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The association of health behaviors prior to cancer diagnosis and functional aging trajectories after diagnosis: Longitudinal cohort study of middle-aged and older US cancer survivors

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ABSTRACT

We aimed to determine the influence of modifiable health behaviors prior to a cancer diagnosis on functional aging trajectories after diagnosis among middle-aged and older cancer survivors in the United States. Data were from biennial interviews with 2,717 survivors of a first incident cancer diagnosis after age 50 in the population-based US Health and Retirement Study from 1998 to 2016. Smoking status, alcohol use, and vigorous physical activity frequency were assessed at the interview prior to cancer diagnosis. Confounder-adjusted multinomial logistic regression was used to determine the associations between each pre-diagnosis health behavior and post-diagnosis trajectories of memory function and limitations to activities of daily living (ADLs), which were identified using group-based trajectory modeling. Overall, 20.7 % of cancer survivors were current smokers, 30.6 % drank alcohol, and 27.1 % engaged in vigorous physical activity >=once a week prior to their diagnosis. In the years following diagnosis, those who had engaged in vigorous physical activity > once a week were less likely to have a medium–high (OR: 0.5; 95 % CI: 0.2–0.9) or medium–low memory loss trajectories (OR: 0.6; 95 % CI: 0.3–1.0) versus very low memory loss trajectory, and were less likely to have a high, increasing ADL limitation trajectory (OR: 0.3; 95 % CI: 0.2, 0.6) versus no ADL limitation trajectory. Vigorous physical activity, but not smoking or alcohol use, was associated with better post-diagnosis functional aging trajectories after a first incident cancer diagnosis in mid-to-later life in this population-based study. Identification of modifiable risk factors can inform targeted interventions to promote healthy aging among cancer survivors.

1. Introduction

By 2030, the population of cancer survivors in the United States (US) is expected to grow by 31% to 22.2 million people, with the majority being over age 65 (National 2021). Cancer and its treatments can have a variety of effects on cancer survivors, including acceleration of the aging process and declines in physical and cognitive function (Ahles and Root, 2018; Ahles et al., 2012). Functional status and quality of life are outcomes that are highly valued by middle-aged and older cancer survivors, and are important dimensions of healthy aging (Fried et al., 2002). There is a need to understand modifiable drivers of post-cancer diagnosis cognitive and physical functional aging trajectories, in order to identify survivors who could be at high risk and may potentially benefit from interventions to support their healthy aging. Among modifiable risk factors, strong evidence suggests that health behaviors including physical activity, smoking, and alcohol use can influence both cognitive and physical health in later-life and therefore, the engagement of these health behaviors prior to a cancer diagnosis could impact survivorship after a cancer diagnosis (Beydoun et al., 2014; Lee et al., 2010).

1.1. Vigorous physical activity

In the cancer-free population, engaging in physical activity has been found to be protective against both cognitive and physical decline

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(Nuzum et al., 2020; Lautenschlager et al., 2008; Stewart, 2005; Lin et al., 2020). Aichberger et al., found that individuals who participated in any type of physical activity had less cognitive decline compared to those who didn't exercise regularly, with this benefit being more pronounced when vigorous physical activity was done more than once a week compared to doing vigorous physical activity less than once a week (Aichberger et al., 2010). Physical activity can support healthy aging by reducing frailty and risks of falls, which can help prevent limitations to daily activities and physical disability (Theou et al., 2011) and can improve cognitive health by increasing blood flow to the brain, promoting neurogenesis and maintaining hippocampus volume (Cass, 2017). Physical activity can further support healthy aging by preventing and managing comorbidities including hypertension and diabetes (Eckstrom et al., 2020).

1.2. Smoking

Smoking is a known risk factor for myriad of negative health outcomes (Risks, 2021). The adverse effects of smoking can often be compounded in older adults by exacerbating negative outcomes associated with chronic conditions such as heart disease, hypertension, and diabetes (U.S. Department of Health and Human, 2014). Smoking exacerbates vascular damage and cerebral ischemia in the brain, which is associated with higher risk of cognitive decline and dementia (Elbejjani et al., 2019), as well as increases the risk of frailty and disability (Peters et al., 2008; Anstey et al., 2007; Amiri and Behnezhad, 2019).

