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Association between prognostic nutritional index (PNI) and depression: the NHANES 2005–2018

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Article

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Abstract

Depression, impacting millions worldwide, necessitates the identification of predictive markers for risk assessment. The Prognostic Nutritional Index (PNI), an indicator of immune and nutritional status, is correlated with various diseases' prognoses. This study explores the correlation between PNI and depression in the National Health and Nutrition Examination Survey (NHANES) dataset spanning 2005 to 2018.Utilizing NHANES data, we included 32,739 participants after applying exclusion criteria. The PNI was calculated from serum albumin levels and lymphocyte counts. Depressive symptoms were assessed using the Patient Health Questionnaire-9. Logistic regression models estimated the odds ratios for depression across PNI levels, adjusted for various demographic and health variables. The mean age of participants was 47.78 years, with a prevalence of depressive symptoms observed in 7.82% of the sample. A nonlinear association between PNI levels and depression risk was observed, with lower PNI linked to higher depression odds. Subgroup analyses supported the consistency of the PNI-depression association across different cohorts. The relationship between lower PNI and increased depression risk suggests the potential of PNI as a tool for depression risk assessment. This study underscores the significance of PNI as a marker in understanding the relationship between nutritional status and depression, providing insights into preventive and therapeutic strategies in mental health care.

1. Introduction

Depression represents a pervasive mental health condition impacting an estimated 264 million individuals globally, as reported by the World Health Organization (WHO)[1]. With increasing acknowledgment of mental well-being, the pursuit of effective diagnostic and therapeutic approaches for depression has intensified. Nonetheless, the etiology of depression is multifaceted, and treatment responses vary due to individual differences[2], thereby necessitating the identification of reliable predictive markers for depression risk[3].

In recent years, the role of chronic inflammation in psychiatric disorders, particularly depression, has garnered attention[4,5]. The Prognostic Nutritional Index (PNI), an integrative marker of immune and nutritional status, has been correlated with the prognosis in various diseases[6–9]. Calculated based on serum albumin levels and peripheral blood lymphocyte counts, the PNI was originally employed to assess preoperative nutritional status and surgical risk[10], but its applications have since expanded across numerous medical disciplines[11,12].

Despite this, the relationship between PNI and disease risk within the context of depression remains underexplored. Given that both immune dysregulation and malnutrition are considered potential risk factors for depression[13,14], the PNI might serve as a valuable tool in assessing the risk of depression. Utilizing data from the National Health and Nutrition Examination Survey (NHANES) 2005–2018, this study aims to explore the correlation between these two factors and further investigate their intrinsic relationship and characteristics.

Through this investigation, we aspire to provide clinicians with a convenient screening tool for depression risk and offer new insights into preventive and interventional strategies for depression. Furthermore, our findings may elucidate the role of nutrition and immune status in the pathogenesis of depression, laying a scientific foundation for future therapeutic approaches.

2. Materials and methods

2.1. Study participants

Participants for this investigation were selected from the National Health and Nutrition Examination Survey (NHANES) data spanning from 2005 to 2018. NHANES is an ongoing, multistage, probability-sampling, cross-sectional survey designed to assess the health and nutritional status of the civilian, noninstitutionalized U.S. population[15]. All data utilized in this study are publicly accessible on the CDC website. A total of 32,739 participants remained after excluding 23262 participants age under 18 years old, 3638 participants with missing depression data, as well as 203 participants without serum albumin and lymphocyte data (Figure. 1). Ethical approval for the NHANES was granted by the Institutional Review Board of the National Center for Health Statistics, with written informed consent procured from all participants. More detailed information about the NHANES is available at www.cdc.gov/nchs/nhanes.htm.

2.2. Study Variables

2.2.1. Depressive symptoms

The Patient Health Questionnaire-9 (PHQ-9) was employed to assess depressive symptoms experienced over the preceding two weeks. This instrument comprises nine items, each rated on a 0–3 scale (0 signifying 'none', 1 'several days', 2 'more than half the days', 3 'nearly every day'), yielding a cumulative score between 0 and 27. The PHQ-9's internal consistency was validated using SPSS 26.0 software, evidencing a Cronbach's alpha of 0.84. As delineated in prior research[16], a score of 10 or higher on the PHQ-9 was indicative of clinically significant depressive symptoms. Accordingly, depressive symptoms were coded as: “0” = no (0–9 points); 1 = yes (10–27 points).

