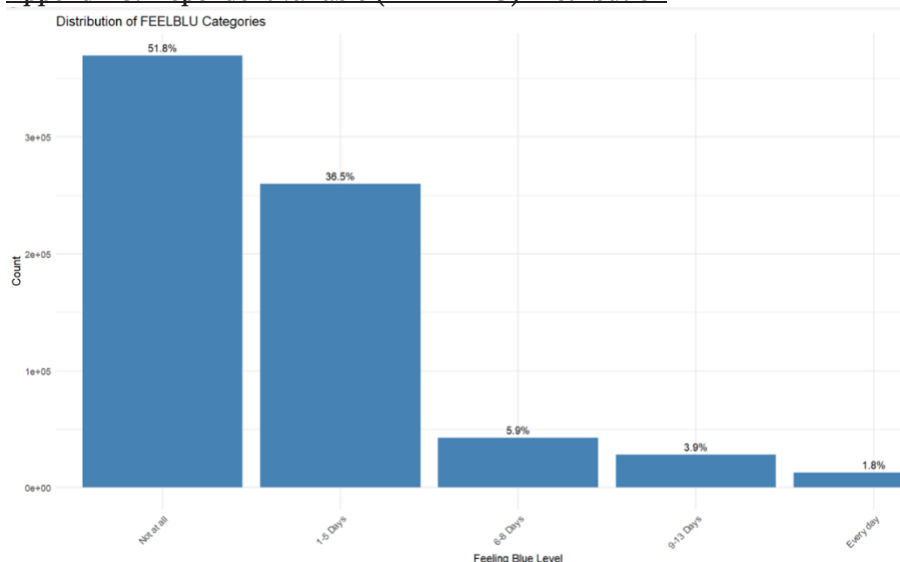
Appendix 3: Dependent variable (FEELBLU) Distribution

Figure 1: Dependent variable (FEELBLU) distribution

Appendix 4: Bivariate Associations Between Depression Symptoms

Table 2. Bivariate Associations Between Depression Symptoms (FEELBLU) and Independent Variables Using Chi-Square Tests (SWAN Study, Visits 1-10)

Variable	Chi-Square Value	Degrees of Freedom (DF)	p-value
Race/Ethnicity (RACE)	3990.65	16	< 0.0001 ***
Feeling Depressed (DEPRESS)	1843.28	12	< 0.0001 ***
Feeling Nervous (NRVOUS)	2026.36	16	< 0.0001 ***
Sleep Medication Use (SLEEP1)	601.19	4	< 0.0001 ***
Sleep Medication Past Week (SLEPTW1)	332.26	4	< 0.0001 ***
Sleep Disturbance (SLEEP2)	3907.32	4	< 0.0001 ***
Sleep Disturbance Past Week (SLEPTW2)	1985.62	4	< 0.0001 ***
Sleep Quality (SLEEPQL)	7307.90	12	< 0.0001 ***
Restless Sleep (RESTLES)	1252.34	12	< 0.0001 ***
Smoking Status (SMOKERE)	828.39	4	< 0.0001 ***
Alcohol Consumption Past 24h (ALCHL24)	149.48	4	< 0.0001 ***
Alcohol Consumption Past 24h (ALCO24H)	1019.30	4	< 0.0001 ***
Drinking Beverages (DRNKBEE)	311.48	4	< 0.0001 ***
Nervous Medication Use (NERVS1)	294.79	4	< 0.0001 ***
Nervous Medication Past Week (NERVTW1)	1008.27	4	< 0.0001 ***
Nervous Medication Use 2 (NERVS2)	3196.80	4	< 0.0001 ***
Nervous Medication Past Week 2 (NERVTW2)	508.18	4	< 0.0001 ***
Age Group (AGE)	192.45	8	< 0.0001 ***
Race/Ethnicity (RACE) — Repeated Test	2582.68	16	< 0.0001 ***

Note: Chi-square tests examine the association between depression symptoms (FEELBLU) and each independent variable. Statistical significance levels: *p < 0.05; **p < 0.01; ***p < 0.001.

