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The depression-heart connection: cardiovascular risks in cancer patients from NHANES 2005–2018

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Abstract

Background Previous studies have proved that depression is an independent risk factor of cardiovascular disease (CVD) in the general population. We conducted this analysis to explore whether depression symptoms are associated with an increased risk of developing CVD among cancer patients in the United States.

Methods The data for this study were obtained from the National Health and Nutrition Examination Survey (NHANES) conducted between 2005 and 2018, with a total of 1890 cancer patients included in the analysis. A stratified multistage probability sampling design was used to select a nationally representative sample, ensuring demographic groups were proportionally represented. Depressive symptoms were assessed using the Patient Health Questionnaire-9 (PHQ-9), and CVD risk was determined based on clinical and self-reported data. A weighted multivariate logistic regression analysis was conducted to assess the relationship between depression and CVD risk, adjusting for confounding factors. Subgroup analyses were performed to explore the associations across demographic subgroups.

Results After adjusting for all covariates in the fully adjusted model (Model 3), CVD risk showed a significant association with depression severity. For each unit increase in PHQ-9 score, the adjusted odds ratio (AOR) for CVD was 1.09 (95% CI: 1.05–1.14, $P < 0.001$). Participants with severe depression exhibited markedly higher odds of CVD compared to those without depression (AOR=6.82,95%CI: 2.39–19.50, $P < 0.001$). Trend analysis revealed a graded relationship, with CVD risk increasing progressively across depression severity categories (P for trend < 0.001). Restricted cubic spline analysis confirmed a linear dose–response relationship (P for nonlinearity $= 0.424$), indicating that CVD risk escalates continuously with worsening depression severity.

Conclusion Our findings suggest that more severe depression is associated with higher CVD incidence in cancer populations. These observations highlight the need to consider depressive symptom monitoring as part of comprehensive care approaches that may help address cardiovascular risks in this vulnerable group.

Keywords Depression, Cardiovascular disease, Cancer, NHANES, Cross-sectional study

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Introduction

Cardiovascular disease (CVD) and cancer are the two leading causes of death globally, significantly affecting public health. In 2019, CVD accounted for 32% of global deaths, while cancer contributed to 16.8% [1, 2]. These two diseases not only overlap epidemiologically but also share interconnected pathophysiological mechanisms. Chronic inflammation, oxidative stress, and shared genetic vulnerabilities (e.g., TP53 mutations) create a biological link between CVD and cancer [3, 4].Their bidirectional relationship, where cancer treatments may accelerate the progression of atherosclerosis [5] and pre-existing CVD complicates cancer treatment [6], presents complex clinical challenges.

As the burden of CVD continues to rise, fueled by hypertension, diabetes, and obesity in aging populations, there is also an increasing recognition of treatment-related cardiovascular toxicity [7]. Chemotherapeutic agents (e.g., anthracyclines) induce cardiomyopathy through inhibition of topoisomerase IIβ and mitochondrial dysfunction [8], while radiation therapy promotes coronary artery disease through endothelial damage [9]. Cancer patients face dual stressors, including the physiological impacts of treatments and psychological distress from diagnostic and prognostic uncertainty. Depression affects 15–25% of cancer patients and may exacerbate cardiovascular risk through neurohormonal activation, chronic inflammation, and autonomic imbalance [10–12].

This intersection has led to the development of cardio-oncology, a field focused on mitigating treatment-related cardiovascular risks [13]. The Cardiometabolic Index (CMI) has emerged as a tool for assessing cardiovascular risk, particularly relevant in cancer survivors with metabolic syndrome from androgen deprivation therapy or immune checkpoint inhibitors [14]. Given the overlap of these factors in cancer patients, CMI may be useful in evaluating their cardiovascular risk by considering both psychological and physiological contributors to heart health [15].

Cancer patients are particularly vulnerable to depression due to chemotherapy-induced neuroinflammation and dysregulation of the hypothalamic–pituitary–adrenal axis [16, 17]. This burden worsens existing cardiovascular risks, leading to higher cardiovascular morbidity and mortality [18, 19]. As cancer survival rates increase, longitudinal studies reveal that 10-year cardiovascular mortality exceeds cancer-specific mortality in breast and prostate cancer survivors [20].

The importance of addressing both depression and CVD in cancer patients is underscored by a retrospective cohort study showing that pharmacological management of depression (SSRIs) reduced incident heart failure by 38% in lymphoma survivors [21]. Cardiovascular outcomes in CVD patients can be markedly improved through the screening and management of depressive symptoms, a practice that is now routinely integrated into cardiovascular care [22].