2.2.2. Prognostic Nutritional Index Assessment

PNI was calculated for each participant using the formula: 10 × serum albumin value (g/dL) + 0.005 × total lymphocyte count (per mm^3)[10]. Serum albumin and lymphocyte counts were obtained from blood samples collected at the mobile examination centers, the NHANES laboratory methods were employed to analyze these blood samples. The complete blood count (CBC) is a commonly utilized laboratory test to evaluate the influence of dietary intake and various factors on overall blood nutrient levels and immune competence, encompassing the assessment of total lymphocyte count. The methodology employed for acquiring CBC parameters is based on the Beckman Coulter counting and classification

approach[17]. Serum albumin levels, serving as a consistent indicator of nutritional status, are quantified using the bromocresol purple method within the NHANES database.

2.2.3. Assessment of other variables

In this study, the CDC employed the Computer Assisted Personal Interviewing system to gather a comprehensive range of data encompassing demographic details, lifestyle factors, self-reported health status, physical measurements, and biochemical markers. The demographic variables collected included age, gender, race, educational attainment, marital status, and the income-to-poverty ratio. Lifestyle variables comprised smoking and alcohol consumption statuses. Smoking status was classified into two categories: 'never smokers', defined as individuals who have smoked less than 100 cigarettes in their lifetime, and 'smokers', defined as those who have smoked more than 100 cigarettes. Alcohol consumption status was categorized as ‘drinkers’ (defined as having consumed more than 12 drinks of any type of alcoholic beverage in a year) and ‘nondrinkers’ (defined as having consumed fewer than 12 drinks of any type of alcoholic beverage in a year). Health data were gathered on the presence of stroke, hypertension, diabetes, and cardiovascular disease (CVD), with diagnoses based on physician notification of stroke, coronary heart disease, congestive heart failure, or heart attack. Diabetes mellitus and hypertension were identified either through doctor diagnosis or the use of antihypertensive or hyperglycemic medications. Body Mass Index (BMI) was calculated by dividing an individual's weight in kilograms by the square of their height in meters. C-reactive protein levels were measured using latex-enhanced nephelometry.

2.3. Statistical analysis

Continuous variables were stratified based on their distributional characteristics. Weighted means (standard error) were computed for continuous variables, while weighted frequency percentages were calculated for categorical variables. Chi-squared test or Kruskal-Wallis H test was employed to assess variations among quartile groups categorized by the PNI. Potential nonlinear relationships between PNI levels and depression were explored utilizing restricted cubic spline curves. The association between PNI levels and depression was assessed through logistic analysis. Logistic regression models were employed to estimate the odds ratio (OR) measuring the correlation between PNI index levels and depression.

Covariates were chosen based on their relevance to the outcomes of interest or substantial (> 10%) changes in effect estimation. Three models were constructed: Model 1 (Non-adjusted model); Model 2 adjusted for: age, gender, race; Model 3 adjusted for: age, gender, race, educational level, marital status, smoking habits, alcohol consumption, stroke, CVD, hypertension, diabetes, BMI, income-to-poverty ratio, and C-reactive protein. Stratified analyses based on subgroup variables were conducted using the fully adjusted Model 3. The log-likelihood ratio test was employed to assess interaction effects between the PNI index and subgroup variables.

Weighted analyses were applied to account for the complex sampling design of NHANES. The detail was in this website as followed: https://wwwn.cdc.gov/nchs/nhanes/tutorials/module3.aspx

All statistical analysis was conducted using R (version 3.5.3) and EmpowerStats 2.2 (http://www.empowerstats.com). Statistical significance was determined by P values < 0.05.

