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ORIGINAL RESEARCH

Depression as a Risk Factor for Gynecological Cancers: Evidence from NHANES Data

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Purpose: Depression is one of the leading sources of disease burden globally and plays a significant role in the occurrence and development of many cancers, representing an important health risk. However, the relationship between depression and the risk of gynecologic cancers has not been fully assessed. This study aims to explore the association between depression and the risk of gynecologic cancers.

Patients and Methods: We selected 11,574 participants from the NHANES 2009–2018 cycles, among which 274 had gynecologic cancer (GC), 137 had cervical cancer (CC), 48 had ovarian cancer (OC), and 89 had endometrial cancer (EC). Box plots were used to assess the differences in PHQ-9 depression scores between cancer and non-cancer groups. Logistic regression models and restricted cubic spline (RCS) models were employed to evaluate the relationship between PHQ-9 scores and gynecologic cancers. Subgroup analyses and interaction tests examined the consistency of the association across different characteristics.

Results: There was a significant difference in PHQ-9 scores between the cancer group and the non-cancer group. In the multivariable logistic regression analysis, PHQ-9 scores were positively correlated with GC, OC, and EC, while no significant association was found with CC risk. Additionally, the RCS model also indicated no nonlinear association between PHQ-9 scores and CC risk. Additionally, subgroup analyses suggested that the relationship between PHQ-9 scores and CC and OC was consistent across groups, whereas the association between PHQ-9 scores and GC and EC showed heterogeneity in relation to race and marital status.

Conclusion: Depression is positively correlated with gynecologic cancers. Specifically, higher levels of depression are associated with an increased risk of OC and EC, while no significant association was found with CC risk. Future attention should be given to the impact of depression on the incidence of gynecologic cancers, particularly OC and EC.

Keywords: gynecological cancers, depression, NHANES, epidemiology

Introduction

Depression, also known as depressive disorder, is a prevalent mental health condition characterized by a high incidence rate, high clinical cure rate, but low treatment acceptance and a high recurrence rate.[1] Its main characteristics include significant and persistent low mood. Depression is primarily manifested through symptoms such as low mood, loss of interest, and lack of energy.[2] Approximately 5% of adults globally experience depression annually, and this condition is more prevalent among women than men.[3] The development of depression involves various factors, including hormone levels, immunity, unhealthy lifestyles, inflammation, and others.[4] Many studies have found that depression is associated with various diseases, including cardiovascular disease, diabetes, irritable bowel syndrome, and cancer, among others.[5–8] Similarly, depression is also related to gynecological diseases.[9] Gynecological cancers are common among gynecological diseases, yet there is a lack of sufficient research on the correlation between depression and gynecological cancers.

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Globally, while the incidence of gynecological malignancies is not among the highest, they remain a significant threat to women's health.[10] Gynecological malignancies affect the uterus, ovaries, cervix, vulva, vagina, fallopian tubes, and peritoneum.[11] In the United States, the most common gynecological malignancy is EC, followed by OC and CC.[12] Among these, OC and EC are the fifth and sixth leading causes of cancer-related deaths in women.[13] Although early screening and prevention have reduced the incidence and mortality of gynecological cancers, many cases are still diagnosed at advanced stages, resulting in poorer prognosis.[14] The risk factors for gynecological cancers include individual factors, obesity, infectious factors, and lifestyle factors.[15,16] Previous research has found that patients with gynecological cancers often exhibit significant emotional changes, which may be related to factors such as inflammation, neuroendocrine dysregulation, and impaired immune function.[17]

Considering the above factors, we propose that these emotional changes may be a potential risk factor for the development of gynecological cancers. However, it remains unclear whether these emotional changes are related to the incidence of gynecological cancers, and there is a lack of large-scale studies investigating depression as a risk factor for gynecological cancers.[18] To address this issue, the present study analyzes NHANES data to explore the association between depression and the risk of common gynecological cancers—cervical, ovarian and endometrial cancers.

Methods

Study Population

This study included 49,693 participants from the National Health and Nutrition Examination Survey (NHANES) conducted between 2009 and 2018. Based on the research requirements, we excluded male participants (n = 24,533), individuals over the age of 20 (n = 8,031), those with missing gynecological cancer questionnaire data (n = 9), other cancer patients (n = 1,173), and individuals with missing PHQ-9 questionnaire data (n = 2,126). Ultimately, a total of 11,574 participants were retained for further analysis (Figure 1).

