Proceedings of the 2nd International Conference on Modern Medicine and Global Health
DOI: 10.54254/2753-8818/8/20240463

Estradiol in adult females and its association with depression: NHANES 2013-2016

Haoran He

Department of Statistics, University of Pittsburgh, Pittsburgh, Pennsylvania, The United States, 15213

q56586668@gmail.com

Abstract. In the contemporary era of rapid global development, a growing proportion of individuals are dedicating extended hours to their professional endeavors, driven by the desire to attain enhanced financial remuneration and an improved quality of life. Consequently, a significant majority of the population finds themselves immersed in an environment characterized by elevated levels of stress and strain. Consequently, there is a growing prevalence of depression among individuals, with a particular emphasis on the female population. At present, there is a paucity of studies pertaining to the correlation between estradiol levels in women and the occurrence of depression. In order to investigate this issue, an experimental study is done to examine the relationship between estradiol levels and depression scores. The present study utilizes a sample derived from the 2013-2016 US National Health and Nutrition Examination Survey (NHANES) to investigate the relationship between estradiol levels and depression. This analysis employs various statistical techniques, including exploratory data analysis, linear regression, logistic regression, Poisson regression, and chi-squared test. Additionally, the study controls for several covariates, namely age, sex, race, marital status, work minutes, sedentary activity, vitamin D levels, and diabetes status. The findings indicate a negative association between estradiol levels and depression.

Keywords: Estradiol, Depression, Females, NHANES.

1. Introduction

Estrogen is a crucial sex hormone in females that plays a vital role in maintaining sexual and reproductive well-being. The levels of estrogen undergo natural fluctuations throughout the menstrual cycle and experience a gradual reduction during the menopausal phase. Persistently elevated or diminished levels of estrogen may indicate a medical problem that necessitates the attention of a healthcare provider [1].

There exist three primary variants of estrogen, namely Estrone, Estradiol, and Estriol. Estrone (E1) is the predominant endogenous estrogen synthesized by the body subsequent to the onset of menopause. Estradiol (E2) is the predominant estrogenic hormone present in the human body during the reproductive phase of life. This particular type of estrogen is highly powerful. Estriol (E3) is recognized as the predominant estrogenic hormone during the gestational period [1].

Estradiol (E2), is a steroid hormone classified as an estrogen and serves as the primary sex hormone in females. The entity in question plays a role in the control of the estrous and menstrual

DOI: 10.54254/2753-8818/8/20240463

cycles in female reproductive systems. Estradiol plays a pivotal role in the development of female secondary sexual features, including the formation of breasts, broadening of the hips, and the establishment of a fat distribution pattern consistent with the female gender. The role of estrogen is crucial in the growth and sustenance of female reproductive tissues, including the mammary glands, uterus, and vagina, during the stages of puberty, maturity, and pregnancy. Additionally, it exerts significant impacts on various other tissues, such as bone, adipose tissue, dermis, hepatic tissue, and the central nervous system [1].

Depression is classified as a mental condition characterized by a prolonged state of melancholy and diminished interest. Major depressive disorder, often known as clinical depression, has a profound impact on an individual's emotions, cognition, and behaviors, potentially resulting in a range of psychological and physiological complications. The user's text is too short to be rewritten in an academic manner. Individuals may encounter difficulties in doing routine daily tasks and may experience a sense of existential despair, questioning the value of life itself [2]. Depression affects 3.8% of the population, according to available data. This includes 5% of adults, 4% men and 6% women. About 5.7% of people 60 and older have depression. Around 280 million people worldwide suffer from depression. Depression affects 50% more women than males. Depression affects almost 10% of pregnant and postpartum women worldwide [2].

Prior research has indicated that instances of female depression frequently coincide with hormonal disturbances, such as premenstrual phases, postpartum periods, and menopausal stages [3]. As previously mentioned, there is a higher prevalence of depression among females compared to males. The prevalence and, in certain instances, intensity of depression are linked to the presence or absence of ovarian hormones. Previous studies have demonstrated a positive association between female estrogen levels and the occurrence of depression in women [4]. Nevertheless, there is a limited number of scholarly articles that examine the precise correlation between estradiol levels and depression ratings utilizing data from the National Health and Nutrition Examination Survey (NHANES) [5]. Furthermore, it should be noted that the NHANES 2013-2014 and 2015-2016 datasets exclusively include the necessary paperwork and data files pertaining to the subject matter. Hence, the primary objective of this study is to investigate the potential correlation between levels of estradiol and scores of depression through the analysis of datasets obtained from NHANES 2013-2016 [5].

