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Joint association of depressive symptoms and dietary patterns with mortality among US cancer survivors: a population-based study

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Abstract

Background Depression and diet are both common modifiable factors related to mortality rates among individuals with cancer, but their combined effects remained underexplored. We aimed to comprehensively evaluate the independent and joint association of depressive symptoms and dietary patterns with mortality among cancer survivors.

Methods A cohort of US cancer survivors (3,011 eligible participants, representing 20 million cancer patients) were collected from the National Health and Nutrition Examination Survey (NHANES) between 2005 and 2018. Depressive symptoms were assessed with the Patient Health Questionnaire (PHQ-9). Based on dietary data from 24-hour recall, several well-developed dietary pattern indices were calculated, including Healthy Eating Index-2020 (HEI-2020), Alternative Healthy Eating Index (AHEI), Alternate Mediterranean Diet Score (aMED), MED Index in serving sizes from the PREDIMED trial (MEDI), Dietary Approaches to Stop Hypertension Index (DASH), DASH Index in serving sizes from the DASH trial (DASHI), Dietary Inflammation Index (DII), and DII excluding alcohol (DII [No EtOH]). Kaplan-Meier curves and multivariable Cox proportional hazards regression models were conducted to investigate the relationships of independent and combined prognostic effects of PHQ-9 score and dietary pattern indices with survival among cancer survivors.

Results In joint analysis, combinations of lower PHQ-9 score with higher HEI-2020, AHEI, aMED or DASH were favorably linked to lower risks of overall and noncancer mortality. Representatively, cancer survivors with no to minimal depressive symptoms (PHQ-9 score: 0–4) and high adherence to the HEI-2020 had lower risk of all-cause (HR = 0.43, 95% CI: 0.24–0.75) and noncancer (HR = 0.29, 95% CI: 0.15–0.55) mortality, when compared to those with PHQ-9 score ≥ 10 and low adherence to the HEI-2020. Additionally, a combination of higher adherence to the MEDI and lower PHQ-9 scores was linked to a reduced risk of noncancer mortality.

Conclusions The joints of depressive symptoms and certain dietary patterns were associated with risks of all-cause, cancer-specific, and noncancer mortality among cancer survivors. Early psychological counseling and individualized dietary strategies are crucial to reduce mortality risk and improve quality of life for this population.

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Keywords Depression, Dietary pattern, Cancer survivors, Mortality, NHANES

Background

To date, cancer has represented a significant public health and economic challenge worldwide, with approximately 20 million new cases and 9.7 million cancer-related deaths in 2022 [1]. For individuals up to 74 years of age, the lifetime risk of developing cancer is estimated to be around 20.2% [2]. In the UK population, roughly two out of every five people are affected by cancer during their entire lifetime [3]. Despite gradual advancements in early detection and therapeutic interventions over recent decades [4, 5], cancer survivors are still faced with considerably reduced life expectancy compared to those without cancer. The survival of cancer patients could be affected by a range of factors, including physiological characteristics, socioeconomic status, lifestyle choices, comorbidities, tumor types and stages, as well as personalized treatments [6]. Notably, cancer survivors are considered to encounter greater mental difficulties which may adversely affect both their quality of life and long-term survival [6, 7]. Moreover, dietary patterns are another modifiable factor that can be readily altered to impact survival outcomes [8, 9]. Therefore, it is essential to identify mental risk factors and develop appropriate dietary strategies to improve the well-being of cancer survivors and reduce their risk of mortality.

In recent years, increasing attention has been given to the mental health challenges faced by individuals with cancer, alongside their physical hardships. Studies have shown that individuals diagnosed with cancer, such as prostate and breast cancer, are at higher risk for depression, anxiety, and suicide [10–12]. For instance, depression, one of the most common mental disorders, is far more prevalent in cancer patients, among which up to 20% are affected [13]. Besides, it was reported that men with high-risk prostate cancer had nearly double the risk of developing major depression and dying by suicide [10]. In turn, mental health problems could also adversely affect carcinogenesis, progression, therapeutic efficacy and outcomes of cancer. A meta-analysis of cohort studies revealed that depression was associated with an increased cancer-specific mortality risk across various cancer types, including lung, bladder, breast, colorectal, hematopoietic, kidney, and prostate cancers [14]. Although the relationship between depression and cancer outcomes has been well-established as described above, existing research remains inadequate due to various limitations, such as study design, insufficient follow-up, interference from confounding factors, and substantial heterogeneity across different cancer types [14]. In addition to depressive symptoms, dietary patterns are also an established modifiable factor that could significantly affect the incidence and mortality of cancer. According to the guidelines of the American Cancer Society (ACS) and the American Society for Clinical Oncology (ASCO), cancer survivors were recommended to adopt improved dietary and nutritional management strategies, including preferring to acquire macronutrients and micronutrients from a plant-based diet, avoiding the overuse and misuse of dietary supplements, and following food safety practices [8, 15]. Notably, high-quality meta-analytic evidence supported only a limited number of associations between individual food/nutrient and incidence and mortality of cancer, such as alcohol consumption and various cancers [16–18]. Moreover, it is difficult to comprehensively reflect eating habits based on individual food/nutrient, which also makes it challenging to adhere to. Compared to individual food components or nutrients, the effect of dietary patterns on clinical outcomes among cancer survivors has been highlighted in recent studies [19–21]. Nevertheless, to our knowledge, current literature offers limited systematic evaluations of the effects of different dietary patterns on the mortality rates among cancer survivors. Previous research has highlighted the close link between depressive symptoms and dietary patterns. Specifically, healthier diets, characterized by high intake of fruits, vegetables, and healthy fats, were associated with a reduced risk of depression, while diets rich in processed foods tend to increase the risk [22]. However, the distinct and combined influences of depressive symptoms and dietary patterns remain insufficiently understood.

In the current study, we aimed to investigate the independent and joint associations of depressive symptoms and several well-established dietary patterns with all-cause, cancer-specific, and non-cancer mortality among US cancer survivors. Since different dietary health indices were examined, we extended our evaluation to determine whether the combination of any two indices could serve as a promising predictor of cancer outcomes. The findings of this study were expected to provide novel insights regarding appropriate psychological interventions and dietary strategies for cancer survivors, which could lead to improved survival outcomes and overall quality of life.

Methods

Study population

The participants for this population-based study were chosen from a nationally representative sample of the US

population, collected by the National Health and Nutrition Examination Survey (NHANES) of Centers for Disease Control and Prevention (CDC) [23]. Recognized as the most in-depth survey assessing the health and nutritional status of US children and adults, the NHANES has examined approximately 5,000 noninstitutionalized individuals annually from 15 different counties across the country since 1999, with each two-year span constituting a complete cycle [23]. Invited participants responded to demographic, socioeconomic, dietary, and health questionnaires, and underwent medical and physical examinations, as well as laboratory tests. The stratified, multistage probability sampling design of NHANES enables estimates to represent the entire US population. All NHANES protocols received approval from the National Center for Health Statistics Ethics Review Board, and written informed consent was obtained from all participants. Detailed survey plans and operations of NHANES have been described elsewhere [23]. Since this study utilized previously collected anonymized data and involved no human participants, the requirement for informed consent and institutional review board approval was waived.

In the current study, we included all adult cancer survivors ≥ 20 years old from NHANES 2005–2018. We examined questions related to cancer history from the "Medical Conditions" questionnaire section. The presence of cancer was determined by "Have you ever been told by a doctor or other health professional that you had cancer or a malignancy of any kind?" The participants who answered "Yes" to this question were identified as cancer survivors. Types of cancer were determined by "What kind of cancer was it?" Age when cancer first diagnosed was determined by "How old were you when [type of cancer] was first diagnosed?" Cancer types were further grouped into ten categories: respiratory system tumors (lung, laryngeal, and tracheal), gastrointestinal tumors (esophageal, gastric, hepatocellular, gallbladder, pancreatic, and colorectal), breast tumors, gynecologic tumors (uterine, ovarian, and cervical), urologic tumors (kidney, bladder, prostate, and testicular), hematologic malignancies (blood, leukemia, and lymphoma), skin tumors (melanoma and nonmelanoma), head and neck tumors (mouth/tongue/lip and thyroid), other types of tumors (brain, nervous system, bone, and soft tissue), and multiple tumors (≥ 2 types of cancer). Participants with missing information on depressive scores, dietary data required for calculating dietary patterns, or follow-up were excluded from this study. The flowchart of the participant selecting process is presented in Supplementary Figure S1.

Assessment of depressive symptoms

The Patient Health Questionnaire (PHQ-9), a validated 9-item instrument for depression screening, was used to evaluate the frequency and severity of depressive symptoms among cancer survivors over the preceding two weeks [24]. This tool incorporates the DSM-IV criteria for diagnosing depression [25]. Each item is scored from 0 to 3, with response options ranging from "not at all" to "nearly every day". The total PHQ-9 scores, ranging from 0 to 27, were calculated and categorized into three levels based on predefined cut-points: no to minimal (0–4), mild (5–9), and moderate to severe (≥ 10) depressive symptoms. The nine items of the PHQ-9 and the scoring cut-offs have been thoroughly detailed in a previous publication [24].

Assessment of dietary patterns

The NHANES collected dietary intake data from eligible participants through two 24-hour dietary recall interviews: the first was conducted in-person at the Mobile Examination Center (MEC), while the second was conducted by telephone 3 to 10 days later. Apart from consumption of individual foods, estimated total nutrients intake was also provided. Due to the greater prevalence of missing information in the second 24-hour dietary recall, we relied on the dietary data from the first recall for the primary analysis. To provide a broader understanding of dietary behaviors rather than individual food intakes, several well-developed dietary pattern indices were chosen and calculated, including Healthy Eating Index-2020 (HEI-2020) [26], Healthy Eating Index-2015 (HEI-2015) [27], Alternative Healthy Eating Index (AHEI) [28], Alternate Mediterranean Diet Score (aMED) [29], MED Index in serving sizes from the PREDIMED trial (MEDI) [30], Dietary Approaches to Stop Hypertension Index (DASH) [31], DASH Index in serving sizes from the DASH trial (DASHI) [32, 33], Dietary Inflammation Index (DII) [34], and DII excluding alcohol (DII [No EtOH]). To adhere to a standardized dietary index computation process and avoid inaccuracies, these dietary pattern indices were calculated with the R package "dietaryindex" (version 1.0.3) [35], which adopted a structured 2-step computation process with validated accuracy. Detailed information on which and how dietary components are scored can be found in the supplementary materials of the referenced publication. To note, since the computed HEI-2015 values were basically the same as HEI-2020 values in the NHANES 2005–2018 dataset, they were not included in subsequent analysis. Due to the unavailability of dietary data for certain foods or nutrients: trans-fat was not included in the AHEI score; 27 out of 45 required foods or nutrients were used for calculation of DII. In this study, the dietary pattern indices were divided into low, intermediate and high levels based on the weighted tertile values.

