Yao et al. BMC Cancer (2025) 25:570
https://doi.org/10.1186/s12885-025-13578-2

BMC Cancer

RESEARCH Open Access

Association between sedentary behavior, depressive symptoms, and the risk of all-cause and cause-specific mortality among U.S. cancer survivors

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Abstract

Background Sedentary behavior and depressive symptoms are commonly observed in cancer survivors. However, the combined impact of these factors on the mortality outcomes of cancer survivors remains unknown.

Methods Cancer survivors from the National Health and Nutrition Examination Survey (NHANES) (2007–2018) were selected. Multivariate-adjusted Cox regression analyses were employed to examine the intendent and joint prognostic effects of sedentary behavior and depressive symptoms on the mortality outcomes of cancer survivors.

Results A total of 2,460 US adult cancer survivors (men = 1,143 and women = 1,317) were included. Severe sedentary behavior (≥ 8 h/day) was linked to higher all-cause [hazard ratio (HR) = 1.68, 95% confidence interval (CI): 1.36–2.09, $p < 0.001$] and noncancer mortality (HR = 1.80, 95% CI: 1.35–2.40, $p < 0.001$) in cancer survivors. Each additional hour of sedentary time increased the risk of all-cause (HR = 1.05, 95% CI: 1.02–1.08, $p < 0.001$) and noncancer mortality (HR = 1.07, 95% CI: 1.04–1.11, $p < 0.001$). Depressive symptoms (PHQ-9 ≥ 5) were also associated with higher all-cause (HR = 1.22, 95% CI: 1.01–1.48, $p = 0.040$) and noncancer mortality (HR = 1.27, 95% CI: 1.01–1.61, $p = 0.045$). In the joint analysis, cancer survivors with both depressive symptoms and severe sedentary behavior had the highest risk of all-cause mortality (HR = 2.06, 95% CI: 1.47–2.88, $p < 0.001$). Survivors with no depressive symptoms but severe sedentary behavior also had a higher risk (HR = 1.44, 95% CI: 1.10–1.88, $p = 0.008$). Additionally, the combination of depressive symptoms and severe sedentary behavior increased risks of cancer-specific (HR = 1.56, 95% CI: 1.04–2.34, $p = 0.001$), noncancer (HR = 1.86, 95% CI: 1.34–2.57, $p < 0.001$), and CMD-related mortality (HR = 1.74, 95% CI: 1.04–2.93, $p = 0.037$). In subgroup analysis, cancer survivors with endocrine-related and gastrointestinal cancers were more sensitive to these effects.

Conclusion Our study highlighted the importance of considering both sedentary behavior and mental health in making effective long-term follow-up recommendations for cancer survivors.

Keywords Cancer survivor, Sedentary behavior, Depressive symptoms, Mortality risk, Cohort study

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Introduction

Currently, the number of new cancer cases and related deaths is continuing to increase worldwide, contributing to a large global burden of disease [1–4]. In the US population, it is estimated that there are approximately 200 million new cancer cases and 0.6 million cancer-associated deaths are projected to occur in 2024 [1]. With great advances in new drugs and therapeutic modalities, patients diagnosed with cancer are not only living longer but also facing the long-term consequences of cancer and related treatment [5, 6]. Therefore, how to improve the long-term outcomes of cancer survivors has become a crucially important topic in public health issues [7]. In addition, identifying additional independent prognostic factors for cancer survivors could further extend their survival prospects [8].

In recent decades, sedentary behavior has become prevalent and stable among the general population and has been independently determined to be associated with deleterious health effects [9–11]. In particular, accumulating evidence has demonstrated that sustained sedentary behavior is not only associated with the occurrence of cancer but also related to long-term adverse effects on postdiagnosis cancer survivors [11–13]. For example, two recent systemic reviews and meta-analyses concluded that severe sedentary behavior was associated with a nearly 1.18- to 1.22-fold risk of all-cause mortality among cancer survivors [12, 14]. However, the strength of the evidence was relatively low, and some potential confounders, such as obesity, were not adequately adjusted [12, 14]. Although links between sedentary behavior and all-cause and cancer mortality have been established, whether sedentary behavior impairs cardiometabolic disease (CMD) survival is worth further exploration [15, 16].

In addition to lifestyle characteristics, mental health, especially depressive symptoms, has been determined to be an independent predictor of cancer onset and prognosis [5, 17, 18]. Several possible underlying mechanisms at both the biological and behavioral levels have been proposed to explain this association [19]. Depressive symptoms impair the systemic endocrine system, as well as the immune response, which could consequently impair immunosurveillance and cause chronic circulatory inflammation and oxidative stress to induce carcinogenesis and poor clinical outcomes [20, 21]. Notably, a bidirectional relationship between depressive symptoms and sedentary behavior has been observed in recent epidemiological and Mendelian randomization studies [22–24]. Specifically, adults with depression were more likely to have unhealthy lifestyle habits, such as being sedentary, whereas adults with long-term sedentary behavior had a greater risk of developing depressive symptoms. Considering the potential interactions between sedentary behavior and depressive symptoms, a combined evaluation of their effects on health outcomes could provide clinicians with an in-depth understanding of the effects of physical and mental health on the mortality outcomes of cancer survivors. Nevertheless, the epidemiological evidence regarding the joint prognostic effects of sedentary behavior and depressive symptoms on the survival of US cancer survivors is limited.

To fill these research gaps, we aimed to explore the independent and joint prognostic effects of sedentary behavior and depressive symptoms with the mortality outcomes of US cancer survivors based on the cohort from the National Health and Nutrition Examination Surveys (NHANES) project. This is a representative population-based study to investigate the joint prognostic effects of lifestyle factors and mental health on all-cause and cause-specific mortality in cancer survivors.

Materials and methods

Data collection

Data were obtained from the National Health and Nutrition Examination Survey (NHANES) between 2007 and 2018, covering six interview cycles. NHANES collected nationally representative health data from noninstitutionalized US civilians using a stratified, multistage probability sampling design [25]. Details regarding NHANES objectives and protocols are available elsewhere [26]. Participants under 20 years of age, without a history of cancer, missing data on sitting time or depressive symptoms, with a body mass index (BMI) below 18.5 kg/m^2, with non-melanoma skin cancer, or who lacked follow-up information were excluded. The participant selection process is illustrated in Fig. 1.