While the link between depression and CVD is well established in the general population, the unique cardiotoxic environment of cancer therapy may potentiate this relationship through shared pathways such as NLRP3 inflammasome activation [23]. This study hypothesizes that depression exacerbates cardiovascular morbidity in cancer patients, and that the relationship between depression and cardiovascular risk is intensified by cancer treatment-related cardiotoxicity. By exploring this relationship using data from the National Health and Nutrition Examination Survey (NHANES), we aim to provide evidence that may inform clinical guidelines and healthcare practices for managing cardiovascular and mental health risks in cancer patients.

This study hypothesizes that depressive symptoms exacerbate cardiovascular risk in cancer patients, contributing to poorer long-term health outcomes. By examining this relationship, we aim to demonstrate the importance of integrating routine depression screening into cancer care. Our findings could inform policy by supporting the adoption of early screening and tailored interventions, potentially reducing cardiovascular incidence and mortality in cancer survivors, and improving their overall health and quality of life.

Materials and methods

Data sources

This research utilized data collected by the NHANES ranging from 2005 to 2018. NHANES is a comprehensive study performed in the US every two years to evaluate the health and nutritional condition of the whole US population. This survey included a mixture of health interviews, examination components, laboratory tests, and various surveys. The selection of participants for NHANES was done by employing a sophisticated method called complex, stratified, multistage probability-cluster sampling design.This method ensures that individuals from the non-institutionalized civilian population in the US were chosen for in-home interviews and visits to a mobile examination center [24]. Our study was exempted from the Institutional Review Board because all participants had provided written informed consent in the initial survey and their personal information had been completely de-identified. For comprehensive information, please visit http://www.cdc.gov/nchs/nhanes.htm.

Study design and population

This research screened data from 39,749 participants ≥ 20 years of age, collected from the NHANES ranging from 2005 to 2018. The criteria for selection was strictly designed to ensure the integrity of the data. The initial analysis included a total of 3277 cancer patients who were identified by asking whether they had ever received a diagnosis of cancer or any form of malignancy from a doctor or other healthcare professional. A total of 274 individuals were eliminated from the study because they did not have any essential PHQ-9 scores ($n = 274$). Out of the remaining 3003 participants, 1113 individuals lacking complete covariate information were eliminated. In result, a total of 1890 participants met the criteria for further study (Fig. 1).

Definition of depression

Depression was diagnosed employing the PHQ-9, a questionnaire made up of nine items that assess depressive symptoms suffered over the previous two weeks, as defined by the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. A 4-point scale was used to score each symptom item, ranging from 0 ("not at all") to 3 ("nearly every day"). Therefore, a total score between 0 and 27 points was obtained for the entire questionnaire. Participants were classified into different groups, namely "no" (0–4), "mild" (5–9), "moderate" (10–14), and "severe" (15–27), based on their total score, reflecting the degree of depression as defined by previous studies [25–27]. Additionally, we computed a dichotomous PHQ-9 variable to identify participants with clinically significant depressive symptoms (PHQ-9 ≥ 10) and those without (PHQ-9 < 10). And higher scores correlate with higher levels of depressed symptoms. In addition, the total score was analyzed as a continuous variable to further validate the results we obtained.

Ascertainment of outcomes

CVD in participants was determined by self-reported diagnoses obtained through an individual interview utilizing a standardized questionnaire. The participants were questioned about whether a doctor or other health professional had ever informed them of their assessment of CHF/CHD/angina pectoris/MI/stroke. The individual was considered to have CVD if they responded affirmatively to any of the mentioned disease. The result was converted into a binary variable [28].

