HHS Public Access

Author manuscript

Cancer. Author manuscript; available in PMC 2019 August 01.

Published in final edited form as:

Cancer. 2018 August ; 124(16): 3417–3426. doi:10.1002/cncr.31572.

Putting the life in lifestyle: Lifestyle choices after a diagnosis of cancer predicts overall survival

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Abstract

Background—The aims of the present study were to examine predictors of health behaviors over time and the link between health behaviors and survival after a diagnosis of advanced cancer.

Methods—Patients with a diagnosis of advanced cancer were administered a battery of questionnaires measuring optimism, depressive symptoms, physical activity, intake of fruits and vegetables, and alcohol and tobacco use over an 18-month period. Analyses included generalized linear mixed models and Cox regression survival analyses.

Results—Of the 411 patients enrolled in the study, the mean age at cancer diagnosis was 62; the majority were male (62.3%) and white (91%). Twenty percent of patients reported using alcohol, 19% using tobacco, 19% eating fewer fruits and vegetables than recommended by the Center for Disease Control, and 28% physical inactivity after diagnosis of advanced cancer. Clinical levels of

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Support and Financial Disclosure Declaration: National Cancer Institute R01CA176809

There is no conflict of interest disclosures from any authors.

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depressive symptoms were associated with lower intake of fruits and vegetables [t=2.67, p=.007] and inactivity [t=2.11, p=.035]. Dispositional optimism was positively associated with physical activity [t=−2.16, p=0.031] and lower frequency of tobacco use [Z =−2.42, p=.015]. Multivariable analyses revealed that after adjusting for demographic variables (age, gender), depressive symptoms, and disease-specific factors (diagnosis, tumor size, cirrhosis, vascular invasion, number of lesions), alcohol use [χ^2 =4.1186, p=.042] and physical inactivity [χ^2 =5.6050, p=0.018] were linked to increased risk of mortality.

Conclusions—Greater dissemination and implementation of effective interventions to reduce alcohol use and increase physical activity in cancer patients are recommended.

Keywords

cancer; oncology; health behaviors; depression; optimism; survival

Introduction

Health behaviors, such as substance use, diet, and physical activity, have been studied in relation to the development of cancer.[1–5] However, few studies have focused on health behaviors after a diagnosis of cancer except for cancers in which health behaviors were a primary contributing factor (e.g., lung cancer).[6,7] Tobacco and alcohol use after a diagnosis of cancer is associated with increased recurrence rates and poorer survival in head and neck and lung cancer.[6,7] Higher levels of physical activity were associated with longer survival in patients with colon cancer and breast cancer.[8,9] Furthermore, physical inactivity is a predictor of all-cause mortality and a 42% increase of recurrence in breast cancer.[8,10] Higher intake of fruits and vegetables has been associated with increased survival in patients diagnosed with colorectal cancer.[10]

Research regarding the links between health behaviors and survival has advanced our understanding of the importance of lifestyle choices after a diagnosis of cancer. However, a major limitation of previous research is that health behaviors have been studied individually despite their comorbidity (e.g., alcohol use often accompanies tobacco use, poor diet often accompanies inactivity). As a result, prior studies may not have adequately accounted for the shared variance associated with various health behaviors when examining the link with survival. Furthermore, many of these studies have not assessed changes in health behaviors over time after a diagnosis of cancer and the association with survival in patients diagnosed with cancer.

Health behaviors are modifiable.[11,12] As such, understanding what factors may predict these behaviors may further facilitate effective intervention. In the general population, optimism and depressive symptoms have been shown to consistently predict health behaviors such as substance use and factors contributing to obesity.[13,14] However, these predictors have not been studied in the context of cancer where the rate of depressive symptoms and poor health behaviors have been shown to be higher than in the general population. Changes in health behaviors may also occur, without intervention, more frequently after a diagnosis of cancer.[11,15,16] Therefore, we expect that there may be a differential relationship between depressive

symptoms, optimism, and health behaviors in those diagnosed with cancer when compared to the general population.