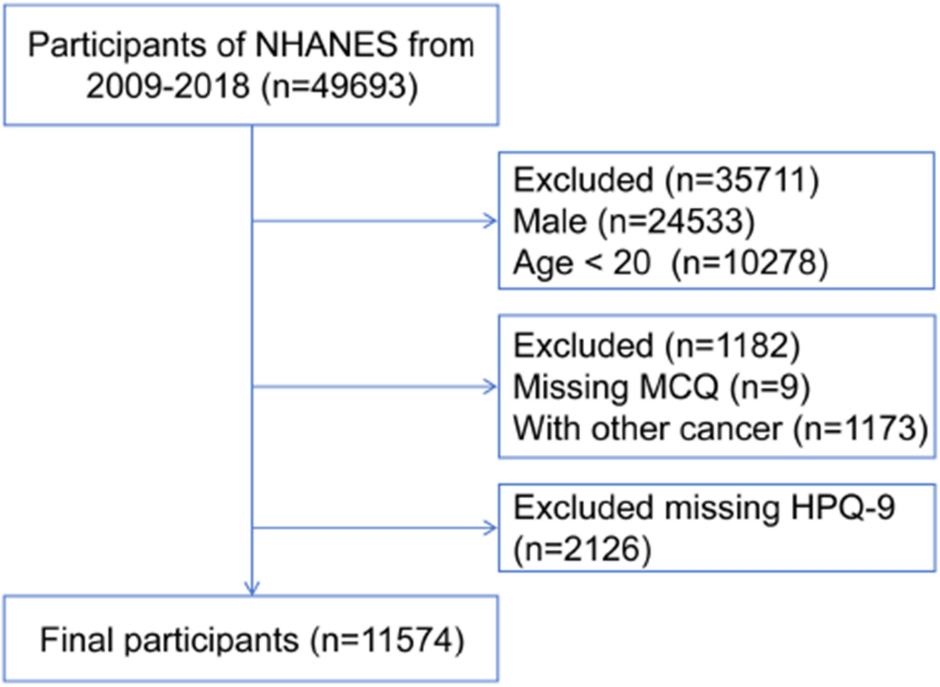

Figure 1 Flow chart of participants' enrollment process.
Abbreviations: NHANES, National Health and Nutrition Examination Survey; PHQ-9, Patient Health Questionnaire-9; MCQ, medical conditions.

Gynecological Cancers

The diagnosis of gynecological cancers was determined through a questionnaire survey. First, participants were assessed for cancer status based on their response to the question "Ever told you had cancer or malignancy?" Then, the type of gynecological cancer was identified based on their response to the question "What kind of cancer?" It is required that the answers to both questions be based on a physician's diagnosis.

Depression

The PHQ-9 (Patient Health Questionnaire-9) is a commonly utilized self-report instrument for evaluating depressive symptoms experienced in the last two weeks.[19] It consists of 9 items addressing core symptoms of depression, including low mood, loss of interest, sleep disturbances, fatigue, appetite changes, guilt, concentration difficulties, psychomotor changes, and suicidal thoughts. Each item is scored based on frequency, with scores that range from 0 to 27. Higher scores reflect a greater severity of symptoms. PHQ-9 scores from NHANES were used to categorize depression into five levels: minimal-G1 (0–4 scores), mild-G2 (5–9 scores), moderate-G3 (10–14 scores), moderately severe-G4 (15–19 scores), and severe-G5 (20–27 scores).[20]

Covariates

Continuous variables include age, poverty income ratio (PIR), and body mass index (BMI). Age is divided into three groups: "20–40", "40–65", and "≥65". PIR is categorized into three groups: "<1.3", "1.3–3.5", and "≥3.5". BMI is classified as <25 kg/m² and ≥25 kg/m². Categorical variables include ethnicity, education level, marital status, current smoking status, past-year alcohol drinking, diabetes mellitus, and hypertension, all categorized into groups based on survey data.

Statistical Analysis

This study did not involve any weighted variables. Missing values in the variables were imputed using multiple imputation to ensure data integrity. Chi-square tests were used to assess all variables, and results were presented as absolute values (n) or percentages (%). First, univariate and multivariate logistic regression analyses were conducted to calculate odds ratios (ORs) and 95% confidence intervals (CIs) to explore the relationship between PHQ-9 scores and the risk of gynecological cancers. Potential confounders were adjusted to ensure the reliability of the results. The crude model did not adjust for any covariates. Model I adjusted for age, ethnicity, BMI, and diabetes. Model II adjusted for all covariates. Next, for the CC group, where no linear relationship was observed, restricted cubic splines (RCS) were used to further examine the potential nonlinear association with PHQ-9 scores, with knots at the 10th, 50th, and 90th percentiles. Finally, subgroup analysis and interaction tests were performed on potential confounding variables to examine the consistency of the relationship between PHQ-9 scores and gynecological cancers across different subgroups and to identify sources of variation. All statistical analyses were conducted using R software (version 4.4.1). P-value < 0.05 was considered statistically significant.