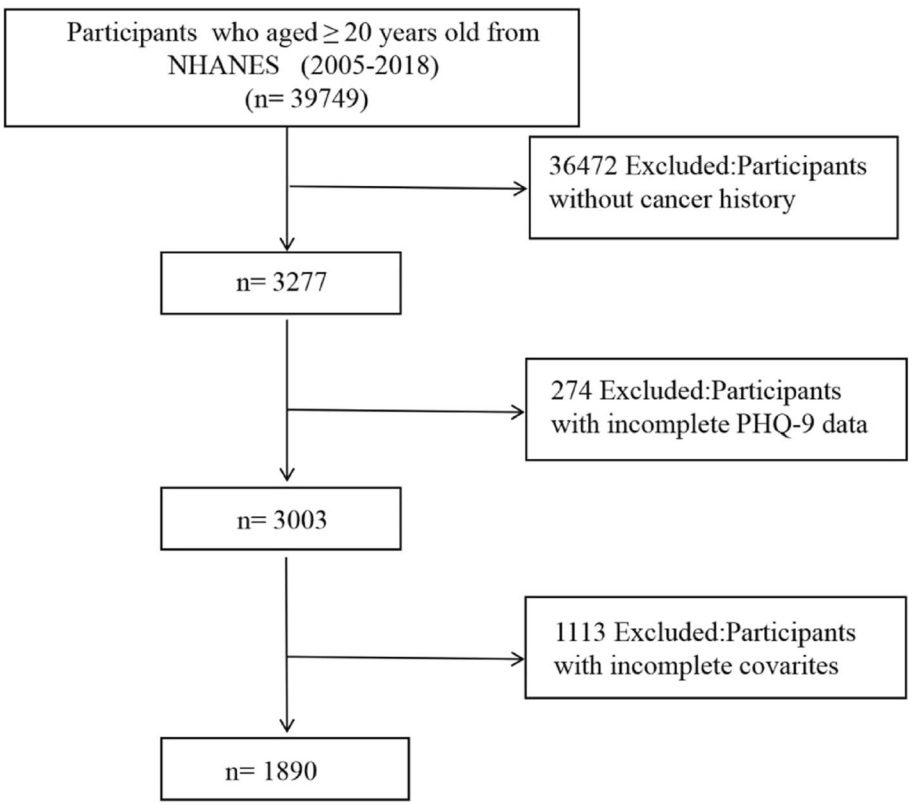

Fig. 1 Flow chart of the research study design

Covariates

In order to offset the influence of confounding factors on conclusions, we adjusted for various variables such as age, gender (male, female), education level (below high school, high school or above), race/ethnicity (Mexican American, Other Hispanic, Non-Hispanic White, Non-Hispanic Black, and Other Race), marital status (married/cohabitant, widowed, divorced or separated, never married), poverty-income ratio (PIR), and smoking status was assessed with the question, "Have you ever smoked at least 100 cigarettes in your lifetime?". Participants who answered "yes" were classified as smokers, while those who answered "no" were categorized as never smokers. Smokers were further asked, "Are you currently smoking?" Those who continued to smoke were classified as current smokers, while those who had stopped were categorized as former smokers [29]. Drinking status was defined using the NHANES ALQ101 questionnaire, where participants were categorized as never, former, mild, moderate, or heavy drinkers based on whether they consumed at least 12 alcoholic drinks in the past year [30, 31].The body mass index (BMI) was measured by dividing the weight in kilograms by the square of the height in meters. The data was grouped into three categories based on: < 25.0 kg/m2, 25.0–29.9 kg/m^2, and ≥ 30.0 kg/m2. The Physical Activity Questionnaire (PAQ) was used to obtain Metabolic Equivalent (MET) scores based on activity type and intensity. The weekly total physical activity (PA) volume was calculated by summing the MET scores for work, recreational, and walking/bicycle activities. Physical activity levels were classified into low (1.0–3.0 MET), moderate (3.0–6.0 MET), and high (> 6.0 MET) categories [32, 33]. Chronic diseases such as hypertension, diabetes mellitus (DM), and hyperlipidemia were diagnosed based on index measurements and identified using a self-reported medical history questionnaire. The diabetes category was subdivided into three distinct conditions: diabetes mellitus (DM), impaired fasting glycemia (IFG), and impaired glucose tolerance (IGT). All of these factors have been demonstrated in relation to CVD [34]. Cancer patients were further asked about the specific type of cancer they were diagnosed with, which was then categorized into the following groups: breast, digestive system, gynecological, hematological, respiratory, skin or soft tissue, urinary system, and other tumor types.

Statistical analysis

In this study, missing data were addressed using a complete case analysis approach. Participants with missing data on any key variables, including depression status, CVD status, and important covariates, were excluded from the analysis. This approach is appropriate when the data are missing completely at random (MCAR) and provides unbiased estimates under this assumption. To mitigate the impact of reduced sample size, all analyses incorporated NHANES sampling weights (wtmec4 year), stratification, and clustering to ensure representativeness and accuracy.

Statistical analysis was conducted using R version 4.3.2 and the "survey" package. The baseline characteristics were analyzed by grouping participants based on the presence or absence of cardiovascular disease (CVD). Continuous variables are presented as weighted means ± standard error (SE), and categorical variables as weighted counts and percentages (%). Comparisons between groups were made using independent samples t-tests for continuous variables and chi-squared tests for categorical variables (see Table 1 for detailed results).

