BMC Cancer

RESEARCH

Open Access

The association between life's crucial 9 and all-cause, cancer-specific and cardiovascular mortality in US cancer survivors: a cohort study of NHANES

Hongyang Gong[1†], Ming Gao[2†] and Zhiwen Zeng[3,4*]

Abstract

Background Life's Crucial 9 (LC9) is a recently proposed cardiovascular health (CVH) scoring system that integrates psychological well-being with Life's Essential 8 (LE8). However, its prognostic value remains unclear. This study aims to investigate the association between LC9 and outcomes among cancer survivors.

Methods A total of 2,558 cancer survivors from the National Health and Nutrition Examination Survey (NHANES) 2005–2018 were included in this study. LC9, representing a dimension of psychological health, was calculated as the average of the LE8 score and the depression score. Cox proportional hazards regression, restricted cubic spline (RCS) analysis, subgroup analysis, and Kaplan-Meier survival curves were employed to evaluate the association between LC9 and mortality risk, with adjustments for potential confounders.

Results During an average follow-up period of 80 months, 640 deaths occurred, including 205 from cancer and 128 from cardiovascular disease. After adjusting for all covariates using Cox regression, a 10-point increase in the LC9 score was associated with a 24% reduction in all-cause mortality (HR: 0.76; 95% CI: 0.68–0.84), a 19% reduction in cancer-specific mortality (HR: 0.81; 95% CI: 0.68–0.97), and a 28% reduction in cardiovascular mortality (HR: 0.72; 95% CI: 0.58–0.90). Kaplan-Meier survival curves indicated lower rates of all-cause, cancer-specific, and cardiovascular mortality among participants with higher LC9 scores. RCS analysis revealed a linear inverse association between LC9 and all-cause and cancer-specific mortality and a nonlinear inverse association with cardiovascular mortality.

Conclusion Among cancer survivors in the United States, higher LC9 scores were independently associated with lower risks of all-cause, cancer-specific, and cardiovascular mortality. This finding highlights the potential link between cardiovascular health and survival outcomes in cancer survivors, suggesting that improving cardiovascular health may serve as an important preventive strategy to enhance survival rates in this population.

Keywords Life's crucial 9, Cancer survivors, All-cause mortality, Cancer-specific mortality, Cardiovascular mortality

[†]Hongyang Gong and Ming Gao contributed equally to this work.

*Correspondence:
Zhiwen Zeng
454690568@qq.com
[1]Department of Physiology, College of Medicine, Chosun University, Gwangju, Republic of Korea
[2]Department of Gastroenterology, The First Hospital of Jilin University, Changchun, Jilin, China
[3]Department of Oncology, NANCHANG PEOPLE'S HOSPITAL, Nanchang, Jiangxi, China
[4]Department of Oncology, NANCHANG PEOPLE'S HOSPITAL, No. 2, Xiangshan South Road, Nanchang 330009, China

Introduction

According to the latest estimates from the International Agency for Research on Cancer (IARC), approximately one in five men or women will develop cancer during their lifetime, and about one in nine men and one in ten women will die from the disease [1]. Over the past three decades, advancements in medicine have reduced overall cancer mortality rates by approximately 32% [2]. With improvements in cancer diagnosis, the implementation of screening programs, and the continuous development of new therapies, the number of cancer survivors is expected to increase significantly with an aging population [3]. By 2030, the number of cancer survivors in the United States is projected to rise to 22.1 million [4, 5]. The primary determinant of survival among cancer patients is access to treatment from specialized healthcare providers. However, it is crucial to recognize that complications arising from cancer and its treatment can negatively impact physical functioning, lifestyle, and psychological well-being, ultimately reducing life expectancy [6]. Many cancer survivors face complex health challenges, including malnutrition, inflammation, and psychological issues, which may increase the risk of cancer recurrence and adversely affect post-diagnosis survival rates [7]. Survivors often have multiple modifiable factors, such as physical activity, dietary intake, smoking, alcohol consumption, and weight management [8]. Therefore, identifying modifiable factors that can improve the long-term prognosis of cancer survivors is essential.

In 2010, the American Heart Association (AHA) defined cardiovascular health (CVH) and introduced Life's Simple 7, an accessible and actionable metric designed to improve CVH [9]. In 2020, as evidence on CVH expanded, the AHA launched an enhanced approach for assessing CVH: Life's Essential 8 (LE8). This updated definition incorporated sleep as a component and revised the scoring algorithm for its elements [10]. LE8 consists of four health behaviors—diet, physical activity, nicotine exposure, and sleep duration—and four health factors: body mass index (BMI), non-high-density lipoprotein (HDL) cholesterol, blood glucose, and blood pressure [10]. Recently, the importance of psychological health in preventing cardiovascular disease (CVD) has been emphasized, leading to the development of a new metric, Life's Crucial 9 (LC9), which integrates psychological health into the LE8 framework [11].

LC9 is an extension of LE8 that incorporates mental health, which is a critical yet often overlooked dimension of cardiovascular and overall health. While LE8 focuses on biomedical indicators (e.g., blood pressure, blood glucose, cholesterol) and lifestyle factors (e.g., diet, physical activity, smoking), mental health significantly affects health outcomes, particularly in cardiovascular and cancer-related contexts. For instance, mental health conditions such as depression and anxiety have been associated with poor outcomes in cancer survivors [12]. By including mental health, LC9 provides a more holistic and scientifically comprehensive approach to assessing cardiovascular health, especially in complex populations such as cancer survivors. Moreover, mental health is significantly associated with increased all-cause mortality among cancer survivors. Psychological burdens, including depression and distress, are prevalent in this population and can exacerbate long-term health risks [13]. Assessing the predictive value of mental health not only complements LE8 but also sheds light on its unique contribution to mortality risk in cancer survivors. To the best of our knowledge, no prior studies have examined the association between LC9 and long-term outcomes in cancer survivors. Our research addresses this gap by evaluating the role of LC9 in predicting mortality, offering new insights into its utility in this specific population. This approach underscores the value of including mental health to enhance the predictive power of cardiovascular health metrics, ultimately informing future strategies for health management in cancer survivors.

This study aims to analyze the association between LC9 scores and mortality outcomes, including all-cause mortality, cardiovascular mortality, and cancer-specific mortality, using a representative sample of U.S. cancer survivors from 2005 to 2018. Insights gained from this research are expected to provide a foundation for developing quantitative lifestyle guidelines for cancer survivors.

Materials and methods

Study population and design

The National Health and Nutrition Examination Survey (NHANES) is an ongoing program designed to assess the health and nutritional status of individuals in the United States. The survey combines in-home health interviews with health measurements conducted in mobile examination centers, utilizing modern equipment to ensure data reliability and quality. Data for this study were obtained from the 2005–2018 NHANES cycles, which employed a complex probability sampling method to provide a nationally representative sample of the U.S. population. All NHANES surveys conducted by the National Center for Health Statistics (NCHS) were approved by the NCHS Ethics Review Board, and participants provided written informed consent. Since participant data were pre-collected and anonymized, NHANES datasets are publicly accessible without requiring additional approval from local ethics committees [14]. All data are freely available on the NHANES website (https://wwwn.cdc.gov/nchs/nhanes/Default.aspx).

We utilized baseline data from seven NHANES cycles collected between 2005 and 2018. Initially, the study

included 70,190 participants, of whom 66,408 were excluded due to no self-reported history of cancer. Additionally, 9 participants under 20 years of age or who were pregnant were excluded. Furthermore, 1,214 participants with incomplete data for variables of interest and 1 participant with incomplete mortality data were excluded. Ultimately, the study included a total of 2,258 adult participants (Fig. 1).