Results

Baseline Characteristics of Participants

As detailed in Table 1 and Supplementary Tables 1–3, the study included 11574 participants from the NHANES cycles between 2009 and 2018. Of these, 274 were diagnosed with GC, 137 with CC, 48 with OC, and 89 with EC. Participants were categorized into the gynecological cancer group (n = 274) and the non-gynecological cancer group (n = 11,300). Significant differences were observed among groups regarding age, ethnicity, education level, PIR, marital status, BMI, diabetes mellitus and hypertension (all $P < 0.05$). No meaningful differences were found for current smoker status and past-year alcohol drinking. Additionally, Figure 2A–D shows significant differences in PHQ-9 scores between gynecological cancer groups and non-gynecological cancer groups (GC:P < 0.0001, CC and: P < 0.01, OC and EC: P < 0.05).

Table 1 Baseline Characteristics of Participants with and without Gynecological Cancers

Variables	Total (n = 11574)	Non-Gynecological Cancers (n = 11300)	Gynecological Cancers (n = 274)	P-value
Age, n (%), years				<0.001
20–40	4039 (34.90)	3987 (35.28)	52 (18.98)	
40–65	5163 (44.61)	5010 (44.34)	153 (55.84)	
≥ 65	2372 (20.49)	2303 (20.38)	69 (25.18)	
Ethnicity, n (%)				<0.001
Mexican American	1757 (15.18)	1717 (15.19)	40 (14.60)	
Other Hispanic	1314 (11.35)	1287 (11.39)	27 (9.85)	
Non-Hispanic White	4355 (37.63)	4200 (37.17)	155 (56.57)	
Non-Hispanic Black	2598 (22.45)	2566 (22.71)	32 (11.68)	
Other	1550 (13.39)	1530 (13.54)	20 (7.30)	
Education level, n (%)				0.027
Less than 12th grade	2543 (21.97)	2468 (21.84)	75 (27.37)	
High school	2492 (21.53)	2427 (21.48)	65 (23.72)	
College or more	6539 (56.50)	6405 (56.68)	134 (48.91)	
PIR, n (%)				0.009
< 1.3	3925 (33.91)	3812 (33.73)	113 (41.24)	
1.3–3.5	4571 (39.49)	4464 (39.50)	107 (39.05)	
≥ 3.5	3078 (26.59)	3024 (26.76)	54 (19.71)	
Marital status, n (%)				<0.001
Married	5306 (45.88)	5194 (45.99)	112 (41.03)	
Never married	2215 (19.15)	2190 (19.39)	25 (9.16)	
Other	4045 (34.97)	3909 (34.61)	136 (49.82)	
BMI (kg/m^2)				0.037
< 25.0	3357 (29.00)	3293 (29.14)	64 (23.36)	
≥ 25.0	8217 (71.00)	8007 (70.86)	210 (76.64)	
Current smoker status, n(%)				0.159
Not at all	4428 (38.26)	4310 (38.14)	118 (43.07)	
Some days	910 (7.86)	886 (7.84)	24 (8.76)	
Every day	6236 (53.88)	6104 (54.02)	132 (48.18)	
Past-year alcohol drinking, n(%)				0.653
Non-drinker	5000 (43.20)	4880 (43.19)	120 (43.80)	
1–3 drinks	4984 (43.06)	4872 (43.12)	112 (40.88)	
≥ 4 drinks	1590 (13.74)	1548 (13.70)	42 (15.33)	
Diabetes mellitus, n(%)				0.003
Yes	1425 (12.31)	1381 (12.22)	44 (16.06)	
No	9853 (85.13)	9637 (85.28)	216 (78.83)	
Borderline	296 (2.56)	282 (2.50)	14 (5.11)	
Hypertension, n(%)				<0.001
Yes	4129 (35.67)	3985 (35.27)	144 (52.55)	
No	7445 (64.33)	7315 (64.73)	130 (47.45)	

Abbreviations: PIR, family poverty income ratio; BMI, body mass index.

