

v1: 20 July 2023

## Research Article

# The Impact of physical exercise and alcohol conditions on self-reported health among cancer patients? An analysis of the Health Information National Trends Survey 2019

Peer-approved: 20 July 2023

© The Author(s) 2024. This is an Open Access article under the CC BY 4.0 license.

Qeios, Vol. 5 (2023)  
ISSN: 2632-3834

Ming Guan<sup>1</sup>

1. Xuchang University, Jiangguanchi, China

**Background and objective:** Sleep hours, physical exercise, and alcohol conditions were report to reduce or increase the detrimental side effects of cancer treatment. This study was aimed to evaluate the associations of outcomes of physical exercise and alcohol conditions with poor health among cancer patients when controlling socioeconomic factors. The secondary aim was to evaluate the joint effects of multiple cancers in the association of sleep hours, physical exercise, and alcohol conditions with poor health among cancer patients.

**Methods:** The data were from the Health Information National Trends Survey (HINTS) Wave 5 Cycle 3 administered by the National Cancer Institute since 2003 in the United States of America. Chi-square test and orthogonality tables were employed to assess the difference between pairs of variables. Logit regressions with marginal odds ratios (MOR) and 95% confidence intervals (95% CI) were conducted to examined the associations of socioeconomic variables with disadvantages of alcohol conditions and benefits of physical activity, respectively. King et al.'s (2000) simulation-based approach was employed to explore the moderating effects of multiple cancers on the associations of interest. Simulation extrapolation was conducted to examine the roles of socioeconomic factors, benefits of physical activity, and disadvantages of alcohol conditions in the fair/poor self-reported health (SRH) among cancer patients.

**Results:** The mean age of the sample was  $69.79 \pm 7.10$ , (range = 60 to 99) years old. Compared to cancer patients aged <60 years, cancer patients aged  $\geq 60$  years had significant associations with alcohol-related cancer risk (MOR = 1.503, 95% CI: 1.029–2.196), alcohol-related heart disease (MOR = 3.015, 95% CI: 1.965–4.626), alcohol-related diabetes (MOR = 2.300, 95% CI: 1.440–3.673), helping sleep (MOR = 2.033, 95% CI: 1.267–3.263), and reducing anxiety (MOR = 1.918, 95% CI: 1.218–3.021). Multiple cancers had limited moderating effects on the associations of sleep hours with outcomes of physical exercise and alcohol conditions. Socioeconomic factors (Coefficient = -0.311, 95% CI: -0.529, -0.094) and benefits of physical activity (Coefficient = -0.417, 95% CI: -0.737, -0.096) were mainly drivers of fair/poor SRH.

**Conclusion:** A high proportion of cancer patients are abnormal sleepers, insufficiently active and alcoholic. Socioeconomic factors and physical exercise were mainly drivers of health changes among them. Multiple cancers and sleep hours had limited effects on outcomes of physical exercise and alcohol conditions.

## Introduction

There were some sleep disturbances, mental disorders, and pain among cancer patients. For example, several studies documented anxiety and depression in patients with gastrointestinal cancer (de Sousa, et al. 2020), metastatic cancer (McFarland, et al. 2022), digestive tract cancer (Chen, et al. 2021), and lung cancer (Chen, et al. 2015). Cancer-related sleep disturbances were often reported during cancer treatment (Wu, et al. 2022). Improving quality of sleep does ease the

symptoms of cancer-related fatigue (Dean, 2022). Multiple current studies documented opioid use disorder (Merlin, et al. 2021), immunotherapy (Wu, et al. 2022), tapentadol extended-release (Jung, et al. 2022), pain education (Eisen, et al. 2021), caregiver interventions (Smith, et al. 2022) in the treatment of cancer-related pain. Thus, it is difficult to control and mitigate the disadvantages of cancers.

Physical exercises were confirmed to be beneficial to cancer patients. Multiple systematic reviews and meta-analyses indicated physical exercise was confirmed to beneficial in reducing fatigue (Medeiros Torres, et al. 2022; Belloni, et al.

2021) and improve quality of life (Lopez-Garzon, et al. 2022; Rendeiro, et al. 2021; Soares Falcetta, et al. 2018) in cancer patients. A systematic review with meta-analysis indicated people with advanced cancer engaged in exercise experienced an increase in quality of life, fitness and strength and a decrease in fatigue in the palliative care phase (Toohey, et al. 2023). Physical exercise could reduce the severity of fatigue and improve quality of life in advanced cancer patients (Navigante, et al. 2023; Rodríguez-Cañamero, et al. 2022). For women with early breast cancer, physical exercise was associated with a better quality of life, less depression and anxiety, and fewer adverse events of adjuvant therapy (Vehmanen, et al. 2022). Multiple studies indicated physical exercise can improve cognitive function (Ren, et al. 2022), emotional well-being (Wiggenraad, et al. 2020), cardiovascular system (Wang, et al. 2021), insulin-like growth factor system (Han & Kim, 2021) in breast cancer patients. Likewise, a present cross-sectional study indicated physical exercise was positively correlated with gastric cancer, colon cancer, breast cancer, thyroid cancer, and prostate cancer in the adult population  $\geq 40$  years old (Kim, et al. 2021).