Measurement of LC9

The LC9 score is determined by the average score of 9 individual cardiovascular health (CVH) indicators, which include the 8 components of the Life's Essential 8 (LE8) score [10] (4 health behaviors: diet, physical activity, tobacco exposure, and sleep duration; 4 health factors: body mass index (BMI), non-high-density lipoprotein (HDL) cholesterol, blood glucose, and blood pressure) as well as the average depression score. The diet indicator is assessed using the Healthy Eating Index 2015 (HEI-2015). Dietary information is collected through two 24-hour

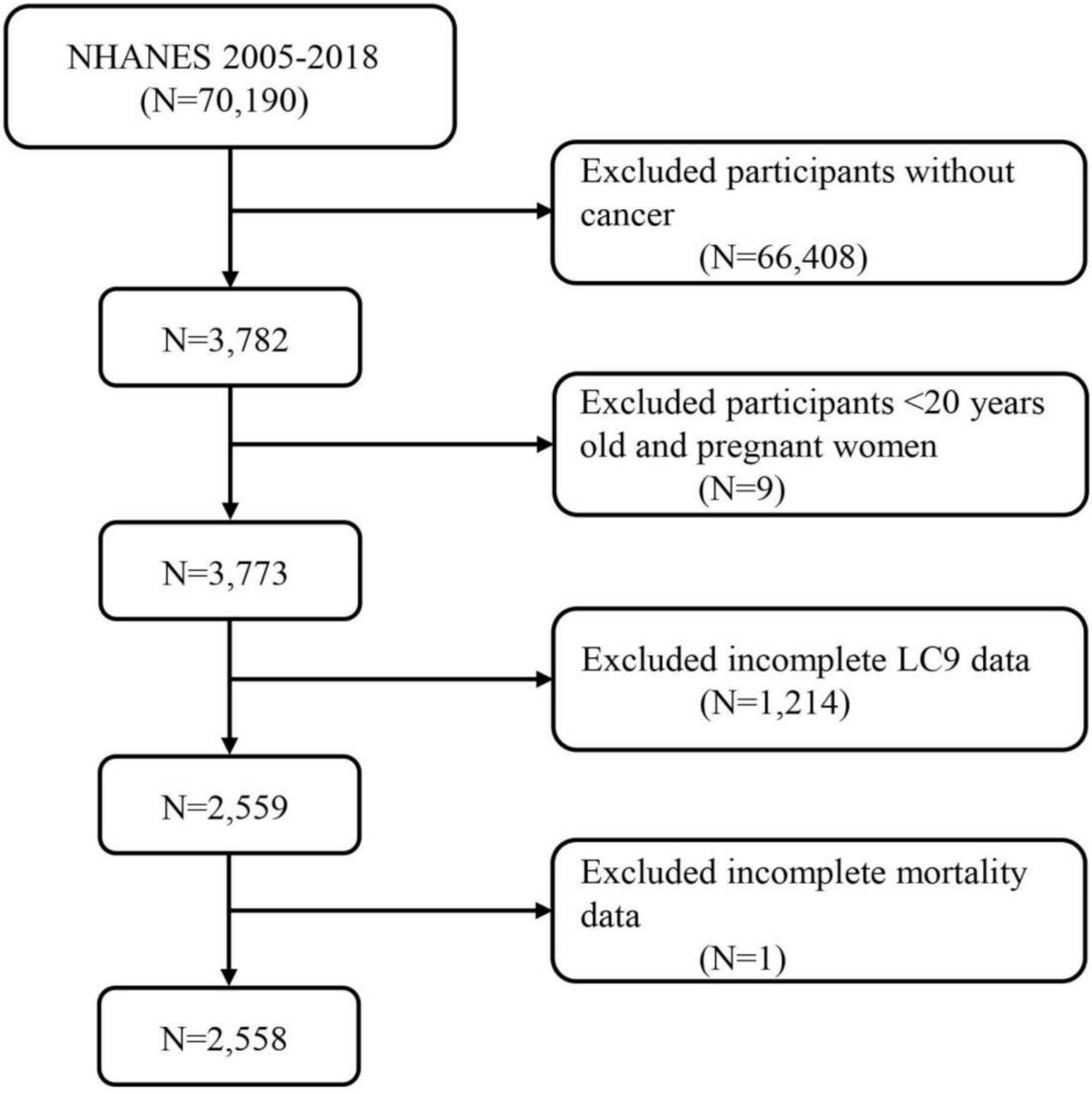

Fig. 1 A flow diagram of eligible participant selection in the National Health and Nutrition

dietary recalls and combined with data from the U.S. Department of Agriculture's Food Patterns Equivalent Database to construct and calculate the HEI-2015 score on an individual basis [15]. The components and scoring criteria of HEI-2015 are detailed in Table S2. Physical activity, tobacco exposure, sleep duration, history of diabetes, and medication history are collected through standardized self-report questionnaires. Height, weight, and blood pressure are measured during physical exams. BMI is calculated as weight (kg) divided by height (m) squared. After blood samples are collected, they are sent to a central laboratory for lipid, fasting glucose, and glycated hemoglobin measurement [15]. The depression score is calculated based on the Patient Health Questionnaire-9 (PHQ-9) score, a validated structured questionnaire for depression screening, where higher scores indicate more pronounced depressive symptoms. Depression scores are assigned based on the PHQ-9 score range as follows: 0–4 points = 100, 5–9 points = 75, 10–14 points = 50, 15–19 points = 25, and 20–27 points = 0 [16]. Each CVH indicator has a score range of 0 to 100, with scores assigned by an expert panel using the modified Delphi method based on the relationship between health outcomes and risks [10]. Detailed instructions for calculating each participant's LC9 score using the NHANES database are provided in Table S1.

Mortality outcomes collection

Mortality data were obtained from the National Death Index (NDI) database maintained by the Centers for Disease Control and Prevention (CDC) (https://www.cdc.gov/nchs/data-linkage/mortality-public.htm). The most recent follow-up was conducted on December 31, 2019. Causes of death were determined based on the International Classification of Diseases, 10th edition (ICD-10) codes. The primary outcomes of this study focus on mortality associated with all-cause, cardiovascular diseases (including codes I00-I09, I11, I13, I20-I25, I26-I51, and I60-I69), and cancer (codes C00-C97) [17, 18].

Covariates

Based on previously published studies [17, 18], this study includes the following covariates: (1) demographic variables, including age (20–65 years old, >65 years old), sex (Male and Female), race (Mexican American, Non-Hispanic Black, Non-Hispanic White, Other Race), household income (Poor: <1.3; Not Poor:>=1.3), education level (Below high school, High School or above), and marital status; (2) lifestyle factors and conditions, including obesity (BMI > = 30), smoking (never smoker defined as <100 cigarettes in a lifetime, current smoker defined as ≥100 cigarettes in a lifetime, and former smoker defined as ≥100 cigarettes and had quit smoking), and alcohol use (heavy drinking: ≥4 drinks/day for men, ≥3 drinks/day for women, or ≥5 days of drinking in a month; moderate drinking: ≥3 drinks/day for men, ≥2 drinks/day for women, or ≥2 days of drinking in a month; mild drinking: ≤2 drinks/day for men, ≤1 drink/day for women, and ≥12 drinks in a year; and never-drinking: total number of drinks in a year < 12, and dietary alcohol content of 0%); (3) chronic comorbidities, including diabetes (defined as a history of previous diabetes, HbA1c level ≥ 6.5%, or fasting blood glucose level ≥ 126 mg/dL), hypertension (self-reported hypertension history, the utilization of antihypertensive medication, a systolic blood pressure (SBP) ≥ 140mmHg, or a diastolic blood pressure (DBP) ≥ 90mmHg), and hyperlipidemia (Triglyceride (TG) levels ≥ 150 mg/dl (1.7 mmol/L); Total cholesterol (TC) levels ≥ 200 mg/dl (5.18 mmol/L); Low-density lipoprotein (LDL) levels ≥ 130 mg/dl (3.37 mmol/L); High-density lipoprotein (HDL) levels: Men: <40 mg/dl (1.04 mmol/L); Women: <50 mg/dl (1.30 mmol/L); Individuals taking cholesterol-lowering drugs). Detailed information on these covariates is provided in Table S3.