2. Methods

2.1. Data Background and study population

The research datasets come from the National Health and National Examination Survey (NHANES) [5]. It is a program of studies designed to assess the health and nutritional status of adults and children in the United States every 2 years. NHANES is a major program of the Centers for Disease Control and Prevention (CDC). It combines interviews and physical examinations and has Demographics Data, Dietary Data, Examination Data, Laboratory Data, Questionnaire Data and Limited Access Data [7].

The datasets included Demo.xpt, BMX.xpt, TST.xpt, VID.xpt, DIQ.xpt, DPQ.xpt, PAQ.xpt and RHQ.xpt [6], which contained the information about body measures, sex steroid hormone – serum, Vitamin D, diabetes, mental health - depression screener, physical activity and reproductive health.

The study sample comprised persons who were enrolled in two consecutive 2-year cycle surveys conducted throughout the periods of 2013-2014 and 2015-2016. Among the 19,357 participants in the examination, the author excluded those who are younger than 18 $(n = 7698)$, who were males(n=5582), whose estradiol data (n=547) and depression data (n=564) were missing. Finally, 4966 individuals were included in the cross-sectional study. The flow chart can be seen in Figure 1.

DOI: 10.54254/2753-8818/8/20240463

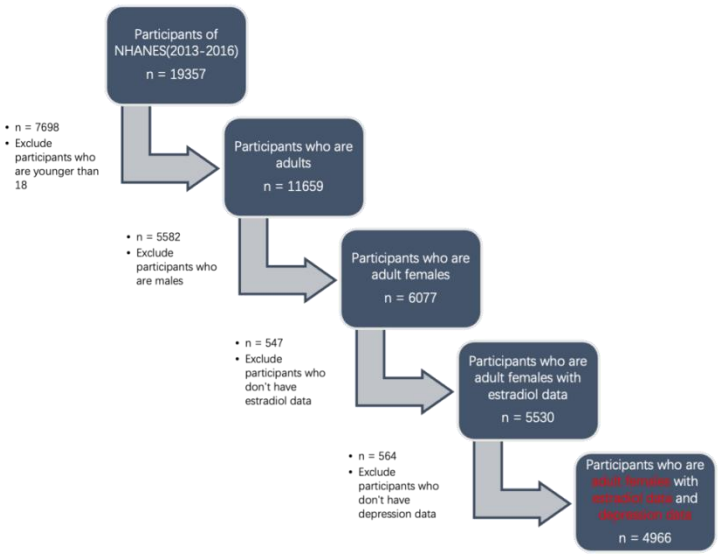

Figure 1. Flow Diagram of the Screening and Enrollment of Study Participants.

2.2. Variables

The examination of serum estradiol levels was conducted using the isotope dilution liquid chromatography tandem mass spectrometry (ID-LC-MS/MS) method, which has been established by the Centers for Disease Control and Prevention (CDC) for regular measurements. The serum samples underwent processing, storage, and shipment to the Division of Laboratory Sciences, National Centre for Environmental Health, Centers for Disease Control and Prevention, located in Atlanta, GA, in order to facilitate analysis. The Estradiol's lower limit of detection was reported as 2.994pg/ml [8].

The depression assessment utilized the Patient Health Questionnaire (PHQ-9), a screening tool consisting of nine items. These items inquire about the frequency of depressive symptoms experienced by individuals throughout the preceding two-week period. The response categories of "not at all," "several days," "more than half the days," and "nearly every day" were assigned scores ranging from 0 to 3. A comprehensive score was computed, encompassing a range of values from 0 to 27. A score of 10 or above has been extensively validated and is frequently employed in clinical research to establish the presence of depression [9].

2.3. Covariates

Other possible factors in this study include age, race (Mexican American, Other Hispanic, Non-Hispanic White, Non-Hispanic Black, and other races), BMI (Normal: BMI < 25kg/m^2; Overweight: 25<= BMI < 30 kg/m^2; Obese: BMI >= 30kg/m^2), Marital Status (Married, Widowed, Divorced, Separated, Never married, Living with partner), Diabetes (Yes, No, Borderline), taking birth control pills (Yes, No), using female hormones (Yes, No), vigorous-intensity work minutes, moderate-intensity work minutes, moderate recreational activity minutes, sedentary activity minutes, Vitamin D (nmol/L) [10].