Alcohol conditions were confirmed to be harmful to cancer patients. In the field of public health, multiple studies documented alcohol-related esophageal cancer (Du, et al. 2022), colorectal cancer (Zheng, et al. 2019), and breast cancer (Kopp, et al. 2016). Several studies reported the associations of alcohol consumption with the risks of new-onset stroke (Cui, et al. 2023) and coronary heart disease (O'Neill, et al. 2018). But, another study indicated that alcohol intake could increase risk of breast cancer and decrease risk of coronary heart disease (Dam, et al. 2016). Two studies documented the causal relationship between alcohol intake and glucose levels (Ishihara, et al. 2023; Jee, et al. 2016).

The purpose of this study is to determine whether benefits of physical exercise can tradeoff disadvantages of alcohol conditions in the health change among the cancer patients. The data from the Health Information National Trends Survey (HINTS) are employed in the current study. The logistic regression model was used to empirically examine the associations of socioeconomic variables with disadvantages of alcohol conditions and benefits of physical activity, respectively. The present study used simulation-based approach to explore moderating effects of multiple cancers on the associations of sleep hours with disadvantages of alcohol conditions and benefits of physical activity, respectively. This study used simulation extrapolation to judge how benefits of physical activity and disadvantages of alcohol conditions influence individual self-reported health (SRH) among cancer patients.

## Methods

### Data source

This study analyzed publicly available data from the National Cancer Institute's 2019 Health Information National Trends Survey 5 (HINTS 5), Cycle 3 (<http://hints.cancer.gov>). The participants who were not diagnosed as cancer patients were excluded from the analysis. After dropping the missing values of the variable "time since diagnosed with cancer", 826 observations were obtained. All the variables related to this

study were decoded the responses options with "missing data", "inapplicable", "unreadable or non-conforming numeric response", and "question answered in error".

### Main variables

#### Dependent variables

The dependent variables were benefits of physical activity (helping sleep, reducing anxiety, and reducing pain) and disadvantages of alcohol conditions (cancer, heart disease, and diabetes). Benefits of physical activity were assessed by the question: "As far as you know, does physical activity help with sleep? Reduce anxiety and depression? Reduce pain?" The response options were "yes", "no", and "don't know". The disadvantages of alcohol conditions were assessed by the question: "Which of the following health conditions do you think can result from drinking too much alcohol?" The choices were cancer, heart disease, diabetes, and liver disease. The response options were "yes", "no", and "don't know". All the responses with the option of "don't know" were excluded.

General health was assessed by the question: "In general, would you say your health is excellent, very good, good, fair, or poor?" Thus, fair/poor self-reported health (SRH) was obtained by dichotomizing the response options into binary values: 1 (= fair/poor) and 0 (= excellent/very good/good).

#### Socioeconomic factors

The continuous age ( $n=826$ ) was grouped by aged  $<65$  years ( $=0$ ) and aged  $\geq 65$  years ( $=1$ ). Gender ( $n=819$ ) was divided into female ( $=0$ ) and male ( $=1$ ). Marital status ( $n=823$ ) was distributed by married (47.27%), living as married or living with a romantic partner (3.40%), divorced (19.32%), widowed (18.47%), separated (2.19%), and single, never been married (9.36%). Thus, partnered status was defined as no ( $=0$ : divorced, widowed, separated, and single, never been married) and yes ( $=1$ : married and living as married or living with a romantic partner).

Educational attainment ( $n=822$ ) was distributed by less than 8 years (0.73%), 8 through 11 years (3.77%), 12 years or completed high school (18.73%), post high school training other than college (vocational or technical) (8.39%), some college (24.09%), college graduate (23.84%), and postgraduate (20.44%). Thus, higher education was defined as no ( $=0$ : less than 8 years, 8 through 11 years, 12 years or completed high school, post high school training other than college (vocational or technical)) and yes ( $=1$ : some college, college graduate, and postgraduate).

Race/Ethnicity ( $n=737$ ) was distributed by Hispanic (7.06%), Non-Hispanic White (78.43%), Non-Hispanic Black or African American (8.55%), Non-Hispanic American Indian or Alaska Native (0.27%), Non-Hispanic Asian (2.31%), Non-Hispanic Native Hawaiian or other Pacific Islander (0.14%), and Non-Hispanic Multiple Races Mentioned (3.26%). Thus, non-Hispanic white was defined as no ( $=0$ : Hispanic, Non-Hispanic Black or African American, Non-Hispanic American Indian or Alaska Native, Non-Hispanic Asian, Non-Hispanic Native Hawaiian or other Pacific Islander, Non-Hispanic Multiple Races Mentioned) and yes ( $=1$ : Non-Hispanic White).

Income ranges (n=815) were distributed by \$0 to \$9,999 (5.77%), \$10,000 to \$14,999 (8.10%), \$15,000 to \$19,999 (5.28%), \$20,000 to \$34,999 (15.83%), \$35,000 to \$49,999 (15.58%), \$50,000 to \$74,999 (17.55%), \$75,000 to \$99,999 (10.06%), \$100,000 to \$199,999 (15.58%), and \$200,000 or more (6.26%). Thus, high income was defined as no (=0: <=\$49,999) and yes (=1: >\$50,000).

BMI category (n=804) was distributed by underweight (1.37%), normal weight (30.22%), overweight (36.82%), and obese (31.59%). Thus, normal weight was defined as no (=0: underweight, overweight, and obese) and yes (=1: normal weight).