In addition, PHQ-9 scores were categorized into four levels (no, mild, moderate, and severe). Multivariate logistic regression models were used to evaluate the relationship between depression level and CVD risk. PHQ-9 scores were analyzed separately as both a continuous variable and as a categorical variable representing different levels of depression severity, with each analysis adjusted for relevant covariates. The odds ratio (OR) and 95% confidence interval (CI) for the association between depression and CVD risk were estimated using three models: (1) Model 1 was adjusted for age, gender, and ethnicity. This basic model aimed to capture the general relationship between depression and CVD risk with minimal confounding; (2) Model 2 was adjusted for age, gender, ethnicity, educational level, marital status, alcohol consumption, smoking status, and PIR,in order to control for more comprehensive social and behavioral factors; (3) Model 3 included all adjustments from Model 2, along with additional potential covariates, such as hypertension, diabetes, stroke, physical activity levels, hyperlipidemia, and tumor type.This model aimed to account for clinical conditions that may further confound or mediate the relationship between depression and CVD risk (See Table 2 for detailed results). All odds ratios from these multivariable logistic regression models are reported as adjusted odds ratios (AORs) to explicitly indicate control for covariates, distinguishing them from crude (unadjusted) associations. Furthermore, to assess the non-linear relationship between PHQ-9 scores and CVD risk, we used restricted cubic spline (RCS) models with four knots at the 25th, 50th, 75th, and 95th percentiles of the PHQ-9 distribution, using the 50th percentile as the reference. These knots were selected to reflect key distribution points while maintaining flexibility in the model, especially in the central range where most observations were concentrated (see Fig. 2 for detailed results). The choice of four knots strikes a balance between capturing the potential non-linearity in the relationship and

Table 1 Baseline characteristics of participants by CVD categories from NHANES 2005–2018

Characteristic	Participants	No CVD	CVD	*P*-value
	Total (*N* = 1890)	(*N* = 1510)	(*N* = 380)	
Age, mean(SE)	60.61(0.45)	59.08(0.50)	69.38(0.74)	< 0.0001
Gender,%				< 0.001
Male	955(45.34)	712(43.12)	243(58.05)	
Female	935(54.66)	798(56.88)	137(41.95)	
Ethnicity,%				0.29
Mexican	104(1.97)	87(1.97)	17(1.98)	
White	1343(88.04)	1063(88.44)	280(85.76)	
Black	253(4.45)	196(4.07)	57(6.61)	
Other	190(5.54)	164(5.52)	26(5.65)	
Education level,%				< 0.0001
High school or above	1782(97.56)	1440(98.08)	342(94.58)	
Below high school	108(2.44)	70(1.92)	38(5.42)	
PIR	3.52(0.06)	3.60(0.06)	3.04(0.11)	< 0.0001
BMI (kg/m^2),%				0.02
< 25	552(30.70)	455(31.60)	97(25.55)	
25–29.9	647(34.10)	519(34.77)	128(30.28)	
≥ 30	691(35.20)	536(33.63)	155(44.17)	
Marital status,%				< 0.001
Married/ Cohabitant	1193(68.87)	966(69.49)	227(65.32)	
Widowed	257(10.45)	184(9.17)	73(17.75)	
Divorced/ Separated	320(15.02)	259(15.30)	61(13.41)	
Never married	120(5.66)	101(6.03)	19(3.52)	
Drinking status,%				< 0.0001
Former	353(14.59)	256(12.79)	97(24.88)	
Heavy	207(12.10)	180(12.84)	27(7.85)	
Mild	882(48.79)	692(48.51)	190(50.40)	
Moderate	253(16.79)	220(18.20)	33(8.73)	
Never	195(7.73)	162(7.65)	33(8.14)	
Smoking status,%				< 0.001
Former	744(38.08)	556(36.03)	188(49.84)	
Never	837(45.82)	716(47.96)	121(33.59)	
Now	309(16.10)	238(16.01)	71(16.57)	
MET				0.03
Low	432(21.42)	334(20.60)	98(26.11)	
Moderate	325(17.46)	239(16.78)	86(21.37)	
High	1133(61.12)	937(62.62)	196(52.51)	
PHQ-9 score	2.81(0.13)	2.60(0.12)	4.02(0.34)	< 0.0001
PHQ-9 groups				< 0.0001
None	1455(78.94)	1190(80.92)	265(67.58)	
Mild	277(14.10)	209(12.95)	68(20.70)	
Moderate	102(4.59)	76(4.34)	26(6.04)	
Severe	56(2.37)	35(1.79)	21(5.68)	
Hypertension,%				< 0.0001
No	760(46.53)	689(50.97)	71(21.14)	
Yes	1130(53.47)	821(49.03)	309(78.86)	
Hyperlipidemia,%				< 0.001
No	409(21.64)	358(23.13)	51(13.16)	
Yes	1481(78.36)	1152(76.87)	329(86.84)	
Diabetes,%				< 0.0001
DM	445(19.80)	311(17.22)	134(34.55)	
IFG	102(5.85)	74(5.14)	28(9.90)	
IGT	92(4.11)	72(4.03)	20(4.55)	
No	1251(70.25)	1053(73.62)	198(50.99)	
Tumor type,%				0.003
Breast	279(15.16)	234(15.28)	45(14.47)	
Digestive system	137(4.91)	103(4.62)	34(6.54)	
Gynecological	231(12.58)	200(13.19)	31(9.10)	
Hematological	72(3.74)	61(4.01)	11(2.18)	
Respiratory	41(1.68)	29(1.41)	12(3.21)	
Skin or soft tissue	593(39.85)	482(40.89)	111(33.91)	
Urinary system	319(11.05)	235(9.80)	84(18.18)	
Other	218(11.03)	166(10.79)	52(12.41)	