2.4. Statistical Analysis

The statistical studies were performed using R version 4.3.1 and RStudio version 2023.06.1-524. The author employed exploratory data analysis techniques to describe the primary characteristics of the variables, and conducted an analysis of the datasets using histograms, boxplots, and scatterplots.

The data that follows a normal distribution can be assessed using either a T-test or a Z-test. Normally distributed variables are typically represented by their mean value plus or minus the standard deviation. On the other hand, nonnormally distributed variables are typically represented by the median value together with the interquartile range, which is calculated as the difference between

DOI: 10.54254/2753-8818/8/20240463

the third quartile (Q3) and the first quartile (Q1). A comparison was conducted between the median values of depression estradiol levels and depression categories. The chi-square test was employed to assess the presence of a statistically significant relationship between the categories of the two variables [11].

The researcher employed univariate and multivariate linear regression models to establish the curve's fit and ascertain the association between each covariate and estradiol levels. Subsequently, the author observed that the distribution of estradiol exhibited a right-skewed pattern, prompting the utilization of a log transformation to appropriately align the model. Because the level of estradiol was log-transformed, the percent differences of estradiol was calculated by the equation: percent change = (e^ß−1) ∗100%. For outliers of Estradiol, the decision range is [Q1−1.5∗IQR, Q3+1.5∗IQR]. Any data point less than the Lower Bound or more than the Upper Bound is considered as an outlier. The author conducted a sensitivity analysis by excluding participants with estradiol level < 2.994 pg/mL or > 187.4375 pg/mL or points more than 3 standard deviations from the mean [12].

Additionally, the author employed univariate and multivariate linear regression models to examine the association between each covariate and categories of depression. In each instance of regression analysis, the researcher obtained residuals, multiple R-squared, adjusted R-squared, and regression coefficients, which encompass estimated coefficients, standard error, t-value, and p-value.

Additionally, stratified analyses by race (Mexican American, Other Hispanic, Non-Hispanic White, Non-Hispanic Black, and other races), BMI (Normal: BMI < 25kg/$\sqrt{m^2}$; Overweight: 25<= BMI < 30 kg/$\sqrt{m^2}$; Obese: BMI >= 30kg/$\sqrt{m^2}$), Martial Status (Married, Widowed, Divorced, Separated, Never married, Living with partner), Diabetes (Yes, No, Borderline), taking birth control pills (Yes, No) and using female hormones (Yes, No) were performed to examine the association between depression and log-transformed estradiol.

3. Results

3.1. Exploratory data analysis

The utilization of histograms was employed by the author to visually represent the distribution of estradiol and estradiol data points, with the exclusion of any outliers. The author discovered that there were outliers present in the estradiol data, rendering the estradiol histogram unsuitable for analysis. The histogram depicting the distribution of estradiol, after removing outliers, exhibited improved characteristics, enabling the author to ascertain that estradiol follows a right-skewed distribution. The author also employed boxplots to represent the distribution of estradiol levels, both with and without outliers. According to the author's findings, it was determined that the inclusion of outliers should be avoided while analyzing estradiol data. Subsequently, a boxplot was utilized to visually represent the median, lower bound, and upper bound of the estradiol values [13].

The author employed scatterplots to examine the relationship between estradiol and depression, revealing a negative correlation wherein higher depression ratings were associated with lower estradiol levels. Consequently, he hypothesized that there might exist a negative correlation.

3.2. Analysis results

A total of 4,966 individuals were involved in this research and categorized into five racial groups: Mexican American (n = 837), Other Hispanic (n = 594), Non-Hispanic White (n = 1886), Non-Hispanic Black (n = 984), and other races (n = 665). Participants also were divided into six marital groups: Married (n = 2209), Widowed (n = 487), Divorced (n = 635), Separated (n = 186), Never married (n = 838), Living with partner (n = 361). Participants also were divided into three BMI (Body Mass Index) categories: Normal (n = 1486), Overweight (n = 1310), Obese (n = 2126). Participants also were divided into three Diabetes groups: Yes (n = 621), No (n = 4205), Borderline (n = 135). Participants also were divided into two groups about birth control pills: Yes, No (n = 1738). Participants also were divided into two groups about using female hormones: Yes (n = 822), No (n = 3865) [10].