Sedentary behavior assessment

Participant responses to the Global Physical Activity Questionnaire (GPAQ) were used to assess daily sitting time, with the questionnaire demonstrating moderate to good reliability in NHANES and being previously validated for measuring physical activity and sedentary behavior [27]. Total sitting time was calculated based on daily activities, including time spent sitting at home, work, school, commuting, and socializing. Based on prior research [28, 29], sitting time was categorized as no sedentary behavior (< 6 h/d), moderate sedentary behavior (6–8 h/d), or severe sedentary behavior (> 8 h/d).

Depressive symptom assessment

Depressive symptoms were measured using the Patient Health Questionnaire-9 (PHQ-9) in NHANES, a validated tool widely used in clinical and research settings [30]. Scores ranged from 0 to 27, with higher scores indicating greater symptom severity. Participants were classified into two groups: no depressive symptoms (0–4) and having depressive symptoms (≥ 5).

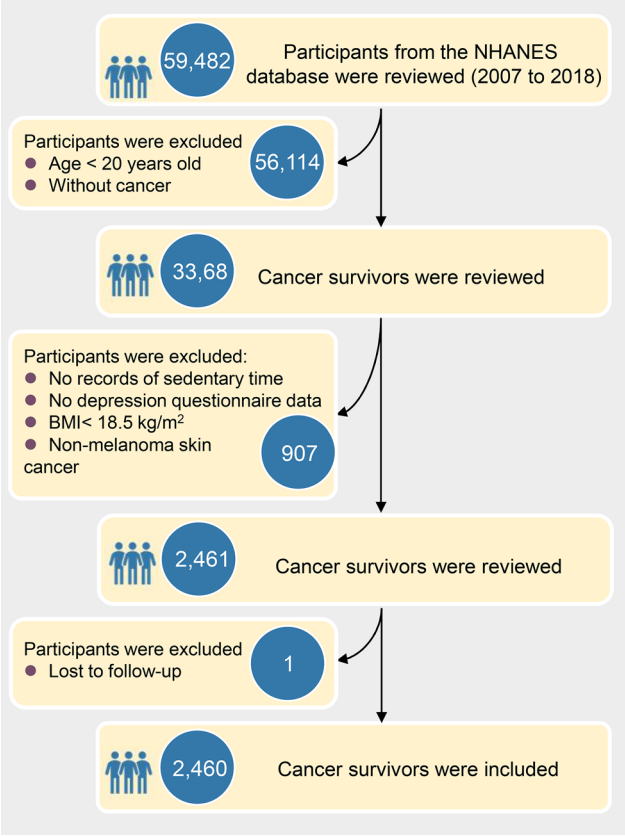

Fig. 1 The selection process for the cancer survivors in this study. NHANES: National Health and Nutrition Examination Survey. BMI: body mass index

Diagnosis of cancer

Cancer history was determined through the NHANES 'Medical Conditions' section, where cancer survivors were identified by a positive response to the question of whether they had been told they had cancer. For this study, cancers were grouped into major organ-based categories like previous studies [29, 31]. These included endocrine-related cancers (including thyroid, breast, and prostate cancers), gynecologic cancers (including breast, cervical, ovarian, and uterine cancers), male urologic cancers (including prostate and testicular cancers), gastrointestinal cancers (including colorectal, esophageal, gallbladder, hepatocellular, pancreatic, rectal, and gastric cancers), respiratory system cancers (including lung and laryngeal/tracheal cancers), head and neck cancers (including laryngeal/tracheal, oral/tongue/lip, and thyroid cancers), urologic cancers (including bladder and kidney cancers), hematologic malignancies (including leukemia, lymphoma, and other blood cancers), melanoma skin cancer, and other types of cancers (including bone, brain, nervous system, and soft tissue cancers). To enhance statistical power and ensure the robustness of the results, cancer types were grouped into broader organ-based categories. Besides, due to relatively small sample sizes, hematologic malignancies and urologic cancers were excluded from the joint subgroup analysis.

Furthermore, obesity-related cancers, including breast, colorectal, liver, pancreas, stomach, thyroid, ovary, uterus, brain, blood, gallbladder, kidney, and esophagus cancers, were specifically selected for analysis based on existing evidence linking these cancers to obesity and its metabolic consequences [32]. Other cancers were categorized as non-obesity-related. This refined categorization approach allows for a more robust examination of the associations between sedentary behavior, depressive symptoms, and mortality across different cancer types, improving the depth and specificity of the analysis while addressing sample size limitations.

Study outcomes measurement

Mortality data were obtained from the NHANES-linked death files, using the National Death Index (NDI) and ICD-10 codes to ascertain causes of death. All-cause mortality was defined as death from any cause, regardless of the underlying disease. Cancer mortality was defined as death due to cancer, with the specific cancer type identified based on ICD-10 codes. Noncancer mortality refers to deaths caused by factors other than cancer. CMD-related mortality was defined as death caused by cardiovascular and metabolic diseases, including heart disease, stroke, and diabetes, as classified by relevant ICD-10 codes. The follow-up period lasted until the participant's death or December 31, 2019 [33]. The primary aim of this study was to evaluate the independent and joint associations of sedentary behavior and depressive symptoms with all-cause mortality in cancer survivors. Secondary outcomes included cancer, noncancer, and CMD mortality.

Assessment of demographic factors and covariates

The selection of study variables was based on previous study findings elucidating the association between lifestyle factors and the outcomes of interest [29, 34]. This approach ensured that the chosen variables were relevant and likely to capture meaningful relationships, thereby enhancing the validity and interpretability of the study findings. This approach ensured that the chosen covariates were both relevant and likely to capture meaningful relationships, thereby enhancing the validity and interpretability of the study findings. In this study, a range of sociodemographic, behavioral, and health-related covariates were considered.