### *Multiple cancers*

Number of cancers was assessed by the question: "What type of cancer did you have?" Among the available 825 observations, the responses options were distributed by bladder cancer only (2.06%), bone cancer only (0.36%), breast cancer only (13.70%), cervical cancer only (4.36%), colon cancer only (3.27%), endometrial cancer only (2.18%), head/neck cancer only (0.73%), Hodgkin's only (0.24%), renal cancer only (2.18%), leukemia only (1.70%), liver cancer only (0.48%), lung cancer only (2.18%), melanoma only (4.85%), non-Hodgkin's only (1.82%), oral cancer only (0.24%), ovarian cancer only (1.45%), pancreatic cancer only (0.12%), pharyngeal cancer only (0.12%), prostate cancer only (9.94%), rectal cancer only (0.48%), skin cancer only (23.88%), more than one cancer checked (19.15%), and other cancer only (4.48%). Thus, multiple cancers was defined as no (=0: one cancer only) and yes (=1: more than one cancer checked).

### *Statistical analyses*

For categorical variables, Chi-squared tests were used to determine the differences in multiple cancers by socioeconomic variables, outcomes of physical exercise and alcohol conditions and fair/poor SRH. For continuous variables, orthogonality tables were used to determine the differences in multiple

cancers by sleep hours. Then, we examined the associations of socioeconomic variables with disadvantages of alcohol conditions and benefits of physical activity using logistic regressions with marginal odds ratios (MOR) and 95% confidence intervals (95% CI), respectively. Moderating effects of multiple cancers on the associations of interest were examined by King et al.'s (2000) simulation-based approach. Simulation extrapolation was conducted to examine how socioeconomic factors, benefits of physical activity, and disadvantages of alcohol conditions influence self-reported poor health among cancer patients.

## **Results**

### *Sample characteristics*

In Table 1, mean age of the sample was 69.79 (Standard deviation = 7.10, range = 60 to 99, n=826) years old. 24.50% of respondents reported poor health status. Among 826 cancer patients, most participants (65%) reported they were aged 65+ years (65.33%, n=825), males (55.19%, n=819), educated by college and above (76.73%, n=821), non-Hispanic white (70.06%, n=825), physically active (65.80%, n=801), and earned \$20,000 and above (80.84%, n=814). Among the available 808 respondents, the short (< or =6 hours), normal (7-8 hours), and long (> or =9 hours) sleep duration groups were distributed by 38.00%, 53.58%, and 8.42%, respectively.

Forty-three percent developed 1 or more cancers. There were significant differences between multiple cancers diagnosed with respect to helping sleep due to physical activity, reducing pain due to physical activity, and fair/poor SRH. Considering disadvantages of alcohol conditions, most of the sample reported alcohol-related cancer (65.45%, n=440), heart disease (83.98%, n=543), and diabetes (86.11%, n=540). Regarding benefits of physical activity, most of the sample reported helping sleep (95.65%, n=712), reducing anxiety and depression (95.13%, n=677), and reducing pain (69.58%, n=595). Less than a quarter of the sample reported fair/poor SRH.

	Multiple cancers		chi2	P value
	No (%)	Yes (%)		
Age (N=826)			2.0536	0.152
<65 years	28.93	5.69		
≥65 years	51.94	13.44		
Gender (N=819)			1.8309	0.176
Female	45.67	9.52		
Male	35.41	9.40		
Partnered status(N=823)			0.0017	0.967
No	40.07	9.44		
Yes	40.80	9.69		
Higher education (N=822)			0.0090	0.924
No	25.79	6.17		
Yes	55.08	12.95		
non-Hispanic white (N=737)			1.1017	0.294
No	24.94	5.08		
Yes	55.93	14.04		
Normal weight (N=804)			0.7571	0.384
No	56.54	14.04		
Yes	24.33	5.08		
High income (N=815)			0.8106	0.368
No	40.80	10.41		
Yes	40.07	8.72		
Cancer risk (N=440)			0.4010	0.527
No	27.95	6.59		
Yes	54.55	10.91		
Heart disease risk (N=543)			0.3564	0.551
No	12.71	3.31		
Yes	68.88	15.10		
Diabetes risk (N=540)			1.0134	0.314
No	11.85	2.04		
Yes	69.26	16.85		
Helping sleep (N=712)			3.5339	0.060*
No	2.95	1.40		
Yes	77.81	17.84		
Reducing anxiety (N=677)			2.5804	0.108
No	3.40	1.48		
Yes	77.10	18.02		
Reducing pain (N=595)			3.2634	0.071*
No	23.53	6.89		
Yes	58.15	11.43		
Fair/poor SRH (N=826)			3.6370	0.057*

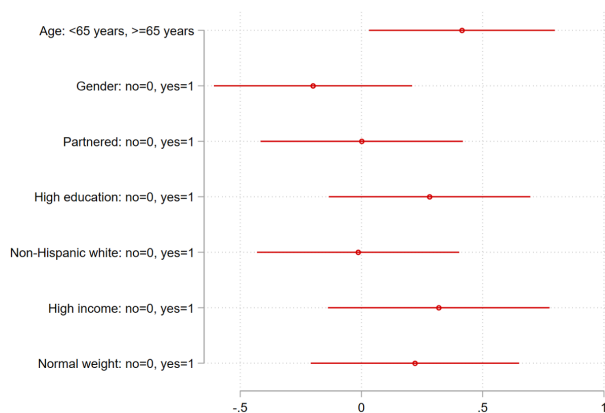
	Multiple cancers		chi2	P value
	No (%)	Yes (%)		
No	63.56	13.68		
Yes	17.31	5.45		
Sleep hours (N=808)			Difference	
Mean	12.159	17.089	-4.930	0.000***
Standardized errors	0.468	1.027	1.085	
N	668	158		

**Table 1.** Sample characteristics

Note: \*\*\*, \*\* and \* indicates 1%, 5% and 10% significance level, respectively.