1.3. Alcohol use

The evidence on alcohol use and healthy aging is mixed, with some studies finding that moderate alcohol use compared with no drinking is beneficial for healthy aging including physical and cognitive health (Ronksley et al., 2011; Britton et al., 2008; Kojima et al., 2018), while others studies have found a u-shape association between alcohol use and cognitive impairment with mild/moderate alcohol use having lower risk of dementia compared to either no drinking or heavy drinking (Krivanek 2021). The impact of alcohol use on cognitive and functional aging outcomes is often a result of confounding (Fillmore et al., 2007), as moderate alcohol use is highly correlated with both socioeconomic status and education (Collins, 2016) which are shown to be influential in cognitive and physical functioning (Lövdén et al., 2020). However, even after controlling for these factors, studies have found similar associations (Lang et al., 2007). The impact of alcohol use on cognitive health is not fully understand and the role of alcohol use prior to a cancer diagnosis on cognitive aging after diagnosis is not known.

1.4. Current study

Most previous research on health behaviors among cancer survivors has focused on the influence of pre-diagnosis health behaviors on cancer incidence, or on post-diagnosis health behaviors on the health outcomes of cancer survivors (Chen et al., 2019; Lacombe et al., 2019; Spei et al., 2019; Cortés-Ibáñez et al., 2020). Fewer have examined the influence of pre-cancer diagnosis health behaviors on longer-term post-cancer diagnosis outcomes such as cognitive and physical functional aging trajectories. Cognitive reserve, or the characteristic of an individual to maintain cognitive function despite underlying brain pathology, has been proposed as a potential reason for individual differences in cognitive aging trajectories and rates of cognitive decline (Stern, 2009). Smoking and alcohol use prior to a cancer diagnosis could lessen the levels of cognitive reserve increasing susceptibly to cognitive decline after diagnosis, while engaging in vigorous physical activity could increase cognitive research and provide a buffer to the biological affects of cancer (Clare et al., 2017; The National Institute on Aging, 2020). Furthermore, these health behaviors could have a similar affect to physical function trajectories. It's possible that engaging in beneficial health behaviors prior to a cancer diagnosis could protect against the affects of cancer and its treatment whereas engaging in more adverse health behaviors could weaken the cognitive and functional reserves making some individuals more vulnerable to the effects of cancer and its treatment. Despite the growing population of older cancer survivors, there is a paucity of evidence on how pre-cancer diagnosis health behaviors could influence long-term cognitive and physical functional aging trajectories after a cancer diagnosis.

We aimed to determine the associations between pre-cancer diagnosis vigorous physical activity, smoking, and alcohol use and previously identified post-cancer diagnosis functional aging trajectories, defined as separate memory loss trajectories and activities for daily living (ADL) limitation trajectories, in a cohort of middle-aged and older cancer survivors in the US. We hypothesized that: 1) older cancer survivors who engaged in vigorous physical activity at least once a week (versus <once per week) prior to diagnosis will have better functional aging trajectories; 2) current smoking prior to diagnosis (versus never smoking) will be associated with worse functional aging trajectories; and 3) alcohol use prior to diagnosis (versus no alcohol use) will be associated with better functional aging trajectories.

2. Methods

2.1. Study design and sample

This study used data from 1998 to 2016 from survivors of a first incident cancer after age 50 years in the population-based US Health and Retirement Study (HRS) (Sonnega et al., 2014). The HRS data are collected in biennial interview waves through in-person and telephone interviews. Proxy interviews with a spouse, other family member, or friend are conducted for HRS participants who are too impaired to directly participate due to physical or cognitive limitations (Wu et al., 2013). Eligible participants were US adults born before 1949 who participated in the 1998 HRS interview with no self-reported cancer history prior to 1998, and who had a new diagnosis of any cancer type except non-melanoma skin cancer over the follow-up period (n=3,747). Hispanic participants were excluded (n = 280) because the memory score algorithm we used to retain memory data from proxy participants did not validate well for most Hispanic participants in the HRS (Ofstedal et al., 2005). Additional exclusions are described in Fig. 1. The final analytic sample included 2,717 individuals (Fig. 1). This study was approved by the University of Michigan Institutional Review Board.