Assessment of covariates

Potential covariates were selected based on our prior knowledge of factors influencing the prognosis of cancer survivors. Physiological characteristics included age (continuous), sex (male, female), race/ethnicity (non-Hispanic White, non-Hispanic Black, Mexican American, and other),

body mass index (BMI < 25, ≥ 25 and < 30, and ≥ 30 kg/m^2). Socioeconomic status included educational level (less than high school, high school graduate, greater than high school), marital status (married/living with partner, not married), family poverty income ratio (< 1.3, 1.3–3.5, and > 3.5), and health insurance coverage (yes, no). Lifestyle choices included smoking status (never, former, and current), alcohol use (never, former, and current), sleep duration (≤ 7 h, > 7 h), and energy intake (quartile). Health conditions included hypertension, hypercholesterolemia, diabetes, and cardiovascular disease (CVD), and cancer history (described earlier in the text). The presence of CVD was determined by self-reported history of congestive heart failure, coronary heart disease, angina, heart attack, or stroke.

Assessment of mortality

Data of eligible cancer survivors in this study were linked to death certificate records from the National Death Index (NDI), which have been updated to include follow-up records up to December 31, 2019. The primary outcome of this study was all-cause mortality, while cancer (defined by the 10th revision of International Statistical Classification of Diseases [ICD-10] codes C00-C97) and noncancer (other ICD-10 codes) mortality served as secondary outcomes. The duration of follow-up was determined from the date of the initial interview to the date of death or the last update, whichever occurred first.

Statistical analysis

In adherence to the NHANES analytic tutorials, all analysis in this study accounted for the sample weights, stratification, and clustering to ensure proper variance estimation and national representativeness of US cancer survivors. We assumed that the covariates were missing at random and applied multiple imputation by chained equations using the R package "mice" (version 3.16.0) to minimize uncertainty arising from missing data and ensure valid statistical inferences. All covariates from the primary analysis, together with sample weights, stratification, and clustering, were included as predictors. We generated a total of ten imputed datasets and pooled them to produce the overall results.

Baseline characteristics were presented according to the PHQ-9 score (0–4, 5–9, and ≥ 10). Continuous and categorical variables were compared by using Wilcoxon rank-sum test and chi-squared test, respectively. Moreover, baseline characteristics in the origin and imputation datasets were also displayed and compared. Weighted Kaplan-Meier curves and Log- rank test were applied to evaluate the effects of PHQ-9 score and different dietary pattern indices on all-cause mortality among US cancer survivors, without covariate adjustment. Dietary pattern indices were divided based on weighted tertile, median, and quartile values. Multivariable Cox proportional hazards regression models were performed to assess the association of depressive symptoms and dietary patterns with all-cause, cancer and noncancer mortality among cancer patients, respectively. Risk estimates were represented by hazard ratios (HR) with 95% confidence intervals (CIs). The fully adjusted Cox models accounted for age, sex, race/ethnicity, BMI, educational level, marital status, family poverty income ratio, health insurance coverage, smoking status, alcohol use, sleep duration, energy intake, hypertension, hypercholesterolemia, diabetes, CVD, the number of cancer types and years since first cancer diagnosis. To evaluate the joint associations, participants were categorized based on depressive levels and tertiles of dietary pattern indices to estimate mortality risks. Subgroup analyses according to sex, cancer type, hypertension, hypercholesterolemia, diabetes, and CVD were further performed. When different cancer types were considered, the dietary health indices were converted into binary variables (low and high, based on median values) and only all-cause mortality was assessed for respiratory system, gynecologic, hematologic, head, neck and other cancers, owing to the limited number of outcome cases. To investigate the shapes and relationships of PHQ-9 score and dietary pattern indices with all-cause mortality, restricted cubic splines (RCS) with 3 nodes were applied, using the median value as a reference point. The analysis was adjusted for the same set of covariates applied in the Cox models. To assess the robustness of the results and mitigate the impact of reverse causality, sensitivity analyses were conducted using dietary data from two 24-hour dietary recall interviews, excluding participants died within 2 years of follow-up, and excluding participants with missing covariates, respectively.

All analysis and graphics were conducted in statistical software R (version 4.3.3, R Development Core Team, Austria). Statistical significance was evaluated based on a two-sided *P* value of < 0.05.

Results

Baseline characteristics

As presented in Table 1, a total of 3,011 eligible participants were included in this study, representing 20,428,257 US cancer survivors. Population-weighted mean age was 63.01 years old, 43.08% were male (n = 1,421), and 86.04% were non-Hispanic White (n = 2,061). A high prevalence of overweight/obesity was observed. Participants were divided into three levels based on PHQ-9 score, indicating no to minimal (0–4), mild (5–9), and moderate to severe (≥ 10) depressive symptoms, respectively. Cancer survivors with moderate to severe depressive symptoms (PHQ-9 score ≥ 10) were more likely to be younger, female, obese, less educated, not married, with lower family poverty income ratio, not covered by health insurance, current smokers, worse at general health condition, and had shorter sleep time. Moreover, survivors with

Table 1 Baseline characteristics of US cancer survivors in the current study according to the PHQ-9 score

Characteristic	Overall ($n=3011$)	PHQ-9 score			
		0–4 ($n=2223$)	5–9 ($n=480$)	≥ 10 ($n=308$)	*P* value
Age (years)	63.01 (13.90)	63.88 (13.55)	63.10 (13.77)	55.67 (14.76)	< 0.001
Sex					< 0.001
Male	1,421 (43.08%)	1,144 (46.07%)	178 (34.78%)	99 (32.41%)	
Female	1,590 (56.92%)	1,079 (53.93%)	302 (65.22%)	209 (67.59%)	
Race/ethnicity					0.009
Non-Hispanic White	2,061 (86.04%)	1,544 (86.86%)	330 (86.54%)	187 (78.46%)	
Non-Hispanic Black	438 (5.49%)	327 (5.17%)	69 (5.91%)	42 (7.45%)	
Mexican American	190 (2.45%)	128 (2.26%)	27 (2.29%)	35 (4.26%)	
Other	322 (6.02%)	224 (5.71%)	54 (5.27%)	44 (9.83%)	
BMI (kg/m^2)					< 0.001
< 25	785 (27.79%)	594 (28.39%)	119 (27.28%)	72 (23.57%)	
≥ 25 and < 30	1,059 (34.98%)	830 (37.18%)	143 (28.96%)	86 (26.68%)	
≥ 30	1,132 (37.23%)	780 (34.43%)	209 (43.76%)	143 (49.75%)	
Education level					< 0.001
Less than high school	609 (12.17%)	408 (10.50%)	103 (15.13%)	98 (20.95%)	
High school graduate	677 (20.60%)	472 (18.57%)	131 (26.45%)	74 (27.53%)	
Greater than high school	1,724 (67.23%)	1,343 (70.93%)	246 (58.42%)	135 (51.52%)	
Marital status					< 0.001
Married/living with partner	1,827 (65.98%)	1,414 (68.54%)	276 (60.46%)	137 (54.23%)	
Not married	1,182 (34.02%)	807 (31.46%)	204 (39.54%)	171 (45.77%)	
Family poverty income ratio					< 0.001
< 1.3	669 (15.07%)	388 (11.57%)	134 (19.08%)	147 (37.23%)	
1.3–3.5	1,141 (35.89%)	850 (34.21%)	194 (42.94%)	97 (37.94%)	
> 3.5	971 (49.04%)	816 (54.22%)	115 (37.98%)	40 (24.83%)	
Health insurance coverage	2,820 (94.59%)	2,116 (96.06%)	442 (92.09%)	262 (86.61%)	< 0.001
Smoking status					< 0.001
Never	1,364 (46.40%)	1,051 (49.21%)	207 (40.81%)	106 (32.66%)	
Former	1,186 (38.08%)	907 (38.67%)	190 (40.65%)	89 (28.89%)	
Current	460 (15.52%)	264 (12.11%)	83 (18.53%)	113 (38.45%)	
Alcohol use					< 0.001
Never	372 (9.77%)	279 (10.12%)	53 (8.75%)	40 (8.57%)	
Former	976 (26.81%)	671 (24.11%)	190 (37.28%)	115 (31.37%)	
Current	1,654 (63.42%)	1,265 (65.77%)	237 (53.96%)	152 (60.07%)	
Sleep duration (h)					< 0.001
≤ 7	1,595 (50.47%)	1,123 (47.61%)	281 (57.08%)	191 (63.14%)	
> 7	1,403 (49.53%)	1,093 (52.39%)	197 (42.92%)	113 (36.86%)	
Energy intake (kcal)	1,945.10 (816.13)	1,966.84 (806.60)	1,854.83 (775.45)	1,917.65 (942.56)	0.12
General health status					< 0.001
Excellent	210 (8.52%)	195 (10.34%)	11 (3.05%)	4 (2.66%)	
Very good	790 (30.98%)	715 (37.40%)	64 (14.22%)	11 (6.23%)	
Good	1,172 (38.70%)	906 (39.07%)	191 (43.07%)	75 (28.26%)	
Fair	651 (17.25%)	352 (11.35%)	170 (33.40%)	129 (38.68%)	
Poor	188 (4.57%)	55 (1.83%)	44 (6.26%)	89 (24.18%)	
Hypertension	1,728 (52.09%)	1,249 (50.34%)	287 (59.00%)	192 (54.95%)	0.024
Hypercholesterolemia	1,551 (54.05%)	1,152 (53.95%)	245 (55.67%)	154 (52.03%)	0.8
Diabetes	712 (19.11%)	489 (17.78%)	133 (24.44%)	90 (21.08%)	0.017
CVD	543 (14.85%)	365 (12.82%)	92 (18.17%)	86 (25.97%)	< 0.001
Number of cancer types					0.2
1	2,721 (90.11%)	2,027 (90.67%)	428 (88.99%)	266 (87.35%)	
2	258 (8.84%)	176 (8.45%)	48 (10.03%)	34 (10.13%)	
≥ 3	32 (1.05%)	20 (0.89%)	4 (0.98%)	8 (2.52%)	
Cancer type					< 0.001

Table 1 (continued)