Self-reported socio-demographic variables included age, sex (men and women), race (Hispanic, non-Hispanic white, non-Hispanic black, and other races), marital status (not married, married/living with partner), educational attainment (≤ high school, college, and > college), and family poverty income ratio (PIR, categorized as

< 1.3, 1.3–3.5, and > 3.5). Self-reported behavioral factors including smoking status (never, current, and former), alcohol use (never, current, and former), sleep duration (< 7 h/d, 7–9 h/d, and > 9 h/d), and dietary quality (assessed using the Healthy Eating Index 2015, categorized as < 60 and ≥ 60) were also included. BMI was categorized as < 25 kg/m², ≥ 25 kg/m² and < 30 kg/m², and ≥ 30 kg/m², based on measurements taken during mobile health center visits. Physical activity was measured (minutes/week) according to the GPAQ [27] and also controlled during the analysis.

Besides, health conditions of interest, including hypertension, hyperlipidemia, diabetes mellitus, and cardiovascular disease (CVD), were included. These comorbidities were ascertained through self-reported physician diagnoses obtained during individual interviews. This comprehensive selection of covariates allowed for a thorough assessment of factors influencing mortality outcomes, ensuring the rationale of our statistical analyses and strengthening the interpretation of our findings.

Statistical analysis

According to the NHANES analytic tutorials for weights in making estimates that were representative of the US civilian noninstitutionalized population, all analyses in this study incorporated adequate sample weights, clustering, and stratification to estimate appropriate variance and ensure national representation of the US cancer survivors. The baseline characteristics are presented by daily sitting time (< 6 h/d, 6–8 h/d, > 8 h/d), with normally distributed variables as mean (SD), non-normally distributed variables as median (IQR), and categorical variables as count (percentage). Comparisons were made using the Student's *t*-test for normally distributed continuous variables, the Kruskal-Wallis test for non-normally distributed variables, and the Chi-Square test for categorical variables. Multivariate Cox regression models were applied to determine the independent and joint associations of sedentary behavior and depressive symptoms with all-cause and cause-specific mortality. Model 1 referred to the crude model with no adjustments. Model 2 served as a less adjusted model with adjustments for age, sex, and race. In the fully adjusted model, Model 3 accounted for age, sex, race, marital status, educational level, PIR, smoking status, alcohol use, sleep time, dietary quality, physical activity, BMI, hypertension, hyperlipidemia, diabetes mellitus, and CVD. The sedentary behavior and depressive symptoms were mutually adjusted in the independent analysis.

To analyze the joint effects on all-cause mortality, participants were classified into six subgroups: no depressive symptoms and no sedentary behavior (Reference), no depressive symptoms with moderate sedentary behavior, no depressive symptoms with severe sedentary behavior, depressive symptoms with no sedentary behavior, depressive symptoms with moderate sedentary behavior, and depressive symptoms with severe sedentary behavior. For the analysis of cancer-, noncancer-, and CMD mortality, sedentary behavior categories were combined into two groups (no sedentary behavior, < 6 h/d, and sedentary behavior, ≥ 6 h/d) due to small case numbers in each category. Consequently, participants were classified into four subgroups: no depressive symptoms with no sedentary behavior (Reference), no depressive symptoms with moderate/severe sedentary behavior, depressive symptoms with no sedentary behavior, and depressive symptoms with moderate/severe sedentary behavior. Multivariable Cox proportional hazards regression models were employed to estimate the mortality risk associated with these different phenotypes.

All analyses were conducted in different subpopulations, including overall, female, male, younger (< 65 years), older (≥ 65 years), obesity-related, and non-obesity-related cancer subgroups. In addition, subgroup analyses of primary outcomes were performed among cancer survivors with different cancer types. Variables with missing data were imputed using the median imputation method, as the proportion of missing data was small and the data were not normally distributed. This method was chosen to maintain the distribution of the variables and minimize potential bias due to missing values. Sensitivity analysis was conducted by excluding participants who died within 24 months of follow-up to reduce the potential impact of reverse causality.

All the statistical analyses were conducted using R software (version 4.3.2). A two-tailed p-value < 0.05 was considered to indicate statistical significance.

Results

The demographic characteristics of the study population

Among the six cycles, 2,460 adult cancer survivors [1,143 men (weighted: 44.2%) and 1,317 women (weighted: 57.8%)] were included in this study, with a median age of 65.00 years. The non-Hispanic white population (n = 1,516) accounted for a majority of cancer survivors, with a weighted proportion of 83.0%. Almost 66.3% of cancer survivors had educational levels above college. In addition, 15.2% (n = 596) of cancer survivors had a PIR less than 1.3. Regarding personal habits, 15.6% of cancer survivors (n = 394) were still smoking and 66.8% were still drinking (n = 1,454). Over 50% of the cancer survivors had cardiometabolic-related comorbidities. Depressive symptoms were identified in 25.9% of the cancer survivors (n = 688) and 57.7% of cancer survivors (n = 1,341) had moderate to severe sedentary behavior. Among the study population, the median time since cancer diagnosis before the interview was 8 years. During a median follow-up of 68 months, 592 deaths were observed in the study

population, with 216 attributed to cancer, 376 attributed to noncancer, and 156 attributed to CMD causes. In cancer survivors with moderate to severe sedentary behavior, 52.8% of them ($n = 386$) had depressive symptoms. A significant correlation between sitting time and PHQ-9 score was observed ($r^2 = 0.103$, $p < 0.001$) (Fig S1), and cancer survivors with severe sedentary behavior (> 8 h/d) showed higher PHQ-9 scores (Fig S2). With comparisons of other subgroups, cancer survivors with a setting time above 8 h/d were more likely to be younger age, non-Hispanic white, higher educational levels, higher PIR, and higher BMI but lower physical activity intensity. The specific clinical factors of the cancer survivors are presented in Table 1.