NHANES National Health and Nutrition Examination Survey, *BMI* Body Mass Index, *CHD* Coronary Heart Disease, *PIR* Poverty Income Ratio, *DM* Diabetes mellitus, *IFG* Impaired fasting glycemia, *IGT* Impaired glucose tolerance. A *P*-value < 0.05 indicates statistical significance

minimizing the risk of overfitting, particularly considering the sample size. This approach is consistent with common practices in large, nationally representative datasets such as NHANES, where percentiles are often used for knot placement to enhance model stability and interpretability. Subgroup analyses were conducted to control for potential confounding factors and assess effects across different subgroups. Forest plots were used to visualize the significance of interactions and the effects within each subgroup (see Fig. 3 for detailed results). To address the risk of Type I errors from multiple comparisons, we applied appropriate correction methods to adjust *P*-values using the R forestplot package, ensuring the results' reliability. The adjusted *P*-values, displayed in the forest plots, were used to evaluate subgroup interactions, with caution emphasized when interpreting differences. A two-sided *P*-value of < 0.05 was regarded as statistical significance.

Results

Baseline characteristics of study participants

A total of 1890 cancer patients (Table 1) were included in this cross-sectional analysis, with males accounting for 45.34% of the cohort. These cancer patients

Table 2 Adjusted Odds Ratios (AOR) and 95% Confidence Intervals (CI) for the association between depression symptoms and CVD risk

Total PHQ-9 score	Model I[a] (AOR,95%CI,*P*-value)	Model II[b] (AOR, 95% CI, *P*-value)	Model III[c] (AOR, 95% CI, *P*-value)
Continuous	1.14(1.09–1.18), $P<0.0001$	1.12(1.07–1.16), $P<0.0001$	1.09(1.05–1.14), $P<0.001$
Four categorical groups			
None	ref	ref	ref
Mild	2.39(1.59–3.61), $P<0.0001$	2.19(1.41–3.39), $P<0.001$	1.70(0.91– 3.17), $P=0.09$
Moderate	2.92(1.13–7.53), $P=0.030$	2.09(0.85–5.16), $P=0.110$	2.28(0.91–5.73), $P=0.08$
Severe	9.58(4.06–22.60), $P<0.0001$	7.55(3.12–18.25), $P<0.0001$	6.82(2.39–19.50), $P<0.001$
P for trend	$P<0.0001$	$P<0.0001$	$P<0.001$

[a] Model I included modifications for age, ethnicity, and gender

[b] Model II included modifications for age, ethnicity, gender, marital status, BMI, degree of education, alcohol intake, cigarettes smoked, and PIR

[c] Model III included modifications for all confounding factors previously mentioned

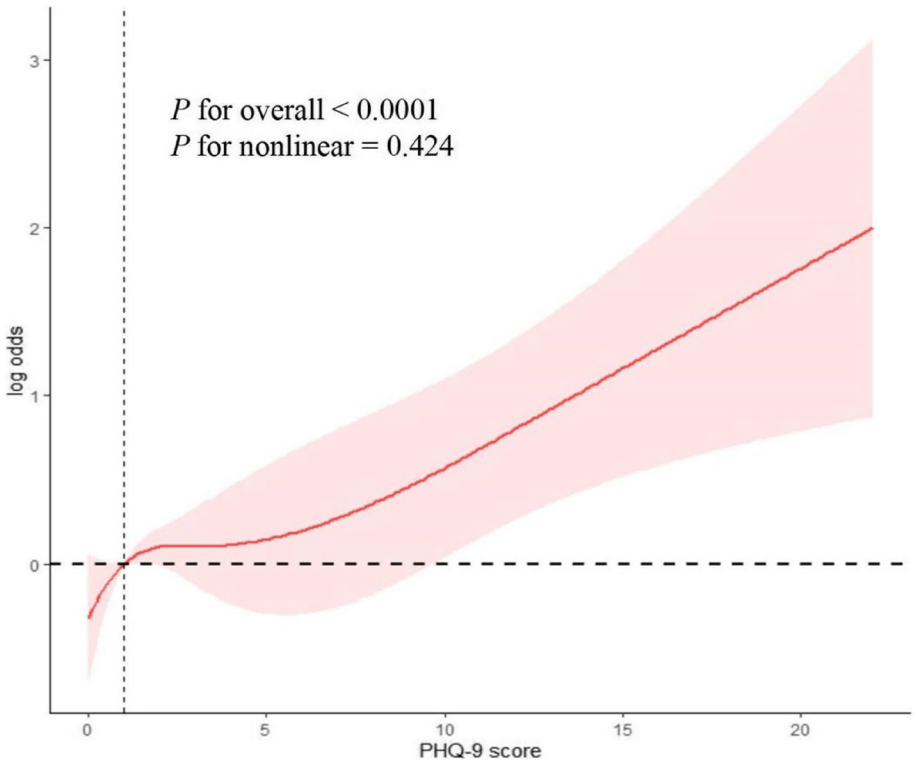

Fig. 2 The RCS curve illustrates the association between depression symptoms and CVD risk among all US adults. RCS regression was modified for all confounding factors previously mentioned