Characteristic	Overall (*n* = 3011)	PHQ-9 score			*P* value
		0–4 (*n* = 2223)	5–9 (*n* = 480)	≥ 10 (*n* = 308)	
Respiratory system tumors	65 (1.99%)	52 (2.08%)	10 (2.48%)	3 (0.38%)	
Gastrointestinal tumors	215 (5.53%)	147 (5.43%)	39 (5.85%)	29 (5.87%)	
Breast tumors	445 (14.22%)	325 (14.15%)	73 (15.35%)	47 (12.97%)	
Gynecologic tumors	375 (12.40%)	217 (10.23%)	84 (15.69%)	74 (24.68%)	
Urologic tumors	574 (12.73%)	471 (13.89%)	72 (10.72%)	31 (6.55%)	
Hematologic malignancies	97 (2.96%)	73 (2.91%)	16 (3.17%)	8 (3.04%)	
Skin tumors	847 (36.95%)	666 (38.66%)	118 (32.56%)	63 (30.29%)	
Head and neck tumors	77 (2.49%)	54 (2.30%)	13 (3.03%)	10 (3.15%)	
Other types of tumors	26 (0.83%)	22 (1.02%)	3 (0.15%)	1 (0.41%)	
Multiple tumors	290 (9.89%)	196 (9.33%)	52 (11.01%)	42 (12.65%)	
Age at cancer first diagnosed (years)					< 0.001
< 40	580 (23.74%)	363 (21.09%)	115 (26.85%)	102 (40.51%)	
40–60	1,197 (44.01%)	875 (44.84%)	186 (40.64%)	136 (42.76%)	
> 60	1,223 (32.25%)	979 (34.06%)	179 (32.52%)	65 (16.74%)	
Dietary health					
HEI-2020	53.26 (13.90)	53.73 (13.83)	52.98 (14.25)	49.84 (13.38)	< 0.001
HEI-2015	53.26 (13.90)	53.73 (13.83)	52.98 (14.25)	49.84 (13.38)	< 0.001
AHEI	42.14 (13.30)	42.92 (13.22)	41.13 (13.14)	37.41 (13.23)	< 0.001
aMED	3.73 (1.66)	3.82 (1.65)	3.60 (1.65)	3.26 (1.60)	< 0.001
MEDI	3.60 (1.25)	3.66 (1.25)	3.45 (1.28)	3.38 (1.23)	0.013
DASH	23.91 (5.77)	24.30 (5.75)	23.57 (5.65)	21.30 (5.49)	< 0.001
DASHI	3.77 (1.55)	3.76 (1.55)	3.83 (1.65)	3.70 (1.41)	0.9
DII	0.89 (1.87)	0.77 (1.83)	1.09 (1.89)	1.50 (1.97)	< 0.001
DII (No EtOH)	0.72 (1.85)	0.61 (1.81)	0.89 (1.88)	1.31 (1.96)	< 0.001

Abbreviations: PHQ-9 score, Patient Health Questionnaire-9 score; BMI, body mass index; CVD, cardiovascular disease; HEI-2020, Healthy Eating Index-2020; HEI-2015, Healthy Eating Index-2015; AHEI, Alternative Healthy Eating Index; aMED, Alternate Mediterranean Diet Score; MEDI, MED Index in serving sizes from the PREDIMED trial; DASH, Dietary Approaches to Stop Hypertension Index; DASHI, DASH Index in serving sizes from the DASH trial; DII, Dietary Inflammation Index; EtOH, alcohol

lower scores on dietary indices such as HEI-2020, HEI-2015, AHEI, aMED, MEDI, DASH, along with higher scores on the DII and DII (No EtOH) were more prone to exhibit higher PHQ-9 scores. Multiple imputation was applied to missing data on family poverty income ratio ($n = 230$, 8%), hypercholesterolemia ($n = 162$, 5%), BMI ($n = 35$, 1%), and other covariates ($n = 24$, < 1%). Detailed baseline characteristics of the imputation datasets were shown in Supplementary Table 1.

Relationship between PHQ-9 score, dietary pattern indices, and mortality

During 20,096 person-years of follow-up (median, 6.2 years), 786 deaths occurred, with 268 attributed to cancer and 518 to noncancer causes. Weighted Kaplan-Meier curves demonstrated that, when dietary pattern indices were divided by tertiles, high levels of the aMED ($P = 0.031$, Fig. 1D) and MEDI ($P = 0.003$, Fig. 1E) scores were associated with lower risk of all-cause mortality among US cancer survivors. The results remained largely consistent when the dietary pattern indices were stratified by both the weighted median and quantile values (Supplementary Figure S2-S3). The fully adjusted multivariable Cox proportional hazards regression models revealed that cancer survivors with no to minimal depressive symptoms (PHQ-9 score: 0–4) had lower risks of noncancer (HR = 0.62, 95% CI: 0.42–0.92) mortality when compared to those with moderate to severe depressive symptoms (PHQ-9 score: ≥10) (Table 2). As for dietary patterns, participants with intermediate adherence to the DASH diet showed a lower risk of cancer mortality(HR = 0.66, 95% CI: 0.49–0.89), while those with high adherence to the aMED diet had a lower noncancer mortality risk (HR = 0.74, 95% CI: 0.57–0.96) relative to the low-adherence group, respectively (Table 2).

Joint association of PHQ-9 score and dietary pattern indices with mortality

In joint analysis, combinations of lower PHQ-9 score with higher HEI-2020, AHEI, aMED or DASH were favorably linked to lower risks of overall and noncancer mortality (Fig. 2, Table S2). For instance, cancer survivors with PHQ-9 score ranging from 0 to 4 and high scores on HEI-2020 had lower risk of all-cause (HR = 0.43, 95% CI: 0.24–0.75) and noncancer (HR = 0.29, 95% CI: 0.15–0.55) mortality, when compared to those with PHQ-9 score ≥ 10 and low scores

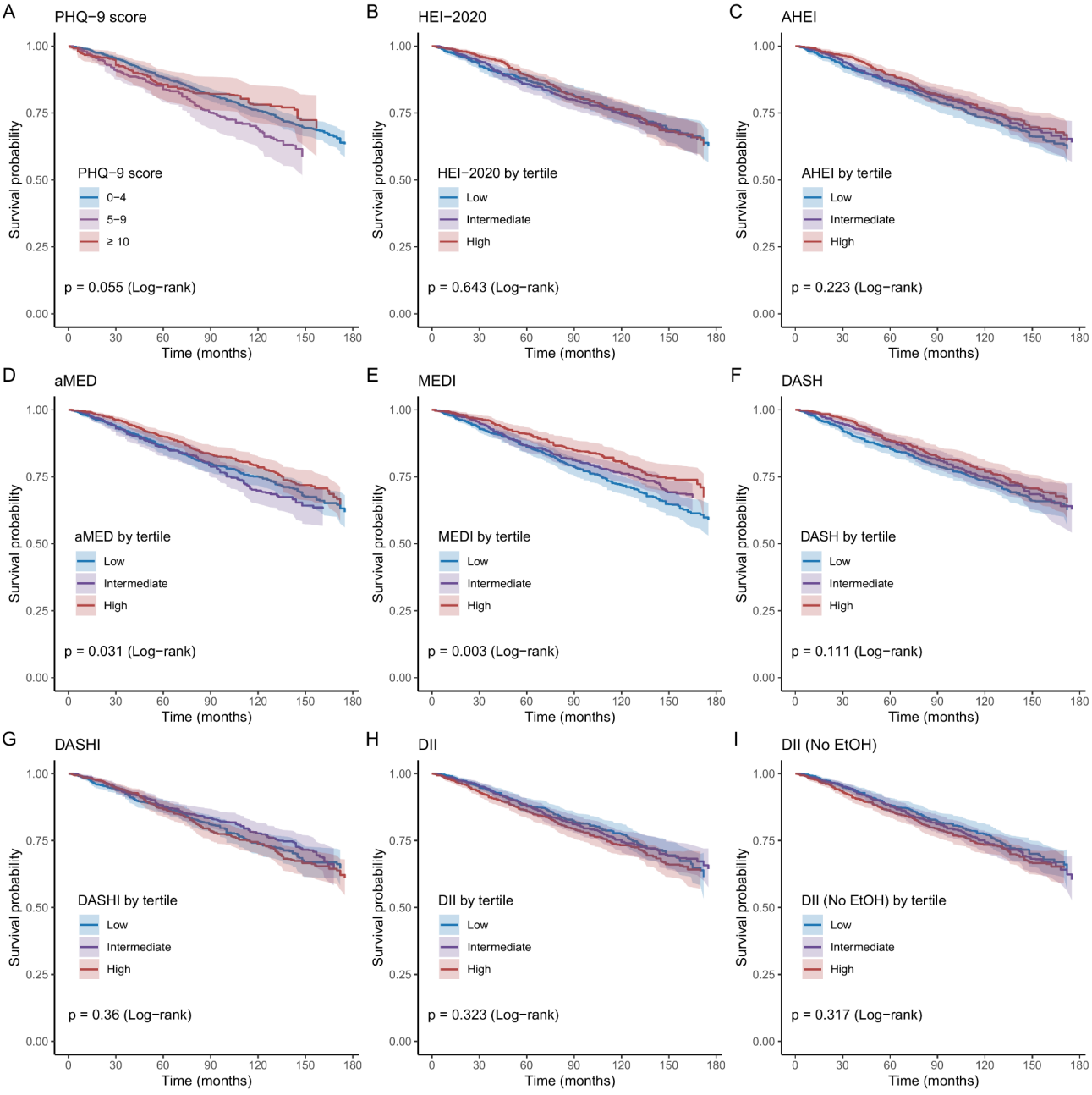

Fig. 1 Weighted Kaplan-Meier curves for all-cause mortality among US cancer survivors by PHQ-9 score and different dietary pattern indices divided by tertiles, NHANES 2005–2018. The dietary pattern indices were divided into low, intermediate and high levels based on the weighted tertile values. Abbreviations: NHANES, the National Health and Nutrition Examination Survey; PHQ-9 score, Patient Health Questionnaire-9 score; HEI-2020, Healthy Eating Index-2020; AHEI, Alternative Healthy Eating Index; aMED, Alternate Mediterranean Diet Score; MEDI, MED Index in serving sizes from the PREDIMED trial; DASH, Dietary Approaches to Stop Hypertension Index; DASHI, DASH Index in serving sizes from the DASH trial; DII, Dietary Inflammation Index; EtOH, alcohol

on HEI-2020. Besides, combinations of higher adherence to MEDI and lower PHQ-9 score were found to be associated with reduced risk of noncancer mortality. Notably, among participants with a PHQ-9 score of ≥ 10, intermediate (HR = 0.15, 95% CI: 0.04–0.66) and high (HR = 0.19, 95% CI: 0.04–0.85) adherence to the DASH diet were linked to significantly lower cancer-specific mortality risks, compared to low adherence. The evaluation of combinations of any two dietary pattern indices demonstrated that the pairings of AHEI and MEDI, aMED and DASHI, and DASH and DII might serve as potential indicators in guiding dietary strategies of cancer patients to improve long-term outcomes (Fig. 3; Table S3). Nevertheless, these