2.2. Measures

2.2.1. Incident cancer ascertainment

Incident cancer status was defined as a self-reported newly reported physician diagnosis of cancer and was assessed at each interview with the question, "*Has a doctor ever told you that you have cancer or a malignant tumor, excluding minor skin cancers?*" (yes/no). The month and year of cancer diagnosis was self-reported, allowing us to determine the timing of the memory assessments and covariates relative to cancer diagnoses. For participants who died between interviews, we ascertained cancer diagnoses from post-death interviews with a spouse, family member, or friend. The HRS does not report information on cancer type in the publicly available data and does not collect information on cancer stage. For this analysis, baseline was considered the interview wave immediately prior to which the participant reported a cancer diagnosis.

2.2.2. Memory and ADL limitations

Memory was assessed at each biennial study interview as immediate and delayed recall of a 10-word list read out loud by the interviewer (Jorm, 1994). For participants represented by a proxy, memory was assessed by the proxy informant using the 16-item version of the Jorm Informant Questionnaire for Cognitive Decline (IQCODE) and a 5-point Likert scale of proxy-reported memory (Jorm et al., 1991; Jorm et al.,

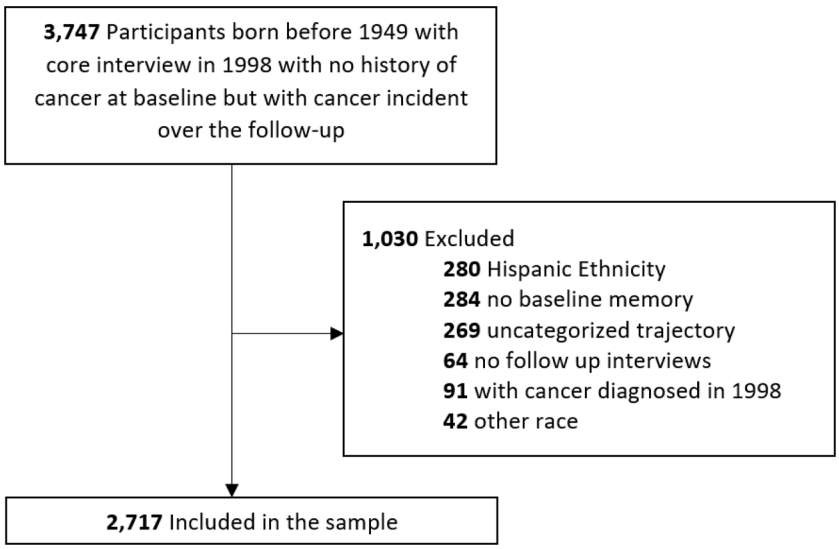

Fig. 1. Selection of the study population from the Health and Retirement Study.

2000; Katz et al., 1963). To reduce the bias that could be introduced by excluding participants represented by a proxy, the direct and proxy assessments of memory were combined using a validated algorithm developed by Wu et al, (Wu et al., 2013) allowing us to retain participants across the full range of cognitive function. Limitations to ADLs were assessed using self-reported difficulty with each of eating, bathing, dressing, transferring, toileting, and walking across a room (Katz et al., 1963). For each activity, difficulty was recorded as present (i.e., difficulty with activity or cannot/does not do) or absent (no difficulty). A 6-point ADL summary score was computed for each individual based on the sum of reported difficulties across all 6 activities.

2.2.3. Pre-cancer diagnosis vigorous physical activity, smoking, and alcohol use

Self-reported vigorous physical activity, ever and current smoking, and alcohol use were measured at the interview wave prior to a cancer diagnosis (baseline) and therefore could differ by participant. These health behaviors were chosen because of the strong evidence that lifestyle factors can influence both cognitive and physical health in later-life and were available in the HRS. (Anstey et al., 2007; Kojima et al., 2018; Lin et al., 2020; Song et al., 2022; The National Institute on Aging, 2020).

2.2.4. Vigorous physical activity

For interviews conducted in 1998, 2000, and 2002, respondents were asked "*On average over the last 12 months have you participated in vigorous physical activity or exercise three times a week or more? By vigorous physical activity, we mean things like sports, heavy housework, or a job that involves physical labor*." Respondents answered "yes" or "no". From the 2004 forward, participants were asked "*How often do you take part in sports or activities that are vigorous, such as running or jogging, swimming, cycling, aerobics or gym workout, tennis, or digging with a spade or shovel*". Response options were "every day", "more than once per week", "once per week", "one to three times per month", or "never". Due to these cross-wave, we coded vigorous physical activity as those who participated in vigorous physical activity more than once a week, once a week or less, and never.