### Associations of socioeconomic factors

Logistic regressions on disadvantages of alcohol conditions, benefits of physical activity, and fair/poor SRH could be shown in Supplementary table 1. In Figure 1, compared to cancer patients aged <60 years, cancer patients aged ≥60 years had a 50.3% higher alcohol-related cancer risk (marginal odds ratios (MOR) = 1.503, 95% Confidence Interval (95% CI): 1.029–2.196,  $p=0.035$ ).



**Figure 1.** Association with cancer risk

	Cancer risk	Heart disease risk	Diabetes risk	Help sleeping	Reducing anxiety	Reducing pain						
	aOR	95% CI	aOR	95% CI	aOR	95% CI	aOR	95% CI	aOR	95% CI	aOR	95% CI
Older adult	Ref. : <65		Ref. : <65		Ref. : <65		Ref. : <65		Ref. : <65		Ref. : <65	
>:65	1.513**	1.032-2.220	3.115***	2.017-4.810	2.406***	1.508-3.838	2.270**	1.191-4.326	2.187**	1.136-4.213	0.959	0.678-1.356
Gender	Ref.:female		Ref.:female		Ref.:female		Ref.:female		Ref.:female		Ref.:female	
Male	0.819	0.544-1.232	1.120	0.707-1.773	0.890	0.544-1.456	1.776	0.845-3.735	1.105	0.548-2.227	0.923	0.634-1.346
Partnered status	Ref.:no		Ref.:no		Ref.:no		Ref.:no		Ref.:no		Ref.:no	
Yes	1.001	0.659-1.519	1.350	0.843-2.160	0.995	0.600-1.650	1.751	0.826-3.713	2.020*	0.989-4.125	0.879	0.602-1.284
Higher education	Ref.:no		Ref.:no		Ref.:no		Ref.:no		Ref.:no		Ref.:no	
Yes	1.324	0.874-2.007	1.889***	1.207-2.955	2.303***	1.441-3.683	6.239***	3.125-12.456	11.361***	5.137-25.125	1.877***	1.302-2.705
Non-Hispanic white	Ref.:no		Ref.:no		Ref.:no		Ref.:no		Ref.:no		Ref.:no	
Yes	0.986	0.650-1.497	1.107	0.702-1.747	1.738**	1.086-2.780	1.884*	0.953-3.721	1.485	0.761-2.894	1.080	0.746-1.563
High income	Ref.:no		Ref.:no		Ref.:no		Ref.:no		Ref.:no		Ref.:no	
Yes	1.375	0.871-2.172	1.283	0.765-2.151	1.435	0.829-2.485	4.965***	1.641-15.022	3.810***	1.387-10.467	1.626**	1.085-2.436
Normal weight	Ref.:no		Ref.:no		Ref.:no		Ref.:no		Ref.:no		Ref.:no	
Yes	1.247	0.811-1.916	1.203	0.731-1.979	1.461	0.836-2.552	2.116*	0.938-4.777	1.820	0.831-3.987	2.005***	1.325-3.036
N	439		541		536		706		671		590	

**Supplementary Table 1.** Logistic regressions on disadvantages of alcohol conditions, benefits of physical activity, and fair/poor SRH.

Note: \*\*\*, \*\* and \* indicates 1, 5 and 10% significance level, respectively. aOR= adjusted odds ratio. SRH= self-reported health.

In Figure 2, cancer patients aged  $\geq 60$  years had a 201.5% higher alcohol-related heart disease (MOR = 3.015, 95% CI: 1.965–4.626,  $p=0.000$ ) than cancer patients aged  $<60$  years. Cancer patients with higher education was also associated with an 81.6% increase in alcohol-related heart disease (MOR = 1.816, 95% CI: 1.211–2.725,  $p=0.004$ ) than cancer patients without.

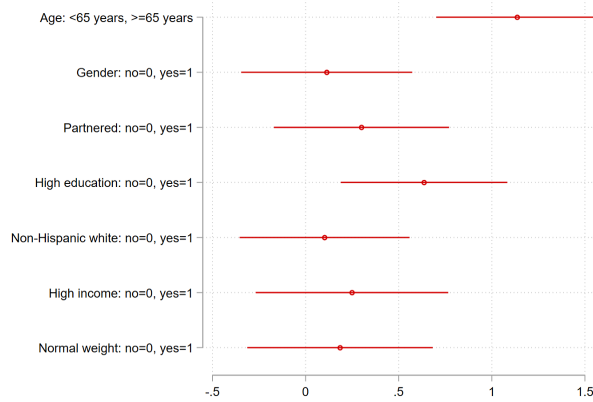


Figure 2. Association with heart disease risk

In Figure 3, cancer patients aged  $\geq 60$  years had a 140.6% higher alcohol-related diabetes (MOR = 2.300, 95% CI: 1.440–3.673,  $p=0.001$ ) than cancer patients aged  $<60$  years. Cancer patients with higher education was also associated with a 120.4% increase in alcohol-related diabetes (MOR = 2.204, 95% CI: 1.434–3.386,  $p=0.000$ ) than cancer patients without. Non-Hispanic white cancer patients was also associated with a 68.3% increase in alcohol-related diabetes (MOR = 1.683, 95% CI: 1.093–2.593,  $p=0.018$ ) than other race/ethnicity.