Table 2 Association of PHQ-9 score and dietary health with all-cause, cancer, and noncancer mortality among US cancer survivors, NHANES 2005–2018

Mortality outcome	Death/No.	Weighted death (%)	Model 1		Model 2		Model 3	
			HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value
All-cause mortality								
PHQ-9 score								
≥ 10	74/308	341,067 (18.2)	1 [Reference]		1 [Reference]		1 [Reference]	
5–9	140/480	717,775 (22.8)	0.73 (0.48, 1.10)	0.127	0.89 (0.60, 1.33)	0.568	0.96 (0.64, 1.44)	0.842
0–4	572/2223	2,748,863 (17.8)	**0.48 (0.35, 0.67)**	**<0.001**	**0.67 (0.48, 0.93)**	**0.018**	0.74 (0.53, 1.04)	0.080
HEI-2020								
Low	286/1059	1,271,103 (18.7)	1 [Reference]		1 [Reference]		1 [Reference]	
Intermediate	252/962	1,318,089 (19.3)	0.95 (0.76, 1.20)	0.681	1.09 (0.85, 1.38)	0.511	1.05 (0.84, 1.32)	0.675
High	248/990	1,218,513 (18)	**0.66 (0.52, 0.82)**	**<0.001**	0.88 (0.68, 1.14)	0.322	0.83 (0.65, 1.08)	0.163
AHEI								
Low	308/1068	1,386,527 (20.3)	1 [Reference]		1 [Reference]		1 [Reference]	
Intermediate	258/1007	1,268,183 (18.7)	**0.78 (0.64, 0.95)**	**0.013**	0.92 (0.74, 1.13)	0.422	0.90 (0.73, 1.11)	0.346
High	220/936	1,152,995 (16.9)	**0.61 (0.48, 0.78)**	**<0.001**	0.84 (0.65, 1.10)	0.204	0.82 (0.64, 1.07)	0.144
aMED								
Low	400/1447	1,839,838 (19)	1 [Reference]		1 [Reference]		1 [Reference]	
Intermediate	179/643	886,089 (21)	0.92 (0.71, 1.18)	0.492	1.04 (0.8, 1.35)	0.783	1.02 (0.78, 1.33)	0.909
High	207/921	1,081,778 (16.5)	**0.62 (0.50, 0.76)**	**<0.001**	0.80 (0.64, 1.00)	0.051	0.81 (0.65, 1.02)	0.069
MEDI								
Low	428/1509	2,016,594 (20.3)	1 [Reference]		1 [Reference]		1 [Reference]	
Intermediate	224/867	1,109,435 (18.4)	0.87 (0.72, 1.06)	0.165	0.97 (0.80, 1.16)	0.713	0.92 (0.76, 1.11)	0.377
High	134/635	681,675 (15.3)	**0.72 (0.58, 0.90)**	**0.004**	0.96 (0.75, 1.21)	0.721	0.94 (0.74, 1.19)	0.597
DASH								
Low	330/1204	1,476,138 (19.7)	1 [Reference]		1 [Reference]		1 [Reference]	
Intermediate	243/903	1,168,859 (19)	**0.73 (0.61, 0.86)**	**<0.001**	0.89 (0.74, 1.07)	0.221	0.86 (0.71, 1.04)	0.123
High	213/904	1,162,707 (17.1)	**0.56 (0.44, 0.70)**	**<0.001**	0.79 (0.61, 1.03)	0.081	0.78 (0.60, 1.00)	0.054
DASHI								
Low	269/1045	1,247,586 (18.3)	1 [Reference]		1 [Reference]		1 [Reference]	
Intermediate	225/928	1,101,753 (16.2)	0.96 (0.76, 1.21)	0.750	1.11 (0.90, 1.38)	0.335	1.09 (0.88, 1.35)	0.451
High	292/1038	1,458,365 (21.4)	0.86 (0.69, 1.08)	0.199	1.07 (0.84, 1.36)	0.564	1.03 (0.82, 1.31)	0.773
DII								
Low	224/916	1,179,275 (17.3)	1 [Reference]		1 [Reference]		1 [Reference]	
Intermediate	260/993	1,243,275 (18.3)	1.11 (0.92, 1.35)	0.284	1.12 (0.91, 1.37)	0.289	1.15 (0.94, 1.40)	0.166
High	302/1102	1,385,154 (20.4)	**1.31 (1.08, 1.59)**	**0.006**	1.17 (0.90, 1.52)	0.236	1.22 (0.94, 1.58)	0.134
DII (No EtOH)								
Low	225/930	1,174,171 (17.2)	1 [Reference]		1 [Reference]		1 [Reference]	
Intermediate	259/991	1,257,313 (18.5)	1.14 (0.93, 1.39)	0.212	1.18 (0.98, 1.42)	0.081	1.18 (0.98, 1.42)	0.073
High	302/1090	1,376,221 (20.2)	**1.33 (1.09, 1.63)**	**0.005**	1.25 (0.97, 1.62)	0.086	1.29 (1.00, 1.67)	0.052
Cancer mortality								

Table 2 (continued)

Mortality outcome	Death/No.	Weighted death (%)	Model 1		Model 2		Model 3	
			HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value
PHQ-9 score								
≥ 10	28/308	104,728 (5.6)	1 [Reference]		1 [Reference]		1 [Reference]	
5–9	46/480	228,739 (7.3)	0.95 (0.51, 1.77)	0.871	1.28 (0.69, 2.36)	0.431	1.32 (0.70, 2.51)	0.391
0–4	194/2223	903,677 (5.9)	0.67 (0.38, 1.18)	0.166	1.01 (0.58, 1.75)	0.971	1.05 (0.59, 1.87)	0.873
HEI-2020								
Low	116/1059	494,699 (7.3)	1 [Reference]		1 [Reference]		1 [Reference]	
Intermediate	68/962	330,043 (4.8)	**0.63 (0.40, 0.97)**	**0.038**	0.71 (0.45, 1.12)	0.139	0.71 (0.45, 1.12)	0.139
High	84/990	412,402 (6.1)	**0.63 (0.44, 0.89)**	**0.010**	0.85 (0.56, 1.28)	0.436	0.85 (0.56, 1.29)	0.446
AHEI								
Low	110/1068	454,774 (6.7)	1 [Reference]		1 [Reference]		1 [Reference]	
Intermediate	88/1007	398,275 (5.9)	0.77 (0.50, 1.19)	0.238	0.92 (0.59, 1.44)	0.728	0.93 (0.59, 1.45)	0.744
High	70/936	384,095 (5.6)	0.67 (0.45, 1.00)	0.050	0.95 (0.61, 1.49)	0.834	0.95 (0.60, 1.50)	0.833
aMED								
Low	140/1447	555,327 (5.7)	1 [Reference]		1 [Reference]		1 [Reference]	
Intermediate	65/643	342,582 (8.1)	1.25 (0.81, 1.95)	0.318	1.42 (0.92, 2.18)	0.113	1.39 (0.90, 2.15)	0.136
High	63/921	339,235 (5.2)	0.70 (0.48, 1.01)	0.057	0.93 (0.64, 1.36)	0.716	0.97 (0.66, 1.43)	0.880
MEDI								
Low	138/1509	586,227 (5.9)	1 [Reference]		1 [Reference]		1 [Reference]	
Intermediate	79/867	383,446 (6.4)	1.02 (0.75, 1.38)	0.907	1.13 (0.82, 1.56)	0.461	1.13 (0.84, 1.52)	0.429
High	51/635	267,471 (6)	0.95 (0.66, 1.36)	0.778	1.27 (0.86, 1.87)	0.235	1.29 (0.86, 1.92)	0.217
DASH								
Low	130/1204	553,848 (7.4)	1 [Reference]		1 [Reference]		1 [Reference]	
Intermediate	68/903	299,742 (4.9)	**0.52 (0.39, 0.71)**	**< 0.001**	**0.65 (0.48, 0.86)**	**0.003**	**0.66 (0.49, 0.89)**	**0.006**
High	70/904	383,554 (5.7)	**0.54 (0.38, 0.76)**	**< 0.001**	0.78 (0.53, 1.15)	0.213	0.78 (0.53, 1.15)	0.209
DASHI								
Low	96/1045	427,615 (6.3)	1 [Reference]		1 [Reference]		1 [Reference]	
Intermediate	75/928	343,012 (5)	0.83 (0.55, 1.25)	0.377	0.95 (0.62, 1.44)	0.796	0.94 (0.63, 1.41)	0.766
High	97/1038	466,517 (6.9)	0.86 (0.61, 1.20)	0.371	1.08 (0.76, 1.54)	0.669	1.07 (0.75, 1.53)	0.696
DII								
Low	74/916	384,409 (5.6)	1 [Reference]		1 [Reference]		1 [Reference]	
Intermediate	95/993	404,370 (5.9)	1.09 (0.79, 1.50)	0.603	1.14 (0.82, 1.58)	0.444	1.13 (0.81, 1.58)	0.462
High	99/1102	448,365 (6.6)	1.28 (0.91, 1.79)	0.156	1.20 (0.81, 1.78)	0.361	1.16 (0.79, 1.70)	0.439
DII (No EtOH)								
Low	75/930	391,981 (5.8)	1 [Reference]		1 [Reference]		1 [Reference]	
Intermediate	94/991	395,776 (5.8)	1.06 (0.76, 1.49)	0.726	1.13 (0.81, 1.58)	0.461	1.10 (0.79, 1.52)	0.573
High	99/1090	449,387 (6.6)	1.27 (0.90, 1.79)	0.169	1.24 (0.84, 1.84)	0.279	1.21 (0.82, 1.77)	0.344
Noncancer mortality								
PHQ-9 score								

Table 2 (continued)