Logistic Regression Analysis Between PHQ-9 Scores and Gynecological Cancers

Univariate logistic regression analysis indicated that the association between PHQ-9 scores and gynecological cancers was noteworthy in Supplementary Table 4 (all $P < 0.05$). Furthermore, as shown in Table 2, multivariate logistic regression analysis revealed a significant association between PHQ-9 scores and gynecological cancers (G 2: Crude model: OR = 1.62, P = 0.001; Model 1: OR = 1.56, P = 0.003; Model 2: OR = 1.42, P = 0.021; G 3: Crude model: OR = 1.97, P < 0.001; Model 1: OR = 1.82, P = 0.004; Model 2: OR = 1.52, P = 0.045; all P for trend < 0.05). Similar associations were also found between PHQ-9 scores and OC (G2: Crude model: OR = 2.21, P = 0.018; Model 1: OR = 2.10, P = 0.028; Model 2: OR = 2.14,

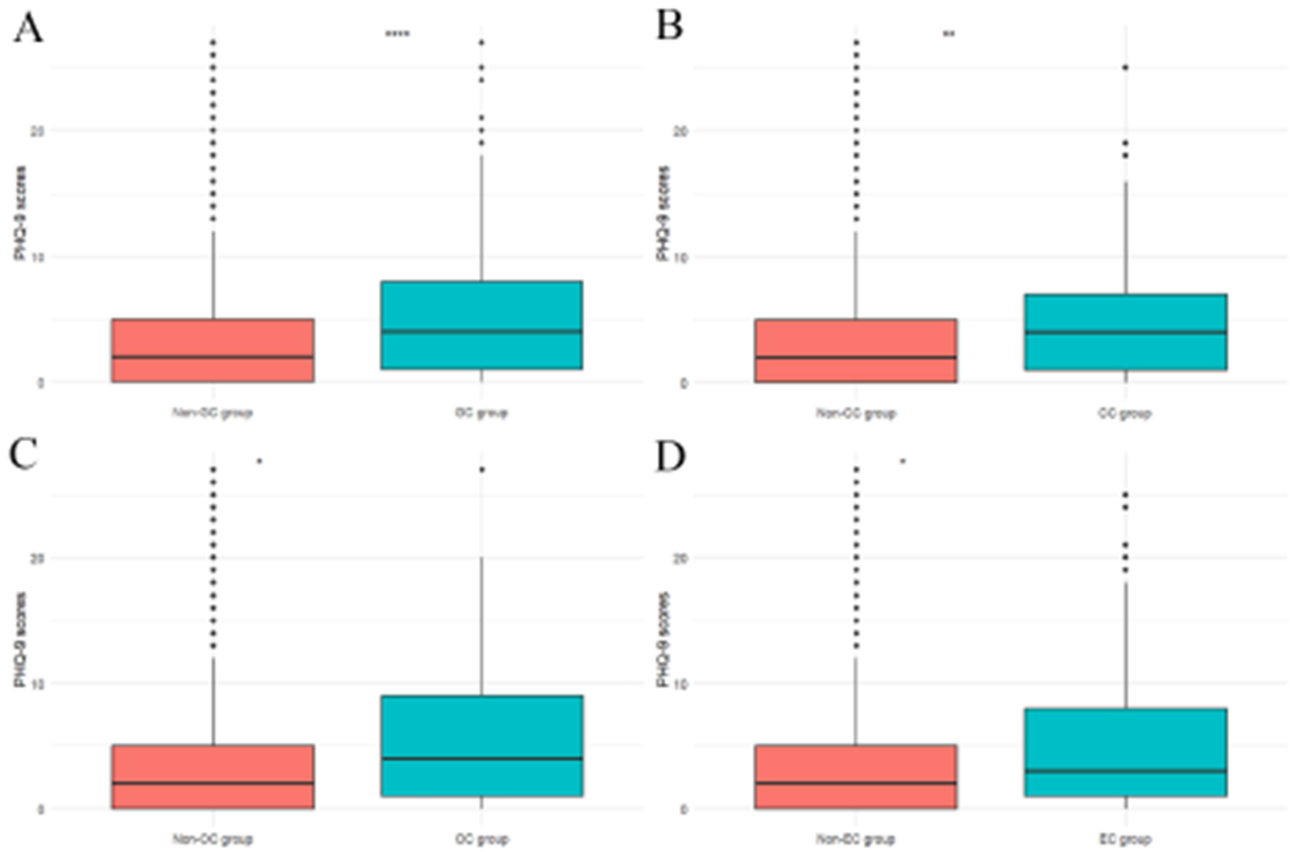

Figure 2 Comparison of PHQ-9 scores between gynecological cancers and non-gynecological cancer groups. (**A**) PHQ-9 scores in the GC group compared to the non-GC group. (**B**) PHQ-9 scores in the CC group compared to the non-CC group. (**C**) PHQ-9 scores in the OC group compared to the non-OC group. (**D**) PHQ-9 scores in the EC group compared to the non-EC group. ****: $P < 0.0001$, **: $P < 0.01$, *: $P < 0.05$.
Abbreviations: PHQ-9, Patient Health Questionnaire-9; GC, gynecologic cancer; CC, cervical cancer; OC, ovarian cancer; EC, endometrial cancer.