Statistical analysis

In all our analyses, sample weights were considered to obtain national estimates. The analysis used the appropriate sampling weight (1/7 × WTMEC2YR) to account for the complex survey design employed in the NHANES survey [19]. Continuous variables are presented as means and standard deviations (SD), with *p*-values calculated using t-tests or one-way analysis of variance (ANOVA). Categorical variables are represented by counts and weighted percentage frequencies (%), with *p*-values determined using weighted chi-square tests. Participants were categorized into three groups based on LC9 score tertiles (T1: <62.77, T2: 62.77–74.44, T3: ≥74.44).

Multivariable Cox proportional hazards regression models were used to calculate hazard ratios (HR) and their corresponding 95% confidence intervals (CI) to assess the association between LC9 and all-cause mortality, cancer-specific mortality, and cardiovascular mortality. Three statistical models were constructed. Model 1 was unadjusted for any covariates. Model 2 adjusted for demographic characteristics, including age, sex, education level, marital status, poverty-to-income ratio (PIR), and race. To assess whether factors such as obesity, smoking, diabetes, hypertension, and hyperlipidemia exert an influence on outcomes (all-cause mortality, cancer-specific mortality, and cardiovascular mortality) beyond what is captured by the total LC9 score, we incorporated these variables as independent adjustments in the model. This approach helps clarify the relationship between LC9 and mortality risk while enhancing the robustness and interpretability of the results. Therefore, Model 3 was further adjusted for current lifestyle conditions and comorbidities, including obesity, smoking,

drinking, hypertension, diabetes, and hyperlipidemia, in addition to the covariates in Model 2.

Kaplan-Meier survival analysis and log-rank tests were used to assess the prognostic differences among the LC9 score groups. Restricted cubic splines (RCS) were employed to evaluate the linear or nonlinear relationship between LC9 scores and mortality. Subgroup analyses were conducted to explore whether the relationship between LC9 scores and mortality varied by age, sex, education level, marital status, PIR, race, obesity, smoking, drinking, hypertension, diabetes, and hyperlipidemia. All statistical analyses were performed using R (version 4.3.1). A two-tailed p-value of less than 0.05 was considered statistically significant.

Results

Population characteristics

This study included 2,258 cancer survivors, with a total of 640 deaths, of which 205 participants died from cancer, and 128 died from heart disease. Table 1 presents the baseline characteristics of the study population, stratified by LC9 score. The weighted mean (SD) LC9 score for all participants was 68.42 (13.28). Overall, 51% of participants were aged over 65 years, and 56% were female. Compared to participants with lower LC9 scores, those with higher LC9 scores exhibited lower all-cause mortality, cancer-specific mortality, and cardiovascular mortality. Table S4 presents the baseline characteristics of the study population by survival status, showing that participants who survived had higher LC9 scores compared to those who died.

Association of LC9 with mortality

Table 2 illustrates the association between LC9 scores and all-cause mortality, cancer-specific mortality, and cardiovascular mortality, as assessed using Cox regression models. Three different models were used to evaluate the relationship between LC9 and mortality, all of which showed a significant negative correlation between LC9 and mortality (all $p < 0.01$). Specifically, in Model 3, after adjusting for various covariates, a 10-point increase in LC9 score was associated with a 24% reduction in all-cause mortality (HR: 0.76; 95% CI: 0.68–0.84; $p < 0.001$), a 19% reduction in cancer mortality (HR: 0.81; 95% CI: 0.68–0.97), and a 28% reduction in cardiovascular mortality (HR: 0.72; 95% CI: 0.58–0.90). Additionally, when LC9 was classified as Low (0–49), Moderate (50–79), and High (80–100), the risk of all-cause mortality was 36% lower in the LC9 High group compared to the LC9 Low group (HR: 0.36; 95% CI: 0.22–0.59; P for trend < 0.001). In addition, the results remained consistent when LC9 was categorized into tertiles (T1, T2, T3), the risk of all-cause mortality was 36% lower in the LC9 T3 group compared to the LC9 T1 group (HR: 0.64; 95% CI: 0.48–0.87; P for trend = 0.003) (Table S5). Additionally, the Psychological Health score remained significantly negatively associated with all-cause mortality (Table 2).

Figure 2 presents the results of the RCS analysis, which further confirms a significant linear negative correlation between LC9 and all-cause mortality after adjusting for relevant variables (overall $P < 0.001$; non-linear $P = 0.589$, Fig. 2A), indicating that the risk of all-cause mortality decreases linearly with an increase in LC9 score. However, LC9 showed a non-linear negative correlation with cardiovascular mortality (overall $P = 0.001$; non-linear $P = 0.046$, Fig. 2C), with a turning point at an LC9 score of 67.78.

Furthermore, Kaplan-Meier curves showed that when divided by tertiles, the highest LC9 group (T3) had a significantly lower incidence of all-cause mortality, cancer-specific mortality, and cardiovascular mortality compared to the lowest LC9 group (T1) (Log-rank $P < 0.05$, Figs. 3A-C).

Subgroup analysis

To further investigate the relationship between LC9 scores and all-cause, cancer-specific, and cardiovascular mortality, subgroup analyses were conducted (Table 3). The subgroup analysis revealed that the negative association between LC9 scores and all-cause mortality was consistent across various subgroups, including age, sex, marital status, education level, obesity, hypertension, and diabetes. No significant interactions were observed.

Additionally, the study found a significant negative association between LC9 scores and cancer mortality in the following groups: younger individuals (aged 20–65 years, HR 0.67; 95% CI 0.49–0.91), married individuals (HR 0.74; 95% CI 0.56–0.98), those not living in poverty (HR 0.80; 95% CI 0.65–0.98), individuals with higher education levels (HR 0.79; 95% CI 0.63–0.98), non-smokers (HR 0.62; 95% CI 0.47–0.83), and those without hyperlipidemia (HR 0.48; 95% CI 0.29–0.79). No significant interactions were found in these subgroups.

Furthermore, a significant negative association between LC9 scores and cardiovascular mortality was observed in the following subgroups: older individuals (aged > 65 years, HR 0.70; 95% CI 0.54–0.89), males (HR 0.70; 95% CI 0.54–0.91), married individuals (HR 0.67; 95% CI 0.49–0.90), individuals with lower poverty levels (HR 0.70; 95% CI 0.55–0.91), individuals with higher education levels (HR 0.73; 95% CI 0.56–0.94), those without obesity (HR 0.65; 95% CI 0.48–0.90), hypertensive patients (HR 0.72; 95% CI 0.57–0.92), hyperlipidemia patients, and individuals with diabetes. No significant interactions were observed in these subgroups.

Table 1 The demographic characteristics of the Cancer survivors population in the present study were stratified by LC9