represented a population of 9,327,251 adults in the United States. Notably, 14.88% (380) of the cancer patients had a diagnosis of CVD. Among males, 243 (58.05%) had CVD, while 712 (43.12%) did not. Among females, 137 (41.95%) had CVD, while 798 (56.88%) did not.Cancer patients with CVD tended to be older (mean age = 69.38) and had a higher percentage of males. Those with CVD also exhibited a lower proportion of BMI ≥ 30, lower educational levels, and lower PIR(3.04). Maritally, widowed cancer patients were more prevalent in the CVD group, whereas those without CVD had a higher proportion of never-married individuals. Lifestyle factors revealed higher rates of mild drinkers and smokers among cancer patients with CVD. Physical activity (MET) levels were lower in those with CVD, with a lower proportion reporting

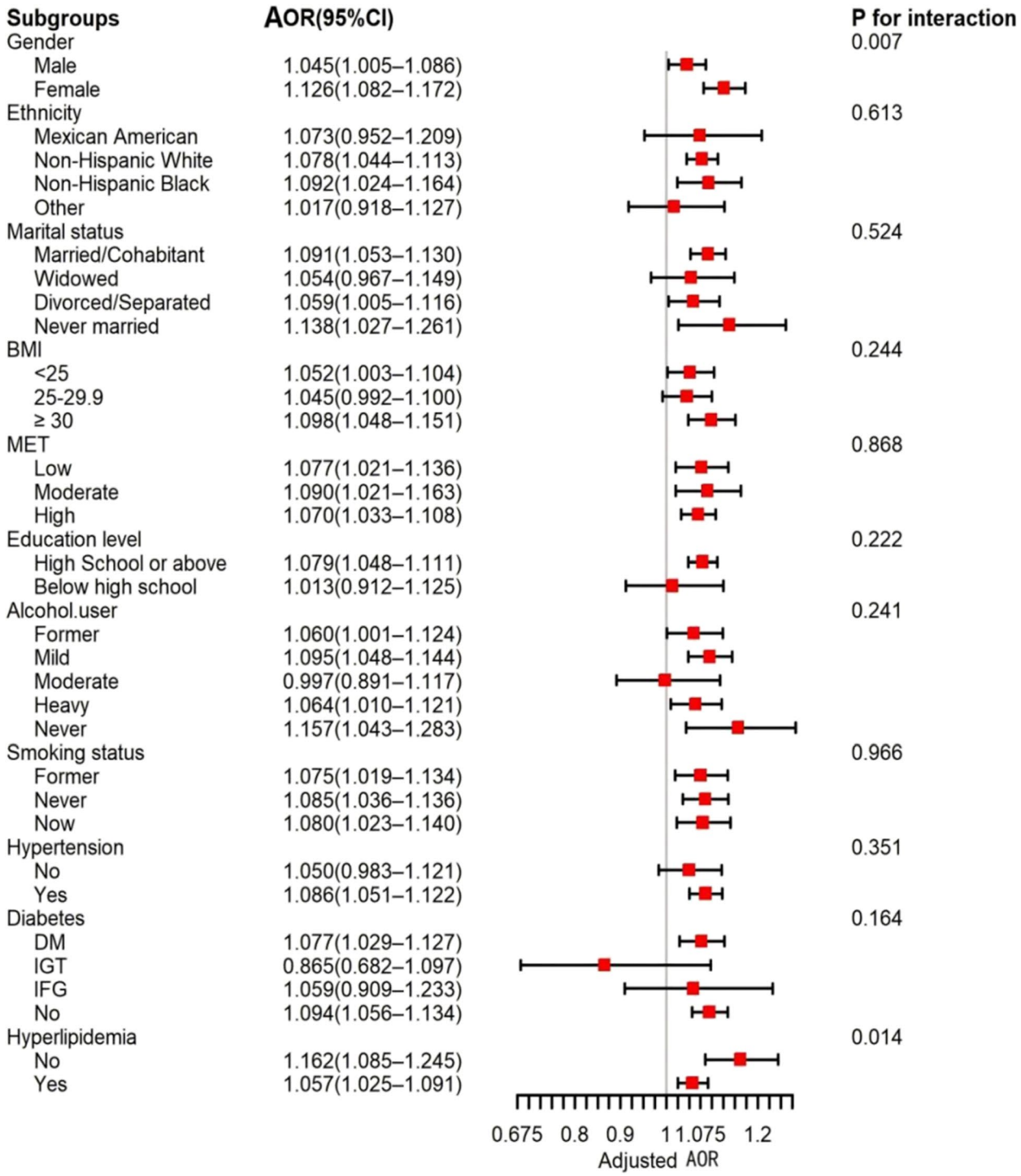

Fig. 3 Subgroup analysis explored the association between depression symptom and CVD risk. Each stratification was adjusted for gender, ethnicity, marital status, BMI, MET, degree of education, alcohol intake, cigarettes smoked, hypertension, diabetes and hyperlipidemia