P = 0.027; G5: Crude model: OR = 4.68, P = 0.037; Model 1: OR = 4.67, P = 0.040; Model 2: OR = 4.81, P = 0.040; all P for trend < 0.05) and EC (G5: Crude model: OR = 4.45, P = 0.005; Model 1: OR = 3.61, P = 0.016; Model 2: OR = 3.25, P = 0.031; all P for trend < 0.05). However, no linear relationship was found between PHQ-9 scores and CC (P for trend > 0.05). Additionally, both adjusted and unadjusted RCS models did not show a nonlinear relationship between PHQ-9 scores and CC (P for nonlinear = 0.058 in the unadjusted model, P for nonlinear = 0.089 in the adjusted model) (Figure 3A and B).

Subgroup Analysis

We conducted stratified and interaction analyses for each gynecological cancer group to assess result robustness and explore potential modifying factors. Figure 4 and Supplementary Figure 1 present the results for gynecological cancers and EC, respectively. A consistent positive correlation was observed between PHQ-9 scores and both gynecological cancers and EC across most subgroups. Significant interactions were found in the ethnicity (GC: P for interaction = 0.033; EC: P for interaction = 0.031) and marital status (GC: P for interaction = 0.026; EC: P for interaction = 0.041) subgroups, suggesting that ethnicity and marital status may modify the relationship between PHQ-9 scores and the risk of both GC and EC. Supplementary Figures 2 and 3 indicate the robustness of the relationship between PHQ-9 scores and CC as well as OC. Notably, age subgroup analyses across all cancer groups suggest that the risk of gynecological cancers associated with PHQ-9 scores decreases with increasing age.

Discussion

With changes in lifestyle, an aging population, and the widespread use of screening technologies, the current status of gynecological cancers shows a diversified trend of development, where early detection and active intervention are key to

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Table 2 Multivariate Logistic Regression Analysis of PHQ-9 Score for Risk of Gynecological Cancers

	Crude Model		Model I		Model II	
	Crude OR (95% CI)	**P-value**	**Adjusted OR (95% CI)**	**P-value**	**Adjusted OR (95% CI)**	**P-value**
Gynecological cancers						
PHQ-9 score	1.06 (1.04 ~ 1.08)	<0.001	1.05 (1.03 ~ 1.07)	<0.001	1.04 (1.01 ~ 1.06)	0.002
G 1	Reference		Reference		Reference	
G 2	1.62 (1.21 ~ 2.17)	0.001	1.56 (1.16 ~ 2.09)	0.003	1.42 (1.05 ~ 1.91)	0.021
G 3	1.97 (1.33 ~ 2.94)	<0.001	1.82 (1.22 ~ 2.72)	0.004	1.52 (1.01 ~ 2.30)	0.045
G 4	2.21 (1.28 ~ 3.79)	0.004	2.02 (1.17 ~ 3.50)	0.012	1.59 (0.91 ~ 2.77)	0.106
G 5	2.57 (1.18 ~ 5.58)	0.017	2.21 (1.01 ~ 4.86)	0.048	1.68 (0.76 ~ 3.74)	0.200
P for trend	<0.001		<0.001		0.006	
Cervical cancer						
PHQ-9 score	1.04 (1.01 ~ 1.08)	0.005	1.03 (1.01 ~ 1.07)	0.035	1.01 (0.98 ~ 1.04)	0.629
G 1	Reference		Reference		Reference	
G 2	1.55 (1.03 ~ 2.33)	0.035	1.50 (0.99 ~ 2.26)	0.055	1.28 (0.84 ~ 1.95)	0.244
G 3	1.88 (1.08 ~ 3.28)	0.026	1.64 (0.93 ~ 2.88)	0.087	1.22 (0.68 ~ 2.17)	0.504
G 4	1.96 (0.90 ~ 4.26)	0.092	1.78 (0.80 ~ 3.92)	0.155	1.20 (0.54 ~ 2.69)	0.655
G 5	0.68 (0.09 ~ 4.95)	0.707	0.56 (0.08 ~ 4.09)	0.567	0.35 (0.05 ~ 2.55)	0.298
P for trend	0.017		0.078		0.829	
Ovarian cancer						
PHQ-9 score	1.08 (1.03 ~ 1.13)	0.002	1.07 (1.02 ~ 1.13)	0.003	1.08 (1.03 ~ 1.13)	0.003
G 1	Reference		Reference		Reference	
G 2	2.21 (1.14 ~ 4.29)	0.018	2.10 (1.08 ~ 4.09)	0.028	2.14 (1.09 ~ 4.19)	0.027
G 3	2.53 (1.03 ~ 6.20)	0.043	2.45 (0.99 ~ 6.07)	0.052	2.53 (1.01 ~ 6.36)	0.049
G 4	1.87 (0.44 ~ 7.95)	0.395	1.71 (0.40 ~ 7.37)	0.469	1.77 (0.40 ~ 7.74)	0.448
G 5	4.68 (1.10 ~ 20.00)	0.037	4.67 (1.07 ~ 20.34)	0.040	4.81 (1.08 ~ 21.54)	0.040
P for trend	0.004		0.007		0.008	
Endometrial cancer						
PHQ-9 score	1.06 (1.03 ~ 1.10)	<0.001	1.06 (1.02 ~ 1.09)	0.003	1.05 (1.01 ~ 1.09)	0.021
G 1	Reference		Reference		Reference	
G 2	1.41 (0.83 ~ 2.40)	0.201	1.33 (0.78 ~ 2.27)	0.289	1.26 (0.74 ~ 2.17)	0.394
G 3	1.79 (0.88 ~ 3.64)	0.111	1.66 (0.81 ~ 3.42)	0.165	1.46 (0.70 ~ 3.03)	0.315
G 4	2.66 (1.14 ~ 6.25)	0.024	2.34 (0.98 ~ 5.54)	0.054	1.92 (0.80 ~ 4.63)	0.146
G 5	4.45 (1.59 ~ 12.49)	0.005	3.61 (1.27 ~ 10.29)	0.016	3.25 (1.12 ~ 9.47)	0.031
P for trend	<0.001		0.002		0.016	