2.2.5. Smoking

For ever smoking, respondents were asked, "*Have you ever smoked cigarettes?*" with responses coded as "yes" or "no". Those who responded as ever having smoked cigarettes were coded as an ever smoker, while those who responded having never smoked cigarettes were coded as never smoker. For current smoking, respondents were asked, "*Do you smoke cigarettes now?*" regardless of whether they had previously smoked. Current smokers were those who responded 'yes', while those who responded 'no' were coded as nonsmoker/former smoker.

2.2.6. Alcohol use

Participants were asked, "*In the last three months, on the days you drink, about how many drinks do you have?*" For respondents who said they never drink alcohol, this variable was set to zero while those who drank any alcohol this variable was set to 1. We additionally examined the continuous number of drinks per day.

2.2.7. Covariates

Potential confounders were assessed at the wave immediately prior to cancer diagnosis and were: age (years), sex (male; female), race (White; Black), education (years), self-reported history of each physician-diagnosed hypertension, diabetes, and stroke (yes; no for each), body mass index (BMI; calculated as weight in kilograms divided by height in meters squared), depressive symptoms (measured using the 8-item Center for Epidemiologic Studies Depression scale [CES-D] (Radloff, 1977) and treated as a continuous variable with higher values indicating more depressive symptoms), ADL limitations (continuous with a range of 1–5), and memory scores (continuous, with a range of −1.84, 2.44).

2.3. Statistical analysis

Previously, we identified memory loss and ADL limitation trajectories at the time of cancer diagnosis using latent growth curve modeling (Westrick et al., 2022). Based on a combination of interpretability and model fit, we identified five memory loss trajectories: very low memory loss; low memory loss; medium–low memory loss; medium–high memory loss; and high memory loss (reference outcome category); and four ADL limitation trajectories: no limitations (reference outcome category); low limitations; medium limitations, and high, increasing limitations (Westrick et al., 2022). For the present study, descriptive statistics were generated, including means and standard deviations (SD) for continuous variables, and counts and percentages for categorical variables. To assess how each pre-diagnosis health behavior was associated with post-diagnosis memory loss and ADL limitation trajectories, we specified multinomial logistic regression models, controlling for confounders with sampling weights (Lee et al., 2021), for each of the memory loss and ADL limitation trajectories as outcomes. All analyses were conducted using

Stata/SE version 16.0 (StataCorp).

3. Results

Baseline characteristics of study participants are shown in Table 1. Half of the sample was male (50.6%) and the majority was white (86.6%). The mean age at baseline was 73.2 (8.7) years (Table 1). The median follow-up time after a cancer diagnosis was 1 year (IQR: 0 – 5 years). Of the 2,717 cancer survivors, 27.1% reported engaging in vigorous physical activity more than once a week, 66.3% reported having ever smoked, 20.7% reported being a current smoker, and 30.6% reported drinking alcohol at the interview wave prior to their self-reported diagnosis. More men than women reported engaging in vigorous physical activity-one or more times a week (58.8% vs 41.2%; $p < 0.001$), having smoked (57.4% vs 42.6%; $p < 0.001$), and consuming any alcohol (63.2% vs 36.8%; $p < 0.001$) prior to their cancer diagnosis.

Participants who reported engaging in no vigorous physical activity were more likely to be in the high memory loss and medium–high memory loss trajectories than those who engaged in vigorous physical activity (8.5% vs 3.4% and 22.6% vs 11.1%, respectively; Table 1) while those who reported no vigorous physical activity also were more likely to be in the high, increasing ADL limitation trajectory compared to those who engaged in vigorous physical activity more than once a week (11.3% vs 1.9%, $p < 0.001$; Table 1). More non-smokers than smokers were in the high memory loss trajectory (6.9% vs 3.4, Table 1) while more participants who drank alcohol than those who did not drink alcohol were in the low and very low memory loss trajectories (32.2% vs 25.7% and 22.9% vs 19.1%, respectively, $p < 0.001$; Table 1).