3. Results

After applying the exclusion criteria, a total of 32,739 individuals from the NHANES dataset spanning 2005 to 2018 were included in this study, depicted in Figure. 1. Participants were stratified into four distinctive groups based on their PNI values: Q1 (PNI < 40.0), Q2 (40.0 ≤ PNI < 43.0), Q3 (43.0 ≤ PNI < 45.0), and Q4 (PNI ≥ 45.0). The comprehensive demographic and clinical attributes of the participants are delineated in Table 1. The average age of the cohort was 47.78 ± 18.50 years, and 7.82% (n = 2560) of the subjects displayed depressive symptoms, as ascertained by the PHQ-9. As detailed in Table 1, it was noted that individuals with a lower PNI tended to be older, predominantly non-Hispanic black, either divorced or separated, and had a prior medical history encompassing hypertension, diabetes, CVD, and stroke, along with a comparatively lower level of educational attainment. Additionally, they exhibited a history of smoking and alcohol consumption.

Table 1
Characteristics of the study population from NHANES 2005–2018.

	PNI Quartiles n (%)					
	Total	**Q1** (n = 8184) PNI□40.0	**Q2** (n = 8185) 40.0 ≤ PNI < 43.0	**Q3** (n = 8185) 43.0 ≤ PNI < 45.0	**Q4** (n = 8185) PNI ≥ 45.0	**P-value**
Age (years)	47.78 ± 18.50	50.63 ± 18.06	49.01 ± 18.91	48.65 ± 17.02	42.82 ± 20.03	< 0.001
Gender (%)						< 0.001
Male	48.98	37.84	45.62	52.36	60.15	
Female	51.02	62.16	54.38	47.64	39.85	
Race/ethnicity (%)						< 0.001
Mexican American	8.41	6.57	7.66	9.26	10.15	
Other Hispanic	5.17	4.04	5.54	5.34	5.74	
Non-Hispanic White	68.70	69.04	68.85	68.64	68.28	
Non-Hispanic Black	10.70	14.56	10.62	9.79	7.84	
Other Race	7.02	5.79	7.33	6.98	7.99	
Education level (%)						< 0.001
Less than high school	19.94	25.82	22.76	16.02	15.15	
High school	25.33	27.31	26.25	24.02	23.73	
More than high school	54.74	46.87	50.99	59.96	61.13	
Marital status (%)						< 0.001
Married	54.47	55.94	57.16	55.11	49.68	
Living with partner	7.63	6.17	7.14	7.32	9.89	
Divorced/separated/widowed	20.61	24.59	20.96	18.83	18.06	
Never married	17.29	13.30	14.74	18.74	22.37	

	PNI Quartiles n (%)					
Smoking status (%)						0.003
Ever smoker	47.27	51.98	46.46	45.54	45.08	
Never smoker	52.74	48.02	53.54	54.46	54.92	
Alcohol status (%)						< 0.001
Drinkers	74.04	78.43	72.82	75.23	69.67	
Nondrinkers	25.96	21.57	27.18	24.77	30.33	
Stroke (%)						< 0.001
Yes	4.54	7.13	5.18	3.11	2.75	
No	95.46	92.87	94.82	96.89	97.25	
CVD (%)						< 0.001
Yes	11.07	16.61	10.52	8.92	8.23	
No	88.93	83.39	89.48	91.08	91.77	
Hypertension (%)						< 0.001
Yes	26.64	33.59	28.21	24.31	20.46	
No	73.36	66.41	71.79	75.69	79.54	
Diabetes (%)						< 0.001
Borderline/Diabetic	12.45	14.48	13.46	12.47	9.38	
Not Present	87.55	85.52	86.54	87.53	90.62	
BMI (kg/m^2)	28.55 ± 5.90	29.46 ± 6.32	28.59 ± 5.87	28.87 ± 5.84	27.79 ± 5.57	< 0.001
Income to poverty ratio	2.70 ± 1.63	2.10 ± 1.56	2.75 ± 1.63	2.60 ± 1.7	2.94 ± 1.66	< 0.001
C-reactive protein (mg/dl)	2.43 ± 5.81	2.95 ± 6.78	2.50 ± 5.65	2.17 ± 5.48	2.10 ± 5.34	< 0.001
Depression						< 0.001
Yes	7.82	9.11	8.06	7.27	6.92	

	PNI Quartiles n (%)				
No	92.18	90.89	91.94	92.73	93.08

The association between PNI and the risk of depression exhibited a nonlinear pattern (Table 2). Upon adjusting for age, gender, race, educational level, marital status, smoking and alcohol habits, stroke, CVD, hypertension, diabetes, BMI, income-to-poverty ratio, and C-reactive protein, the OR with 95% confidence intervals for depression across varying PNI levels were as follows: 1.00 (reference), 0.92 (0.74, 1.13), 0.86 (0.69, 1.08), and 0.73 (0.56, 0.96). A nonlinear correlation was evident through the smoothing curve analysis (Figure. 2).