Characteristic	Overall, *N* = 2,558 (100%)	Low (LC9 < 50), *N* = 263 (8%)	Moderate (50 ≤ LC9 < 80), *N* = 1,853 (71%)	High (LC9 ≥ 80), *N* = 442 (21%)	*P*Value
Age (%)					0.010
20–65	1,071 (49%)	142 (59%)	734 (46%)	195 (54%)	
> 65	1,487 (51%)	121 (41%)	1,119 (54%)	247 (46%)	
Sex (%)					**0.028**
Female	1,337 (56%)	168 (63%)	923 (54%)	246 (61%)	
Male	1,221 (44%)	95 (37%)	930 (46%)	196 (39%)	
Race (%)					**< 0.001**
Non-Hispanic White	1,812 (88%)	167 (82%)	1,296 (88%)	349 (92%)	
Non-Hispanic Black	317 (4.3%)	50 (9.5%)	236 (4.6%)	31 (1.7%)	
Other	271 (5.5%)	31 (6.4%)	196 (5.7%)	44 (4.8%)	
Mexican American	158 (2.1%)	15 (2.2%)	125 (2.2%)	18 (1.7%)	
Married/live with partner (%)					**0.001**
no	971 (33%)	128 (40%)	711 (34%)	132 (26%)	
yes	1,586 (67%)	135 (60%)	1,141 (66%)	310 (74%)	
Education level (%)					**< 0.001**
Below high school	477 (11%)	99 (26%)	341 (11%)	37 (5.5%)	
High School or above	2,081 (89%)	164 (74%)	1,512 (89%)	405 (94%)	
PIR (%)					**< 0.001**
Poor	530 (13%)	108 (32%)	380 (14%)	42 (4.7%)	
Not Poor	1,832 (87%)	135 (68%)	1,327 (86%)	370 (95%)	
Obesity					**< 0.001**
no	1,604 (64%)	84 (29%)	1,108 (58%)	412 (94%)	
yes	954 (36%)	179 (71%)	745 (42%)	30 (6.0%)	
Smoking (%)					**< 0.001**
never	1,167 (46%)	56 (19%)	817 (43%)	294 (69%)	
former	1,018 (39%)	99 (36%)	780 (42%)	139 (30%)	
current	373 (15%)	108 (45%)	256 (15%)	9 (1.6%)	
Drinking (%)					**< 0.001**
never	301 (9.7%)	36 (13%)	216 (9.6%)	49 (9.1%)	
former	543 (18%)	78 (31%)	409 (19%)	56 (10%)	
mild	1,079 (47%)	78 (38%)	769 (45%)	232 (56%)	
moderate	293 (15%)	19 (5.9%)	209 (15%)	65 (18%)	
heavy	221 (11%)	30 (13%)	165 (11%)	26 (6.8%)	
Hypertension (%)					**< 0.001**
no	920 (42%)	59 (29%)	576 (34%)	285 (70%)	
yes	1,638 (58%)	204 (71%)	1,277 (66%)	157 (30%)	
Diabetes (%)					**< 0.001**
no	1,907 (79%)	132 (56%)	1,355 (76%)	420 (96%)	
yes	651 (21%)	131 (44%)	498 (24%)	22 (4.3%)	
Hyperlipidemia (%)					**< 0.001**
no	448 (17%)	16 (6.0%)	280 (13%)	152 (34%)	
yes	2,110 (83%)	247 (94%)	1,573 (87%)	290 (66%)	
Mean LC9 score (mean (SD))	68.42 (13.28)	42.39 (6.55)	66.05 (7.86)	86.06 (4.65)	**< 0.001**
Mean psychological health score (mean (SD))	88.54 (24.27)	56.29 (39.13)	89.59 (22.11)	97.22 (9.93)	**< 0.001**
Mean HEI-2015 diet score (mean (SD))	45.17 (31.54)	21.27 (23.55)	40.92 (29.96)	68.22 (26.08)	**< 0.001**
Mean physical activity score (mean (SD))	66.45 (43.56)	19.45 (35.77)	63.62 (44.04)	93.52 (20.08)	**< 0.001**
Mean tobacco exposure score (mean (SD))	73.08 (34.55)	41.42 (41.59)	71.56 (34.61)	90.04 (17.57)	**< 0.001**
Mean sleep health score (mean (SD))	84.97 (23.40)	61.01 (31.72)	85.17 (22.63)	93.31 (14.42)	**< 0.001**
Mean body mass index score (mean (SD))	60.97 (32.92)	34.95 (31.55)	56.39 (31.83)	85.93 (20.17)	**< 0.001**
Mean blood lipid score (mean (SD))	60.51 (28.92)	41.60 (28.65)	58.65 (28.17)	73.80 (25.79)	**< 0.001**
Mean blood glucose score (mean (SD))	78.59 (26.44)	58.69 (28.82)	76.00 (26.50)	94.64 (14.51)	**< 0.001**
Mean blood pressure score (mean (SD))	57.51 (32.07)	46.82 (34.46)	52.57 (30.59)	77.87 (27.21)	**< 0.001**

Table 1 (continued)

Characteristic	Overall, *N* = 2,558 (100%)	Low (LC9 < 50), *N* = 263 (8%)	Moderate (50 ≤ LC9 < 80), *N* = 1,853 (71%)	High (LC9 ≥ 80), *N* = 442 (21%)	*P* Value
BMI (mean (SD))	28.86 (6.35)	34.09 (7.71)	29.61 (6.08)	24.40 (3.56)	**< 0.001**
Systolic blood pressure (mean (SD))	127.40 (18.74)	132.32 (21.51)	129.70 (18.33)	117.92 (15.61)	**< 0.001**
Diastolic blood pressure (mean (SD))	68.53 (12.50)	68.71 (13.14)	68.82 (13.01)	67.51 (10.30)	**0.033**
HDL, mmol/L (mean (SD))	1.43 (0.45)	1.19 (0.35)	1.37 (0.41)	1.69 (0.50)	**< 0.001**
Fasting blood glucose, mmol/L (mean (SD))	6.14 (1.66)	7.28 (3.32)	6.24 (1.53)	5.45 (0.66)	**< 0.001**
Physical activity (mean (SD))	830.04 (1,182.30)	620.71 (1,322.13)	828.25 (1,217.17)	856.03 (1,075.92)	**< 0.001**
Mortality (%)					**0.001**
All-cause mortality	640 (19%)	83 (29%)	481 (20%)	76 (11%)	
Cancer-specific mortality	205 (5.9%)	23 (7.1%)	158 (6.3%)	24 (4.3%)	
Cardiovascular mortality	128 (4.0%)	17 (6.3%)	98 (4.4%)	13 (2.0%)	

Mean (SD) for continuous variables: the *P* value was calculated by the weighted one-way analysis of variance (ANOVA)

Percentages (weighted N, %) for categorical variables: the *P* value was calculated by the weighted chi-square test

Abbreviation: LC9, Life's Crucial 9; HDL, high density lipoprotein cholesterol; PIR, Ratio of family income to poverty

Discussion

To the best of our knowledge, this is the first study to use nationally representative data from NHANES to explore the relationship between LC9 scores and the risk of all-cause mortality, cancer-specific mortality, and cardiovascular mortality in cancer survivors. In a cohort of 2,558 cancer survivors from seven NHANES cycles (2005–2018), a significant dose-dependent relationship was observed between LC9 scores and all-cause mortality, cancer mortality, and cardiovascular mortality risk. Notably, for every 10-point increase in LC9 scores, the risk of all-cause mortality, cancer mortality, and cardiovascular mortality was significantly reduced by 24%, 19%, and 28%, respectively. The dose-dependent relationship was particularly significant in the context of all-cause mortality, where a linear relationship was observed. However, cardiovascular mortality showed a non-linear association with LC9 scores. As a powerful tool for quantifying lifestyle, our findings underscore the importance of maintaining high cardiovascular health (CVH) levels in improving the overall health of cancer patients, managing cancer itself, and enhancing cardiovascular health outcomes.

Cancer has become one of the leading causes of premature death globally and remains a prominent issue in global health [20]. In recent years, there has been increasing attention on the impact of lifestyle factors on cancer incidence and progression. Studies show that individuals adopting a healthy lifestyle have a 52% lower risk of cancer mortality compared to those with unhealthy lifestyles [21]. Furthermore, research indicates that cancer survivors face higher cardiovascular disease (CVD) risks due to a combination of factors, such as cancer treatments, lifestyle changes, and other underlying risk factors [22, 23]. The impact of cardiovascular health (CVH) on the quality of life of cancer survivors has garnered increasing attention, particularly in terms of depression, anxiety, and chronic or traumatic stress. Despite significant advances in cancer treatments that have substantially improved survival rates, many survivors continue to face long-term health challenges, which may stem from the effects of cancer treatments on the cardiovascular system [21].