3.1. Regression analysis: Memory loss trajectories

For memory loss trajectories, cancer survivors who engaged in vigorous physical activity more than once a week (vs never) prior to their cancer diagnosis were less likely to be in the medium–high (OR: 0.5; 95% CI: 0.2–0.9) or medium–low (OR: 0.6; 95% CI: 0.3–1.0) memory loss trajectories compared to the very low memory loss trajectory (Table 2). Participants who reported ever smoking (vs non smokers) had higher odds of being in the low memory loss trajectory

Table 1
Characteristics of cancer survivors by smoking, alcohol use, and physical activity, the US Health and Retirement Study, 1998–2016, n = 2,717.

		Vigorous Physical Activity			Ever Smoker		Current Smoker		Alcohol Use	
	Total N = 2717	**Never 1155 (42.5)**	**<1/ week 826 (30.4)**	**>=1/ week 736 (27.1)**	**Yes 1800 (66.3)**	**No 902 (33.2)**	**Yes 617 (20.7)**	**No[1] 2,368 (79.3)**	**Yes 913 (30.6)**	**None 2,072 (69.4)**
Age, mean (SD), *years*	73.2 (8.7)	75.3 (8.4)	72.3 (9.15)	71.3 (8.01)	72.6 (8.4)	74.3 (9.1)	70.1 (7.7)	74.0 (8.8)	72.4 (8.41)	73.5 (8.1)
Male, n (%)	1374 (50.6)	509 (44.0)	432 (52.3)	433 (58.8)	1033 (57.4)	333 (36.9)	277 (49.3)	1097 (50.9)	540 (63.2)	834 (44.8)
White, n (%)	2352 (86.6)	985 (85.2)	711 (86.1)	656 (89.1)	1547 (58.9)	791 (87.7)	454 (80.8)	1898 (88.1)	789 (92.4)	1563 (83.9)
Education, mean (SD), *years*	12.6 (2.9)	12.3 (2.8)	12.3 (5.36)	13.1 (2.85)	12.5 (2.8)	12.8 (2.9)	11.9 (2.6)	12.8 (2.9)	13.6 (2.7)	12.1 (2.9)
Depressive symptom score, mean (SD)[2]	1.6 (1.9)	1.9 (2.1)	1.67 (2.03)	1.14 (1.67)	1.6 (2.0)	1.5 (1.9)	1.9 (2.1)	1.5 (1.9)	1.3 (1.8)	1.8 (2.1)
Pre-diagnosis memory z-score, mean (SD)	0.9 (0.5)	0.8 (0.5)	0.88 (0.56)	1.02 (0.42)	0.9 (0.5)	0.9 (0.5)	1.0 (1.4)	0.9 (0.4)	0.9 (0.4)	0.9 (0.5)
Pre-diagnosis number of ADL limitations, mean (SD)	0.3 (0.7)	0.3 (0.9)	0.31 (0.81)	0.11 (0.44)	0.3 (0.7)	0.3 (0.8)	0.3 (0.9)	0.2 (0.7)	0.2 (0.6)	0.3 (0.8)
BMI, mean (SD)	26.9 (5.4)	27.4 (6.1)	26.8 (5.4)	26.4 (4.3)	26.7 (5.4)	27.3 (5.5)	25.6 (5.5)	27.3 (5.4)	26.3 (4.8)	27.2 (5.7)
Post-diagnosis memory loss trajectory										
High memory loss	169 (6.2)	98 (8.5)	46 (5.6)	25 (3.4)	98 (5.4)	71 (7.9)	19 (3.4)	150 (6.9)	32 (3.8)	137 (7.4)
Medium-High memory loss	487 (17.9)	261 (22.6)	144 (17.4)	82 (11.1)	323 (17.9)	161 (17.9)	73 (12.9)	414 (19.2)	113 (13.2)	374 (20.1)
Medium-Low memory loss	755 (27.8)	351 (30.4)	216 (26.2)	188 (25.5)	498 (27.7)	255 (28.3)	144 (25.6)	611 (28.4)	238 (27.9)	517 (27.8)
Low memory loss	754 (27.8)	286 (24.8)	220 (26.6)	248 (33.7)	533 (29.6)	213 (23.6)	194 (34.5)	560 (25.9)	275 (32.2)	479 (25.7)
Very Low memory loss	552 (20.3)	159 (13.8)	200 (24.2)	193 (26.2)	348 (19.3)	202 (22.4)	132 (23.5)	420 (19.5)	196 (22.9)	356 (19.1)
Post-diagnosis ADL limitation trajectory										
High, Increasing limitations	184 (6.8)	131 (11.3)	39 (4.7)	14 (1.9)	120 (6.7)	63 (6.9)	37 (6.6)	147 (6.8)	35 (4.1)	149 (8.0)
Medium limitations	792 (29.0)	327 (28.3)	237 (28.7)	228 (30.9)	538 (29.9)	249 (27.6)	181 (32.2)	611 (28.4)	233 (27.3)	559 (30.0)
Low limitations	784 (28.9)	405 (35.1)	238 (28.8)	141 (19.2)	511 (28.4)	270 (29.9)	108 (17.5)	631 (29.3)	196 (22.9)	588 (31.6)
No limitations	957 (35.2)	292 (25.3)	312 (37.8)	353 (47.9)	631 (35.1)	320 (35.5)	191 (33.9)	766 (35.5)	390 (45.7)	567 (30.4)
Hypertension, n(%)	1589 (58.5)	770 (66.7)	458 (55.4)	361 (49.1)	1041 (58.5)	538 (59.6)	303 (53.9)	1286 (59.7)	450 (52.8)	1139 (61.1)
Diabetes, n(%)	554 (20.4)	304 (26.3)	150 (18.2)	100 (13.6)	359 (19.9)	190 (21.1)	91 (16.2)	463 (21.5)	109 (12.8)	445 (23.9)
Stroke, n(%)	289 (10.6)	151 (13.1)	87 (10.5)	51 (6.9)	215 (11.9)	72 (7.9)	69 (12.3)	220 (10.2)	74 (8.7)	215 (11.5)