Table 2
Relationship between PNI and depression in different models.

OR (95% CI) P-value	**Model 1**	**Model 2**	**Model 3**
PNI	0.94 (0.93, 0.95) < 0.0001	0.96 (0.94, 0.97) < 0.0001	0.97 (0.95, 0.99) 0.0057
PNI quartiles			
Q1	1.0	1.0	1.0
Q2	0.78 (0.67, 0.91) 0.0013	0.83 (0.71, 0.97) < 0.0158	0.92 (0.74, 1.13) 0.4095
Q3	0.67 (0.57, 0.78) < 0.0001	0.74 (0.63, 0.88) 0.0004	0.86 (0.69, 1.08) 0.2065
Q4	0.54 (0.45, 0.65) < 0.0001	0.65 (0.54, 0.79) < 0.0001	0.73 (0.56, 0.96) 0.0255
Model 1: no covariates were adjusted.			
Model 2: age, gender, and race were adjusted.			
Model 3: age, gender, race, educational level, marital status, smoking status, alcohol status			
stroke, CVD, hypertension status, diabetes status, BMI, income to poverty ratio and C-reactive protein were adjusted.			

To assess the consistency of the PNI-depression association across different cohorts, subgroup analyses were conducted. In the adjusted Model 3, stratified analyses reveal that this association remains consistent across most subpopulations, as detailed in Figure. 3 and Table 3.

Table 3
Subgroup multi-factor logistic regression analysis for the association between PNI and depression

Variables	OR (95%CI)	P-value	Interaction P-value
Age (years)			0.0584
< 60	1.09 (0.95, 1.26)	0.0855	
≥ 60	1.13 (1.05, 1.20)	< 0.0001	
Gender (%)			0.3523
Male	1.09 (1.01, 1.18)	< 0.0001	
Female	1.15 (1.08, 1.21)	< 0.0001	
Race/ethnicity (%)			0.3106
Mexican American	1.12 (1.03, 1.22)	0.1051	
Other Hispanic	1.06 (1.00, 1.12)	0.0327	
Non-Hispanic White	1.09 (1.01, 1.18)	0.0563	
Non-Hispanic Black	1.00 (0.92, 1.08)	0.0731	
Other Race	1.07 (0.99, 1.16)	0.0652	
Education level (%)			0.4607
Less than high school	1.08 (1.03, 1.12)	0.1651	
High school	1.04 (0.99, 1.10)	0.1293	
More than high school	1.03 (0.99, 1.08)	0.0006	
Marital status (%)			0.8651
Married	1.04 (1.00, 1.10)	0.0089	
Living with partner	1.05 (0.95, 1.14)	0.3651	
Divorced/separated/widowed	1.06 (1.02, 1.12)	0.0586	
Never married	1.05 (0.99, 1.12)	0.0956	
Smoking status (%)			0.1128
Ever smoker	1.07 (1,05, 1.09)	< 0.0001	
Never smoker	1.05 (1.04, 1.07)	< 0.0001	
Alcohol status (%) (at least 12 alcoholic drinks per year)			0.0355