Associations between sedentary behavior or depressive symptoms and mortality outcomes in cancer survivors

In the separate analysis, sedentary behavior, especially severe sedentary behavior (> 8 h/d), was significantly associated with the mortality outcomes of cancer survivors [hazard ratio (HR) = 1.68, 95% confidence interval (CI): 1.36–2.09, $p < 0.001$ for all-cause mortality; HR = 1.80 95% CI: 1.35–2.40, $p < 0.001$ for noncancer mortality] (Fig. 2). When sedentary behavior was modeled as a continuous variable, each additional hour of sedentary time was associated with an increased risk of all-cause mortality (HR = 1.05, 95% CI: 1.02–1.08, $p < 0.001$) and noncancer mortality (HR = 1.07, 95% CI: 1.04–1.11, $p < 0.001$). Similarly, depressive symptoms (PHQ-9 score ≥ 5) in cancer survivors were associated with all-cause mortality (HR = 1.22, 95% CI: 1.01–1.48, $p = 0.040$; HR = 1.27 95% CI: 1.01–1.61, $p = 0.045$ for noncancer mortality) (Fig. 2). When depressive symptoms were analyzed as a continuous variable, each additional point on the PHQ-9 score was linked to a higher risk of all-cause mortality (HR = 1.02, 95% CI: 1.00–1.04, $p = 0.027$) and noncancer mortality (HR = 1.03, 95% CI: 1.00–1.05, $p = 0.031$). In contrast, no significant associations were detected between sedentary behavior and depressive symptoms with cancer mortality (Sitting time > 8 h/d: HR = 1.34, 95% CI: 0.92–1.94, $p = 0.126$; PHQ-9 score ≥ 5: HR = 1.28, 95% CI: 0.94–1.75, $p = 0.122$) or CMD mortality (Sitting time > 8 h/d: HR = 1.52, 95% CI: 0.97–2.39, $p = 0.067$; PHQ-9 score ≥ 5: HR = 1.03, 95% CI: 0.99–1.07, $p = 0.205$) of cancer survivors. Similar findings were determined when sedentary behavior and depressive symptoms were considered as continuous variables (Fig. 2).

Joint association between sedentary behavior and depressive symptoms and mortality outcomes in cancer survivors

As shown in Fig. 3, the multivariate Cox regression analyses indicated that cancer survivors with any combination of depressive symptoms and varying levels of sedentary behavior experienced increased risks of all-cause mortality compared to those without depressive symptoms or sedentary behavior. Specifically, survivors in the following phenotypes had higher all-cause mortality: no depressive symptoms and moderate sedentary behavior (HR = 1.28, 95% CI: 1.02–1.60, $p = 0.030$), no depressive symptoms and severe sedentary behavior (HR = 1.44, 95% CI: 1.10–1.88, $p = 0.008$), depressive symptoms and moderate sedentary behavior (HR = 1.54, 95% CI: 1.14–2.07, $p = 0.005$), and depressive symptoms and severe sedentary behavior (HR = 2.06, 95% CI: 1.47–2.88, $p < 0.001$) (Fig. 3A). Furthermore, cancer survivors with depressive symptoms and severe sedentary behavior were also at significantly greater risk of cancer-specific mortality (HR = 1.56, 95% CI: 1.04–2.34, $p < 0.001$) compared to those without depressive symptoms or sedentary behavior (Fig. 3B). In addition, both survivors with no depressive symptoms but moderate or severe sedentary behavior and those with both depressive symptoms and moderate/severe sedentary behavior had a significantly higher risk of noncancer mortality (HR = 1.56, 95% CI: 1.20–2.03, $p = 0.001$; HR = 1.86, 95% CI: 1.34–2.57, $p < 0.001$) as well as CMD-related mortality (HR = 1.51, 95% CI: 1.01–2.27, $p = 0.046$; HR = 1.74, 95% CI: 1.04–2.93, $p = 0.037$) compared to cancer survivors without depressive symptoms or sedentary behavior (Fig. 3C, D).

Stratified and sensitivity analyses

According to the independent subgroup analysis, the adverse effects of severe sedentary behavior were more pronounced in cancer survivors with clinical characteristics of female, obesity-related cancer types, and younger age than other subgroups. Besides, males were more vulnerable to the harmful effects of depressive symptoms on mortality risk than females (Table S1). According to the joint subgroup analysis, cancer survivors with cancer types of endocrine-related cancers and gastrointestinal cancers were more sensitive to the joint prognostic effects of severe sedentary behavior and depressive symptoms (Table S2). To check the robustness of the main findings, cancer survivors who died within 24 months after the interview were excluded. As shown in Table S3, cancer survivors with severe sedentary behavior and depressive symptoms still showed significantly higher all-cause mortality risk in comparison to the control subgroup. As for cause-specific mortality, cancer survivors with moderate/severe sedentary behavior and depressive symptoms showed significantly higher cancer-, noncancer-, and CMD mortality than the control subgroup, which were similar to the main findings (Table S4-S6).