[1] Includes never smokers/former smokers.
[2] Depressive symptom score is from the Center for Epidemiologic Studies – Depression (CES-D).

Table 2
Multinomial Logistic Regression of Health-Related Behaviors and Memory Loss Trajectory Group Memberships, the US Health and Retirement Study, 1998 – 2016, n = 2,717.

Pre-diagnosis health behavior	Very Low Memory Loss N = 552 OR (95 % CI)	Low Memory Loss N = 754 OR (95 % CI)	Medium Low Memory Loss N = 755 OR (95 % CI)	Medium High Memory Loss N = 487 OR (95 % CI)	High Memory Loss N = 169 OR (95 % CI)
Model 1: Physical Activity					
(More than once a week vs never)	1 (Reference)	0.7 (0.4, 1.1)	**0.6 (0.3, 1.0)**	**0.5 (0.2, 0.9)**	0.6 (0.3, 1.5)
(Less than once a week vs never)	1 (Reference)	0.7 (0.4, 1.1)	0.8 (0.4, 1.4)	0.9 (0.4, 1.7)	1.0 (0.5, 2.3)
Model 2: Smoking					
Ever Smoker (yes vs no)	1 (Reference)	**1.5 (1.0, 2.4)**	1.2 (0.7, 2.0)	1.2 (0.7, 2.3)	1.1 (0.5, 2.4)
Current Smoker (current smoker vs never smoker/ former smoker)	1 (Reference)	1.1 (0.7, 1.7)	0.9 (0.5, 1.6)	0.8 (0.4, 1.6)	0.7 (0.3, 1.7)
Model 3: Alcohol use					
Alcohol Use (yes vs none)	1 (Reference)	0.9 (0.6, 1.4)	0.9 (0.6, 1.5)	0.6 (0.3, 1.2)	0.6 (0.3, 1.2)
Number of drinks per day	1 (Reference)	1.0 (0.9, 1.2)	1.0 (0.8, 1.2)	0.9 (0.7, 1.1)	0.9 (0.6, 1.4)

*Adjusted for age at diagnosis, sex, race, years of education, comorbidities, BMI, and depressive symptoms, with sampling weights applied.

compared to the very low memory loss trajectory (OR: 1.5; 95% CI: 1.0, 2.4). Being a current smoker (vs non-smoker or former smoker), drinking any alcohol, and number of drinks consumed prior to diagnosis was not associated with post-diagnosis memory trajectories (Table 2).