Variables	OR (95%CI)	P-value	Interaction P-value
Yes	1.16 (1.01,1.32)	0.0935	
No	0.98 (0.84, 1.15)	0.0003	
Stroke (%)			0.0859
Yes	1.05 (1.01, 1.09)	0.0166	
No	1.05 (1.04, 1.07)	< 0.0001	
CVD (%)			0.0032
Yes	1.09 (1.06, 1.11)	< 0.0001	
No	1.04 (1.03, 1.05)	< 0.0001	
Hypertension (%)			0.0764
Yes	1.07 (1.04, 1.10)	0.0005	
No	1.05 (1.04, 1.06)	0.0026	
Diabetes (%)			0.7263
Borderline/Diabetic	1.06 (1.04, 1.07)	< 0.0001	
Not Present	1.04 (1.01, 1.07)	0.0026	
BMI (kg/m^2)			0.1602
< 18	1.04 (0.96, 1.13)	0.0265	
18–25	1.05 (1.03, 1.07)	< 0.0001	
25–30	1.04 (1.02, 1.06)	< 0.0001	
> 30	1.08 (1.01, 1.14)	< 0.0001	

4. Discussion

In this nationally representative cross-sectional study, we evaluated the relationship between the PNI and depression. The pivotal discovery of this research is that a low level of PNI was associated with higher odds of having depression in the US adult population. This association persists even after conducting various stratified and sensitivity analyses. To the best of our knowledge, this study is the inaugural investigation into the correlation between PNI and depression within a general population context.

The intricate relationship between depression and the PNI warrants further exploration, and multiple plausible explanations may shed light on this association. Firstly, individuals experiencing depression often exhibit compromised nutritional status[18], which could be reflected in a lower PNI[10]. Several studies have highlighted the connection between depressive symptoms and poor nutritional intake[18–21],

emphasizing the role of nutritional deficiencies in mental health. Notably, a study encompassing a substantial cohort in the NHANES database demonstrated that a lower PNI was associated with a higher risk of depression. This finding echoes previous research that links depression to malnutrition and supports the potential role of PNI as an indicator in assessing mental health status.

Secondly, the relationship between PNI and depression might be mutual. While a lower PNI signifies nutritional insufficiency, it also serves as a marker for adverse health conditions, including chronic diseases, immune dysfunction, and inflammation[22–25]. These health complications associated with a lower PNI could contribute to the onset or exacerbation of depressive symptoms[26–29]. In our study, individuals with higher depression rates exhibited lower PNIs, indicating a potential interplay between nutritional status and mental health.

Moreover, inflammatory markers and oxidative stress, both influenced by nutritional status[30,31], are recognized contributors to the pathophysiology of depression[32]. Studies have revealed that a diminished PNI correlates with elevated levels of inflammatory markers[33,34]. Furthermore, oxidative stress, known for inducing albumin denaturation, triggers a rapid decline in serum albumin levels[35,36], thereby contributing to a reduction in PNI. These physiological imbalances may implicate a biological link between lower PNI and an increased susceptibility to depression, underscoring the importance of considering nutritional status in mental health management.

Our findings contribute significantly to understanding the intersection of nutritional status and depression, particularly within the general population. Individuals with compromised nutritional status often face metabolic irregularities and immune system dysfunctions, both of which can impact mental well-being[37,38]. Notably, maintaining a healthy PNI might serve as a preventive measure against the development or progression of depression. Additionally, considering the potential impact of nutritional status on mental health, interventions aimed at improving PNI through dietary modifications or nutritional supplementation might be beneficial in alleviating depressive symptoms. Previous studies have highlighted the impact of specific nutrients on mental health outcomes[39,40], emphasizing the role of a well-balanced diet in supporting overall well-being, including mental health[41,42].

However, our study has several limitations that necessitate consideration. Firstly, its cross-sectional design precludes establishing causality between PNI and depression. Furthermore, the findings may not be universally applicable across different ethnic groups or regions, as the study primarily focuses on data from the United States. Additionally, the reliance on self-reported depressive symptoms for a one-time assessment may not fully capture the spectrum of depression severity and longitudinal fluctuations. Moreover, the absence of detailed medication data and its potential influence on both depression and nutritional status poses a limitation in our analysis.

In conclusion, our study underscores the association between Prognostic Nutritional Index and depression within the NHANES cohort. While highlighting the intricate interplay between nutritional status and mental health, it suggests avenues for further research exploring the role of nutritional

interventions in managing depression. Despite limitations, this investigation lays a foundation for future multi-center cohort studies aiming to elucidate the nuanced relationship between PNI and depression and its potential implications for mental health interventions.