Table 1 The demographic characteristics of the study population

Variables	Total ($n=2,460$)	Stratified by sitting time			*p*
		< 6 h/d ($n=1,119$) Weighted %: 42.3	**6–8 h/d ($n=812$) Weighted %: 32.4**	**> 8 h/d ($n=529$) Weighted %: 25.3**	
Age, M (Q_1, Q_3)	65.00 (54.00,74.00)	64.00 (53.00,73.00)	67.00 (58.00,76.00)	62.00 (53.00,74.00)	**< 0.001**
Physical activity, M (Q_1, Q_3)	840.00 (0.00,2,880.00)	1,628.12 (240.00,5,280.00)	720.00 (0.00,2,266.01)	200.00 (0.00,1,320.00)	**< 0.001**
PHQ-9 score, n (%)					
0–4	1,772 (74.1)	817 (74.8)	584 (73.3)	371 (73.9)	0.845
≥ 5	688 (25.9)	302 (25.2)	228 (26.7)	158 (26.1)	
Sex, n (%)					0.749
Men	1,143 (42.2)	523 (41.1)	382 (42.8)	238 (42.3)	
Women	1,317 (57.8)	596 (58.9)	430 (57.2)	291 (57.7)	
Race, n (%)					**< 0.001**
Hispanic	371 (6.2)	239 (9.2)	94 (4.8)	38 (2.9)	
Non-Hispanic white	1,516 (83.0)	619 (79.4)	524 (84.3)	373 (87.5)	
Non-Hispanic black	420 (6.6)	197 (7.1)	142 (6.9)	81 (5.3)	
Others	153 (4.2)	64 (4.3)	52 (4.0)	37 (4.3)	
Education level, n (%)					**< 0.001**
≤High school	1,089 (33.7)	558 (40.4)	353 (33.0)	178 (24.3)	
College	750 (32.1)	316 (30.3)	255 (33.9)	179 (33.4)	
> College	621 (34.2)	245 (29.3)	204 (33.1)	172 (42.3)	
Marital status, n (%)					0.344
Not married	1,021(35.2)	427 (33.7)	359 (36.6)	235 (37.9)	
Married/living with partner	1,439 (64.2)	692 (66.3)	453 (63.4)	294 (62.1)	
Poverty income ratio, n (%)					**0.009**
< 1.3	596 (15.2)	291 (16.1)	195 (15.2)	110 (14.0)	
1.3–3.5	1,136 (42.1)	550 (45.9)	371 (40.6)	215 (36.2)	
> 3.5	728 (42.7)	278 (38.0)	246 (44.2)	204 (49.8)	
BMI, n (%), kg/m^2					**< 0.001**
< 25	593 (25.1)	288 (28.7)	187 (22.9)	118 (21.7)	
≥ 25 and < 30	893 (34.7)	441 (38.6)	296 (34.0)	156 (29.6)	
≥ 30	974 (40.2)	390 (32.7)	329 (43.1)	255 (48.7)	
Smoking status, n (%)					0.089
Never	1,117 (46.2)	518 (44.0)	369 (46.7)	230 (47.6)	
Now	394 (15.6)	190 (18.9)	127 (14.6)	77 (12.3)	
Ever	949 (38.2)	411 (37.1)	316 (38.7)	222 (40.1)	
Alcohol use, n (%)					0.436
Never	580 (19.2)	263 (19.4)	201 (21.1)	116 (16.7)	
Now	1,454 (66.8)	648 (65.3)	474 (65.9)	332 (70.1)	
Ever	426 (14.0)	208 (15.3)	137 (13.0)	81 (13.2)	
Hypertension, n (%)					**0.019**
No	1,008 (47.2)	500 (51.0)	301 (43.1)	207 (44.8)	
Yes	1,452 (52.8)	619 (49.0)	511 (56.9)	322 (55.2)	
Hyperlipidemia, n (%)					0.228
No	1,183 (47.9)	558 (51.1)	386 (46.0)	239 (45.8)	
Yes	1,277 (52.1)	561 (48.9)	426 (54.0)	290 (54.2)	
Diabetes mellitus, n (%)					0.127
No	1,903 (81.8)	879 (83.1)	617 (79.2)	407 (82.1)	
Yes	557 (18.2)	240 (16.9)	195 (20.8)	122 (17.9)	
CVD, n (%)					0.250
No	2,011 (85.2)	944 (86.1)	650 (83.3)	417 (84.1)	
Yes	449 (14.8)	175 (13.9)	162 (16.7)	112 (15.9)	
Sleep time, n (%), h/d					0.803
< 7	774 (27.3)	358 (26.1)	251 (28.7)	165 (28.6)	
7–9	1,502 (65.8)	684 (66.6)	501 (64.6)	317 (64.9)	

Table 1 (continued)

Variables	Total ($n=2,460$)	Stratified by sitting time			*p*
		<6 h/d ($n=1,119$) Weighted %: 42.3	6–8 h/d ($n=812$) Weighted %: 32.4	>8 h/d ($n=529$) Weighted %: 25.3	
>9	184 (6.9)	77 (7.3)	60 (6.7)	47 (6.5)	
Dietary quality, n (%)					0.194
<60	1,765 (73.0)	783 (71.2)	587 (74.3)	395 (76.2)	
≥60	695 (27.0)	336 (28.8)	225 (25.7)	134 (23.8)	

Abbreviations: M: median; Q: quartile; h/d: hours per day; n (%): number with weighted percentage

Note: Physical activity calculated as minutes/week; Bold values indicate statistical significance ($p<0.05$)

Discussion

In this study, over half of cancer survivors experienced both sedentary behavior and depressive symptoms. Multivariate regression analysis revealed that both sedentary behavior and depressive symptoms were independently associated with increased all-cause and noncancer mortality among the US cancer survivors, even after adjusting for several relevant covariates. Moreover, this is the first study, to our knowledge, to examine the joint association between sedentary behavior and depressive symptoms with mortality outcomes in cancer survivors using a nationally representative cohort. Specifically, cancer survivors with severe sedentary behavior and depressive symptoms had 2.06-, 1.56-, 1.86-, and 1.74-fold increased risks of all-cause, cancer, noncancer, and CMD mortality, respectively. The findings highlight the importance of integrating assessments of sedentary behavior and depressive symptoms into clinical practice.

Sedentary behavior and depressive symptoms are both prevalent in the general population, especially in terms of cancer survivors [35]. Specifically, accumulating observational evidence revealed that sedentary behavior was associated with adverse health outcomes in different study populations, independent of physical activity [9, 11, 36]. In particular, severe sedentary behavior is not only associated with health-related quality of life (HRQoL) and fatigue but also related to mortality outcomes among cancer survivors [12, 13]. In our analysis, cancer survivors with severe sedentary behavior (>8 h/d) exhibited a remarkably greater risk of mortality, independent of daily physical activity. More importantly, the HRs associated with sitting time and survival outcomes were generally more pronounced for noncancer mortality than for cancer mortality. Although the *p*-value for the association between sedentary behavior and CMD mortality ($p_{category}$ = 0.067 and $p_{continuous}$ = 0.075) did not reach conventional statistical significance, a trend towards increased risk was observed. This finding might be influenced by the relatively small number of events observed in the study, which could limit the statistical power to detect a significant association. Further studies with larger sample sizes or longer follow-up periods may help to clarify this trend.