Life's Simple 7 (LS7), established by the American Heart Association (AHA) in 2010, has served as a standard for cardiovascular health (CVH) assessment. Studies have demonstrated that LS7 is an effective tool for evaluating cardiovascular disease (CVD) risk in cancer survivors, highlighting the critical role of CVH in preventing CVD development [24]. LS7 includes seven key indicators: smoking, physical activity, obesity, diet, total cholesterol, blood pressure, and blood glucose. To further refine CVH assessment, AHA introduced Life's Essential 8 (LE8) standards in 2020, adding sleep quality as a new metric and providing a more detailed cardiovascular health scoring system ranging from 0 to 100 [10]. Results from two cohort studies conducted in the UK Biobank and the U.S. NHANES emphasized the significant association between higher LE8 scores and a reduced overall cancer mortality risk. Specifically, for every standard deviation increase in LE8 score, cancer mortality was reduced by 19% in both the U.S. and UK populations [25]. A cross-sectional study further indicated a reverse gradient relationship between LE8 scores and both all-cause and cardiovascular mortality risks in cancer survivors [26]. These findings align with the results of our study. However, the aforementioned studies did not consider the potential impact of mental health on cardiovascular health and cancer survivors. To address this, our study innovatively introduced the LC9 score [11], exploring its relationship with cancer survivors and emphasizing the importance of mental health in cardiovascular health and cancer survivorship.

In a study, "Association of sleep duration and depressive symptoms with mortality in cancer survivors" [13],

Table 2 HRs (95% CIs) for All-cause mortality, Cancer-specific mortality, and cardiovascular mortality according to LC9 in the Cancer survivors population, weighted

LC9 and Subgroup scores	Model 1 [HR (95% CI)]	Model 2 [HR (95% CI)]	Model 3 [HR (95% CI)]
All-cause mortality			
Continuous (per 10 scores)	0.77(0.71,0.83)	0.76(0.69,0.83)	0.76(0.68,0.84)
Categories			
Low (0–49)	1 (ref.)	1 (ref.)	1 (ref.)
Moderate (50–79)	0.65(0.47,0.88)	0.49(0.34,0.69)	0.52(0.36,0.75)
High (80–100)	0.31(0.20,0.49)	0.30(0.19,0.48)	0.36(0.22,0.59)
P for trend	< 0.001	< 0.001	< 0.001
Psychological Health score	0.99(0.95,1.03)	0.95(0.92,0.98)	0.97(0.94,1.00)
HEI diet score	0.98(0.95,1.02)	0.97(0.93,1.00)	0.98(0.95,1.02)
Physical activity score	0.90(0.88,0.92)	0.92(0.90,0.94)	0.92(0.90,0.94)
Tobacco exposure score	0.99(0.96,1.01)	0.96(0.93,0.99)	1.03(0.90,1.17)
Sleep health score	0.92(0.89,0.95)	0.91(0.88,0.95)	0.93(0.90,0.97)
Body mass index score	1.01(0.98,1.05)	1.01(0.97,1.05)	1.05(0.96,1.15)
Blood lipid score	1.07(1.04,1.10)	1.05(1.02,1.08)	1.04(1.00,1.07)
Blood glucose score	0.90(0.86,0.94)	0.94(0.90,0.99)	1.01(0.94,1.07)
Blood pressure score	0.88(0.86,0.91)	0.94(0.91,0.98)	0.97(0.93,1.02)
Cancer-specific mortality			
Continuous (per 10 scores)	0.81(0.72,0.92)	0.84(0.73,0.97)	0.81(0.68,0.97)
Categories			
Low (0–49)	1 (ref.)	1 (ref.)	1 (ref.)
Moderate (50–79)	0.77(0.42,1.42)	0.70(0.35,1.40)	0.70(0.37,1.36)
High (80–100)	0.44(0.20,0.96)	0.50(0.22,1.16)	0.52(0.20,1.31)
P for trend	0.010	0.090	0.190
Psychological Health score	0.99(0.95,1.07)	0.97(0.91,1.03)	0.98(0.92,1.04)
HEI diet score	0.96(0.90,1.01)	0.95(0.90,1.01)	0.96(0.91,1.03)
Physical activity score	0.90(0.87,0.94)	0.91(0.88,0.95)	0.91(0.88,0.95)
Tobacco exposure score	0.98(0.94,1.02)	0.98(0.93,1.02)	1.28(1.01, 1.61)
Sleep health score	0.92(0.88,0.97)	0.92(0.87,0.98)	0.93(0.88,0.99)
Body mass index score	1.00(0.95,1.06)	1.00(0.94,1.07)	1.02(0.90,1.16)
Blood lipid score	1.09(1.04,1.15)	1.08(1.02,1.15)	1.07(1.01,1.14)
Blood glucose score	0.95(0.87,1.04)	1.02(0.93,1.13)	1.10(0.99,1.23)
Blood pressure score	0.93(0.88,0.98)	0.99(0.93,1.05)	1.00(0.93,1.08)
Cardiovascular mortality			
Continuous (per 10 scores)	0.70(0.60,0.82)	0.66(0.55, 0.80)	0.72(0.58, 0.90)
Categories			
Low (0–49)	1 (ref.)	1 (ref.)	1 (ref.)
Moderate (50–79)	0.61(0.32,1.18)	0.42(0.18, 0.99)	0.47(0.17, 1.32)
High (80–100)	0.22(0.09,0.55)	0.19(0.07, 0.52)	0.32(0.09, 1.11)
P for trend	< 0.001	0.002	0.100
Psychological Health score	0.99(0.94,1.11)	0.93(0.84, 1.04)	0.96(0.86, 1.08)
HEI diet score	1.06(1.00,1.13)	1.04(0.97, 1.11)	1.07(1.00, 1.15)
Physical activity score	0.89(0.84,0.93)	0.90(0.86, 0.95)	0.91(0.87, 0.95)
Tobacco exposure score	1.00(0.94,1.07)	0.96(0.88, 1.04)	0.99(0.67, 1.46)
Sleep health score	0.91(0.85,0.97)	0.89(0.82, 0.96)	0.91(0.84, 0.98)
Body mass index score	0.96(0.88,1.04)	0.95(0.87, 1.05)	0.98(0.75, 1.28)
Blood lipid score	1.05(0.98,1.13)	1.02(0.93, 1.11)	1.02(0.94, 1.10)
Blood glucose score	0.81(0.76,0.87)	0.88(0.81, 0.95)	0.97(0.86, 1.09)
Blood pressure score	0.79(0.74,0.86)	0.86(0.78, 0.95)	0.91(0.81, 1.03)

Model 1: no covariates were adjusted

Model 2: age, sex, education level, marital status, PIR, and race were adjusted

Model 3: age, sex, education level, marital status, PIR, race, obesity, smoking, drinking, hypertension, diabetes, and hyperlipidemia were adjusted

Abbreviation: LC9, Life's Crucial 9; PIR, Ratio of family income to poverty; HR, hazard ratio; CI, confidence interval; ref., reference; HEI diet score, Healthy Eating Index diet score

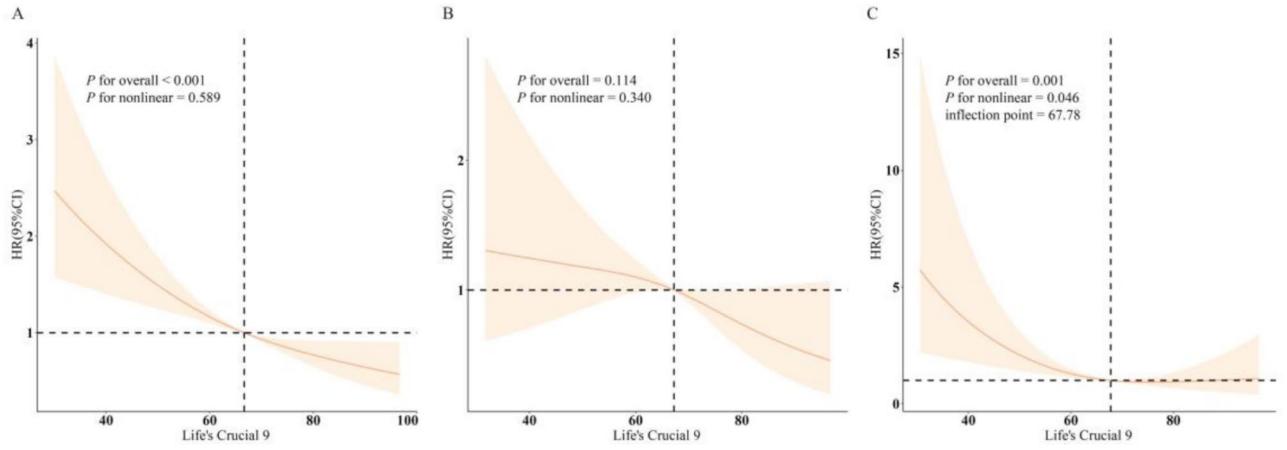

Fig. 2 The association of LC9 with All-cause (**A**), Cancer-specific (**B**), and Cardiovascular mortality (**C**) among Cancer Survivors visualized by restricted cubic spline