DOI: 10.54254/2753-8818/8/20240463

The mean age was 48.05±18.28 years, the mean vigorous-intensity work minutes were 195.062 ± 580.30 minutes, the mean moderate-intensity work minutes were 169.34 ± 375.67 minutes, the mean moderate recreational activity minutes were 69.81 ± 381.86 minutes, the mean sedentary activity minutes were 466.91 ± 845.355 minutes, and the mean Vitamin D was 67.543 ± 30.95 nmol/L. The mean estradiol level was 98.67 ± 642.92 pg/mL while the mean estradiol level excluding outliers was 38.19 ± 46.18 pg/mL. The mean depression score was 3.823 ± 4.60 points. Depression scores were categorized based on validation: Minimal (DPQ_score <= 4), Mild (5<= DPQ_score <=9), Moderate (10 <= DPQ_score <= 14), Moderately severe (15 <= DPQ_score <= 19) and Severe (20 <= DPQ_score <= 27). Using the data, characteristics of the sample population among different Depression categories were summarized in Table 1. There were significant differences among the five groups with respect to age ($p = 0.019$), race ($p < 0.001$), BMI_Category ($p < 0.01$), estradiol ($p = 0.028$), sedentary activity ($p = 0.002$), diabetes ($p < 0.001$) and birth control pills (No) ($p = 0.07$). There was no significant difference among the five groups with respect to marital status, vigorous-intensity work, moderate-intensity work, Vitamin D and using female hormones (No). In conducting the Bonferroni test for intergroup comparison, it was seen that as depression levels grew, there was a progressive decrease in the proportions of race, BMI_category, birth control pill usage (No), and diabetes. Conversely, there was a gradual increase in the proportion of sedentary activity. Furthermore, it was shown that the relationship between age and estrogen levels exhibited fluctuations in conjunction with the escalation of depression levels [14].

The characteristics of participants with different estradiol levels were shown in Table 2. There were significant differences among the four groups with respect to age ($p < 0.001$), race ($p < 0.001$), BMI_category ($p < 0.001$), vigorous-intensity work ($p = 0.022$), moderate-intensity work ($p < 0.001$), moderate recreational activities ($p < 0.001$), DPQ_score ($p = 0.021$), Depression_category ($p = 0.005$), Vitamin D ($p < 0.001$), Diabetes ($p < 0.001$) and using_female_hormones(No) ($p < 0.001$). There was no significant difference among the four groups with respect to marital status, sedentary activity and birth_control_pills (No). Taking the Bonferroni test for intergroup comparison, with the increasing of estradiol levels and the proportion of age. Other Hispanic race, Non-Hispanic White race, Vitamin D and Diabetes (Borderline) decreased gradually, while the proportion of Mexican American race and using_female_hormones(No) increased gradually.

Table 1. Characteristics of the study population disaggregated by depression category.

Characteristics	Depression Category						
	Mild depression	Minimal depression	Moderate depression	Moderately severe depression	Severe depression	p	test
n	960	3458	333	145	70		
Age year	50.00 [34.00, 65.00]	46.00 [32.00, 62.00]	49.00 [34.00, 62.00]	54.00 [37.00, 64.00]	50.00 [41.25, 58.75]	0.019	nonnorm
Race (%)						<0.001	
Mexican American	160 (16.7)	589 (17.0)	49 (14.7)	30 (20.7)	9 (12.9)		
Other Hispanic	116 (12.1)	398 (11.5)	36 (10.8)	29 (20.0)	15 (21.4)		
White	361 (37.6)	1299 (37.6)	141 (42.3)	55 (37.9)	30 (42.9)		
Black	214 (22.3)	663 (19.2)	74 (22.2)	24 (16.6)	9 (12.9)		
Other Race	109 (11.4)	509 (14.7)	33 (9.9)	7 (4.8)	7 (10.0)		
Marital Status (%)						NaN	

DOI: 10.54254/2753-8818/8/20240463

Table 1. (continued).