Dispositional optimism, in the general population, has been found to predict higher levels of physical activity and intake of fruits and vegetables and decreased alcohol and tobacco use.[13,17] Optimism is also associated with a lower risk of mortality in both the general population and in some cohorts of patients diagnosed with cancer.[18–21] Health behaviors have been hypothesized to mediate the link between optimism and mortality in the general population, but little evidence has been found to support this hypothesis.[14]

In the general population, depressive symptoms have been shown to be a significant risk factor for all-cause mortality and this relationship has also been found in patients diagnosed with cancer.[22–25] Depressed smokers were 40% less likely to quit, had a higher overall risk of mortality, and relapse rate that was significantly higher than those who were not depressed.[26] A bidirectional relationship between depression and diet has been observed in otherwise healthy adults.[27,28] Initial adoption of a healthy diet (e.g., higher fruit and vegetable consumption) has been shown to decrease depressive symptoms in the short-term, but the benefits were not sustained.[28] Depressive symptoms have also been shown to be associated with subsequent increases in weight gain, lower rates of exercise, and increased consumption of alcohol in the general population.[29–31] In the general population, major depression was linked to a 43% increase in the risk of death after accounting for sociodemographic characteristics, health behaviors, and health conditions.[32] Health behaviors reduced the hazard ratio for the link between depression and mortality by 17%.[32]

We will build on prior research by examining psychological predictors of health behaviors prospectively to provide new insights that may translate into changes in clinical care aimed at improving quality of life after a diagnosis of cancer. Although these associations have been studied in the general population, due to a diagnosis of advanced cancer, we expect the rates of depression, as well as poor health behaviors, will be higher. This study will also advance our understanding of how all four health behaviors (smoking tobacco, consuming alcohol, physical activity, and fruit and vegetable consumption) contribute to survival independently, and collectively in a cohort of advanced cancer patients.

Methods

Design and Participants

This study was a secondary data analysis of participants from a study conducted at a tertiary care medical center. The Division of Hepatobiliary and Pancreatic Surgery evaluates and treats cancers related to the hepatobiliary-pancreatic system including hepatocellular, cholangio, gallbladder, and pancreatic carcinoma and other primary tumors that have metastasized to the liver (e.g., colorectal, ovarian, breast). Recruitment of patients occurred from November 2012 to June 2014 and patients were followed for 18 months (R01CA176809). Inclusion/exclusion criteria were: (1) patient had biopsy or radiographic-proven diagnosis of advanced cancer affecting the hepatobiliary or pancreatic system; (2) patient was 21 years or older; (3) patient was fluent in English; and (4) patient had no evidence of thought disorder, hallucinations, or delusions. A total of 967 patients were

approached and 541 patients (56%) agreed and consented to participate in the study. Of the 541 patients, a total of 411 completed the battery of questionnaires and were followed for 18 months or until death.

Instruments

The patients were administered questionnaires (see below) at five-time points over the course of the study including at the time of consent and at 4, 8, 12, and 18 months with the exception of optimism which was only measured at baseline due to this construct being considered stable over time (e.g., trait or dispositional optimism).

Sociodemographic—Sociodemographic data included patients' age, body mass index, gender, race, ethnicity, religious preference, educational level, income, occupation, and health insurance status and was reported on a questionnaire specifically designed for this study.

Dispositional Optimism—Dispositional optimism data was obtained using the Life Orientation Test-Revised.[32] This self-report measure has been shown to be reliable and valid.[32] Patients reported the extent of their agreement, *0* (strongly disagree) - *4* (strongly agree) with ten phrases to assess generalized optimism and pessimism. Scales were scored to obtain a continuous overall score.[32]

Depressive Symptoms—Depressive symptoms were assessed using the Center for Epidemiologic Studies - Depression Scale (CES-D). The CES-D is a reliable and valid 20-item self-report questionnaire constructed to measure depression symptoms.[33] The CES-D is recognized as a valid and reliable measure of depression amongst cancer patients.[34]

Alcohol Use—Alcohol use data were obtained by self-report. For current alcohol consumption, patients reported the average number of alcoholic drinks (e.g., one beer, one 4oz glass of wine, one shot of liquor) per week. In addition, information regarding the patients' history of alcohol consumption was gathered, including the age of onset, duration (months or years) of consuming alcohol, and an approximate amount per week. The amount, duration, and history of alcohol use were also crosschecked with patients' medical records. For the purposes of this study, we were interested in alcohol use after a diagnosis of cancer measured over time. Therefore, alcohol use was analyzed as a dichotomous variable with regard to use of alcohol or not at each time point.