Declarations

Author Contribution

J.L. wrote the main manuscript text and prepared figures, J.C. prepared tables. All authors reviewed the manuscript.

Data availability

The datasets utilized in this study are accessible from the NHANES repository, which can be found at www.cdc.gov/nchs/nhanes.htm. All data generated or analyzed during the course of this research have been incorporated into this article.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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Figures

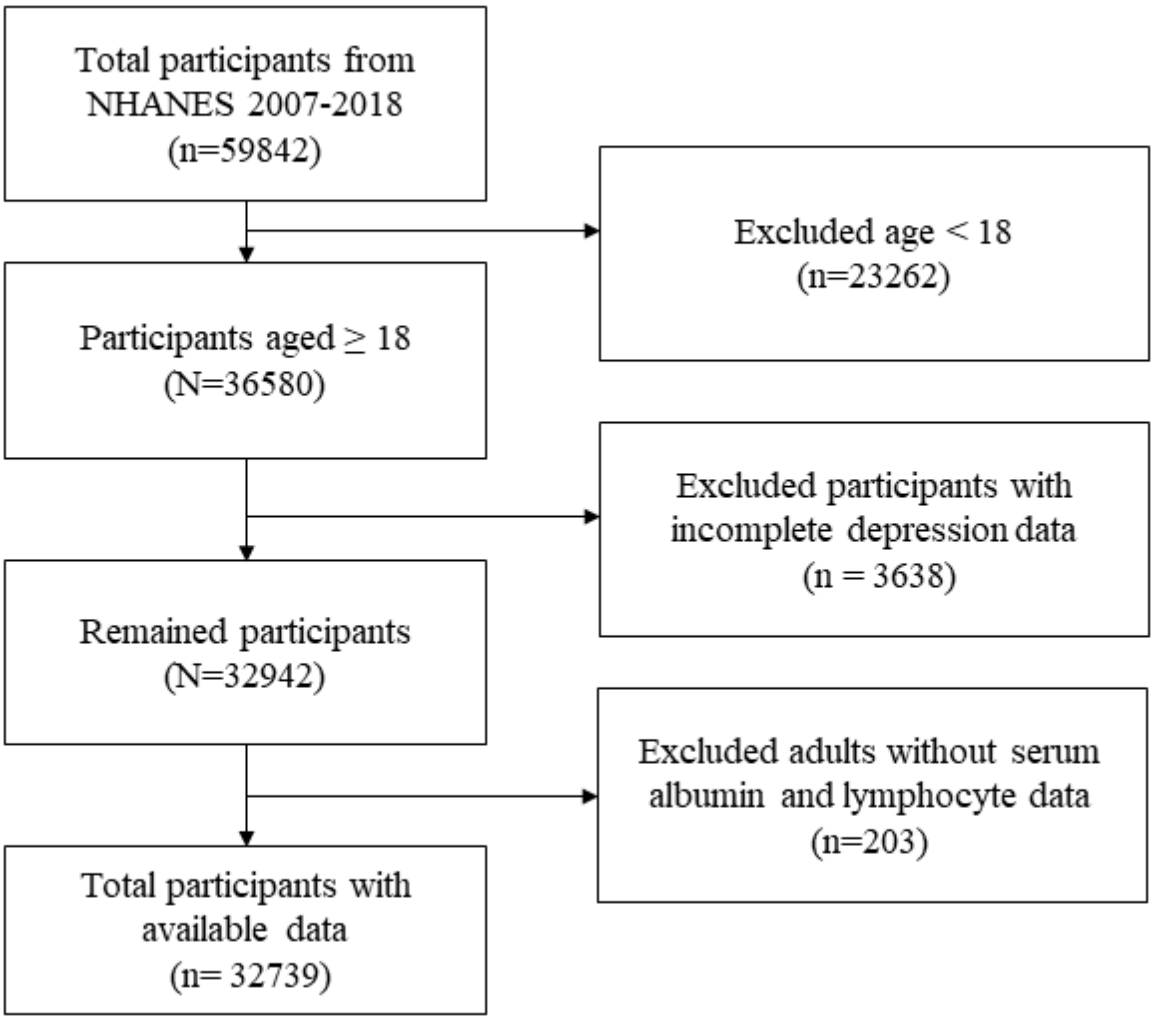


Figure 1

Flow chart of subject selection.