Married	390 (42.7)	1647 (50.3)	108 (33.5)	46 (33.3)	18 (26.1)		
Widowed	104 (11.4)	321 (9.8)	36 (11.2)	15 (10.9)	11 (15.9)		
Divorced	139 (15.2)	393 (12.0)	61 (18.9)	31 (22.5)	11 (15.9)		
Separated	45 (4.9)	103 (3.1)	20 (6.2)	10 (7.2)	8 (11.6)		
Never married	164 (18.0)	567 (17.3)	68 (21.1)	25 (18.1)	14 (20.3)		
Living with partner	71 (7.8)	243 (7.4)	29 (9.0)	11 (8.0)	7 (10.1)		
BMI_category (%)						<0.001	
Normal	246 (25.8)	1116 (32.5)	87 (26.4)	22 (15.5)	15 (21.4)		
Obese	454 (47.7)	1372 (40.0)	171 (52.0)	92 (64.8)	37 (52.9)		
Overweight	252 (26.5)	941 (27.4)	71 (21.6)	28 (19.7)	18 (25.7)		
Estradiol (pg/mL)	15.75 [5.28, 70.03]	21.85 [5.55, 84.18]	19.30 [5.18, 66.30]	11.90 [6.24, 41.30]	14.65 [5.60, 44.84]	0.028	nonnorm
Vigorous-intensity work(min)	120.00 [60.00, 240.00]	120.00 [60.00, 240.00]	120.00 [41.25, 240.00]	60.00 [33.75, 225.00]	60.00 [45.00, 105.00]	0.256	nonnorm
Moderate-intensity work(min)	120.00 [60.00, 240.00]	120.00 [60.00, 240.00]	120.00 [60.00, 180.00]	120.00 [30.00, 240.00]	60.00 [30.00, 180.00]	0.446	nonnorm
Moderate recreational activities(min)	45.00 [30.00, 60.00]	45.00 [30.00, 60.00]	30.00 [30.00, 60.00]	45.00 [30.00, 60.00]	60.00 [30.00, 60.00]	0.579	nonnorm
Sedentary activity(min)	360.00 [240.00, 540.00]	360.00 [240.00, 480.00]	420.00 [300.00, 540.00]	420.00 [240.00, 600.00]	480.00 [300.00, 555.00]	0.002	nonnorm
Vitamin D(nmol/L)	62.85 [45.70, 83.35]	63.90 [45.52, 84.80]	60.40 [42.60, 80.40]	65.30 [43.40, 82.20]	60.30 [46.82, 79.50]	0.339	nonnorm
Diabetes (%)						<0.001	
Yes	170 (17.7)	336 (9.7)	59 (17.8)	39 (26.9)	17 (24.6)		
No	763 (79.6)	3027 (87.6)	260 (78.5)	104 (71.7)	51 (73.9)		
Borderline	26 (2.7)	94 (2.7)	12 (3.6)	2 (1.4)	1 (1.4)		
birth_control_pills = No (%)	334 (35.0)	1235 (35.8)	99 (29.8)	53 (37.1)	17 (24.3)	0.070	
use_femal_hormones = No (%)	722 (80.0)	2704 (83.0)	267 (83.4)	114 (83.2)	58 (84.1)	0.329	

DOI: 10.54254/2753-8818/8/20240463

Table 2. Characteristics of the study population in different estradiol groups.

Characteristics	Estradiol quartiles					
	Q1	Q2	Q3	Q4	p	test
n	1249	1238	1235	1244		
Age (year)	63.00 [55.00, 73.00]	61.00 [52.00, 70.00]	35.00 [26.00, 44.00]	35.00 [26.00, 43.00]	<0.001	nonnorm
Race (%)					<0.001	
Mexican American	180 (14.4)	189 (15.3)	231 (18.7)	237 (19.1)		
Other Hispanic	166 (13.3)	150 (12.1)	148 (12.0)	130 (10.5)		
White	562 (45.0)	510 (41.2)	413 (33.4)	401 (32.2)		
Black	172 (13.8)	272 (22.0)	260 (21.1)	280 (22.5)		
Other Race	169 (13.5)	117 (9.5)	183 (14.8)	196 (15.8)		
Marital Status (%)					NaN	
Married	566 (46.0)	585 (48.1)	519 (46.0)	539 (47.2)		
Widowed	253 (20.6)	197 (16.2)	27 (2.4)	10 (0.9)		
Divorced	200 (16.2)	214 (17.6)	121 (10.7)	100 (8.8)		
Separated	46 (3.7)	48 (3.9)	50 (4.4)	42 (3.7)		
Never married	121 (9.8)	120 (9.9)	291 (25.8)	306 (26.8)		
Living with partner	45 (3.7)	52 (4.3)	120 (10.6)	144 (12.6)		
BMI_category (%)					<0.001	
Normal	497 (40.3)	167 (13.6)	359 (29.2)	463 (37.6)		
Obese	326 (26.4)	748 (60.9)	609 (49.6)	443 (36.0)		
Overweight	410 (33.3)	314 (25.5)	261 (21.2)	325 (26.4)		
Vigorous-intensity work(min)	120.00 [60.00, 240.00]	120.00 [45.00, 240.00]	120.00 [45.00, 180.00]	120.00 [60.00, 240.00]	0.022	nonnorm
Moderate-intensity work(min)	120.00 [60.00, 195.00]	120.00 [30.00, 180.00]	120.00 [60.00, 240.00]	120.00 [60.00, 240.00]	<0.001	nonnorm
Moderate recreational activities(min)	45.00 [30.00, 60.00]	35.00 [30.00, 60.00]	45.00 [30.00, 60.00]	60.00 [30.00, 60.00]	0.001	nonnorm
Sedentary activity(min)	360.00 [240.00, 480.00]	360.00 [240.00, 495.00]	420.00 [240.00, 540.00]	360.00 [240.00, 540.00]	0.083	nonnorm
DPQ_score (median [IQR])	2.00 [0.00, 6.00]	2.00 [1.00, 6.00]	2.00 [0.00, 5.00]	2.00 [0.00, 5.00]	0.021	nonnorm
Depression_category (%)					0.005	
Mild depression	252 (20.2)	263 (21.2)	218 (17.7)	227 (18.2)		
Minimal depression	857 (68.6)	819 (66.2)	879 (71.2)	903 (72.6)		