Tobacco Use—Tobacco use data were obtained by self-report. Current smoking was assessed with regard to the average number of cigarettes per day. The duration the patients had smoked and the amount per week was also assessed. Self-reported cigarette smoking was checked with patient medical records. For the purposes of this study, we were interested in current tobacco use and the change in tobacco use overall over an 18-month period. Tobacco use was analyzed as a dichotomous variable with regard to patient use of a possible response to current tobacco or not at each time point.

Diet—Diet information was obtained using the Rapid Eating Assessment for Patients (REAP). The REAP is a validated and reliable questionnaire designed to facilitate the brief

assessment of diet.[35] Participants rate their agreement with 16 phrases on a scale of *Usually/Often* (0) to *Does not apply* (3), with higher responses indicating poor diet.[35] For the purposes of this study, intake of fruits and vegetables were coded as a dichotomous variable with regard to whether the patient had an intake of fruits and vegetables that met the Center for Disease Control dietary guidelines which included 1.5–2 cups of fruit and 2–3 cups vegetables per day. [36]

Physical Activity—Physical Activity data were obtained via the International Physical Activity Questionnaire (IPAQ).[37] Reliable and valid, the IPAQ assesses five facets of a previous week's physical activity: (1) job-related, (2) transportation-related, (3) housework, house maintenance, and caring for family, (4) recreation, leisure-time, and sport, and (5) time spent sitting.[37,38] The overall score was based on metabolic equivalents (METS).[37]

Medical chart abstraction

Disease-specific characteristics (e.g., diagnosis, tumor size) were abstracted from electronic records by trained members of the research team using a standardized form. Survival was measured from the date of consent until date of death using information in the electronic medical record, and if not found, was collected using the Social Security Death Index.

Procedure

The University of Pittsburgh's Institutional Review Board approved the research study before enrollment began. Patients in the study sample were referred to the study by a UPMC Liver Cancer Center by the medical team. Prior to consent, each patient spoke with a member of the study team about the risks and benefits of the study. After this discussion, written informed consent was obtained from each participant before they completed the study questionnaires.

Data Analysis

Data were entered, verified, and analyzed using SAS (v 9.4, SAS Institute Inc, Cary, NC). Descriptive statistics were performed to obtain measures of central tendency, distribution, and proportions for each variable. Patterns and amounts of missing data were examined prior to performing multiple imputations on the depressive symptoms and optimism variables. Separate generalized linear mixed models using SAS PROC GLIMMIX (multinomial distribution) or PROC GENMOD (binomial distribution) were performed for each of the four outcomes (intake of fruits and vegetables, alcohol and tobacco use, physical activity) with depressive symptoms, optimism, time, and a depressive symptoms*time interaction as the independent variables. Generalized linear mixed models allow for the inclusion of both time-varying (depressive symptoms) and time-invariant (optimism) independent variables. Survival analyses were performed using SAS PROC PHREG and included a main effect of time and a time*predictor interaction to account for predictors that varied over time. A significant interaction would represent that there was a change in the relationship between the outcome variable and the independent variable over time. Depressive symptoms, optimism, intake of fruits and vegetables, alcohol use, physical activity, tobacco use, education, number of lesions, gender, cirrhosis, diagnosis, vascular invasion, age, tumor size, and BMI were examined as predictors of survival. Due to the variable duration in treatment

(months to years) and multimodal approach to treatment (e.g., a combination of regional and systemic chemotherapy with different drugs, duration, and frequency; different types of surgeries including laparoscopic, robotic, and open surgeries; and other treatments such as yttrium-90), we did not include treatments as a variable in the model. Treatment approach was based on clinicians' discretion and the patients were not included in any randomized controlled trials testing the efficacy of cancer-related treatments. Predictors that were significantly associated with survival ($p \leq .10$) were retained and modeled in a multivariable Cox Regression if linked with health behaviors.