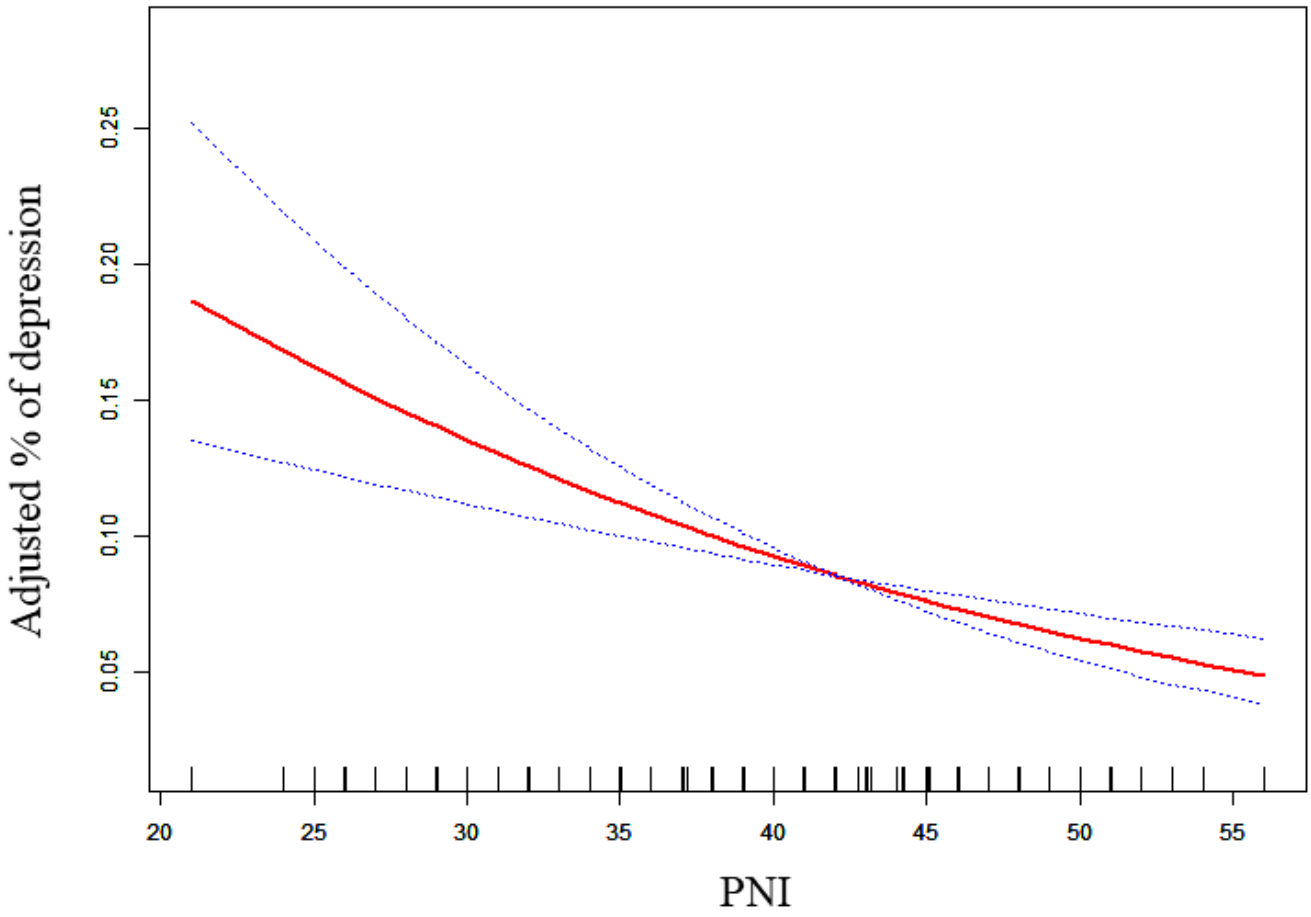


Figure 2

Restricted cubic spline fitting depicting the correlation between PNI levels and depression.