To date, the relationships between sedentary behavior and the incidence and prognosis of cardiometabolic-related diseases have been established [11, 37]. For example, a recent meta-analysis revealed that adults with severe sedentary behavior (>10 h/d) had a significantly greater risk of cardiovascular disease [38]. Similarly, severe sedentary behavior (>7.26 h/d) was also correlated with increased risks of metabolic syndrome (MetS) [39]. Notably, cardiometabolic diseases are prevalent and are among the major causes of death in cancer survivors, especially in those with endocrine-related cancers [40–42]. Emerging evidence suggests that reducing sedentary behavior, particularly prolonged sitting, and incorporating physical activity can significantly enhance cardiovascular fitness and overall health in cancer survivors [16, 43]. While greater amounts of physical activity have demonstrated benefits for survival, such recommendations may not be feasible for all cancer survivors, especially those experiencing cancer-related fatigue or other serious health conditions [8, 44]. Thus, physical activity recommendations should be personalized based on the individual health status and physical capabilities of each cancer survivor. Future research is needed to determine the optimal exercise intensity for cancer survivors at different disease stages, which could ultimately improve long-term outcomes and HRQoL [45].

Alternatively, cross-sectional and longitudinal studies have demonstrated that the presence of depressive symptoms, including those that do not meet the criteria for major depression, is correlated with poor clinical outcomes [20, 46]. In particular, depressive symptoms and anxiety are common in cancer survivors due to the distress of tumor recurrence, pain, or socioeconomic difficulties [47–49]. Moreover, persistent depressive symptoms in cancer survivors predict a worse survival probability [47]. In line with the findings of previous studies [50, 51], approximately 25.9% of cancer survivors experienced depressive symptoms in the current study. In our analysis, cancer survivors with mild or moderate-severe depression exhibited nearly 22% and 27% increased risks of all-cause and noncancer mortality, respectively, compared to those without depressive symptoms. These findings are consistent with results from

Variables	Death/No.	HR (95% CI)	P value
All-cause mortality			
Sedentary time			
<6 h/d	216/1119	Reference	
6-8 h/d	232/812	1.39 (1.15, 1.68)	0.001
> 8 h/d	144/529	1.68 (1.36, 2.09)	<0.001
Continus	/	1.05 (1.02, 1.08)	<0.001
Depressive symptoms			
PHQ-9<5	423/1772		
PHQ-9≥5	169/688	1.22 (1.01, 1.48)	0.040
Continus	/	1.02 (1.00, 1.04)	0.027
Cancer mortality			
Sedentary time			
<6 h/d	90/1119	Reference	
6-8 h/d	76/812	1.10 (0.81, 1.51)	0.539
> 8 h/d	50/529	1.34 (0.92, 1.94)	0.126
Continus	/	1.02 (0.98, 1.07)	0.287
Depressive symptoms			
PHQ-9<5	150/1772	Reference	
PHQ-9≥5	66/688	1.28 (0.94, 1.75)	0.122
Continus	/	1.02 (0.99, 1.05)	0.318
Non-cancer mortality			
Sedentary time			
<6 h/d	126/1119	Reference	
6-8 h/d	156/812	1.51 (1.19, 1.92)	0.001
> 8 h/d	94/529	1.80 (1.35, 2.40)	<0.001
Continus	/	1.07 (1.04, 1.11)	<0.001
Depressive symptoms			
PHQ-9<5	273/1772	Reference	
PHQ-9≥5	103/688	1.27 (1.01, 1.61)	0.045
Continus	/	1.03 (1.00, 1.05)	0.031
CMD mortality			
Sedentary time			
<6 h/d	56/1119	Reference	
6-8 h/d	62/812	1.32 (0.91, 1.91)	0.142
> 8 h/d	38/529	1.52 (0.97, 2.39)	0.067
Continus	/	1.05 (1.00, 1.11)	0.075
Depressive symptoms			
PHQ-9<5	114/1772	Reference	
PHQ-9≥5	42/688	1.32 (0.91, 1.91)	0.145
Continus	/	1.03 (0.99, 1.07)	0.205

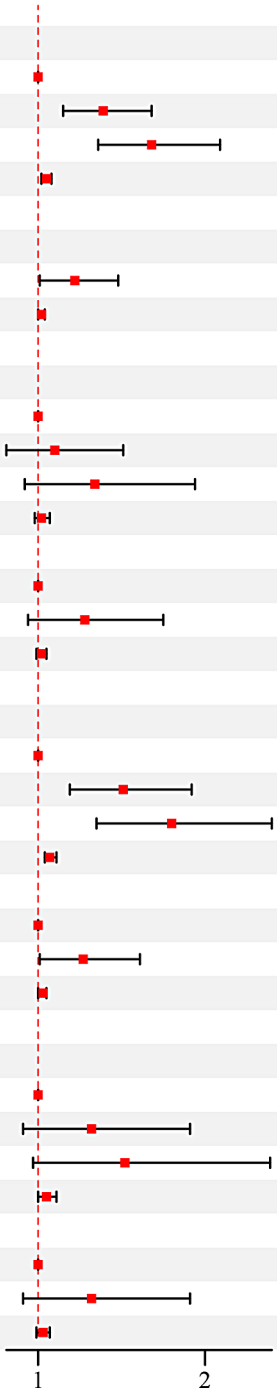

Fig. 2 The multivariate-adjusted associations of sedentary behavior and depressive symptoms with all-cause-, cancer-, noncancer-, and CMD mortality in cancer survivors. HR: hazard ratio; CI: confidence interval; PHQ-9: Patient Health Questionnaire-9. Adjusted for age, sex, race, educational level, marital status, physical activity, family income poverty ratio, BMI, smoking status, alcohol use, hypertension, hyperlipidemia, diabetes mellitus, CVD, dietary quality, and sleep time

an earlier study [52]. In addition, results from previous pan-cancer analyses also revealed the adverse prognostic effects of depressive symptoms on cause-specific mortality outcomes in cancer survivors [19]. Mechanistically, depression induces systemic inflammatory disorders and dysregulation of the hypothalamic–pituitary–adrenal axis, which leads to the release of proinflammatory mediators, thereby undermining immune surveillance