DOI: 10.54254/2753-8818/8/20240463

Table 2. (continued).

Moderate depression	90 (7.2)	80 (6.5)	90 (7.3)	73 (5.9)		
Moderately severe depression	32 (2.6)	55 (4.4)	34 (2.8)	24 (1.9)		
Severe depression	18 (1.4)	21 (1.7)	14 (1.1)	17 (1.4)		
Vitamin D(nmol/L)	78.50 [59.50, 101.00]	67.50 [48.02, 89.60]	56.10 [40.30, 72.70]	55.35 [38.20, 73.12]	<0.001	nonnorm
Diabetes (%)					<0.001	
Yes	218 (17.5)	260 (21.0)	97 (7.9)	46 (3.7)		
No	981 (78.7)	931 (75.3)	1115 (90.4)	1178 (94.8)		
Borderline	48 (3.8)	46 (3.7)	22 (1.8)	19 (1.5)		
birth_control_pills = No (%)	467 (37.7)	407 (33.0)	416 (33.8)	448 (36.1)	0.058	
use_femal_hormones = No (%)	856 (70.3)	890 (73.7)	1026 (91.4)	1093 (96.0)	<0.001	

Table 3 displays the outcomes of both univariable and multivariate linear regression analyses, which were conducted to examine the relationship between each independent variable and log-transformed estradiol. In univariable linear regression analysis, the author found that age, other Hispanic race, white race, widowed, divorced, overweight, DPQ_score and Vitamin D are significantly negatively correlated with estradiol. The author also found that never married status, living with partner status, BMI, minimal depression, Diabetes (No) and using female hormones (No) are significantly positively correlated with estradiol. In multivariate linear regression, the author found that age (estimate estradiol percent difference: −4.62% per year, $p < 0.01$) and white race (estimate estradiol percent difference: −39.32%, $p < 0.01$) were negatively associated with estradiol. And minimal depression (estimate estradiol percent difference: 39.58%, $p = 0.0658$) was nearly positively correlated with estradiol.

Table 3. Univariate and multivariate linear regression analysis predicting log-transformed estradiol.

Variables	Univariable linear regression analysis					Multivariable linear regression analysis				
	Estimated Coef	Std. Error	P-value	R^2	Adjusted R-squared	Estimated Coef	Std. Error	P-value	R^2	Adjusted R-squared
Whole	/	/	/	/	/			6.345E-08	0.3053	0.2238
Age (year)	-0.05566	0.000947	<2e-16	0.4104	0.4102	-0.0462361	0.0073700	1.94E-09		
Race (%)			1.757E-14	0.01411	0.01332			1.757E-14		
Mexican American										
Other Hispanic	-0.30583	0.08463	0.000305			-0.5284143	0.3479841	0.1304		
White	-0.39319	0.06552	2.1E-09			-0.39319	0.06552	2.1E-09		

DOI: 10.54254/2753-8818/8/20240463

Table 3. (continued).