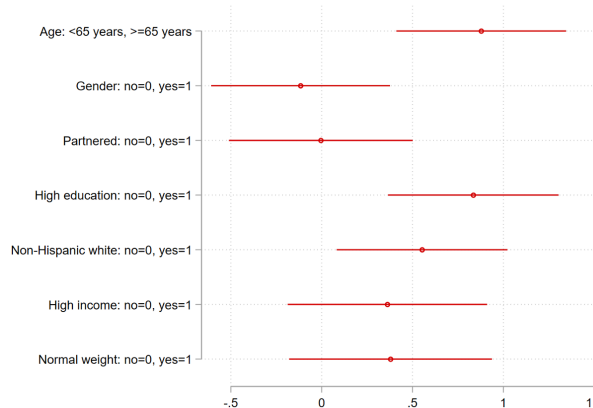


Figure 3. Association with diabetes risk

In Figure 4, cancer patients aged  $\geq 60$  years had a 103.3% higher helping sleep (MOR = 2.033, 95% CI: 1.267–3.263,  $p=0.003$ ) than cancer patients aged  $<60$  years. Cancer patients with Higher education was also associated with a 437.9% increase in helping

sleep (MOR = 5.379, 95% CI: 2.939–9.844,  $p=0.000$ ) than cancer patients without. Non-Hispanic white cancer patients was also associated with a 74.2% increase in helping sleep (MOR = 1.742, 95% CI: 1.057–2.872,  $p=0.030$ ) than other race/ethnicity. Cancer patients with high income was also associated with a 343.1% increase in helping sleep (MOR = 4.431, 95% CI: 1.695–11.580,  $p=0.002$ ) than the patients without. Cancer patients with normal weight were also associated with a 92.6% increase in helping sleep (MOR = 1.926, 95% CI: 0.935–3.968,  $p=0.075$ ) than the patients with abnormal weight.

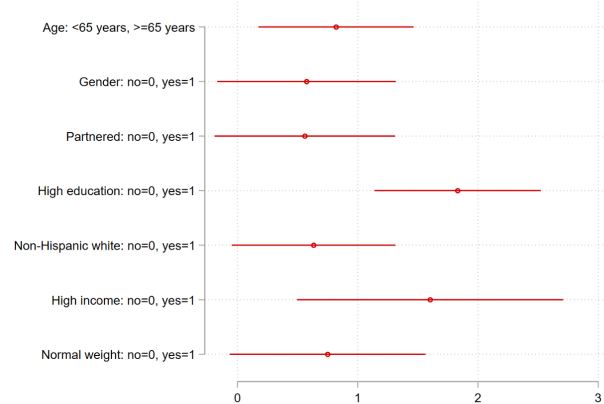


Figure 4. Association with helping sleep

In Figure 5, cancer patients aged  $\geq 60$  years had a 91.8% higher reducing anxiety (MOR = 1.918, 95% CI: 1.218–3.021,  $p=0.005$ ) than cancer patients aged  $<60$  years. Cancer patients with partnered status was also associated with a 82.3% increase in reducing anxiety (MOR = 1.823, 95% CI: 0.963–3.450,  $p=0.065$ ) than single patients. Cancer patients with Higher education was also associated with a 879.9% increase in reducing anxiety (MOR = 9.799, 95% CI: 4.807–19.976,  $p=0.000$ ) than cancer patients without. Cancer patients with high income was also associated with a 234.5% increase in reducing anxiety (MOR = 3.345, 95% CI: 1.283–8.721,  $p=0.014$ ) than the patients without.

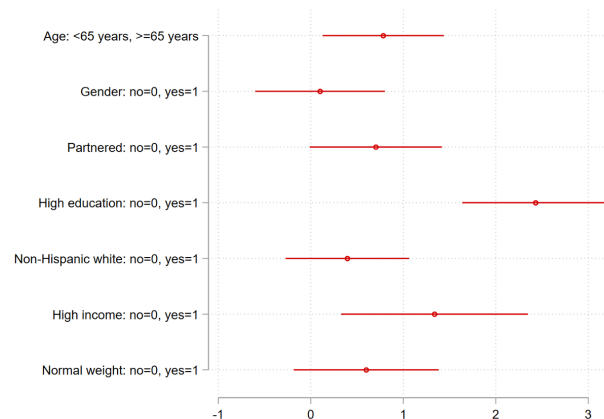
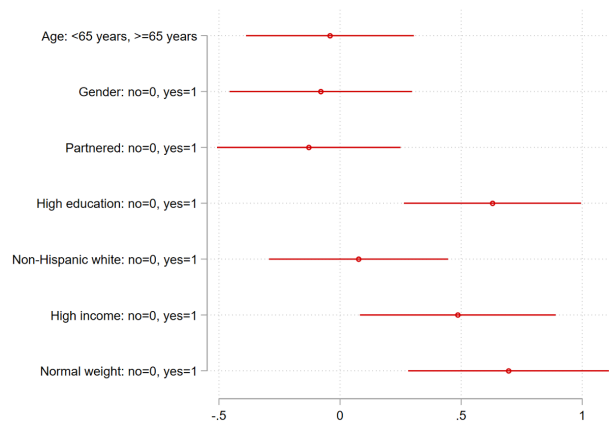