Results

Sociodemographic and Disease-Specific Factors of Patients

A total of 411 participants with cancer affecting the hepatobiliary-pancreatic system were included in the study, 256 (62.3%) male, mean age 62.3, S.D. = 11.1. Ninety-one percent of the sample was white. The average number of lesions was 3.71, S.D. = 2.52; and the mean tumor size was 3.4cm S.D. = 3.5. A total of 42.6% of patients had a primary diagnosis of hepatocellular carcinoma or cholangiocarcinoma, 37.5% had other primary cancers (e.g., breast, ovarian, colorectal) which had metastasized to the liver, 11.9% had neuroendocrine tumors, and 8% had cancer of the appendix, gallbladder, stomach, or pancreas. The majority of the patients had a high school education (57.6%) and 28.4% had completed high school and had a college degree. See Table 1 for sociodemographic and disease-specific characteristics.

Psychological Factors and Health Behaviors

Participants reported levels of low (31.4%), moderate (45.2%), and high (17.4%) dispositional optimism. Approximately one-third of participants (30.2%) reported clinical levels of depressive symptoms using the CES-D cutoff of 16. For those patients using substances after diagnosis, 66 patients reported alcohol use (19.7%) and 80.3% of patients reported consuming no alcohol at the time of assessment. Sixty-five patients reported tobacco use after diagnosis of cancer (19.4%) while 80.6% reported no current tobacco use at the time of baseline assessment. Sixty-five patients reported (19.4%) eating fewer fruits and vegetables than recommended by the Center for Disease Control while 80.6% reported eating the recommended daily amount of fruits and vegetables sometimes or often. Of the total number of patients, 28.4% of patients reported being physically inactive while 71.6% reported moderate to vigorous activity levels.

Approximately 146 (35.5%) of patients were newly diagnosed (< 1 month from the date of consent) while 265 (64.5%) had received a diagnosis of cancer or metastatic spread to the liver greater than one month prior to enrollment in the study. No significant group differences regarding the time since diagnosis were observed between depressive symptoms and tobacco use, fruit and vegetable intake, physical activity, alcohol use or survival. Time since diagnosis was related to optimism, which was only measured at baseline [$F(1,372) = 5.186$, $p = 0.024$]. Patients who were newly diagnosed reported a higher optimism score (Mean=22.5, S.D. =5) versus those who were diagnosed >1 month since consent

(Mean=21.3, S.D. =4.4), however, the differences between groups were not clinically meaningful.

Tables 2–4 depict the relevant statistics for main effects of depressive symptoms and optimism for each of the four outcomes. Using generalized linear mixed models, we found a main effect of clinical levels of depressive symptoms (CESD≥16) for intake of fruits and vegetables [t=2.67, p=.007] and inactivity [t=2.11, p=.035]. Dispositional optimism was positively associated with moderate to vigorous physical activity [t=−2.16, p=0.031] and lower frequency of tobacco use [Z =−2.42, p=.015]. Patients who reported higher levels of dispositional optimism had higher levels of physical activity and lower frequency of tobacco use. There were no significant main effects of depressive symptoms and optimism on alcohol use. Additionally, there were no main effects of time or time*depressive symptoms interaction effects for any of the four health behaviors. The time-by-covariate interactions represent the variable and a linear function of time. Non-significant findings indicate that there was no significant change in the relationship between the outcome and the independent variable over time. All coefficients represent a one-unit increase in the dependent variable due to the independent variable under consideration, with other independent variables held constant. All coefficients represent a one-unit increase in the dependent variable due to the independent variable under consideration, with the other independent variables held constant.

Univariate Cox regression models of demographic, disease-specific, and psychological factors with survival

Cox regression analyses were used to determine significant predictors of survival. Time-varying covariates were modeled using the time by covariate interaction. We examined demographic, disease-specific, and psychological factors that are often associated with survival. The analyses revealed that being male [χ^2=38.59, p<.001]; a diagnosis of gallbladder, stomach, pancreatic, hepatocellular or cholangio carcinoma [χ^2=133.33, p<.001]; presence of cirrhosis [χ^2=144.89, p<.001]; and vascular invasion [χ^2=202.65, p<.001] were significantly associated with poorer overall survival. Cox regression analyses revealed older age at diagnosis [Standardized β=.016, p<.001]; greater number of lesions [Standardized β=−.026, p<.001]; lower body mass index [Standardized β=−.0147, p=.005]; and larger tumor size [Standardized β=.104, p<.001] was associated with poorer overall survival. The Hazard Ratios that are close to 1.0 (e.g., age, number of lesions) should be interpreted cautiously despite being statistical significance.