Variables	Univariable linear regression analysis					Multivariable linear regression analysis				
	Estimated Coef	Std. Error	P-value	R^2	Adjusted R-squared	Estimated Coef	Std. Error	P-value	R^2	Adjusted R-squared
Black	0.02809	0.07418	0.704937			-0.3269706	0.2845447	0.2518		
Other Race	-0.04523	0.08195	0.581032			0.0579279	0.3093879	0.8517		
Marital Status (%)			< 2.2e-16	0.1194	0.1185					
Married										
Widowed	-1.24953	0.07463	< 2e-16			0.0932881	0.3663724	0.7993		
Divorced	-0.40682	0.06713	1.46E-09			-0.3591647	0.4846488	0.4595		
Separated	0.06200	0.11382	0.586			-0.1032525	0.2667746	0.6991		
Never married	0.63338	0.06048	< 2e-16			-0.2329705	0.4623151	0.6148		
Living with partner	0.77571	0.08463	< 2e-16			-0.4838002	0.2452222	0.0498		
BMI	0.009268	0.002850	0.00115	0.002145	0.001942					
BMI_category (%)			3.312E-05	0.004185	0.00378					
Normal										
Obese	0.03816	0.05331	0.474175			0.0232992	0.2331754	0.9205		
Overweight	-0.20588	0.05976	0.000575			0.0050554	0.2378439	0.9831		
DPQ_score(point)	-0.014715	0.004894	0.0026 5	0.001818	0.001617					
Depression_category			0.1702	0.002602	0.001798					
Mild depression										
Minimal depression	0.15592	0.05788	0.00709			0.3958242	0.2140313	0.0658		
Moderate depression	0.05550	0.10091	0.58237			0.4708247	0.3546996	0.1858		
Moderately severe depression	-0.17189	0.14137	0.22407			0.5985204	0.5435798	0.2721		
Severe depression	-0.02159	0.19644	0.91247			-0.5350835	0.7865083	0.4970		
Vigorous-intensity work(min)	120.00 [60.00, 240.00]	120.00 [60.00, 240.00]	120.00 [41.25, 240.00]	60.00 [33.75, 225.00]	60.00 [45.00, 105.00]	0.256	nonnorm			

DOI: 10.54254/2753-8818/8/20240463

Table 3. (continued).

Variables	Univariable linear regression analysis					Multivariable linear regression analysis				
	Estimated Coef	Std. Error	P-value	R^2	Adjusted R-squared	Estimated Coef	Std. Error	P-value	R^2	Adjusted R-squared
Moderate-intensity work(min)	120.00 [60.00, 240.00]	120.00 [60.00, 240.00]	120.00 [60.00, 180.00]	120.00 [30.00, 240.00]	60.00 [30.00, 180.00]	0.446	nonnorm			
Moderate recreational activities(min)	45.00 [30.00, 60.00]	45.00 [30.00, 60.00]	30.00 [30.00, 60.00]	45.00 [30.00, 60.00]	60.00 [30.00, 60.00]	0.579	nonnorm			
Sedentary activity(min)	360.00 [240.00, 540.00]	360.00 [240.00, 480.00]	420.00 [300.00, 540.00]	420.00 [240.00, 600.00]	480.00 [300.00, 555.00]	0.002	nonnorm			
Vitamin D(nmol/L)	-0.0148997	0.0006969	<2e-16	0.08431	0.08413	-0.0010392	0.0035724	0.7714		
Diabetes (%)			< 2.2e-16	0.0394	0.03901					
Yes										
No	0.90685	0.06693	<2e-16			-0.0650675	0.3534530	0.8541		
Borderline	0.18589	0.14784	0.209			-0.5684261	0.7443782	0.4459		
birth_control_pills (%)			0.2218	0.0003019	9.974E-05					
Yes										
No	-0.05776	0.04726	0.222			0.0427099	0.2025550	0.8332		
use_female_hormones (%)			< 2.2e-16	0.07607	0.07587					
Yes										
No	1.15127	0.05862	<2e-16			0.2853555	0.2930601	0.3313		

The author employed the chi-squared test to examine the relationship between two categorical variables, namely Depression categories and Estradiol quartiles. The obtained result suggested a substantial correlation between the variables, with X-squared equaling 28.272 and a p-value of 0.005046.

4. Conclusion

The present study incorporated data from the NHANES 2013-2014 and 2015-2016 surveys, encompassing a sample size of 4,966 women aged 18 years or older. The findings from both univariate and multivariate linear regression analyses indicate a potential negative association between

DOI: 10.54254/2753-8818/8/20240463

depression and estradiol. After removing outliers, the strong negative correlation between depression and estradiol remained intact.