Figure 5. Association with reducing anxiety

In Figure 6, cancer patients with Higher education was also associated with a 83.8% increase in reducing pain (MOR =1.838, 95% CI: 1.287-2.624,  $p=0.001$ ) than cancer patients without. Cancer patients with high income was also associated with a 59.7% increase in reducing pain (MOR =1.597, 95% CI: 1.088-2.344,  $p=0.017$ ) than the patients without. Cancer patients with normal weight were also associated with a 95.1% increase in reducing pain (MOR =1.951, 95% CI: 1.315-2.894,  $p=0.001$ ) than the patients with abnormal weight.

### *Moderating effects of multiple cancers*

In figures 7 to 9, multiple cancers moderated the associations of average night sleep hours with risks of cancer, heart disease, and diabetes, respectively. In figures 10 to 12, multiple cancers moderated the associations of average night sleep hours with benefits of helping sleep, reducing anxiety, and reducing pain, respectively. As observed, the narrow confidence intervals were displayed in the normal sleep hours.



**Figure 6.** Association with reducing pain



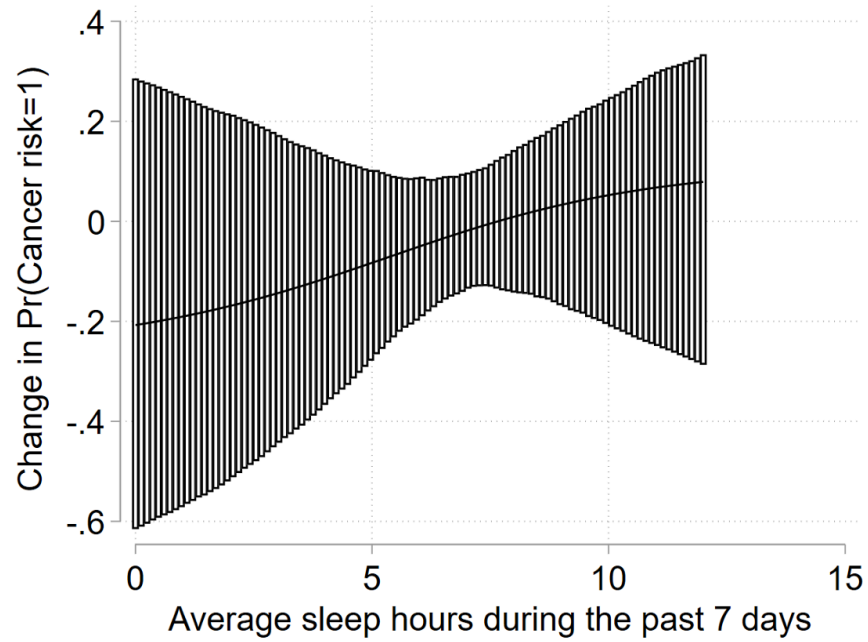


Figure 7. Association with cancer risk

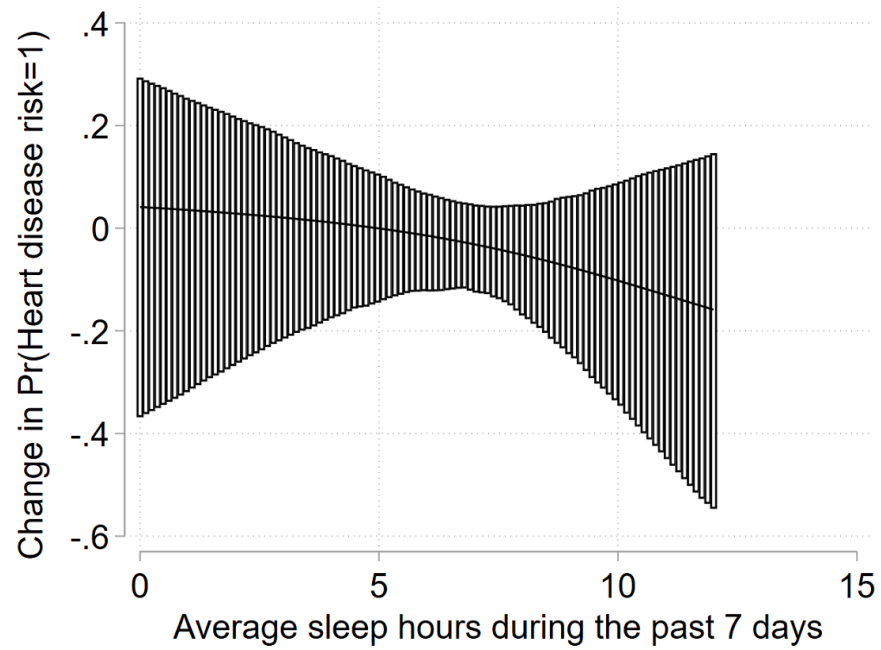


Figure 8. Association with heart disease risk

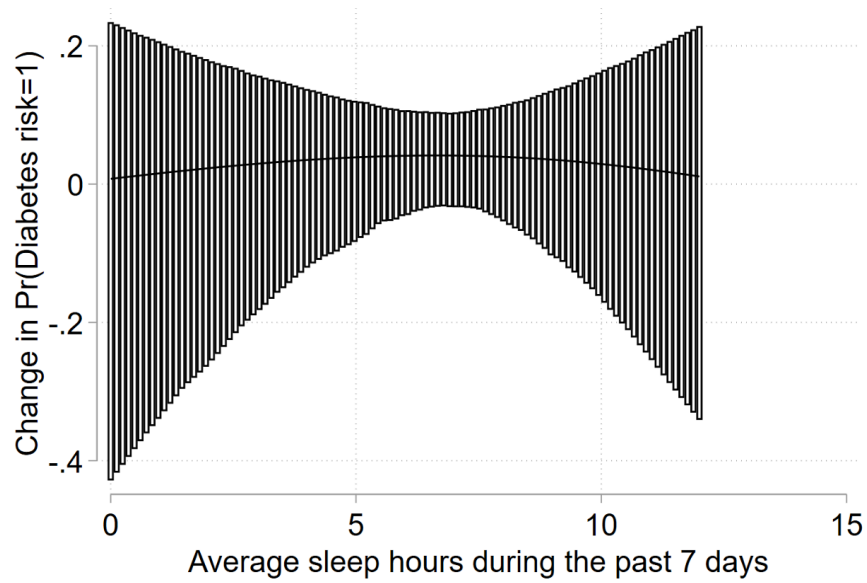


Figure 9. Association with diabetes risk

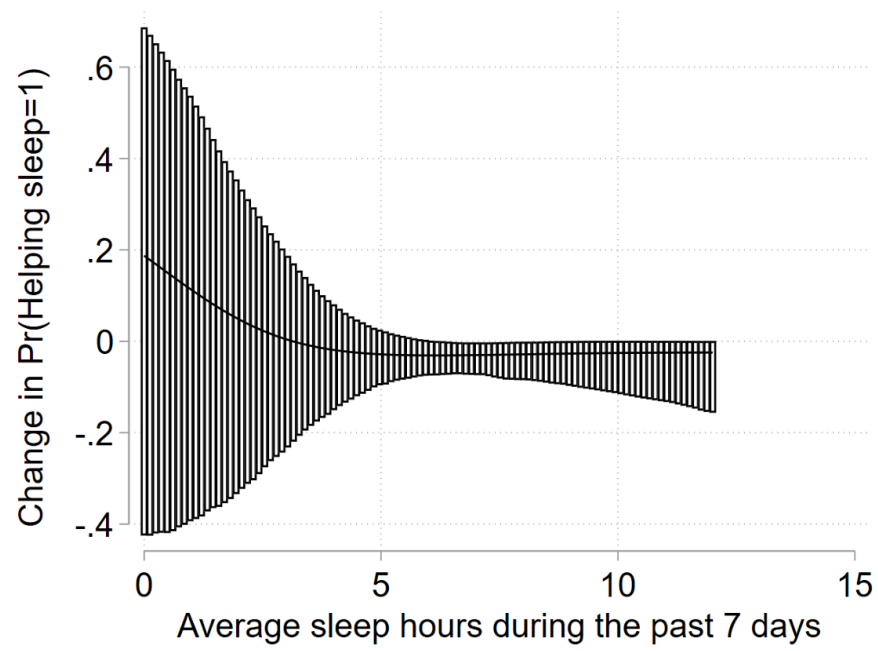


Figure 10. Association with helping sleep

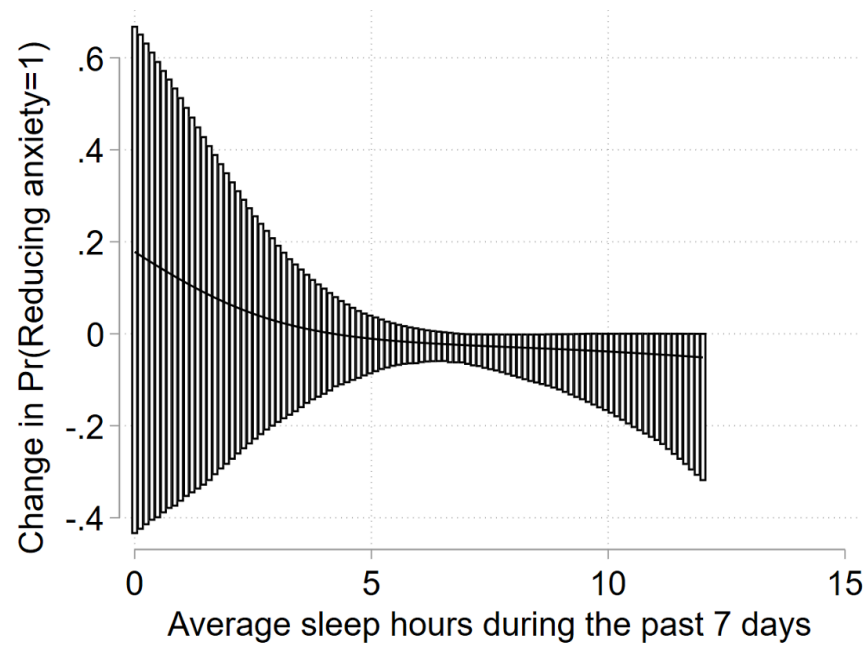


Figure 11. Association with reducing anxiety

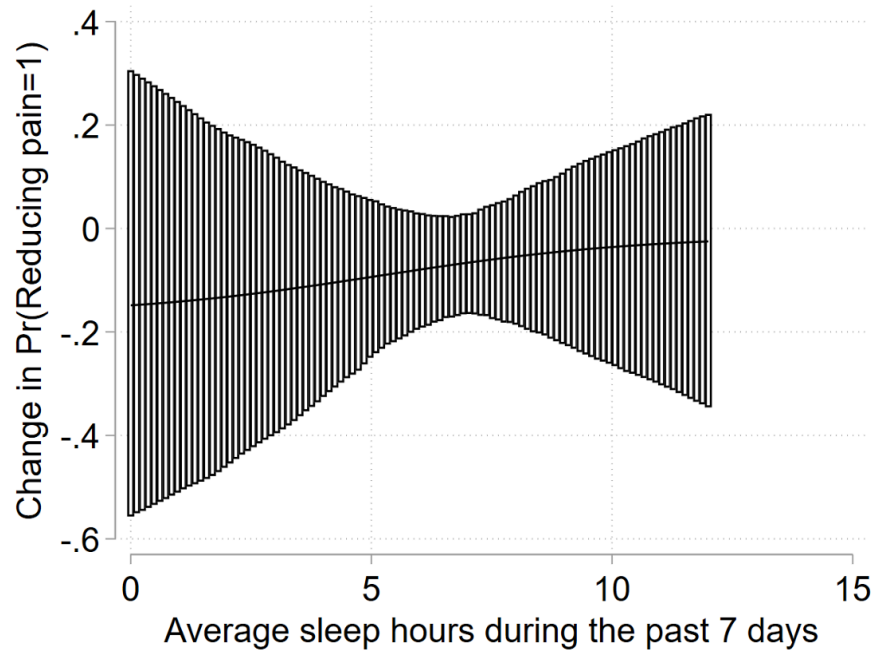


Figure 12. Association with reducing pain