Depressive symptoms were associated with poorer survival [χ^2=3.738, p=.004] but optimism was not linked to survival [χ^2=0.225, p=.635]. We found that not consuming alcohol after a diagnosis of cancer affecting the hepatobiliary and pancreatic system was associated with better survival [χ^2=5.324, p=.021]. A higher level of physical activity was associated with improved survival [χ^2=4.206, p=.040]. Tobacco use [χ^2=1.572, p=.21] and intake of fruits and vegetables [χ^2=.089, p=.735] were not found to be associated with overall survival. (See Table 5).

Multivariable Cox regression testing the role of health behaviors and survival after a diagnosis of cancer

Demographic, disease-specific and psychological variables found to be associated with survival in the univariable analyses ($p<0.10$) were entered into the multivariable model. After adjusting for demographic variables, disease-specific factors, and depressive symptoms; baseline physical activity levels [χ^2 =5.61, p=0.017] and alcohol use after a diagnosis of cancer [χ^2=4.12, p=0.042] remained significantly associated with survival. Changes in physical activity and alcohol use over time was not significantly associated with survival. Vascular invasion [x=129.469, p<0.001] and larger tumor size [x=6.923, p=0.009] were associated with poorer survival in the multivariable model. See Table 6.

Discussion

Health behaviors are often studied with regard to the development of cancer, but are not routinely assessed once an individual has been diagnosed with cancer.[4] However, a diagnosis of cancer can be an opportunity for people to change poor health behaviors, a “teachable moment” when motivation may be high to change maladaptive health behaviors.[11,16] Changing a poor health behavior, such as tobacco use after a diagnosis of cancer, may prevent a second primary cancer and/or development or progression of other health conditions (e.g., coronary heart disease).[4]

Consistent with prior research, we observed that having clinical levels of depressive symptoms was associated with lower levels of fruit and vegetable consumption. Maintenance of weight after a diagnosis of cancer may be protective as there is a link between cachexia and mortality.[39] We did not find a link between diets low in fruits and vegetables and poorer survival in our study. In contrast with previous research, tobacco use after diagnosis was also not linked to poorer survival. We observed that continued alcohol use and physical inactivity after a diagnosis of cancer was linked to poorer survival in patients diagnosed with cancers affecting the hepatobiliary and pancreatic system after adjusting for demographic, psychological, and disease-specific factors.

In this cohort of patients, twenty percent of our patients continued to use alcohol after diagnosis. Few studies to date have examined alcohol use after a cancer diagnosis. Of the studies that have been conducted, a 3.8-fold increase in the development of a second primary tumor was observed in patients with head and neck cancer.[2] Also, those patients who consumed more than 15 alcoholic drinks per week, compared to those who consume less alcohol, had a higher rate of recurrence.[40] People diagnosed with head and neck cancers who reported high alcohol consumption after diagnosis were at a greater risk from dying from cardiovascular, pulmonary, or alcohol-related diseases.[40]

While excessive alcohol use may contribute to the development of some cancers, and people with these cancers may be at a higher risk for alcohol use after diagnosis, only 7% of the patients in this study reported excessive alcohol use prior to their diagnosis. An additional 6.8% of patients diagnosed with hepatitis B and/or C or non-alcohol steatohepatitis, reported moderate alcohol use after a diagnosis of cancer. The findings of this study were not consistent with prior research that has shown that alcohol use was not significantly related to

survival in patients diagnosis with hepatocellular carcinoma.[41] So few studies have focused on the role of alcohol use on survival after diagnosis of pancreatic or other cancers, it is difficult to make definitive conclusions.[42–45]