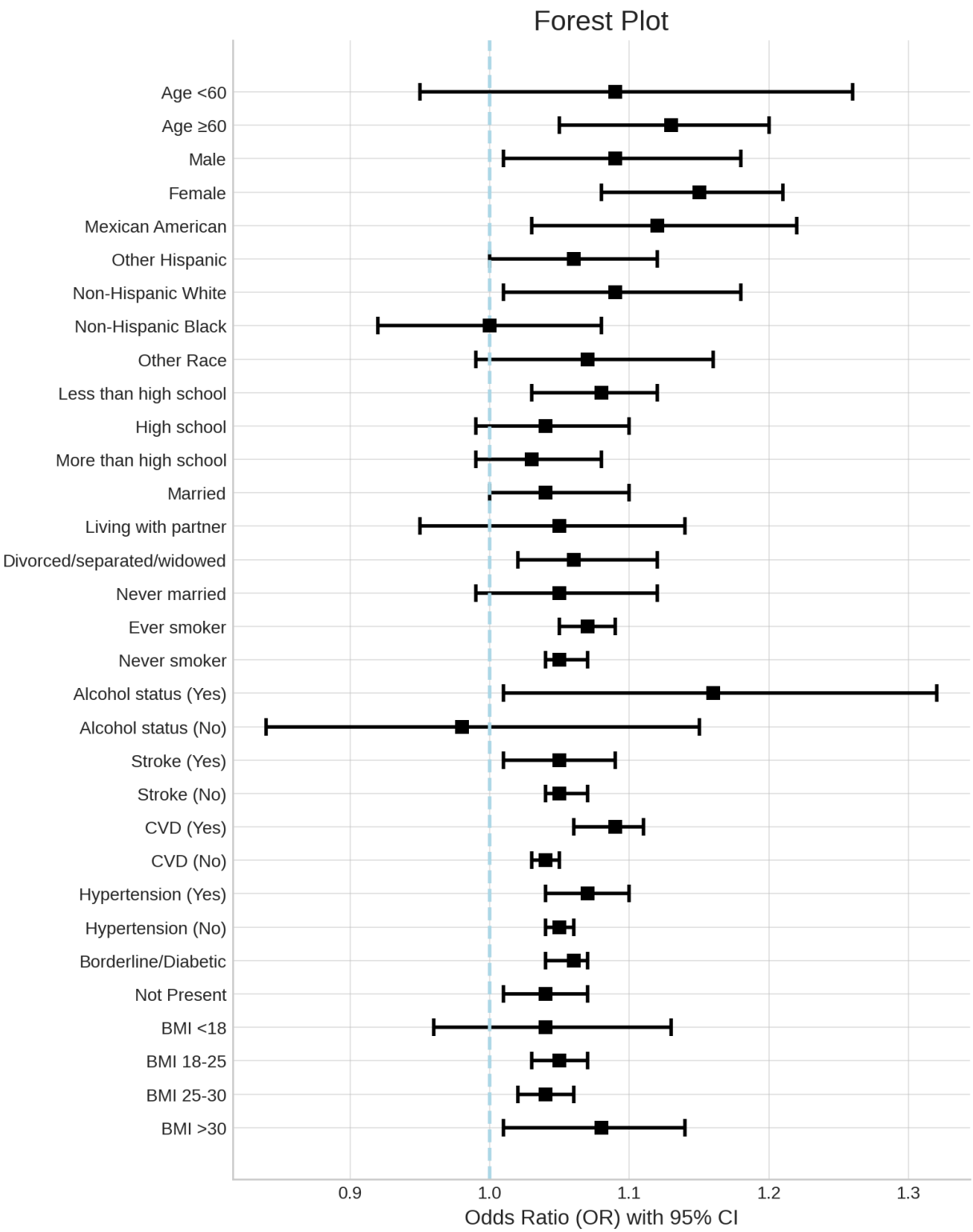


Figure 3

Odds of depression subgroups associated with increasing PNI across various clinical variables.