Mortality outcome	Death/No.	Weighted death (%)	Model 1		Model 2		Model 3	
			HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value
≥ 10	46/308	236,339 (12.6)	1 [Reference]		1 [Reference]		1 [Reference]	
5–9	94/480	489,036 (15.6)	0.64 (0.40, 1.01)	0.053	0.73 (0.47, 1.15)	0.181	0.81 (0.51, 1.28)	0.366
0–4	378/2223	1,845,186 (12)	**0.41 (0.29, 0.60)**	**< 0.001**	**0.54 (0.36, 0.79)**	**0.002**	**0.62 (0.42, 0.92)**	**0.017**
HEI-2020								
Low	170/1059	776,403 (11.4)	1 [Reference]		1 [Reference]		1 [Reference]	
Intermediate	184/962	988,046 (14.5)	1.16 (0.88, 1.51)	0.297	1.33 (1.00, 1.78)	0.052	1.27 (0.95, 1.69)	0.108
High	164/990	806,111 (11.9)	**0.68 (0.52, 0.89)**	**0.005**	0.91 (0.67, 1.22)	0.522	0.84 (0.63, 1.14)	0.265
AHEI								
Low	198/1068	931,754 (13.6)	1 [Reference]		1 [Reference]		1 [Reference]	
Intermediate	170/1007	869,908 (12.8)	0.79 (0.61, 1.01)	0.06	0.91 (0.69, 1.21)	0.531	0.90 (0.68, 1.18)	0.435
High	150/936	768,899 (11.3)	**0.59 (0.44, 0.78)**	**< 0.001**	0.80 (0.59, 1.08)	0.147	0.78 (0.57, 1.05)	0.104
aMED								
Low	260/1447	1,284,510 (13.3)	1 [Reference]		1 [Reference]		1 [Reference]	
Intermediate	114/643	543,507 (12.9)	0.78 (0.58, 1.04)	0.089	0.88 (0.65, 1.20)	0.418	0.86 (0.63, 1.17)	0.326
High	144/921	742,543 (11.3)	**0.58 (0.47, 0.73)**	**< 0.001**	**0.74 (0.57, 0.96)**	**0.025**	**0.74 (0.57, 0.96)**	**0.023**
MEDI								
Low	290/1509	1,430,367 (14.4)	1 [Reference]		1 [Reference]		1 [Reference]	
Intermediate	145/867	725,989 (12)	0.82 (0.64, 1.05)	0.113	0.91 (0.71, 1.16)	0.43	0.84 (0.66, 1.07)	0.156
High	83/635	414,204 (9.3)	**0.63 (0.49, 0.82)**	**0.001**	0.84 (0.64, 1.10)	0.207	0.81 (0.62, 1.07)	0.136
DASH								
Low	200/1204	922,290 (12.3)	1 [Reference]		1 [Reference]		1 [Reference]	
Intermediate	175/903	869,117 (14.1)	0.84 (0.67, 1.05)	0.127	1.02 (0.81, 1.30)	0.838	0.97 (0.76, 1.23)	0.781
High	143/904	779,153 (11.5)	**0.57 (0.43, 0.77)**	**< 0.001**	0.80 (0.58, 1.10)	0.173	0.78 (0.57, 1.06)	0.117
DASHI								
Low	173/1045	819,971 (12)	1 [Reference]		1 [Reference]		1 [Reference]	
Intermediate	150/928	758,741 (11.2)	1.04 (0.79, 1.37)	0.759	1.22 (0.95, 1.58)	0.124	1.20 (0.92, 1.55)	0.171
High	195/1038	991,848 (14.6)	0.86 (0.66, 1.13)	0.279	1.07 (0.79, 1.44)	0.666	1.02 (0.77, 1.35)	0.904
DII								
Low	150/916	794,866 (11.7)	1 [Reference]		1 [Reference]		1 [Reference]	
Intermediate	165/993	838,905 (12.3)	1.12 (0.85, 1.47)	0.408	1.11 (0.84, 1.46)	0.478	1.17 (0.89, 1.53)	0.265
High	203/1102	936,789 (13.8)	1.32 (1.02, 1.71)	0.037	1.15 (0.82, 1.61)	0.403	1.24 (0.89, 1.72)	0.207
DII (No EtOH)								
Low	150/930	782,189 (11.5)	1 [Reference]		1 [Reference]		1 [Reference]	

Table 2 (continued)

Mortality outcome	Death/No.	Weighted death (%)	Model 1		Model 2		Model 3	
			HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Intermediate	165/991	861,537 (12.7)	1.16 (0.88, 1.54)	0.284	1.20 (0.92, 1.57)	0.177	1.23 (0.95, 1.60)	0.121
High	203/1090	926,834 (13.6)	**1.35 (1.04, 1.77)**	**0.025**	1.26 (0.90, 1.75)	0.178	1.33 (0.95, 1.84)	0.093

Notes: Model 1: adjusted for age; Model 2: additionally adjusted for sex, race, BMI, education level, marital status, family income poverty ratio, health insurance coverage, smoking status, alcohol use, sleep duration, and energy intake; Model 3: additionally adjusted for hypertension, hypercholesterolemia, diabetes, CVD, the number of cancer types, and years since first cancer diagnosis. The dietary health indices were divided into low, intermediate and high categories based on the weighted tertile values

Abbreviations: PHQ-9 score, Patient Health Questionnaire-9 score; NHANES, the National Health and Nutrition Examination Survey; HR, hazard ratio; CI, confidence interval; BMI, body mass index; CVD, cardiovascular disease; HEI-2020, Healthy Eating Index-2020; HEI-2015, Healthy Eating Index-2015; AHEI, Alternative Healthy Eating Index; aMED, Alternate Mediterranean Diet Score; MEDI, MED Index in serving sizes from the PREDIMED trial; DASH, Dietary Approaches to Stop Hypertension Index; DASHI, DASH Index in serving sizes from the DASH trial; DII, Dietary Inflammation Index; EtOH, alcohol

findings are exploratory and should be interpreted with caution. The results were similar when different sets of covariates were adjusted (Figure S4, S5, S6, S7).

Subgroup analysis

For the independent effects of depressive symptoms and dietary patterns on mortality, noteworthy differences were observed in subgroup analysis of sex (Table S4), cancer type (Table S5), and health conditions (Table S6, S7, S8, S9). In contrast to male cancer survivors, whose risk patterns were similar to the overall population, most of the dietary pattern indices were observed to have a pronounced influence on the risk of all-cause or noncancer mortality in female participants. In subgroup analysis of nine cancer types, lower PHQ-9 scores were linked to improved survival in survivors with respiratory system tumors, gastrointestinal tumors, and multiple tumors, but showed no impact on survival in other cancer types. Moreover, high levels of DII increased the risk of mortality for survivors with gastrointestinal tumors, gynecologic tumors, and multiple tumors. Depressive symptoms and dietary patterns seemed less likely to greatly influence the survival of participants with urologic tumors, skin tumors, or head, neck and other tumors. Subgroup analysis of health conditions revealed that adherence to DASH was beneficial to outcomes of cancer survivals with hypertension or diabetes, and adherence to the AHEI improved outcomes in those with diabetes. Regarding the combined effects of depressive symptoms and dietary patterns on mortality, the results were observed to be more consistent with the overall population in female survivors, compared to male participants (Figure S8, S9). The combined effects differed depending on the health conditions of cancer survivors (Figure S10-S17). Given the limited case numbers in some combination groups, the subgroup analysis of joint associations should be viewed as exploratory and interpreted cautiously.

Shapes of the relationship between PHQ-9 score, dietary pattern indices, and mortality

As demonstrated in Fig. 4, after fully adjusted for potential confounders, RCS showed a linear association between PHQ-9 score and risk of all-cause mortality ($P_{non-linearity}$ = 0.277), with rising HRs as PHQ-9 score increased. No nonlinear associations between dietary pattern indices and all-cause mortality were observed. Similar results were observed when examining nonlinear associations with cancer-specific and non-cancer mortality (Figure S18, S19).