HR (solid lines) and 95% confidence levels (shaded areas) were adjusted for age, sex, education level, marital status, PIR, race, obesity, smoking, drinking, hypertension, diabetes, and Hyperlipidemia

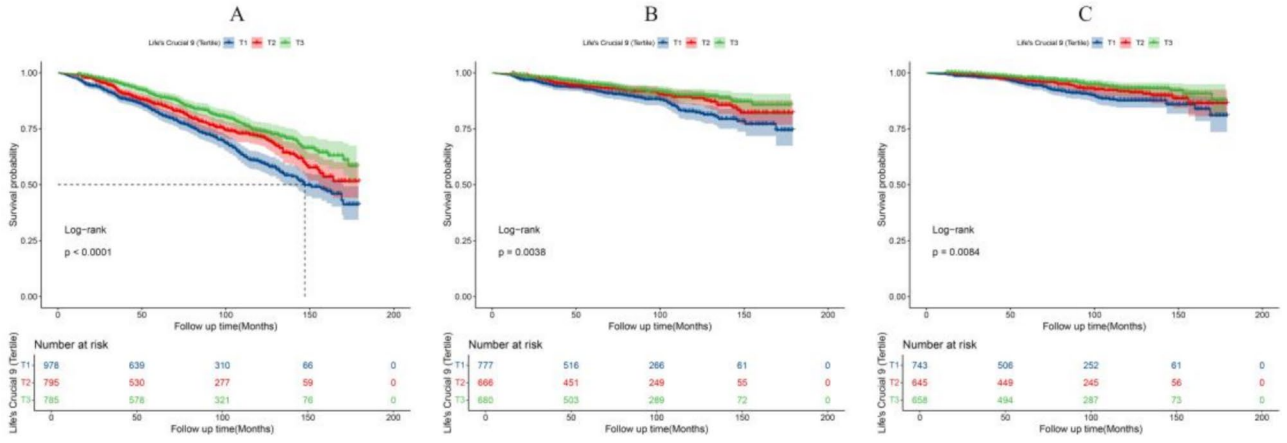

Fig. 3 Kaplan–Meier analyses for mortality among the three groups. T1–T3, Tertiles 1–3; LC9, Life's Crucial 9. (**A**) All-cause mortality; (**B**) Cancer-specific mortality; (**C**) Cardiovascular mortality

it was found that every 1-point increase in depressive symptom score was associated with a 2% increase in all-cause mortality (HR = 1.02; 95% CI: 1.00-1.03). In our study, we found that every 1-point increase in Psychological Health score was associated with a 5% reduction in all-cause mortality (HR = 0.95; 95% CI: 0.92–0.98). Studies have shown that depression can biologically disrupt central stress systems, such as hyperactivity of the hypothalamic-pituitary-adrenal (HPA) axis [27], dysregulation of neuroimmune responses, and imbalances in sympathetic noradrenergic function [28], which may contribute to increased mortality. Therefore, compared to LE8, the inclusion of mental health indicators in LC9 may provide a more comprehensive assessment of long-term prognosis in cancer survivors.

Cardiovascular disease (CVD) and cancer are interrelated to some extent, sharing common risk factors and potential pathophysiological mechanisms, particularly in cancer survivors, where cardiovascular health is closely tied to cancer prognosis [22]. Cancer treatments, including chemotherapy, radiation, and targeted therapies, can have toxic effects on the heart, leading to the development of cardiovascular disease [29, 30]. For instance, doxorubicin (DOX), an effective anthracycline drug, is reported to affect approximately 30% of patients within five years post-chemotherapy, causing permanent cardiac damage [31]. Heart failure (HF) is a major non-cancer cause of death in patients treated with DOX [32]. This highlights the importance of cardiology, an emerging field that integrates the intersection of cancer and cardiovascular disease, focusing on the cardiac effects of cancer treatments and promoting comprehensive health management for cancer patients [30]. CVD and cancer share many common risk factors and can be

Table 3 Subgroup analysis of the relationship between LC9 and mortality in the Cancer survivors population

character	All-cause mortality		Cancer-specific mortality		Cardiovascular mortality	
	HR (95% CI	*p* for interaction	HR (95% CI	*p* for interaction	HR (95% CI	*p* for interaction
Age		0.08		0.42		0.52
20–65	0.76(0.61,0.95)		0.67(0.49,0.91)		0.77(0.32,1.85)	
> 65	0.75(0.67,0.84)		0.87(0.69,1.11)		0.70(0.54,0.89)	
Sex		0.95		0.91		0.96
Female	0.72(0.62,0.83)		0.84(0.65,1.08)		0.70(0.46, 1.05)	
Male	0.78(0.67,0.91)		0.80(0.60,1.08)		0.70(0.54, 0.91)	
Married/live with partner		0.16		0.55		0.61
no	0.82(0.69,0.98)		0.90(0.67,1.21)		0.81(0.54, 1.21)	
yes	0.70(0.60,0.82)		0.74(0.56,0.98)		0.67(0.49, 0.90)	
Education		0.76		0.56		0.37
Below high school	0.81(0.67,0.97)		0.95(0.66,1.38)		0.71(0.44,1.15)	
High School or above	0.77(0.68,0.87)		0.79(0.63,0.98)		0.73(0.56, 0.94)	
PIR		0.41		0.86		0.37
Poor	0.86(0.71,1.04)		0.94(0.65,1.37)		0.95(0.63, 1.44)	
Not Poor	0.74(0.66,0.83)		0.80(0.65,0.98)		0.70(0.55, 0.91)	
Obesity		0.2		0.6		0.96
no	0.77(0.66,0.89)		0.87(0.69,1.09)		0.65(0.48, 0.90)	
yes	0.72(0.60,0.87)		0.73(0.54,0.99)		0.82(0.55, 1.21)	
Smoking		0.2		0.87		0.37
never	0.60(0.51,0.70)		0.62(0.47,0.83)		0.64(0.46,0.90)	
former	0.84(0.73,0.97)		0.85(0.64,1.12)		0.79(0.55,1.14)	
current	0.91(0.66,1.24)		1.07(0.75,1.51)		0.44(0.27,0.73)	
Drinking		0.47		0.09		0.09
never	0.64(0.48,0.85)		1.01(0.58,1.77)		0.46(0.25,0.85)	
former	0.75(0.61,0.92)		0.84(0.65,1.10)		0.60(0.38,0.95)	
mild	0.84(0.70,1.03)		0.91(0.60,1.36)		0.87(0.55,1.36)	
moderate	0.68(0.45,1.03)		0.63(0.32,1.24)		1.48(0.93,2.3)	
heavy	0.70(0.41,1.17)		0.54(0.34,0.86)		0.03(0.02,0.03)	
Hypertension		0.12		0.52		0.94
no	0.78(0.62,0.99)		0.76(0.53,1.09)		0.63(0.33,1.18)	
yes	0.74(0.66,0.83)		0.82(0.67,1.00)		0.72(0.57,0.92)	
Diabetes		0.2		0.42		0.96
no	0.81(0.71,0.92)		0.87(0.70,1.08)		0.77(0.60,1.00)	
yes	0.67(0.56,0.80)		0.66(0.47,0.93)		0.62(0.41,0.95)	
Hyperlipidemia		0.05		0.91		0.11
no	0.82(0.55,1.22)		0.48(0.29,0.79)		2.51(1.48,4.25)	
yes	0.75(0.68,0.83)		0.86(0.73,1.03)		0.69(0.56,0.87)	