### Simulation Extrapolation

In Table 2, risks of cancer, heart disease, and diabetes had no significant associations with fair/poor SRH, respectively. Similarly, helping sleep, reducing anxiety, and reducing pain

had no significant associations with fair/poor SRH, respectively. However, socioeconomic factors had significant associations with fair/poor SRH. Simultaneously, benefits of physical activity had significant associations with fair/poor SRH.

	Model 1		Model 2		Model 3	
	Coefficient	95% CI	Coefficient	95% CI	Coefficient	95% CI
Benefits of physical activity			-0.417**	-0.737, -0.096		
Helping sleep	-0.195	-0.528, 0.137			-0.199	-0.549, 0.151
Reducing anxiety	-0.126	-0.417, 0.166			0.044	-0.259, 0.348
Reducing pain	-0.022	-0.141, 0.096			-0.029	-0.145, 0.087
Disadvantages of alcohol conditions	0.025	-0.152, 0.202				
Cancer risk			0.082	-0.019, 0.183	0.061	-0.048, 0.170
Heart disease risk			0.016	-0.109, 0.141	-0.034	-0.170, 0.103
Diabetes risk			-0.076	-0.218, 0.067	-0.012	-0.155, 0.132
Socioeconomic factors	-0.326***	-0.538, -0.114	-0.311***	-0.529, -0.094	-0.780***	-1.111, -0.449
Constant	0.619***	0.310, 0.929	0.683***	0.381, 0.985	0.770***	0.470, 1.070
No. of observations	294		294		295	

Table 2. Simulation extrapolation on fair/poor SRH.

Note: \*\*\*, \*\* and \* indicates 1, 5 and 10% significance level, respectively.

## Discussion

In this cross-sectional analysis, the sample was dominated by age 65 and more years, males, college and above, non-Hispanic white, income with \$20,000 and above, physically active, and average sleep duration. There were significant differences between multiple cancers diagnosed with respect