Nevertheless, the precise correlation between depression and estradiol remains undetermined. Due to the utilization of a cross-sectional methodology, this study is limited to examining the correlation between levels of depression and estradiol, which is unable to establish causality. The study's sample size is constrained due to the utilization of NHANES information from only the years 2013-2014 and 2015-2016, hence limiting the accuracy of the obtained results. Furthermore, the author is unable to access the most recent data from the National Health and Nutrition Examination Survey (NHANES), potentially rendering the findings outdated at present. Ultimately, the author's analysis was limited in scope and did not extend to examining the causative relationships between depression and estradiol, while recognizing the various constraints and flaws.

The intention is to offer informative content pertaining to the treatment of depression. The author of this study examined a biologically plausible correlation and suggests that additional large-scale prospective studies are necessary to establish a causal relationship between depression and estradiol levels.

References

[1] Estrogen: Hormone, Function, Levels & Imbalances and Estrogen. In: Wikipedia. Accessed August 31, 2023. https://my.clevelandclinic.org/health/body/22353-estrogen, https://en.wikipedia. org/w/index.php?title=Estrogen&oldid=1171482429

[2] Depressive disorder (depression) and Depression (mood). In: Wikipedia.. Accessed August 31, 2023. https://www.who.int/news-room/fact-sheets/detail/depression and https://en.wikipedia.org/w/index.php?title=Depression_(mood)&oldid=1172733106#cite_note-:3-4

[3] Ryan KJ. Biochemistry of aromatase: significance to female reproductive physiology. Cancer Res. 1982;42(8 Suppl):3342s-3344s.

[4] Shors TJ, Leuner B. Estrogen-mediated effects on depression and memory formation in females. J Affect Disord. 2003;74(1):85-96.

[5] NHANES - National Health and Nutrition Examination Survey Homepage. Published July 25, 2023. Accessed August 31, 2023. https://www.cdc.gov/nchs/nhanes/index.htm

[6] NHANES Questionnaires, Datasets, and Related Documentation. Accessed September 9, 2023. https://wwwn.cdc.gov/nchs/nhanes/continuousnhanes/default.aspx?BeginYear=2015

[7] Chen J, Kan M, Ratnasekera P, Deol LK, Thakkar V, Davison KM. Blood Chromium Levels and Their Association with Cardiovascular Diseases, Diabetes, and Depression: National Health and Nutrition Examination Survey (NHANES) 2015–2016. Nutrients. 2022;14(13):2687. doi:10.3390/nu14132687

[8] TST_I. Accessed August 21, 2023. https://wwwn.cdc.gov/Nchs/Nhanes/2015-2016/TST_I.htm

[9] NHANES 2015-2016: Mental Health - Depression Screener Data Documentation, Codebook, and Frequencies. Accessed August 31, 2023. https://wwwn.cdc.gov/Nchs/Nhanes/2015-2016/DPQ_I.htm

[10] Han Y, Zhang Y, Cao Y, et al. Exploration of the association between serum uric acid and testosterone in adult males: NHANES 2011-2016. Transl Androl Urol. 2021;10(1):272-282. doi:10.21037/tau-20-1114

[11] Albert KM, Newhouse PA. Estrogen, Stress, and Depression: Cognitive and Biological Interactions. Annu Rev Clin Psychol. 2019;15:399-423. doi:10.1146/ annurev-clinpsy-050718-095557

[12] Richard A, Rohrmann S, Mohler-Kuo M, et al. Urinary phytoestrogens and depression in perimenopausal US women: NHANES 2005-2008. J Affect Disord. 2014;156:200-205. doi:10.1016/j.jad.2013.12.029

[13] Xie J, Wang M, Long Z, et al. Global burden of type 2 diabetes in adolescents and young adults, 1990-2019: systematic analysis of the Global Burden of Disease Study 2019. BMJ. 2022;379:e072385. doi:10.1136/bmj-2022-072385

DOI: 10.54254/2753-8818/8/20240463

[14] Ruan Z, Lu T, Chen Y, et al. Association Between Psoriasis and Nonalcoholic Fatty Liver Disease Among Outpatient US Adults. JAMA Dermatol. 2022;158(7):745-753. doi:10.1001/jamadermatol.2022.1609