Notes: The crude model was not adjusted for covariates. Model I was adjusted for age, ethnicity, BMI and diabetes mellitus. Model II was adjusted for all covariates.
Abbreviations: PHQ-9, Patient Health Questionnaire-9; G1, minimal level (0–4 scores); G2, mild level (5–9 scores); G3, moderate level (10–14 scores); G4, moderately severe level (15–19 scores); G5, severe level (20–27 scores); OR, odd ratio; CI, confidence interval.

improving prognosis and increasing patient survival rates.[21,22] This study analyzes data from 11,574 participants in the NHANES to explore the association between depression and the risk of gynecological cancers and to assess the heterogeneity of this association with demographic and lifestyle variables.We found a significant difference in depression levels between the cancer group and the non-cancer group. The more severe the depression, the higher the risk of gynecological cancers, OC and EC, while there is no association between CC and depression. Additionally, ethnicity and marital status may play a mediating role in the relationship between depression and GC and EC.

The occurrence of gynecological cancers is caused by various factors. Many previous studies have focused on anxiety and depression in gynecological cancer patients and have confirmed that improving these negative emotions benefits the long-term prognosis of gynecological cancers.[23,24] However, these negative emotions were present even before the diagnosis of cancer.[25] Our study addresses whether this negative emotion (depression) directly leads to the occurrence of gynecological tumors. Furthermore, we attempted to explain the mechanisms underlying this association.Previous studies have confirmed that the mechanisms of gynecological tumor occurrence include hormonal levels, genetic susceptibility,