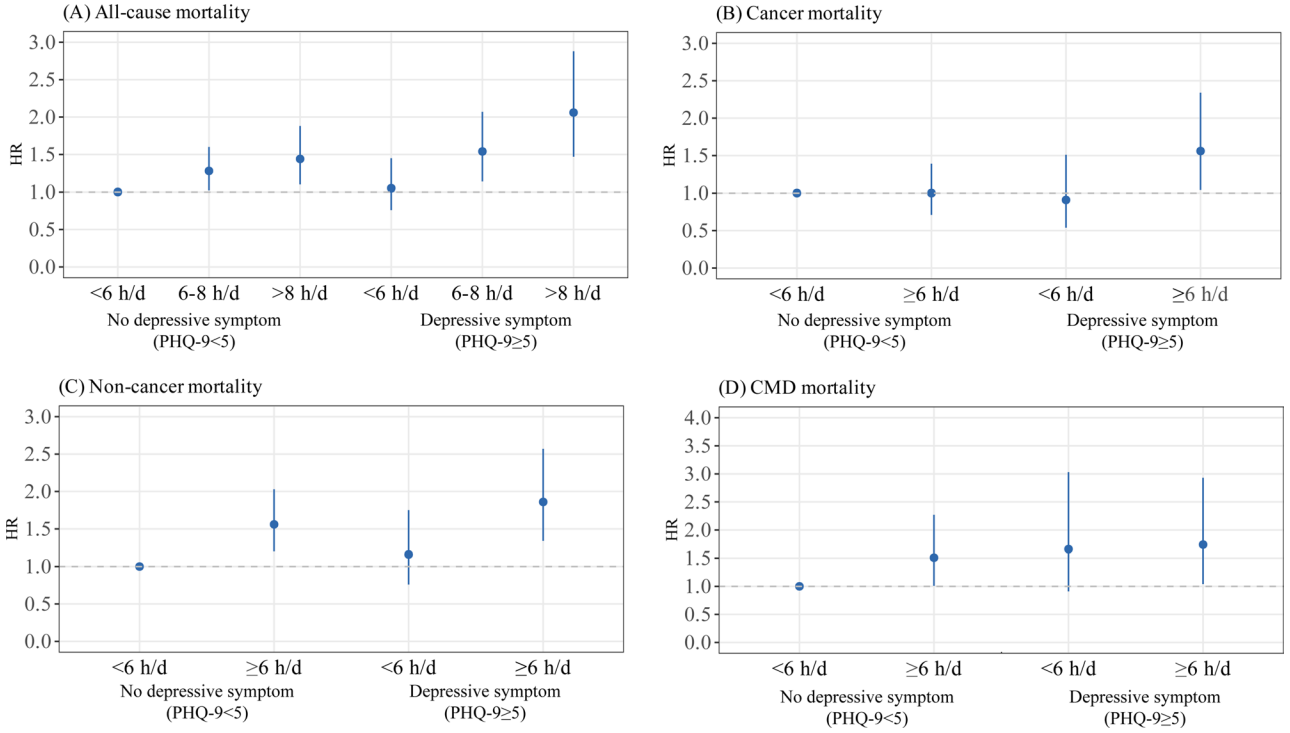

Fig. 3 The multivariate-adjusted joint associations of sedentary behavior and depressive symptoms with all-cause-, cancer-, noncancer-, and CMD mortality in cancer survivors. HR: hazard ratio; CI: confidence interval; PHQ-9: Patient Health Questionnaire-9. Adjusted for age, sex, race, educational level, marital status, physical activity, family income poverty ratio, BMI, smoking status, alcohol use, hypertension, hyperlipidemia, diabetes mellitus, CVD, dietary quality, and sleep time

and facilitating cancer recurrence and progression [20, 21, 53, 54]. Similarly, sedentary behavior is a key risk factor for energy metabolism disorders and cardiovascular complications [55–58]. The combined metabolic disruptions caused by both sedentary behavior and depressive symptoms likely contribute to cancer progression and mortality [11, 19, 59]. Consistent with these mechanisms, our study found that cancer survivors with both severe sedentary behavior and depressive symptoms are at significantly higher risk for all-cause mortality compared to those with either risk factor alone.

Although our study found an association between sedentary behavior and depressive symptoms with all-cause mortality in cancer survivors, no significant relationship was observed for cancer-specific mortality in the independent analysis. In contrast, sedentary behavior and depressive symptoms appeared to have a stronger association with noncancer mortality. These findings suggested that the effects of sedentary behavior and depression may be more pronounced in relation to broader health outcomes, rather than directly impacting cancer-specific mortality. However, it is important to note that the lack of adjustment for factors such as cancer stage and treatment history may limit our ability to draw definitive conclusions about cancer-specific mortality. Future works incorporating more detailed clinical data are needed to further explore these relationships and their underlying mechanisms. First, the relatively low number of cancer-specific events may have limited the statistical power to detect significant associations, making the results less precise. Second, reverse causation may have existed during analysis, as individuals with more advanced cancer are more likely to experience depression and sedentary behavior, which may then contribute to mortality outcomes. Besides, regarding noncancer as well as CMD mortality, we found that the impact of moderate/severe sedentary behavior on mortality risk was more pronounced than that of depressive symptoms. This might reflect the fact that sedentary behavior has a direct influence on cardiovascular health, contributing to increased risks of MetS and other cardiovascular complications, which can subsequently elevate the risk of CMD mortality [60, 61]. Moreover, the direct physiological impact of prolonged sedentary behavior, including endothelial dysfunction, impaired glucose metabolism, and increased inflammation, might have a greater impact than the effects of depressive symptoms in promoting cardiovascular and metabolic-related diseases [55, 60]. On the other hand, depressive symptoms are likely to exert a more complex, indirect influence, often exacerbated by sedentary lifestyles and underlying chronic conditions. These findings highlight the need for comprehensive

lifestyle interventions that target both physical and mental health outcomes. Specifically, strategies to reduce sedentary behavior, promote physical activity, and address depressive symptoms could significantly benefit cancer survivors, who are at heightened risk for mental health challenges and cardiometabolic conditions [59, 61]. Reducing sedentary behavior through regular movement breaks, encouraging physical activity, and providing psychological support may help to improve not only their HRQoL but also their survival outcomes. Incorporating these interventions into cancer care routines could enhance long-term health and reduce mortality risk, making them critical components of survivorship care [62].