high activity(52.51%) compared to those without CVD. Mental health was poorer in the CVD group, as evidenced by a higher average PHQ-9 score of 4.02, with a significantly lower proportion free from depressive symptoms(67.58%) and higher rates of moderate (6.04%) and severe symptoms (5.68%). Furthermore, there were substantially higher rates of hypertension (78.86%) and hyperlipidemia (86.84%) among cancer

patients with CVD. The prevalence of diabetes was also higher, particularly among diagnosed cases (34.55%).

Association between depression and CVD risk

Weighted regression analysis revealed a significant increase in CVD risk associated with higher PHQ-9 scores, as shown in Table 2. Both Model 1 (AOR = 1.14, 95% CI: 1.09–1.18, $P < 0.0001$) and Model 2 (AOR = 1.12, 95% CI: 1.07–1.16, $P < 0.0001$) demonstrated a statistically significant association. After adjusting for potential confounders, Model 3 continued to show a positive correlation between depression and CVD risk, with an AOR of 1.09 (95% CI: 1.05–1.14, $P < 0.001$).

The association remained statistically significant when PHQ-9 scores were categorized into four levels. Although the correlation was not strictly linear, higher PHQ-9 scores were associated with an increased risk of CVD. Notably, individuals with "Severe" depression had a significantly higher CVD risk compared to those with "Mild" or "Moderate" depression. In the fully adjusted model, the AORs (95% CI) for Mild, Moderate, and Severe depression were 1.70 (95% CI: 0.91–3.17), 2.28 (95% CI: 0.91–5.73), and 6.82 (95% CI: 2.39–19.50), respectively. Trend analysis consistently supported this correlation across all three models, with all *P*-values for trend < 0.001.

Analysis of restricted cubic spline regression

To elucidate the association between depression and CVD risk, a RCS regression model was adopted. After neglecting potential confounding factors, we observed a clear and direct correlation between depression and CVD risk in the RCS regression analysis ($P = 0.424$, Fig. 2). As the PHQ-9 score increases, the risk of CVD also significantly increases. There was a virtually log-linear correlation between CVD risk and PHQ-9 score when the score was larger than 5.

Subgroup analysis stratified by clinically important covariates

After adjusting for relevant covariates, Fig. 3 provides additional evidence of a positive correlation between depression symptoms and CVD risk, as indicated by the subgroup analysis. Interaction tests showed no significant differences in the associations between depressive symptoms and CVD risk across ethnicity, marital status, BMI, MET, education level, alcohol consumption, smoking status, hypertension, and diabetes (all *P*-values for interactions > 0.05). These factors did not significantly modify the positive relationship. However, gender and hyperlipidemia appeared to influence the association between depression symptoms and CVD risk, with significant interaction effects (*P*-value for interaction < 0.05).

Discussion

To explore the relationship between depressive symptoms and cardiovascular disease (CVD) risks in cancer patients, we conducted a cross-sectional analysis of 1890 participants using data from NHANES. Our study specifically examines the depression-CVD link within cancer patients, a population with unique biological and psychosocial vulnerabilities that may amplify this connection more than in the general population. Our findings showed a positive correlation between depressive symptoms and CVD risk in cancer patients. RCS analysis revealed a log-linear dose–response relationship, and subgroup analyses confirmed this link across various demographic and clinical groups.

Novelty and contextualization

While previous studies have established a relationship between depression and CVD in the general population [35–37], our findings extend this evidence to cancer patients—a group already at high risk for both conditions. Cancer treatments, such as anthracyclines and radiation, induce cardiotoxicity through mitochondrial dysfunction and endothelial damage, while depression increases cardiovascular risk through neurohormonal activation [38, 39]. This dual burden creates a unique risk profile for cancer patients, distinct from that of the general population. Several surveys have shown higher rates of CVD risk factors in cancer survivors, which may increase their risk of CVD-related mortality [40, 41]. Our study underscores the importance of tailored risk stratification and early intervention in this high-risk group, especially considering the complex interactions between cancer treatment and cardiovascular health.

This study comprehensively assesses the relationship between depression and CVD in cancer patients using a nationally representative dataset.By focusing on this dual vulnerability in cancer patients, our research represents a critical step toward understanding the risks faced by this group.