3.2. Regression analysis: ADL limitation trajectories

Engaging in vigorous physical activity more than once a week (vs never) was associated with lower odds of having high, increasing ADL limitations (OR: 0.3; 95% CI: 0.1–0.6) and lower odds of being in the low ADL limitations trajectory (OR: 0.6; 95% CI: 0.4–0.9), compared to no ADL limitations trajectory (Table 3). Engaging in vigorous physical activity less than once a week (vs never) was associated with decreased odds of being in the high, increasing ADL limitations trajectory compared to no ADL limitations trajectory (OR: 0.3; 95% CI: 0.2–0.6). Having ever smoked, being a current smoker, and consuming any amount of alcohol prior to a first incident cancer diagnosis were not associated with post-diagnosis ADL limitation trajectories (Table 3).

4. Discussion

In this population-based, longitudinal cohort of survivors of a first incident cancer diagnosis after age 50 in the US, we found that engaging in vigorous physical activity immediately prior to a cancer diagnosis was associated with better post-diagnosis trajectories of memory function and ADL limitations. Pre-cancer diagnosis smoking and alcohol use were not associated with post-diagnosis trajectories of memory function and ADL limitations. Results of this study indicate that pre-cancer diagnosis health behaviors may have important implications for post-cancer diagnosis functional aging, emphasizing the need to evaluate pre-cancer diagnosis health factors as a potential factor in identifying survivors at higher risk for accelerated aging after a cancer diagnosis. However, our study was unable to evaluate the amount, intensity, and accumulation of these health behaviors across the life course which are important considerations in understanding these association and should be incorporated into future research.

Table 3
Multinomial Logistic Regression of Health-Related Behaviors and ADL Limitations Trajectory Group Memberships, the US Health and Retirement Study, 1998 – 2016, n = 2,717.

Pre-diagnosis health behavior	No Limitations N = 957 OR (95 % CI)	Low Limitations N = 784 OR (95 % CI)	Medium Limitations N = 792 OR (95 % CI)	High, Increasing Limitations N = 184 OR (95 % CI)
Model 1: Physical Activity				
(More than once a week vs never)	1 (Reference)	**0.6 (0.4, 0.9)**	0.9 (0.7, 1.3)	**0.3 (0.1, 0.6)**
(Less than once a week vs never)	1 (Reference)	0.7 (0.5, 1.0)	0.8 (0.6, 1.0)	**0.3 (0.2, 0.6)**
Model 2: Smoking				
Ever Smoker (yes vs no)	1 (Reference)	**1.4 (1.1, 1.9)**	1.2 (0.9, 1.6)	1.5 (0.9, 2.4)
Current Smoker (current smoker vs never smoker/ former smoker)	1 (Reference)	1.4 (0.9, 2.1)	1.3 (0.9, 1.8)	1.8 (0.9, 3.3)
Model 3: Alcohol use				
Alcohol Use (yes vs none)	1 (Reference)	0.8 (0.6, 1.1)	0.9 (0.7, 1.2)	0.8 (0.5, 1.4)
Number of drinks per day	1 (Reference)	0.9 (0.8, 1.1)	0.9 (0.8, 1.0)	0.9 (0.8, 1.2)

*Adjusted for age at diagnosis, sex, race, years of education, comorbidities, BMI, and depressive symptoms, with sampling weights applied.

4.1. Comparison with existing research

To the best of our knowledge, no other studies have investigated the influence of pre-cancer diagnosis health behaviors on post-diagnosis functional aging trajectories in older cancer survivors. Our results for vigorous physical activity are consistent with previous research which has found physical activity to be beneficial to cancer survivors (Aichberger et al., 2010; Asiamah et al., 2020; Dugan et al., 2018; Eckstrom et al., 2020; Gremeaux et al., 2012), however our results add to the literature by examining the importance of health behaviors prior to diagnosis on long-term aging trajectories among cancer survivors. Lahart and colleagues found that cancer survivors who reported high lifetime recreation physical activity prior to a cancer diagnosis had a significantly lower risk of all cause and breast cancer related death (Lahart et al., 2015). Physical activity after a cancer diagnosis has also been associated with better post-diagnosis quality of life and functional outcomes (Eyl et al., 2018; Garatachea et al., 2015; Lugo et al., 2019). Physical activity including moderate- and vigorous-intensity aerobic exercise can attenuate many aspects of aging, including improving and protecting cardiovascular health and muscle mass (Campbell et al.,

2019; Garatachea et al., 2015). It is possible that being physically active prior to a cancer diagnosis preserves cognitive and physical functioning after a cancer diagnosis. Indeed, a review by Campbell and colleagues found strong evidence that physical activity could improve common cancer-related health outcomes including physical functioning (Campbell et al., 2019). Identifying individuals at the time of cancer diagnosis who did not report engaging in exercise prior to diagnosis could be an important entry point to intervention to improve healthy aging among cancer survivors.