Subgroup analysis was constructed based on Model 3. In each case, the model was not adjusted for the stratification variable itself. HRs were calculated per 10-unit increase in LC9

Abbreviation: LC9, Life's Crucial 9; PIR, Ratio of family income to poverty; HR, hazard ratio; CI, confidence interval

Abbreviation: LC9, Life's Crucial 9; PIR, Ratio of family income to poverty; HR, hazard ratio; CI, confidence interval

interconnected through hormones, cytokines, and metabolic pathways [22]. Chronic inflammation is considered a common underlying factor for various chronic diseases, including CVD and cancer. CVD primarily stems from atherosclerosis, where inflammation and lipid metabolism disorders play a crucial role in its development [33]. Tumor-associated inflammation drives cancer progression and treatment resistance, often involving the infiltration of monocyte-derived tumor-associated macrophages [34]. Modulating inflammatory pathways has shown promising advances in cancer treatment and is a potential strategy for reducing cardiovascular events [35]. Furthermore, metabolic syndrome, which includes hypertension, diabetes, high cholesterol, and obesity, is not only closely linked to CVD but is also an independent risk factor for cancer [36, 37, 38, 39]. Metabolic syndrome accelerates the development of CVD through various molecular mechanisms, including insulin resistance, inflammatory

responses, oxidative stress, and hormonal changes [40], and increases cancer risk [41]. Therefore, comprehensive health management for cancer survivors should include monitoring and intervention for cardiovascular disease to improve their quality of life and prognosis. The new LC9 metric, which incorporates mental health, adds significant value to this study by emphasizing the importance of psychological well-being in the relationship between cardiovascular health and cancer survivorship.

Research has shown that a healthy lifestyle is closely associated with cancer incidence and prognosis [8]. Individuals who adhere to cancer prevention dietary guidelines, especially those for breast cancer, colorectal cancer, and endometrial cancer, exhibit a significantly lower risk of developing these cancers [42, 43]. Regular physical activity is considered an effective means of preventing various cancers. A systematic review found significant associations between physical activity and several cancers, including gastrointestinal and bladder cancers [44]. Exercise reduces cancer risk through multiple mechanisms, including modulation of sex hormones, and metabolic hormones, reducing inflammation, improving immune function, decreasing oxidative stress, and promoting DNA repair [45]. Smoking is one of the most well-established carcinogenic factors. According to the Chinese National Cancer Center, smoking is responsible for approximately 25% of cancer-related deaths [46]. Moreover, sleep disorders can lead to obesity, insulin resistance, weakened immune function, and chronic inflammation, creating an environment conducive to cancer development [47].

This study has several notable strengths: (1) It is the first to examine the relationship between LC9 scores and the risks of all-cause mortality, cancer mortality, and cardiovascular mortality among cancer survivors in the U.S. population, providing scientific guidance for health interventions and management of cancer survivors. (2) The use of a nationally representative sample of U.S. cancer survivors allows for the generalization of the findings at the population level. (3) Through the construction of various models and subgroup analyses, adjusting for confounding factors, the study shows a strong negative correlation between LC9 and cancer survivor mortality, with robust and credible results.

However, it is important to consider several limitations of our study: (1) The study sample is drawn exclusively from the U.S. population and is highly selected from the entire NHANES cohort, which may affect the generalizability of our findings. We plan to include findings from different populations in future research to reduce bias. (2) Some CVH factors, such as diet, physical activity, nicotine exposure, and sleep duration, were collected through self-reported questionnaires, which may introduce measurement and recall bias. (3) NHANES lacks follow-up data, so we were unable to dynamically assess changes in participants' CVH status over time. (4) Measurement errors in relevant individual characteristics and laboratory indicators may affect the accuracy of our results. (5) In this study, we acknowledge the potential issue of "double adjustment" when analyzing the association between LC9 and all-cause, cancer-specific, and cardiovascular mortality. LC9 is a composite measure that includes multiple health factors known to influence mortality risk, such as obesity, smoking, diabetes, hypertension, and hyperlipidemia. Therefore, careful consideration is required when adjusting for these variables to avoid redundancy or confounding effects. Future research should further refine adjustment strategies and explore advanced statistical methods, such as causal inference models, to better characterize the complex relationship between LC9 and mortality risk. Additionally, while LC9 provides a comprehensive assessment of overall health, our study also examined the independent contributions of its individual components to mortality risk, offering valuable insights into the role of specific health factors among cancer survivors.

Conclusion

In conclusion, our study demonstrates that LC9 score, as a novel cardiovascular health (CVH) metric, is independently associated with all-cause mortality, cancer-related mortality, and cardiovascular mortality risks in cancer survivors. Our findings provide new insights for the prevention and management of cancer survivors, highlighting that improving cardiovascular health may help increase cancer survivor survival rates. Implementing such interventions could have a significant public health impact.

Abbreviations

LC9	Life's Crucial 9
LS7	Life's Simple 7
LE8	Life's Essential 8
CVH	Cardiovascular health
NHANES	National Health and Nutrition Examination Survey

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12885-025-14229-2.

Supplementary Material 1

Acknowledgements

We sincerely appreciate the NHANES database for all the data.

Author contributions

H.G. contributed to the original draft, Methodology, and Formal analysis. M.G. contributed to Validation, Formal analysis, Resources, and Data curation. Z.Z. was involved in Writing– review & editing, Supervision, Project administration, and Investigation.

Funding
No specific funding for this research was provided by the government, business, or nonprofit sectors.

Data availability
The corresponding author can provide the datasets used and/or analyzed in this study upon reasonable request.

Declarations

Conflict of interest
The authors state that they have no pertinent financial or non-financial interests to reveal.

Ethics approval and consent to participate
The NCHS Ethics Review Board approved this study's human subjects components, which followed the Declaration of Helsinki. For every subject, written informed permission was acquired.

Consent for publication
All participants gave informed consent for publication.

Clinical trial number
Not applicable.

Received: 17 November 2024 / Accepted: 25 April 2025
Published online: 30 April 2025