In this study, 28% of patients reported physical inactivity and this was linked to poorer survival after adjusting for demographic, disease-specific, and psychological factors. Demark-Wahnefried and colleagues reported that 58% of their respondents reported regular exercise (defined as 30 minutes of exercise for at least 3 days per week).[46] Retrospective studies among patients with breast and colorectal cancer have shown reduced participation in exercise after a cancer diagnosis during treatment.[40] Physical activity after a diagnosis of breast cancer was linked to higher quality and satisfaction with life.[47,48] Interventions aimed at increasing physical activity have been shown to result in 20% improvement in maximal oxygen uptake, reduced fatigue, prevention of weight gain, lower rates of neutropenia, and fewer sleep problems.[49–52] The majority of interventions, however, have been conducted with women diagnosed with breast cancer.[52]

Potential predictors of poor health behaviors included optimism and depressive symptoms. Depressive symptoms have been linked to increased tobacco use, relapse of tobacco use, poor diet, alcohol abuse, and inactivity.[27,53–58] In contrast, dispositional optimism has been found to be linked to a healthier diet, decreased alcohol use and higher levels of physical activity, and lower rates of tobacco use.[13] Our study also confirmed significant associations between dispositional optimism and higher levels of physical activity and lower levels of tobacco use. A trend toward significance was observed between dispositional optimism and fruit and vegetable intake. Dispositional optimism is considered a relatively stable trait throughout one’s life, so it is possible that those who were engaged in poor health behaviors prior to their diagnosis, and had a moderate to high level of optimism, may not have had a change in health behaviors after diagnosis. Consistent with prior research, depressive symptoms were a significant predictor of physical activity which was in turn linked to better overall survival. However, in contrast to earlier research, optimism was not found to be significantly related to survival in this cohort of patients.

The study had many strengths including the inclusion of several health behaviors that were examined simultaneously to understand the potential of shared variance and link to survival, considering these health behaviors are often correlated. The health behaviors and predictors were also assessed longitudinally, so changes over time could be included in the model. A large number of demographic, disease-specific factors, and psychological factors were included in multivariable analyses to adjust for factors linked to survival, which has been a limitation in prior research.[3,57]

The sample was primarily male and Caucasian, which is a limitation of this study. Although we used a valid and reliable measure of physical activity, the use of actigraphy to “objectively” assess physical activity is warranted to confirm these findings.[2,4,54] Alcohol and tobacco use were measured using self-report rather than measurement of nicotine and alcohol in the blood or urine, which was an additional limitation.[55]

Although multidisciplinary teams and multimodal treatment in oncology is recommended, few studies include these multimodal treatment approaches in their analyses of survival.[41,42,59–64] A review examining the relationship between multidisciplinary care and patient survival was inconclusive due to methodological limitations that included a lack of data regarding treatment.[65] There was significant heterogeneity of treatment within and across cancer types. For example, in our cohort of patients, one patient diagnosed with HCC may receive five cycles of transarterial chemoembolization with Cisplatin in 18 months while another patient with the same diagnosis may receive one treatment with 90-Yttrium. Treatment decisions, particularly for advanced cancers, such as the cancers included in this study, are often made based on the clinicians' own experience and the patients' response to treatment. As a result of this heterogeneity of the type, frequency, and duration of treatments within and across cancer types, we did not include treatment as a predictor of survival. We acknowledge this to be a limitation of the study, but prior analyses using treatment at the time of entry into the study were not predictive of survival.[66]

Without clinical intervention, Blanchard and colleagues found that approximately 46% of people diagnosed with cancer quit smoking, 47% of patients improved their dietary habits and 30% exercised more often.[67] Approximately 50–60% of people diagnosed with cancer show interest in interventions to change health behaviors such as diet, exercise, and tobacco use.[67] The development of interventions to increase activity levels in cancer patients is recommended. Due to the rare types of cancers and distance many patients travel to the medical center for treatment, home-based interventions that use technology and can be scalable are recommended. The development of novel interventions to reduce alcohol use, even for patients where alcohol was not considered a contributing factor to their cancer, is important to give these patients the best possible opportunity to improve quality of life and potentially improve their survival. Depression was also an important predictor of health behaviors, particularly physical activity and consumption of fruits and vegetables. It would be important to include assessment and treatment of depression in any interventions designed to target health behaviors. Health behaviors remain an important target for intervention not only before a diagnosis of cancer, but after an individual has been diagnosed with cancer.