We found that pre-cancer diagnosis alcohol use and current or former smoking were not associated with functional aging trajectories after a cancer diagnosis. Most previous research on pre-cancer diagnosis alcohol use and smoking is related to the risk of cancer occurrence (Boffetta and Hashibe, 2006; Shield et al., 2016; U.S. Department of Health and Human, 2014). There is limited research that examines the influence of these behaviors prior to diagnosis on post-diagnosis aging trajectories. The use of alcohol in cancer survivorship is complex, as it is related to both a raised risk for certain cancers but may be cardioprotective in moderation (Corrao et al., 2004). Though not statistically significant, we found that survivors who drank any amount of alcohol prior to their diagnosis were less likely to experience worse functional aging trajectories than those who did not drink. Although we adjusted for several chronic conditions and depressive symptoms prior to diagnosis, it is possible that cancer survivors who completely abstained from alcohol in the years prior to their diagnosis may have done so due to poor health, such as early subclinical cancer.

Additionally, we found that smoking prior to cancer diagnosis was not associated with long-term aging trajectories after diagnosis. As smoking is associated with increased risk of mortality, we may not have observed an association due to a selective survival bias (Weuve et al., 2012). Those smokers who lived to an incident cancer diagnosis might be a healthier subset of smokers than those who did not live long enough to experience a cancer diagnosis. Interestingly, we did find that more non-smokers were more likely to be in both the very low and high memory loss trajectories (versus very low memory loss trajectory) than smokers which warrants more research.

4.2. Strengths and limitations

Limitations of this study include the use of self-reported cancer diagnoses and health behaviors which could be subject to response bias. However, previous research has shown that self-reported cancer diagnoses in the HRS have high sensitivity and specificity (74% sensitivity and 96% specificity, compared to Medicare diagnostic claims as the gold standard) (Mullins et al., 2021). Additionally, we were not able to examine cancer type, stage of diagnosis, or cancer treatment which can affect both lifestyle factors and functional aging trajectories after a cancer diagnosis. Future research should try to elucidate the role that cancer-related factors have in these long-term functional aging trajectories. Additionally, an important next step is to compare how these results could differ to the general cancer-free population to better understand differences in memory and ADL limitation trajectories among cancer survivors above natural aging. Another limitation is the limited number of non-white minority respondents and exclusion of Hispanic participants from our analysis which limits the generalizability of our results. For health behaviors, we were not able to evaluate the nuance in the frequency, duration, and intensity of physical activity, smoking, or alcohol use across the life course, which resulted in a loss of information for these exposure measures. Due to cross-wave differences in the question on physical activity, we were only able to analyze vigorous physical activity as more than once a week, once a week, or none and could not evaluate light or moderate physical activity. For former smokers, we did not have information on how long they had been former smokers. Previous research has shown that former smokers with longer smoking history have worse health compared to former smokers with shorter smoking history (Kramarow, 2020). This limits our ability to understand potential dose–response relationship between these health-related behaviors and post-diagnosis functional aging trajectories. Furthermore, we were not able to assess other lifestyle factor such as diet which have also been shown to be important in aging outcomes. These are important next steps in fully understanding these associations.

4.3. Conclusions

In this population-based, longitudinal study of middle-aged and older survivors of a first incident cancer in the United States, we found that pre-diagnosis vigorous physical activity was associated with better post-diagnosis memory and ADL limitation trajectories. By examining the relationship between pre-diagnosis health behaviors and post diagnosis functional aging, we can identify individuals at a potential higher risk for functional decline post diagnosis. This information can be used as an entry point to interventions programs promoting healthy aging after a cancer diagnosis.

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CRediT authorship contribution statement

Ashly C. Westrick: Conceptualization, Methodology, Formal analysis, Writing – original draft. **Kenneth M. Langa:** Writing – review & editing. **Lindsay C. Kobayashi:** Supervision, Conceptualization, Methodology, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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