Joint exposures	HR (95% CI)	All−cause mortality	P value	HR (95% CI)	Cancer mortality	P value	HR (95% CI)	Noncancer mortality	P value
HEI−2020									
Low, PHQ−9 ≥ 10	1 [Reference]			1 [Reference]			1 [Reference]		
Intermediate, PHQ−9 ≥ 10	0.56 (0.28, 1.11)		0.095	0.86 (0.28, 2.68)		0.793	0.43 (0.19, 0.96)		0.039
High, PHQ−9 ≥ 10	0.38 (0.19, 0.75)		0.005	0.64 (0.21, 1.96)		0.435	0.28 (0.12, 0.69)		0.006
Low, PHQ−9 5−9	0.77 (0.39, 1.53)		0.459	1.57 (0.55, 4.54)		0.401	0.52 (0.23, 1.14)		0.100
Intermediate, PHQ−9 5−9	0.55 (0.31, 0.97)		0.038	0.73 (0.30, 1.79)		0.493	0.44 (0.22, 0.87)		0.018
High, PHQ−9 5−9	0.60 (0.33, 1.10)		0.097	1.13 (0.46, 2.76)		0.787	0.43 (0.22, 0.84)		0.014
Low, PHQ−9 0−4	0.46 (0.27, 0.78)		0.004	1.01 (0.45, 2.26)		0.983	0.29 (0.16, 0.55)		<0.001
Intermediate, PHQ−9 0−4	0.58 (0.34, 1.02)		0.059	0.77 (0.34, 1.75)		0.535	0.48 (0.25, 0.93)		0.030
High, PHQ−9 0−4	0.43 (0.24, 0.75)		0.003	0.90 (0.37, 2.18)		0.818	0.29 (0.15, 0.55)		<0.001
AHEI									
Low, PHQ−9 ≥ 10	1 [Reference]			1 [Reference]			1 [Reference]		
Intermediate, PHQ−9 ≥ 10	0.85 (0.39, 1.83)		0.676	1.03 (0.34, 3.17)		0.957	0.81 (0.28, 2.35)		0.699
High, PHQ−9 ≥ 10	0.52 (0.26, 1.05)		0.068	1.06 (0.27, 4.10)		0.935	0.37 (0.17, 0.82)		0.014
Low, PHQ−9 5−9	0.84 (0.47, 1.49)		0.555	1.61 (0.55, 4.73)		0.386	0.61 (0.31, 1.19)		0.146
Intermediate, PHQ−9 5−9	0.90 (0.48, 1.68)		0.743	1.41 (0.54, 3.73)		0.485	0.73 (0.36, 1.49)		0.393
High, PHQ−9 5−9	0.52 (0.30, 0.91)		0.022	0.92 (0.33, 2.61)		0.879	0.39 (0.20, 0.76)		0.006
Low, PHQ−9 0−4	0.62 (0.38, 1.02)		0.060	1.06 (0.43, 2.61)		0.891	0.48 (0.28, 0.83)		0.009
Intermediate, PHQ−9 0−4	0.56 (0.35, 0.89)		0.014	1.00 (0.41, 2.43)		0.993	0.42 (0.24, 0.73)		0.002
High, PHQ−9 0−4	0.57 (0.34, 0.97)		0.037	1.12 (0.44, 2.90)		0.809	0.42 (0.23, 0.76)		0.004
aMED									
Low, PHQ−9 ≥ 10	1 [Reference]			1 [Reference]			1 [Reference]		
Intermediate, PHQ−9 ≥ 10	1.63 (0.78, 3.42)		0.193	1.70 (0.51, 5.66)		0.391	1.65 (0.55, 4.90)		0.369
High, PHQ−9 ≥ 10	0.61 (0.31, 1.19)		0.149	0.73 (0.21, 2.52)		0.620	0.57 (0.25, 1.32)		0.190
Low, PHQ−9 5−9	1.09 (0.67, 1.75)		0.737	1.48 (0.57, 3.85)		0.417	0.93 (0.53, 1.62)		0.793
Intermediate, PHQ−9 5−9	0.85 (0.48, 1.50)		0.574	1.35 (0.55, 3.32)		0.507	0.66 (0.34, 1.30)		0.231
High, PHQ−9 5−9	0.77 (0.44, 1.38)		0.384	1.27 (0.51, 3.13)		0.607	0.61 (0.31, 1.20)		0.149
Low, PHQ−9 0−4	0.75 (0.50, 1.13)		0.167	0.99 (0.48, 2.03)		0.970	0.65 (0.40, 1.05)		0.081
Intermediate, PHQ−9 0−4	0.78 (0.51, 1.19)		0.246	1.48 (0.68, 3.22)		0.324	0.56 (0.34, 0.91)		0.019
High, PHQ−9 0−4	0.64 (0.42, 0.98)		0.038	1.01 (0.45, 2.31)		0.972	0.51 (0.32, 0.82)		0.005
MEDI									
Low, PHQ−9 ≥ 10	1 [Reference]			1 [Reference]			1 [Reference]		
Intermediate, PHQ−9 ≥ 10	1.06 (0.55, 2.06)		0.859	1.70 (0.59, 4.91)		0.330	0.89 (0.36, 2.19)		0.802
High, PHQ−9 ≥ 10	1.22 (0.53, 2.84)		0.638	3.50 (1.05, 11.65)		0.041	0.63 (0.21, 1.87)		0.401
Low, PHQ−9 5−9	1.15 (0.72, 1.85)		0.557	2.21 (0.96, 5.08)		0.062	0.86 (0.49, 1.52)		0.600
Intermediate, PHQ−9 5−9	0.77 (0.39, 1.51)		0.448	1.81 (0.68, 4.84)		0.238	0.52 (0.25, 1.10)		0.088
High, PHQ−9 5−9	0.93 (0.49, 1.78)		0.838	1.77 (0.57, 5.50)		0.321	0.70 (0.36, 1.37)		0.297
Low, PHQ−9 0−4	0.79 (0.51, 1.22)		0.282	1.45 (0.69, 3.08)		0.328	0.59 (0.37, 0.96)		0.033
Intermediate, PHQ−9 0−4	0.77 (0.50, 1.20)		0.250	1.71 (0.83, 3.52)		0.143	0.54 (0.33, 0.87)		0.011
High, PHQ−9 0−4	0.75 (0.47, 1.21)		0.246	1.88 (0.80, 4.47)		0.150	0.50 (0.29, 0.87)		0.014
DASH									
Low, PHQ−9 ≥ 10	1 [Reference]			1 [Reference]			1 [Reference]		
Intermediate, PHQ−9 ≥ 10	0.63 (0.35, 1.14)		0.125	0.15 (0.04, 0.66)		0.011	0.98 (0.44, 2.17)		0.965
High, PHQ−9 ≥ 10	0.39 (0.18, 0.83)		0.014	0.19 (0.04, 0.85)		0.029	0.49 (0.20, 1.24)		0.132
Low, PHQ−9 5−9	0.78 (0.45, 1.37)		0.390	0.71 (0.29, 1.73)		0.452	0.83 (0.40, 1.71)		0.611
Intermediate, PHQ−9 5−9	0.75 (0.41, 1.36)		0.339	0.69 (0.26, 1.84)		0.452	0.78 (0.38, 1.56)		0.479
High, PHQ−9 5−9	0.57 (0.30, 1.05)		0.072	0.84 (0.37, 1.89)		0.675	0.46 (0.20, 1.04)		0.063
Low, PHQ−9 0−4	0.60 (0.36, 0.98)		0.041	0.70 (0.36, 1.35)		0.282	0.55 (0.29, 1.07)		0.077
Intermediate, PHQ−9 0−4	0.52 (0.32, 0.86)		0.011	0.48 (0.25, 0.93)		0.031	0.54 (0.28, 1.05)		0.070
High, PHQ−9 0−4	0.51 (0.30, 0.86)		0.011	0.55 (0.26, 1.16)		0.116	0.49 (0.25, 0.96)		0.038
DASHI									
Low, PHQ−9 ≥ 10	1 [Reference]			1 [Reference]			1 [Reference]		
Intermediate, PHQ−9 ≥ 10	1.32 (0.68, 2.54)		0.412	0.60 (0.20, 1.76)		0.349	1.91 (0.85, 4.25)		0.116
High, PHQ−9 ≥ 10	0.51 (0.26, 0.99)		0.047	0.41 (0.14, 1.18)		0.098	0.60 (0.25, 1.41)		0.242
Low, PHQ−9 5−9	0.73 (0.41, 1.31)		0.292	0.61 (0.24, 1.55)		0.294	0.81 (0.41, 1.62)		0.552
Intermediate, PHQ−9 5−9	0.95 (0.48, 1.89)		0.889	0.71 (0.22, 2.34)		0.574	1.13 (0.49, 2.56)		0.779
High, PHQ−9 5−9	1.06 (0.59, 1.89)		0.847	1.27 (0.49, 3.25)		0.623	1.00 (0.52, 1.90)		0.989
Low, PHQ−9 0−4	0.71 (0.44, 1.16)		0.172	0.71 (0.33, 1.53)		0.380	0.73 (0.40, 1.34)		0.308
Intermediate, PHQ−9 0−4	0.71 (0.42, 1.19)		0.194	0.68 (0.29, 1.58)		0.368	0.76 (0.42, 1.37)		0.357
High, PHQ−9 0−4	0.71 (0.42, 1.19)		0.192	0.71 (0.30, 1.65)		0.419	0.72 (0.39, 1.35)		0.309
DII									
Low, PHQ−9 ≥ 10	1 [Reference]			1 [Reference]			1 [Reference]		
Intermediate, PHQ−9 ≥ 10	0.97 (0.37, 2.58)		0.954	0.78 (0.19, 3.13)		0.725	1.13 (0.30, 4.26)		0.854
High, PHQ−9 ≥ 10	0.81 (0.37, 1.75)		0.588	0.93 (0.28, 3.12)		0.906	0.78 (0.28, 2.18)		0.631
Low, PHQ−9 5−9	0.64 (0.30, 1.39)		0.261	0.76 (0.22, 2.65)		0.663	0.58 (0.21, 1.58)		0.288
Intermediate, PHQ−9 5−9	1.06 (0.53, 2.13)		0.872	1.94 (0.67, 5.59)		0.221	0.79 (0.28, 2.25)		0.655
High, PHQ−9 5−9	0.93 (0.41, 2.10)		0.858	1.07 (0.30, 3.82)		0.916	0.87 (0.32, 2.38)		0.785
Low, PHQ−9 0−4	0.60 (0.31, 1.16)		0.131	0.90 (0.33, 2.44)		0.841	0.50 (0.19, 1.29)		0.153
Intermediate, PHQ−9 0−4	0.65 (0.33, 1.31)		0.229	0.88 (0.30, 2.56)		0.814	0.58 (0.22, 1.49)		0.254
High, PHQ−9 0−4	0.73 (0.37, 1.42)		0.350	1.05 (0.40, 2.76)		0.920	0.61 (0.24, 1.56)		0.301
DII (No EtOH)									
Low, PHQ−9 ≥ 10	1 [Reference]			1 [Reference]			1 [Reference]		
Intermediate, PHQ−9 ≥ 10	1.00 (0.37, 2.65)		0.993	0.84 (0.20, 3.46)		0.811	1.14 (0.31, 4.20)		0.847
High, PHQ−9 ≥ 10	0.91 (0.41, 2.00)		0.810	1.04 (0.31, 3.51)		0.954	0.86 (0.30, 2.44)		0.780
Low, PHQ−9 5−9	0.67 (0.31, 1.47)		0.316	0.8 0(0.23, 2.77)		0.719	0.60 (0.22, 1.65)		0.324
Intermediate, PHQ−9 5−9	1.13 (0.56, 2.30)		0.731	2.08 (0.72, 6.02)		0.176	0.83 (0.28, 2.43)		0.736
High, PHQ−9 5−9	1.01 (0.46, 2.22)		0.979	1.19 (0.34, 4.13)		0.789	0.93 (0.35, 2.50)		0.891
Low, PHQ−9 0−4	0.62 (0.32, 1.22)		0.166	0.98 (0.36, 2.66)		0.969	0.50 (0.19, 1.31)		0.160
Intermediate, PHQ−9 0−4	0.70 (0.35, 1.37)		0.298	0.90 (0.32, 2.58)		0.850	0.62 (0.24, 1.56)		0.308
High, PHQ−9 0−4	0.79 (0.40, 1.58)		0.509	1.16 (0.43, 3.14)		0.764	0.66 (0.25, 1.71)		0.389

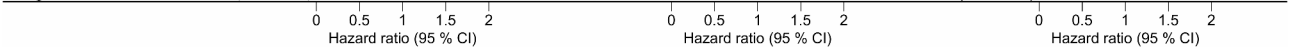

Fig. 2 (See legend on next page.)

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Fig. 2 Joint association of PHQ-9 score and dietary health with all-cause, cancer, and noncancer mortality among US cancer survivors, fully adjusted, NHANES 2005–2018. When the forest plot does not cross the reference line at HR = 1, the result is statistically significant; crossing the line indicates non-significance. The results were adjusted for age, sex, race, BMI, education level, marital status, family income poverty ratio, health insurance coverage, smoking status, alcohol use, sleep duration, energy intake, hypertension, hypercholesterolemia, diabetes, CVD, the number of cancer types and years since first cancer diagnosis. Abbreviations: PHQ-9 score, Patient Health Questionnaire-9 score; NHANES, the National Health and Nutrition Examination Survey; HR, hazard ratio; CI, confidence interval; BMI, body mass index; CVD, cardiovascular disease; HEI-2020, Healthy Eating Index-2020; AHEI, Alternative Healthy Eating Index; aMED, Alternate Mediterranean Diet Score; MEDI, MED Index in serving sizes from the PREDIMED trial; DASH, Dietary Approaches to Stop Hypertension Index; DASHI, DASH Index in serving sizes from the DASH trial; DII, Dietary Inflammation Index; EtOH, alcohol

Sensitivity analysis

Sensitivity analyses were performed to examine the robustness of independent and combined associations of depressive symptoms and dietary patterns with risk of all-cause, cancer-specific, and noncancer mortality. All results remained similar when using dietary data from two 24-hour dietary recall interviews (Table S10, Figure S20), excluding participants died within 2 years of follow-up (Table S11, Figure S21), or excluding participants with missing covariates (Table S10, Figure S22).