Additionally, we further conducted a series of stratified analyses among various subgroups. Especially, we found that male cancer survivors were more susceptible to the impact of depressive symptoms on the risk of all-cause mortality. This finding suggested that depression might have a more pronounced effect on survival outcomes in men compared to women. While previous studies have consistently shown that women are more likely to develop depressive symptoms and anxiety [63], the role of sex in moderating the association between depression and mortality in cancer survivors remains inconclusive. For instance, a meta-analysis by Pinquart et al. found that the relationship between depression and mortality did not differ significantly between sexes [64]. In contrast, Trudel-Fitzgerald et al. reported that male colorectal cancer survivors with depression had a nearly 1.5-fold increased risk of mortality compared to their female counterparts [65]. These contrasting findings underscore the complexity of this issue and highlight the need for further research to clarify the role of sex in depression-related mortality risks. Investigating the potential biological, psychological, and social mechanisms that contribute to these sex differences may provide valuable insights for the development of targeted interventions to improve survival outcomes in cancer survivors [20, 66]. Furthermore, the current study also revealed that cancer survivors with endocrine-related cancers and gastrointestinal cancers were particularly vulnerable to the combined prognostic effects of sedentary behavior and depressive symptoms. The results indicated that underlying factors such as hormonal imbalances and metabolic dysfunctions would play an important role in amplifying the adverse effects of both sedentary behavior and depression on the mortality risk of cancer survivors. For instance, depression can further impair metabolic regulation, while prolonged sedentary behavior may worsen metabolic health, thus creating a feedback loop that worsens survival outcomes [60, 67, 68]. These complex interactions highlight the need for tailored interventions that address both the physical and psychological health of cancer survivors, particularly those with specific cancer types prone to metabolic and hormonal dysfunction. Future studies should investigate the mechanistic pathways linking these factors, which could inform more effective treatment and prevention strategies for this vulnerable subgroup.

Strengths and limitations

There are several notable strengths in the present study. First, the use of a nationally representative cohort of US cancer survivors enables the generalizability of our findings to the broader population of cancer survivors, offering robust evidence for the association between sedentary behavior, depressive symptoms, and different mortality outcomes. Second, this is the first study to investigate the joint effects of sedentary behavior and depressive symptoms on mortality risk among cancer survivors, which helps to fill the research gap in the literature. Third, we controlled for a comprehensive range of potential confounding factors, including demographic characteristics, socioeconomic status, comorbidities, and individual lifestyle factors, thereby minimizing bias and enhancing the internal validity of our results. Last, the use of well-established cohort data, such as NHANES, ensures that our findings are grounded in a high-quality and rigorously collected dataset, further strengthening the reliability of our conclusions.

Nevertheless, some limitations exist in the current study, which indicates our findings need to be interpreted cautiously. First, the sedentary behavior was measured through self-reporting, which may introduce recall and reporting biases. Thus, objective measures for sedentary time can provide more accurate quantitative data and help to determine the optimal sitting time for cancer survivors. Moreover, depressive symptoms were evaluated via self-reports using the PHQ-9. The severity and duration of depression might be calculated in future works. Meanwhile, due to the lack of specific diagnostic information on severe psychiatric conditions in the NHANES database during the study cycles, participants with serious mental health issues, which could influence depression symptoms and sedentary behavior, could not be excluded. Second, the diagnoses and types of cancers were self-reported. Although some studies have indicated good agreement between self-reported cancer history and medical records, self-reported data may be influenced by misclassification during the data recording process [69, 70]. Also, the NHANES database did not collect information regarding cancer stages and treatments. Therefore, the results should be interpreted cautiously. Future studies with specific cancer-associated factors are warranted to evaluate the impact of sedentary behavior and depressive symptoms on the prognosis of cancer survivors with different cancer stages or treatment

modalities. Meanwhile, some site-specific cancer types were not included in the subgroup analysis due to the limited sample size and events. Future studies with larger sample sizes are needed to explore more detailed results for these specific cancer types. Third, the study only measured sedentary behavior and depression at baseline without collecting information on dynamic changes in these factors during the follow-up period. However, previous work indicated fairly stable anxiety or depression levels over several years [71]. Therefore, the main findings of the present study might not be disturbed by repeated assessments of anxiety or depression symptoms in the study population. Also, the study did not include social network factors, which can affect depression and overall health outcomes in cancer survivors. The lack of this information may limit our understanding of the psychosocial factors influencing mortality risk. Future studies incorporating social support variables could provide a more comprehensive understanding of the joint effects of sedentary behavior, depression, and social networks on cancer survivor outcomes. Last, the present study did not include other endpoints, such as HRQoL and physical functioning, which hold significant relevance for patients and their care teams. Future studies are supposed to incorporate these outcomes to provide a more comprehensive understanding of the joint effects of sedentary behavior and depressive symptoms on cancer survivors.

Conclusion

In summary, the findings of this study suggest that severe sedentary behavior and depressive symptoms significantly impact mortality outcomes, particularly all-cause and noncancer mortality, in cancer survivors. These results underscore the importance of healthcare providers considering both physical and mental health factors when making recommendations for this population. Public health interventions should adopt a comprehensive approach to promote physical activity, address depressive symptoms, and ultimately enhance long-term health outcomes for cancer survivors.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12885-025-13578-2.

Supplementary Material 1

Acknowledgements
None.

Author contributions
Conception and design: Ying Zhong and Zhigong Wei Administrative support: Zhigong Wei Provision of study materials: Ping Yao and Zhigong Wei Collection and assembly of data: All authors. Data analysis and interpretation: All authors. Manuscript writing: All authors Final approval of manuscript: All authors.

Funding
None.

Data availability
The public data that support the findings of study are available in the National Health and Nutrition Examination Survey (https://www.cdc.gov/nchs/nhanes/index.htm). The in-house data can be obtained from the corresponding authors upon reasonable request.

Declarations

Ethics approval and consent to participate
As a secondary analysis of anonymized data, this study did not involve human participants. Thus, informed consent and institutional review board approval were not needed. Informed consent was not needed.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 12 November 2024 / Accepted: 21 January 2025
Published online: 28 March 2025

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