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Table 1

Demographic and Disease Specific Factors of the Sample

Variable	n (%)
Gender	
Male	256 (62.3)
Female	155 (37.7)
Race	
Caucasian	374 (91.1)
Non-Caucasian	37 (8.8)
Age at Time of Evaluation	
Mean (S.D)	62.3 (11.1)
Education	
Less than high school	23 (6.1)
High School Only	237 (57.6)
High School and College	117 (28.4)
Number of Lesions	
Mean (S.D.)	3.71 (2.52)
Tumor Size	
Mean (S.D.)	3.4 (3.5)
Diagnosis	
Hepatocellular and cholangio carcinoma	175 (42.6)
Gallbladder, stomach, pancreatic	33 (8.0)
Non-liver primary tumors with liver metastases	154 (37.5)
Neuroendocrine carcinoma	49 (11.9)

Table 2

Psychological predictors of diet and physical activity

Parameters	Estimate	Standard error	C.I. (95%)	t	P-Value
INTAKE OF FRUITS AND VEGETABLES					
Depressive symptoms	0.057	0.021	0.015–0.098	2.67	.007
Dispositional Optimism	−0.031	0.022	−0.074–0.012	−1.40	.161
Depressive symptoms*Time (Diagnosis)	−0.042	0.023	−0.087–0.003	−1.82	.069
Depressive symptoms*Time (4 months)	−0.049	0.027	−0.102–0.003	−1.84	.065
Depressive symptoms*Time (8 months)	−0.037	0.027	−0.091–,0.016	−1.36	0.173
Depressive symptoms*Time (12 months)	−0.006	0.027	−0.060–0.047	−0.25	0.805
Depressive symptoms*Time (18 months)	0.001	0.001	0.001–0.001		
PHYSICAL ACTIVITY					
Depressive symptoms	0.052	0.024	0.003–0.099	2.11	.035
Dispositional Optimism	−0.050	0.023	−0.095–0.004	−2.16	.031
Depressive symptoms*Time (Diagnosis)	−0.010	0.026	−0.050–0.069	−0.40	.686
Depressive symptoms*Time (4 months)	0.009	0.030	−0.102–0.003	0.30	.764
Depressive symptoms*Time (8 months)	0.012	0.031	−0.091–,0.016	0.39	.696
Depressive symptoms*Time (12 months)	−0.017	0.033	−0.082–0.047	−0.54	.591
Depressive symptoms*Time (18 months)	0.001	0.001	0.001 – 0.001		

Table 3

Psychological predictors of tobacco use

Parameters	Estimate	Standard error	C.I. (95%)	Z	P-Value
Depressive symptoms	−0.001	0.013	−0.027 – 0.025	−0.09	0.9251
Dispositional Optimism	−0.058	0.024	−0.105 – 0.011	−2.42	0.016
Depressive symptoms*Time (Diagnosis)	−0.003	0.016	−0.035 – 0.029	−0.19	0.852
Depressive symptoms*Time (4 months)	0.004	0.017	−0.028 – 0.036	0.24	0.810
Depressive symptoms*Time (8 months)	−0.004	0.0150	−0.033 – 0.025	−0.28	0.777
Depressive symptoms*Time (12 months)	−0.011	0.0136	−0.037 – 0.016	−0.78	0.437
Depressive symptoms*Time (18 months)	0.001	0.0001	0.001 – 0.001	.	.

Depressive symptoms*Time – Covariate Interaction

Table 4

Psychological predictors of alcohol use after diagnosis of cancer

Parameters	Estimate	Standard error	C.I. (95%)	Z	P-Value
Depressive symptoms	−0.0013	0.0139	−0.029 – 0.026	−0.09	0.924
Dispositional Optimism	0.015	0.021	−0.026 – 0.055	0.72	0.474
Depressive symptoms*Time (Baseline)	−0.0034	0.017	−0.037 – 0.030	−0.21	0.832
Depressive symptoms*Time (4 months)	−0.013	0.024	−0.059 – 0.034	−0.54	0.587
Depressive symptoms*Time (8 months)	−0.009	0.021	−0.050 – 0.031	−0.45	0.652
Depressive symptoms*Time (12 months)	0.016	0.014	−0.012 – 0.044	1.11	0.265
Depressive symptoms*Time (18 months)	0.001	0.001	0.001 – 0.001	.	.