Discussion

In this population-based study, we comprehensively evaluated the independent and combined effects of depressive symptoms (PHQ-9 score) and dietary patterns (HEI-2020, HEI-2015, AHEI, aMED, MEDI, DASH, DASHI, DII, and DII [No EtOH]) in a cohort of US cancer survivors from NHANES 2005–2018. Our findings revealed the independent contributions of improved mood and healthier dietary patterns to reduced mortality among cancer survivors. Specifically, adherence to the DASH and aMED diets was identified as promising dietary strategies for cancer patients to reduce cancer-specific and noncancer mortality, respectively. For the combined effects of depressive symptoms and dietary patterns, we observed that participants with lower PHQ-9 scores and higher scores on the HEI-2020, AHEI, aMED or DASH, had lower risks of all-cause and noncancer mortality, compared to those with elevated depressive symptoms and low adherence to these diets. Of note, the results showed substantial disparities when stratified by sex, cancer type, and health conditions. To our knowledge, this examination is the first one to investigate the joint effect of depressive symptoms and dietary patterns on mortality among cancer survivors.

Previous studies have documented a higher probability of developing psychological distress among cancer patients during diagnosis and treatment, with about 22.6% of them experiencing depressive symptoms [13, 36]. To be specific, a meta-analysis of 94 interview-based studies demonstrated that the prevalence of clinically diagnosed depression was 16.5% for individuals with cancer in palliative-care settings, and 16.3% for those in oncological and hematological settings [13]. Among the cancer survivors selected from the NHANES population, approximately 9.18%, 15.38%, and 75.45% of them showed moderate to severe (≥ 10), mild (5–9), and no to minimal (0–4) depressive symptoms (defined by PHQ-9 score), respectively. The variations observed might be due to the difference in interview settings, characteristics of participants, and the depression assessment instruments employed. Considering the high prevalence of depressive symptoms in cancer patients, close monitoring and early mental intervention are essential for effective treatment and improving quality of life. Moreover, our findings suggested that cancer survivors with a low level of PHQ-9 score (0–4) had a reduction in all-cause and noncancer mortality by 28% and 39%, respectively, in comparison with those with a PHQ-9 score of ≥ 10. A prior meta-analysis of cohort studies showed that depression and anxiety predicted poorer overall survival of individuals with cancer, with risk ratio (RR) of 1.26 (95% CI: 1.14–1.39) [14]. The site-specific analysis of four cancer types found a significant association only among lung cancer survivors [14]. Their research included a heterogeneous population and did not distinguish between depression and anxiety, whereas ours offered new evidence regarding depressive symptoms in a nationally representative cancer population. Of note, we observed a stronger association between depressive symptoms and mortality in males compared to females. Additionally, our subgroup analysis of nine cancer types identified PHQ-9 scores as prognostic factors for survival of patients with respiratory system tumors, gastrointestinal tumors, and multiple tumors. Our findings highlighted the importance of depression detection and timely intervention, particularly in high-risk cancer patients.

Meanwhile, the prognostic value of nutrition and dietary patterns among cancer populations has been explored [8, 9, 37]. Dietary restriction or supplementation of several nutrients were reported to affect the efficiency of cancer therapies and long-term outcomes, such as glucose restriction and histidine supplementation [37]. Considering that people do not uptake nutrients in isolation, dietary patterns were highly valued, which provided a more comprehensive reflection and quantification of the cumulative influence of various foods [38]. To systematically evaluate the impact of

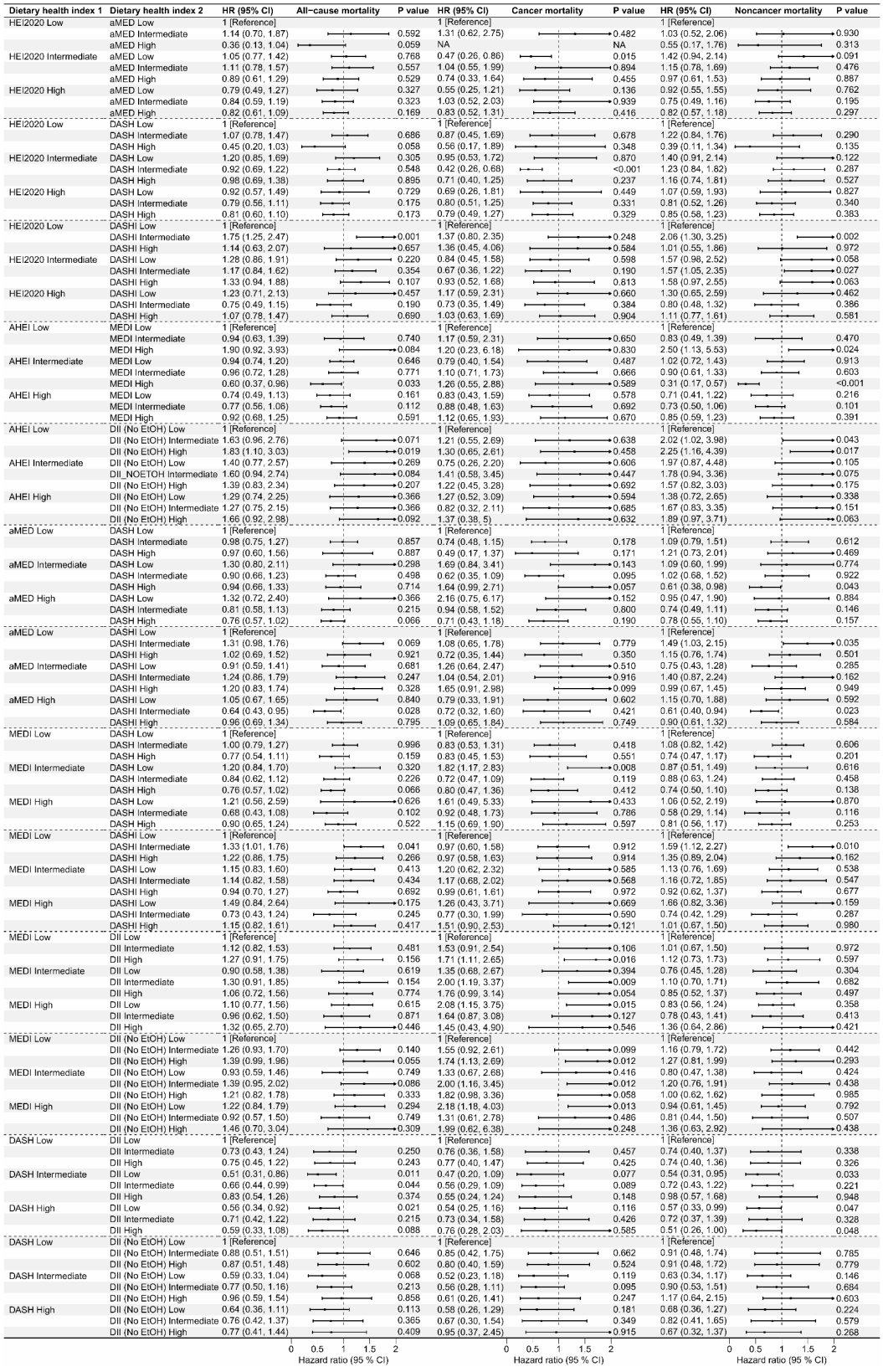

Fig. 3 (See legend on next page.)

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Fig. 3 Joint association of different dietary health Indices with all-cause, cancer, and noncancer mortality among US cancer survivors, fully adjusted, NHANES 2005–2018. When the forest plot does not cross the reference line at HR = 1, the result is statistically significant; crossing the line indicates non-significance. The results were adjusted for age, sex, race, BMI, education level, marital status, family income poverty ratio, health insurance coverage, smoking status, alcohol use, sleep duration, energy intake, hypertension, hypercholesterolemia, diabetes, CVD, the number of cancer types and years since first cancer diagnosis. Abbreviations: NHANES, the National Health and Nutrition Examination Survey; HR, hazard ratio; CI, confidence interval; BMI, body mass index; CVD, cardiovascular disease; HEI-2020, Healthy Eating Index-2020; AHEI, Alternative Healthy Eating Index; aMED, Alternate Mediterranean Diet Score; MEDI, MED Index in serving sizes from the PREDIMED trial; DASH, Dietary Approaches to Stop Hypertension Index; DASHI, DASH Index in serving sizes from the DASH trial; DII, Dietary Inflammation Index; EtOH, alcohol

dietary patterns on mortality, several well-developed dietary indices were selected as the assessment tools in this study, including HEI-2020, AHEI, aMED, MEDI, DASH, DASHI, DII, and DII (No EtOH). The HEI-2020 served as a tool to assess alignment with the 2020–2025 Dietary Guidelines for Americans (DGA) among individuals aged 2 years old and older, comprising 13 components designed to reflect the overall diet quality [26]. Meanwhile, the AHEI was introduced as a refined alternative to the Healthy Eating Index (HEI), offering more detailed dietary measures that are predictive of chronic disease risk [28]. Hower, the effects of HEI-2020 and AHEI on survival of cancer patients remained insufficiently understood [9, 21]. Our analysis indicated that higher HEI-2020 and AHEI scores were linked to a lower risk of mortality in female cancer survivors, but no such association was observed in males or the overall population. This difference highlights the sex-specific impact of dietary health, pointing to the necessity of further exploration in future research. Moreover, adherence to a Mediterranean diet has been demonstrated to extend lifespan and lower mortality rates in both the general population and among cancer patients [19, 21]. Our research employed the aMED and MEDI indices to evaluate adherence to a Mediterranean diet, corroborating previous findings and identifying stronger associations in survivors of gastrointestinal, breast, and multiple tumors. The DASH and DASHI indices were initially developed to manage hypertension and reduce the risk of CVD, while their investigation in relation to mortality from various cancers has been limitedly [21, 31–33]. We observed that intermediate DASH scores were associated with a nearly 33% reduction in cancer mortality among cancer patients, compared to low scores. Notably, the DASH is the only dietary pattern index identified in this study that was found to influence cancer-specific mortality in the overall survivor population. Furthermore, we explored the association between the inflammatory potential of diet and survival, using the DII and its variant excluding alcohol (DII [No EtOH]) [34]. Previous studies have yielded conflicting results, often limited by sample size, confounding factors, and insufficient follow-up time. Our findings revealed that the negative impact of a pro-inflammatory diet was more pronounced in female populations. In general, given the limited prior evidence on the association between various dietary patterns and cancer survivor mortality, our findings offered novel and valuable insights into this relationship and were expected to inform future dietary strategies and improve long-term outcomes of cancer patients.