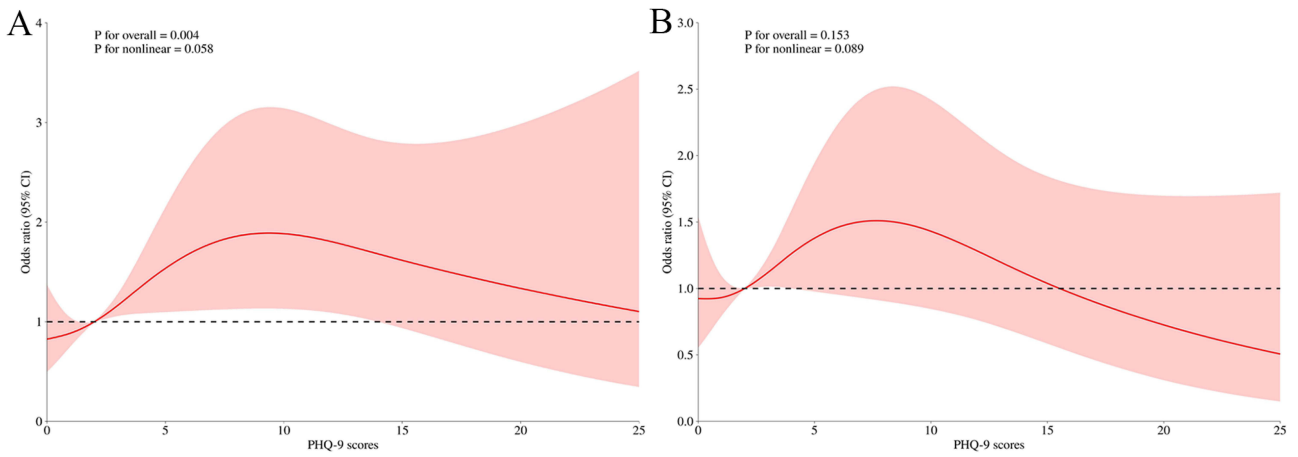

Figure 3 Odds ratio of CC according to PHQ-9 scores in the overall population. The solid line and shadow represented the odds ratio of OA and 95% confidence interval, respectively. (**A**) no covariates were adjusted. (**B**) all covariates were adjusted.
Abbreviations: PHQ-9, Patient Health Questionnaire-9; CC, cervical cancer.

infections, environmental pollutants, immune factors, unhealthy lifestyles, inflammation, and more.[26–28] Depression is associated with changes in hormonal levels, which play an important role in the development of gynecological cancers. For example, depression may lead to an imbalance in estrogen levels, thereby affecting the growth and variation of the endometrium.[29,30] Moreover, patients with depression often experience an imbalance in neurotransmitter levels (such as serotonin and norepinephrine), which may affect immune system function, decreasing the body's ability to monitor tumor cells and thereby increasing the risk of gynecological cancers.[31,32] Studies have also found that inflammatory markers are often elevated in patients with depression, and this chronic inflammatory response may be closely related to cancer development, particularly EC and OC.[33–35] Depression is often accompanied by unhealthy lifestyle choices, such as poor diet, lack of exercise, and smoking, which may increase cancer risk.[36] Therefore, we hypothesize that depression may influence the incidence of gynecological cancers through mechanisms affecting hormone levels, immunity, unhealthy lifestyles, and inflammation.Further research is needed to validate this. It is noteworthy that a Mendelian randomization study has confirmed a causal relationship between depression and CC.[37] However, our study did not find an association between depression and CC. This suggests that other factors may need to be considered, such as whether human papillomavirus (HPV) infection plays a dominant role in the development of cervical cancer or whether early screening could influence the relationship.[38,39] One consideration for future research is the inclusion of longitudinal data to better infer the relationship between depression and CC.

In the subgroup analysis, ethnicity and marital status were also identified as potential mediators in the relationship between depression and the increased risk of gynecological cancers. This may be related to the differences in cancer incidence and living conditions among different ethnic groups, as well as variations in lifestyle based on marital status.[12,40] Additionally, we found that the incidence of CC, OC, and EC decreases with increasing age. However, according to epidemiological statistics, menopause is a peak period for the most common cancers in women, attributed to the gradual decline of ovarian function until it ultimately ceases.[41] This may be due to statistical errors in our data. In summary, not only may the pain and decreased quality of life faced by gynecological cancer patients lead to or exacerbate depressive symptoms, but the anxiety and reduced life satisfaction caused by depression may also promote the occurrence of gynecological cancers. This bidirectional relationship suggests that we should not only focus on the mental health of cancer patients but also recognize the importance of monitoring the mental health of undiagnosed patients.

Our study is pioneering in clearly defining the relationship between depression and the risk of gynecological cancers. Additionally, it utilizes data from participants representing diverse ages, ethnicities, and socioeconomic backgrounds, providing good representativeness. This finding emphasizes the importance of mental health in cancer prevention and offers a basis for public health policy. However, some limitations are unavoidable. First, the PHQ-9 primarily assesses depressive symptoms and does not comprehensively capture the impact of other psychological states, such as anxiety and