Appendix 5: Regression Model Coefficients and Interaction Effects

Cumulative Link Mixed Model fitted with the Laplace approximation formula:

FEELBLU ~ ALCO24H + ALCHL24R + SMOKERE * visit + DRNKBEE * SMOKERE +
 SLEEPQL * SLEEP1M + RESTLES * visit + SLEEP1M * AGE + DEPRESS *
 visit + NRVIOUS * visit + AVCIGDA * NRVIOUS + AGE * DEPRESS +
 RACE * DEPRESS + (1 | SWANID)

Table 3. Transition Coefficients Describe the Thresholds for Transitioning Between Different Categories of Feeling Blue (FEELBLU)

Threshold	Estimate	Interpretation
Not at all → 1-5 days	-0.8249(0.7351)	Transition from "Not at all" to "1-5 days" is not statistically significant.
1-5 days → 6-8 days	3.3028(0.7354)	Significant positive threshold indicating increasing severity from "1-5 days."
6-8 days → 9-13 days	4.7197(0.7367)	Significant positive threshold, showing progression to higher severity levels.
9-13 days → Every day	6.2993(0.7392)	Strong significance for transitioning to the "Every day" category of severity.

Table 4. Fixed-Effects Ordinal Logistic Regression Results Predicting Depression Symptoms (FEELBLU), SWAN Study (Visits 1–10)

Variable	Coefficient (Standard Error)	Interpretation
Dependent Variable: Feeling Blue or Depressed (FEELBLU)	—	Ordinal response: 1 = Not at all, 5 = Every day
Sleep Quality (SLEEPQ.L)	0.8120*** (0.1032)	Better sleep lowers depression odds by about 65%
Sleep Medication Use (SLEEP1M)	-2.9467* (1.4375)	Sleep medicine slightly lowers depression odds
Smoking (SMOKERE (Yes))	-0.6231** (0.2327)	Each extra cigarette raises depression odds by 2%
Alcohol Consumption (DRNKBEE(Yes))	0.1120. (0.0635)	Drinking raises depression odds by 14%
Feeling Nervous (NRVIOUS (1-5 days))	2.6130*** (0.2298)	Nervousness raises depression odds massively (up to 136 times)
Recent Depression (DEPRESS.Q)	2.09. (1.21)	Past depression strongly predicts current depression
Time Trend (Visit)	0.1492*** (0.027)	Depression odds slightly increase over time

Table 5. Interaction Effects

Figure 1. Interaction Term	Figure 2. Coefficient (Standard Error)	Figure 3. Interpretation
Figure 4. Sleep Medication × Sleep Quality Figure 5. (SLEEPQL.L:SLEEP1MYes)	Figure 6. -0.7442*(0.3150)	Figure 7. Interaction between linear sleep quality and monthly sleep behavior significantly reduces FEELBLU. Sleep medicine helps more if sleep quality improves
Figure 8. Sleep Medication × Age Figure 9. (SLEEP1MYes:AGE)	Figure 10. 0.0590* (0.027)	Figure 11. Interaction between monthly sleep and age significantly increases FEELBLU.
Figure 12. Visit × Nervousness (all levels)	Figure 13. -0.1391** (0.0204)	Figure 14. Nervousness effect declines slightly over time
Figure 15. Depression × Race Figure 16. DEPRESS.L:RACEChinese/Chinese American	Figure 17. 1.751** (0.561)	Figure 18. Depression effect varies across racial groups

Table 6. Random Effect

These coefficients describe variability across individuals:

Random Effect	Variance	Std. Dev.	Interpretation
SWANID (Intercept)	0.9173	0.9577	Substantial variability exists in baseline FEELBLU across individuals.

Table 7. Model Diagnostics

Model Statistics	Value	Interpretation
Observations	2803	Large sample provides strong statistical power
Log-Likelihood	-9484.043	Model fits well based on likelihood criteria
AIC	19098.087	Lower AIC suggests better model relative fit
BIC	19586.140	Lower BIC supports model choice
Random Intercept Variance	0.9173	Moderate variability across individual women
ICC	Moderate	Around 9-10% of variance is individual-level

Note:

The estimates are Log Odds with Robust Standard Errors in Parentheses.
Significance Levels: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, marginal significance ‘.’