To our knowledge, the current study is the first one to evaluate the combined effects of depressive symptoms and dietary patterns on mortality, especially in a nationally representative sample of cancer survivors. Since approximately one in every five individuals with cancer encountered depressive symptoms [36], and energy and nutrient intake was primarily derived from diet, numerous studies have investigated the independent effects of depression or diet on cancer patient outcomes [8, 10, 39]. Actually, prior research has also observed the tight correlations between depression and diet. Individuals experiencing severe depressive symptoms tended to develop unhealthy dietary habits, characterized by increased consumption of fast food, fried foods, sugary products, and ultra-processed items [40]. Meanwhile, healthier dietary patterns, such as a high adherence to the Mediterranean diet and anti-inflammatory diet, were beneficial for prevention of depression [22, 41]. However, research on their combined effects appeared to be limited. Our study was thereby designed to fill the research gaps, and is the first to demonstrate that cancer survivors with moderate to severe depression (PHQ-9 score ≥ 10), combined with a low adherence to healthy dietary patterns, are at an elevated risk of mortality. Specifically, lower PHQ-9 scores combined with higher adherence to the HEI-2020, AHEI, aMED, or DASH were associated with decreased risks of all-cause and noncancer mortality. Furthermore, to understand dietary patterns in-depth, we exploratively examined whether the combination of two dietary pattern indices could serve as a viable prognostic factor. Our explorations revealed the potential of combining two or more dietary indices, or developing a new one, to guide targeted dietary strategies for cancer patients. Further research is needed to confirm these findings.

Several plausible biological and behavioral mechanisms might help to explain the observed impact of depression and diet in this study. Depressive symptoms could disturb the hypothalamic-pituitary-adrenal

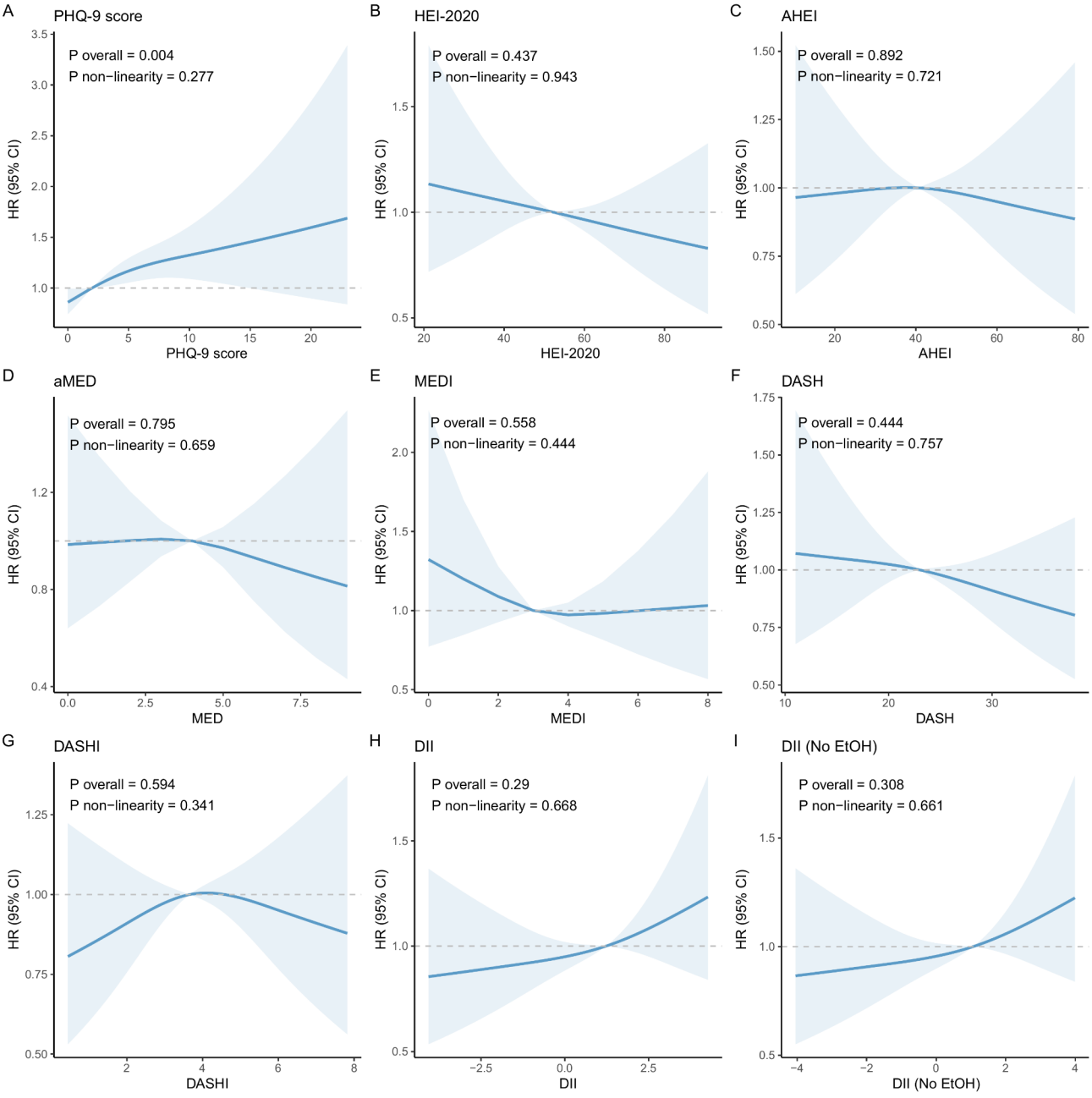

Fig. 4 Shapes of the association of PHQ-9 score and dietary health with all-cause mortality among US cancer survivors, fully adjusted, NHANES 2005–2018. The results were adjusted for age, sex, race, BMI, education level, marital status, family income poverty ratio, health insurance coverage, smoking status, alcohol use, sleep duration, energy intake, hypertension, hypercholesterolemia, diabetes, CVD, the number of cancer types and years since first cancer diagnosis. Abbreviations: PHQ-9 score, Patient Health Questionnaire-9 score; NHANES, the National Health and Nutrition Examination Survey; HR, hazard ratio; CI, confidence interval; BMI, body mass index; CVD, cardiovascular disease; HEI-2020, Healthy Eating Index-2020; AHEI, Alternative Healthy Eating Index; aMED, Alternate Mediterranean Diet Score; MEDI, MED Index in serving sizes from the PREDIMED trial; DASH, Dietary Approaches to Stop Hypertension Index; DASHI, DASH Index in serving sizes from the DASH trial; DII, Dietary Inflammation Index; EtOH, alcohol

(HPA) axis [42], suppress the function of immune cell and DNA repair enzymes [43], and coincide with more unhealthy lifestyle habits (such as smoking, alcohol abuse, and sedentary activities) [44]. Moreover, growing evidence on cancer metabolism has emphasized the critical role of nutritional factors in supporting cancer growth and survival. Dietary modifications could restrict nutritional requirements of tumors, induce selective vulnerabilities of cancer cells, or enhance the efficacy of anti-tumor drugs [37, 45]. Considering that both psychological and nutritional status affected the whole-body systems, there might

be shared mechanisms to underlie their joint effects on survival of cancer patients.

This study has several strengths. The key advantage is that we selected cancer survivors from the NHANES 2005–2018, which offered a prospective cohort, large sample size, rigorous measurement accuracy, and representation of the whole US cancer patients. Second, we comprehensively evaluated the independent and joint associations of depressive symptoms and eight different dietary pattern indices with all-cause, cancer-specific, and noncancer mortality among the overall and subgroup-specific cancer patients. Third, the utilization of multiple imputation by chained equations effectively addressed missing data, reduced bias, and preserved statistical power for more reliable results. Fourth, sensitivity analysis of three groups of participants was performed to verify the robustness of the primary analysis. Some limitations are also noted. First, while NHANES provides a representative sample of the US population, the study population of cancer survivors may not fully reflect the broader cancer survivor population due to the relatively small sample size. Future studies with larger, more specific cancer survivor cohorts are needed to further validate and refine these findings. Second, the dietary data used in this study were derived from one or two 24-hour recalls, which may not fully capture the dietary patterns over the entire follow-up period. Third, due to lack of certain nutrient information, the calculation of certain dietary pattern indices generated results that were specific to our study population. We categorized all indices into tertiles for convenience of comparisons. Moreover, NHANES did not collect information on cancer stages or treatments, as it was not intended to function as a cancer-specific database. Finally, as the study population was restricted to US cancer survivors, additional research is necessary to validate our results in diverse populations.

Conclusions

In conclusion, this population-based study of US cancer survivors demonstrated that the combinations of depressive symptoms and certain dietary patterns were associated with risks of all-cause, cancer-specific, and noncancer mortality among individuals with cancer. Of note, pronounced disparities were observed when stratified by sex, cancer type, and health conditions. Early assessment of depressive symptoms and development of individualized dietary strategies are of great importance to reduce long-term mortality risk of cancer survivors and improve their quality of life.

Abbreviations

ACS	American Cancer Society
AHEI	Alternative Healthy Eating Index
aMED	Alternate Mediterranean Diet Score
ASCO	American Society for Clinical Oncology
BMI	Body mass index
CDC	Centers for Disease Control and Prevention
CI	Confidence interval
CVD	Cardiovascular disease
DASH	Dietary Approaches to Stop Hypertension Index
DASHI	DASH Index in serving sizes from the DASH trial
DII	Dietary Inflammation Index
HEI-2020	Healthy Eating Index-2020
HR	Hazard ratio
ICD	International Statistical Classification of Diseases
MEC	Mobile Examination Center
MEDI	MED Index in serving sizes from the PREDIMED trial
NHANES	National Health and Nutrition Examination Survey
No	EtOH, DII excluding alcohol
PHQ-9	Patient Health Questionnaire

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12885-025-13945-z.

Supplementary Material 1

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Author contributions

LXL, ZYL and CY contributed to the project development, authored the initial manuscript draft, and validated the underlying data. ZYL and YLS were involved in data collection. ZYL, CY and JQH played roles in the statistical analyses. JLL, JZ and QP contributed to the data interpretation. All authors participated in manuscript revisions and provided approval for the final version. The guarantor (LXL) has confirmed that all listed authors meet the authorship criteria, and no eligible contributors have been omitted.

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Data availability

Data are available in a public, open access repository. To access the data and reference documents used in this study, please visit the website of NHANES (https://wwwn.cdc.gov/nchs/nhanes/default.aspx).

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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