Depressive symptoms*Time – Covariate Interaction

Table 5

Univariate Cox Regression analyses examining predictors of survival

Parameters	**β**	**Standard error**	χ^2	***p*-value**	**HR (95% CI)**
Depressive symptoms	0.021	0.011	3.738	.004	1.02 (1.01,1.04)
Optimism	−0.037	0.008	0.225	.635	0.99 (0.98,1.01)
Alcohol (reference: no use)	1.679	0.728	5.324	.021	2.27 (1.71,4.16)
Physical Activity (METS)	−0.423	0.206	4.206	.040	0.75 (0.64,0.88)
Diet (reference: recommended intake of fruits of vegetables)	−0.039	0.131	0.089	.765	0.97 (0.87,1.08)
Tobacco Use (reference: no use)	−0.052	0.413	1.572	.210	0.86 (0.57,1.28)
Gender (reference: male)	0.402	0.066	38.589	<.001	1.50 (1.32,1.71)
Cirrhosis (reference: no cirrhosis)	0.740	0.061	144.887	<.001	2.09 (1.86,2.36)
Education (reference: high school and college) Less than high school	0.026	0.144	0.034	.854	1.02 (0.77,1.36)
High school	−0.012	0.079	0.223	.880	0.99 (0.85,1.15)
Diagnosis (reference: NET) Gallbladder, stomach, pancreatic	0.701	0.080	77.602	<.001	2.02 (1.72,2.38)
Hepatocellular and cholangio carcinoma	0.453	0.124	13.267	.001	1.57 (1.23,2.01)
Non-liver primaries with liver metastases	−0.065	0.091	0.500	.479	0.94 (0.78,1.12)
Vascular invasion (reference: absent)	0.976	0.070	194.865	<.001	2.65 (2.31,3.04)
Age at diagnosis	0.016	0.003	35.080	<.001	1.02 (1.01,1.02)
Largest tumor size (cm)	0.104	0.007	218.840	<.001	1.11 (1.09,1.13)
Body mass index	−0.015	0.005	7.960	.005	0.99 (0.98,0.99)
Number of Lesions	−0.026	0.012	4.470	.035	0.97 (0.95,0.99)

HR – Hazard Ratio

Unless reference indicated, all variables are continuous

Table 6

Multivariable Cox regression analyses examining predictors of survival

Parameter	χ^2	p-value	HR (95% CI)
Time	3.356	.500	1.31 (1.08,1.56)
Age at diagnosis	0.869	.351	1.01 (0.98,1.03)
Gender (reference: male)	2.703	.100	1.45 (0.93,2.25)
Body mass index	2.573	.109	0.97 (0.94,1.01)
Diagnosis (reference: NET)	---	---	---
Gallbladder, Pancreatic, stomach carcinoma	2.336	.126	0.59 (0.29,1.23)
Hepatocellular and cholangiocarcinoma	0.103	.749	0.89 (0.40,1.96)
Non-liver primaries with liver metastases	0.384	.536	0.82 (0.46,1.46)
Number of lesions	1.534	.216	1.06 (0.97,1.15)
Largest tumor size (cm)	6.923	.009	1.08 (1.02,1.15)
Cirrhosis	3.012	.083	1.78 (0.93,3.45)
Vascular invasion (reference: absent)	129.469	<.001	2.23 (1.35,3.67)
Depressive symptoms	0.526	.468	1.03 (1.01,1.04)
Depressive symptoms*Time	2.656	.617	0.97 (0.91, 1.04)
Alcohol use (reference: no use)	4.119	.042	4.67 (1.05,20.66)
Alcohol use (reference: no use)*Time	2.695	.610	1.36 (0.78,2.38)
Physical activity (METS)	5.605	.018	0.57 (0.35,0.90)
Physical activity (METS)*Time	3.714	.446	0.88 (0.71,1.14)

Depressive symptoms*Time – Covariate Interaction

Alcohol Use*Time – Covariate Interaction

Physical Activity*Time – Covariate Interaction

Unless reference indicated, all variables are continuous