Variables	OR (95% CI)	P for interaction
All patients	1.06 (1.04 ~ 1.08)	
Age		0.143
20-40	1.09 (1.05 ~ 1.15)	
40-65	1.05 (1.03 ~ 1.08)	
>= 65	1.02 (0.97 ~ 1.08)	
Past-year alcohol drinking		0.577
Non-drinker	1.05 (1.02 ~ 1.09)	
1-3 drinks	1.07 (1.04 ~ 1.11)	
>= 4 drinks	1.04 (0.99 ~ 1.09)	
PIR		0.982
< 1.3	1.05 (1.02 ~ 1.08)	
1.3-3.5	1.06 (1.02 ~ 1.09)	
>= 3.5	1.06 (1.00 ~ 1.12)	
BMI		0.723
< 25.0	1.06 (1.01 ~ 1.12)	
>= 25.0	1.05 (1.03 ~ 1.08)	
Ethnicity		0.033
Mexican American	1.07 (1.02 ~ 1.13)	
Other Hispanic	1.02 (0.96 ~ 1.09)	
Non-Hispanic White	1.05 (1.02 ~ 1.08)	
Non-Hispanic Black	1.03 (0.96 ~ 1.10)	
Other	1.17 (1.10 ~ 1.25)	
Marital status		0.026
Married	1.09 (1.06 ~ 1.13)	
Never married	1.07 (1.00 ~ 1.14)	
Other	1.03 (1.00 ~ 1.06)	
Current smoker status		0.338
Not at all	1.07 (1.04 ~ 1.10)	
Some days	1.07 (1.00 ~ 1.14)	
Every day	1.03 (1.00 ~ 1.07)	
Diabetes mellitus		0.777
Yes	1.04 (0.99 ~ 1.09)	
No	1.06 (1.04 ~ 1.09)	
Borderline	1.04 (0.93 ~ 1.16)	
Hypertension		0.602
Yes	1.05 (1.02 ~ 1.08)	
No	1.06 (1.02 ~ 1.09)	
Education level		0.928
Less than 12th grade	1.05 (1.01 ~ 1.09)	
High school	1.06 (1.01 ~ 1.10)	
College or more	1.06 (1.02 ~ 1.09)	

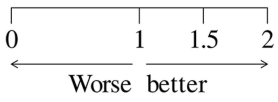

Figure 4 The relationship between PHQ-9 scores and risk of GC according to different subgroups.
Abbreviations: PHQ-9, Patient Health Questionnaire-9; GC, gynecologic cancer; OR, odds ratio; CI, confidence interval; PIR, family poverty income ratio; BMI, body mass index.

stress, on cancer risk. Second, cancer diagnoses in this study rely on self-reported physician diagnoses, which may lead to misclassification. Third, although we found no association between depression and CC risk, we are unable to provide a reasonable explanation due to the limitations of this study. Fourth, the relatively small number of ovarian cancer cases (n = 48) included in this study may limit the robustness of our findings. Finally, it is important to note that the data used is limited to the years 2009–2018, which may not accurately reflect current or future trends.

Conclusions

Depression is significantly positively associated with gynecological cancers. Specifically, higher levels of depression are linked to increased risk of ovarian and endometrial cancers, while no significant association was found with cervical cancer risk. Future efforts should focus on mitigating the impact of depression on the incidence of gynecological cancers, particularly ovarian and endometrial cancer. These findings may encourage further integration of mental health screening and interventions into gynecological cancer prevention strategies to enhance early detection and comprehensive treatment outcomes.

Abbreviations

GC, gynecologic cancer; CC, cervical cancer; OC, ovarian cancer; EC, endometrial cancer; PHQ-9, Patient Health Questionnaire-9; RCS, restricted cubic spline; PIR, family poverty income ratio; BMI, Body mass index; G, group; CI, confidence interval; OR, odds ratios; NHANES, National Health and Nutrition Examination Survey; HPV, papillomavirus.

Data Sharing Statement

The datasets used for these analyses are publicly available (https://www.cdc.gov/nchs/nhanes/index.htm). All necessary permissions for data use have been obtained.

Ethics Approval and Consent to Participate

The study protocol (Protocol Number: Protocol #2005–06, Protocol #2011–17, and Protocol #2018–01) was approved by the NCHS Research Ethics Review Board (ERB) and all participants provided written informed consent prior to participation (https://www.cdc.gov/nchs/nhanes/irba98.htm).

Based on Item 1 and Item 2 of Article 32 of the Measures for Ethical Review of Life Science and Medical Research Involving Human Subjects, dated February 18, 2023, China, our study is exempt from additional ethical approval.

The relevant legislation details are as follows:

Article 32: Research involving human data or biological samples, where no harm is caused to individuals and no sensitive personal information or commercial interests are involved, may be exempt from ethical review. This is to reduce unnecessary burdens on researchers and to facilitate the progress of life science and medical research involving humans.

(1) Research using publicly available data that has been legally obtained, or data generated through observation without interference with public behavior.
(2) Research using anonymized data.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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