Interpreting cross-sectional findings

The bidirectional relationship between depression and CVD in cancer patients calls for cautious interpretation. While depressive symptoms may exacerbate CVD through inflammatory pathways [42], reverse causality is also a possibility. For example, cancer patients with undiagnosed CVD (e.g., subclinical atherosclerosis) may develop depression due to the physical burden of the disease. Moreover, the complex interplay of comorbidities in cancer patients could increase vulnerability to both depression and cardiovascular risk. Therefore, our results highlight the importance of recognizing this critical

comorbidity cluster that requires integrated management, rather than suggesting a unidirectional causality. Depression and CVD risk in cancer patients may evolve together, each exacerbating the other.

Interventional evidence and clinical implications

Emerging intervention studies suggest that managing depression could help reduce CVD risks in cancer patients. Cognitive-behavioral therapy (CBT) has been shown to reduce depressive symptoms and improve cardiovascular risk profiles in cancer survivors, particularly those with breast cancer [43, 44]. Additionally, combining pharmacotherapy with lifestyle counseling has proven effective in lowering cardiovascular risks in cancer patients with depression. This integrated approach has been linked to better clinical outcomes, including a reduction in major adverse cardiovascular events [45]. These findings support the need for integrated care models that address both mental health and cardiovascular health. Early screening and treatment of depression in cancer patients may play a crucial role in mitigating their long-term cardiovascular burden.

Cancer treatment phase and comorbidity dynamics

When interpreting our findings, it is important to consider the cancer treatment phase. Depression severity can fluctuate depending on the treatment stage. For example, chemotherapy can induce neuroinflammation, contributing to depressive symptoms [46]. The ongoing side effects of treatment may exacerbate both psychological and cardiovascular risks. In contrast, during survivorship, patients may experience existential distress and persistent depressive symptoms due to lingering effects of treatment, which could further complicate their cardiovascular health. A study [47] found that persistent depression during chemotherapy was associated with significantly higher CVD risk, highlighting the complex relationship between mood disorders, cancer treatment, and long-term health outcomes. Future studies should stratify by treatment phase (e.g., active treatment vs. survivorship) to refine risk prediction and develop phase-specific interventions.

Limitations and future directions

Although our study provides valuable insights, there are several limitations to consider. Self-reported CVD diagnoses may miss subclinical conditions, such as endothelial dysfunction, which could be detected using advanced diagnostic techniques like flow-mediated dilation. Furthermore, the cross-sectional design prevents us from drawing conclusions about causality, so future longitudinal studies are needed to assess the temporal relationship between depression and CVD risk in cancer patients. The lack of data on treatment phase limits our understanding of how acute versus chronic depression impacts cardiovascular health, underscoring the need for future research to incorporate treatment phase as a variable.

Moreover,the relatively small sample size and reliance on self-reported data introduce potential biases, affecting the generalizability of the findings. Larger, more balanced sample sizes are necessary for more definitive conclusions. Future studies should also explore how cancer-related risk factors, such as cancer treatments and disease progression, interact with depression to elevate cardiovascular risk, and incorporate detailed cancer staging data to improve our understanding of these complex relationships.

Conclusion

In conclusion, this study confirms a significant association between depressive symptoms and CVD risk in cancer patients. These findings underscore the importance of integrating mental health assessments and interventions into routine cancer care to mitigate cardiovascular risks and improve patient outcomes. Given the complex interplay between depression and CVD, addressing both conditions simultaneously may enhance overall patient well-being and reduce long-term health risks.

Future research should focus on key areas: (1) longitudinal studies to establish the causal relationship between depression and CVD in cancer patients; (2)intervention trials to evaluate the effectiveness of integrated care models that combine oncology and mental health treatment to improve both cancer and cardiovascular outcomes;and(3) investigations into the biological mechanisms linking depression and CVD to identify potential therapeutic targets. Additionally, exploring gender-and age-related differences, as well as determining the optimal timing and methods for managing depressive symptoms across different cancer types, will further inform targeted treatment strategies.

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Clinical trial number

Not applicable.

Authors' contributions

Zheling Chen Wrote the original draft; Xiuxiu Qiu focus on data management; Hao Chi supervised the manuscript. Jingfeng Rong revised and edited.All authors reviewed the manuscript.

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Data Availability
NHANES data is accessible to the public and can be obtained through https://www.cdc.gov/nchs/nhanes/index.htm.

Declarations

Ethics approval and consent to participate
This study uses publicly available, de-identified NHANES data, in accordance with the ethical principles of the Helsinki Declaration. The NHANES project received ethical approval from the NCHS Research Ethics Review Board, and all participants provided informed consent.The information is available on the NHANES website (https://www.cdc.gov/nchs/nhanes/participant.htm).

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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