References

1. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2024;74:229–63.
2. Baughman C, Norman K, Mukamal K. Adherence to American Cancer society nutrition and physical activity guidelines among Cancer survivors. JAMA Oncol. 2024;10:789–92.
3. Nong J, Tong J, Wang R, Shi K, Zhang Y. Associations of sleep disorders with all-cause and cause-specific mortality in cancer survivors: a cross-sectional analysis of the NHANES 2005–2016. BMC Psychiatry. 2024;24:118.
4. Liu Q, He H, Yang J, Feng X, Zhao F, Lyu J. Changes in the global burden of depression from 1990 to 2017: findings from the global burden of disease study. J Psychiatr Res. 2020;126:134–40.
5. Mitchell AJ, Chan M, Bhatti H, Halton M, Grassi L, Johansen C, et al. Prevalence of depression, anxiety, and adjustment disorder in oncological, haematological, and palliative-care settings: a meta-analysis of 94 interview-based studies. Lancet Oncol. 2011;12:160–74.
6. Cao C, Friedenreich CM, Yang L. Association of daily sitting time and Leisure-Time physical activity with survival among US Cancer survivors. JAMA Oncol. 2022;8:395–403.
7. Emery J, Butow P, Lai-Kwon J, Nekhlyudov L, Rynderman M, Jefford M. Management of common clinical problems experienced by survivors of cancer. Lancet. 2022;399:1537–50.
8. Rock CL, Thomson CA, Sullivan KR, Howe CL, Kushi LH, Caan BJ, et al. American Cancer society nutrition and physical activity guideline for cancer survivors. CA Cancer J Clin. 2022;72:230–62.
9. Lloyd-Jones DM, Hong Y, Labarthe D, Mozaffarian D, Appel LJ, Van Horn L, et al. Defining and setting National goals for cardiovascular health promotion and disease reduction: the American heart association's strategic impact goal through 2020 and beyond. Circulation. 2010;121:586–613.
10. Lloyd-Jones DM, Allen NB, Anderson CAM, Black T, Brewer LC, Foraker RE, et al. Life's essential 8: updating and enhancing the American heart association's construct of cardiovascular health: A presidential advisory from the American heart association. Circulation. 2022;146:e18–43.
11. Gaffey AE, Rollman BL, Burg MM. Strengthening the pillars of cardiovascular health: psychological health is a crucial component. Circulation. 2024;149:641–3.
12. Yi JC, Syrjala KL. Anxiety and depression in Cancer survivors. Med Clin North Am. 2017;101:1099–113.
13. Liu Y, Feng Y, Wang J, Peng J, Su M, Shao D, et al. Association of sleep duration and depressive symptoms with mortality in cancer survivors. BMC Cancer. 2024;24:1573.
14. Inoue K, Tsugawa Y, Mayeda ER, Ritz B. Association of daily step patterns with mortality in US adults. JAMA Netw Open. 2023;6:e235174.
15. Krebs-Smith SM, Pannucci TE, Subar AF, Kirkpatrick SI, Lerman JL, Tooze JA, et al. Update of the healthy eating index: HEI-2015. J Acad Nutr Diet. 2018;118:1591–602.
16. Zhang Z, Jackson SL, Gillespie C, Merritt R, Yang Q. Depressive symptoms and mortality among US adults. JAMA Netw Open. 2023;6:e2337011.
17. Xu Z, Liu D, Zhai Y, Tang Y, Jiang L, Li L, et al. Association between the oxidative balance score and all-cause and cardiovascular mortality in patients with diabetes and prediabetes. Redox Biol. 2024;76:103327.
18. Fan C, Zhu W, He Y, Da M. The association between life's essential 8 and all-cause, cancer and non-cancer mortality in US Cancer survivors: A retrospective cohort study of NHANES. Prev Med. 2024;179:107853.
19. Curtin LR, Mohadjer LK, Dohrmann SM, Montaquila JM, Kruszan-Moran D, Mirel LB et al. The National health and nutrition examination survey: sample design, 1999–2006. Vital Health Stat 2. 2012;:1–39.
20. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;71:209–49.
21. Zhang Y-B, Pan X-F, Chen J, Cao A, Zhang Y-G, Xia L, et al. Combined lifestyle factors, incident cancer, and cancer mortality: a systematic review and meta-analysis of prospective cohort studies. Br J Cancer. 2020;122:1085–93.
22. Koene RJ, Prizment AE, Blaes A, Konety SH. Shared risk factors in cardiovascular disease and Cancer. Circulation. 2016;133:1104–14.
23. Abdel-Qadir H, Austin PC, Lee DS, Amir E, Tu JV, Thavendiranathan P, et al. A Population-Based study of cardiovascular mortality following Early-Stage breast Cancer. JAMA Cardiol. 2017;2:88–93.
24. Kaneko H, Suzuki Y, Ueno K, Okada A, Fujiu K, Matsuoka S, et al. Association of life's simple 7 with incident cardiovascular disease in 53 974 patients with cancer. Eur J Prev Cardiol. 2022;29:2324–32.
25. Lin L, Hu Y, Lei F, Huang X, Zhang X, Sun T, et al. Cardiovascular health and cancer mortality: evidence from US NHANES and UK biobank cohort studies. BMC Med. 2024;22:368.
26. Liu W, Wang J, Wang M, Hou H, Ding X, Wang M, et al. Associations between life's essential 8 and risks of all-cause and cardiovascular mortality in cancer survivors: A prospective cohort study from NHANES. Heliyon. 2024;10:e36954.
27. Vreeburg SA, Hoogendijk WJG, van Pelt J, Derijk RH, Verhagen JCM, van Dyck R, et al. Major depressive disorder and hypothalamic-pituitary-adrenal axis activity: results from a large cohort study. Arch Gen Psychiatry. 2009;66:617.
28. Dowlati Y, Herrmann N, Swardfager W, Liu H, Sham L, Reim EK, et al. A meta-analysis of cytokines in major depression. Biol Psychiatry. 2010;67:446–57.
29. Moslehi JJ. Cardiovascular toxic effects of targeted Cancer therapies. N Engl J Med. 2016;375:1457–67.
30. Lenneman CG, Sawyer DB. Cardio-Oncology: an update on cardiotoxicity of Cancer-Related treatment. Circ Res. 2016;118:1008–20.
31. Kim H, Kang HJ, Park KD, Koh K-N, Im HJ, Seo JJ, et al. Risk factor analysis for secondary malignancy in Dexrazoxane-Treated pediatric Cancer patients. Cancer Res Treat. 2019;51:357–67.
32. Schirone L, D'Ambrosio L, Forte M, Genovese R, Schiavon S, Spinosa G, et al. Mitochondria and Doxorubicin-Induced cardiomyopathy: A complex interplay. Cells. 2022;11:2000.
33. Soehnlein O. Multiple roles for neutrophils in atherosclerosis. Circ Res. 2012;110:875–88.
34. Nguyen HT, Kan EL, Humayun M, Gurvich N, Offeddu GS, Wan Z, et al. Patient-specific vascularized tumor model: blocking monocyte recruitment with multispecific antibodies targeting CCR2 and CSF-1R. Biomaterials. 2025;312:122731.
35. Libby P, Kobold S. Inflammation: a common contributor to cancer, aging, and cardiovascular diseases-expanding the concept of cardio-oncology. Cardiovasc Res. 2019;115:824–9.
36. Guzik TJ, Touyz RM. Oxidative stress, inflammation, and vascular aging in hypertension. Hypertension. 2017;70:660–7.
37. Cheng Q, Liu X-C, Chen C-L, Huang Y-Q, Feng Y-Q, Chen J-Y. The U-Shaped association of Non-High-Density lipoprotein cholesterol levels with All-Cause and cardiovascular mortality among patients with hypertension. Front Cardiovasc Med. 2021;8:707701.

38. Iyengar NM, Gucalp A, Dannenberg AJ, Hudis CA. Obesity and Cancer mechanisms: tumor microenvironment and inflammation. J Clin Oncol. 2016;34:4270–6.
39. Yuan T, Yang T, Chen H, Fu D, Hu Y, Wang J, et al. New insights into oxidative stress and inflammation during diabetes mellitus-accelerated atherosclerosis. Redox Biol. 2019;20:247–60.
40. Ramesh PR, Krishnan P, Prabu S, Srinivasan V, Niranjan V. Diagnosis and management of metabolic dysfunction- associated steatotic liver disease in South Asians- A clinical review. Obes Pillars. 2024;12:100142.
41. Gallagher EJ, LeRoith D. Epidemiology and molecular mechanisms tying obesity, diabetes, and the metabolic syndrome with cancer. Diabetes Care. 2013;36(Suppl 2 Suppl 2):S233–239.
42. Kohler LN, Garcia DO, Harris RB, Oren E, Roe DJ, Jacobs ET. Adherence to diet and physical activity Cancer prevention guidelines and Cancer outcomes: A systematic review. Cancer Epidemiol Biomarkers Prev. 2016;25:1018–28.
43. Clinton SK, Giovannucci EL, Hursting SD, The World Cancer Research Fund/American Institute for Cancer Research Third Expert. Report on diet, nutrition, physical activity, and cancer: impact and future directions. J Nutr. 2020;150:663–71.
44. McTiernan A, Friedenreich CM, Katzmarzyk PT, Powell KE, Macko R, Buchner D, et al. Physical activity in Cancer prevention and survival: A systematic review. Med Sci Sports Exerc. 2019;51:1252–61.
45. Brown JC, Winters-Stone K, Lee A, Schmitz KH. Cancer, physical activity, and exercise. Compr Physiol. 2012;2:2775–809.
46. Zheng R, Zhang S, Zeng H, Wang S, Sun K, Chen R, et al. Cancer incidence and mortality in China, 2016. J Natl Cancer Cent. 2022;2:1–9.
47. Mogavero MP, DelRosso LM, Fanfulla F, Bruni O, Ferri R. Sleep disorders and cancer: state of the Art and future perspectives. Sleep Med Rev. 2021;56:101409.

Publisher's note