to helping sleep, reducing pain, and fair/poor SRH. The empirical analyses showed that cancer patients aged  $\geq 60$  years had higher likelihood to face alcohol-related risks of cancer, heart disease, and diabetes than cancer patients aged  $< 60$  years. Similarly, cancer patients aged  $\geq 60$  years had higher likelihood to receive physical activity-related benefits of helping sleep, reducing anxiety, and reducing pain than cancer patients aged  $< 60$  years. Simultaneously, socioeconomic factors had significant influence on fair/poor SRH. This study provided evidence to support moderating effect of multiple cancers on physical exercise and alcohol conditions on poor health among cancer patients. Therefore, the results provided useful insights into the roles of alcohol and physical activity in the health evaluations among the older adults.

The associations of socioeconomic factors could be explained by several early studies. For example, alcohol use was reported to substantially influence socioeconomic inequalities in male cancer mortality in several western countries (Menvielle, et al. 2007). Another study reported that alcohol consumption for cancer incidence was impacted by social class (Batchelor, et al. 2023). Also, race disparities in selected alcohol-related cancer incidence and prevalence were reported in U.S. (Polednak, 2007). Luckily, a mass media campaign could increase awareness of alcohol as a risk factor for cancer (Christensen, et al. 2019).

The existence of alcohol-related risks of cancer, heart disease, and diabetes among cancer patients could be in line with early studies. Alcohol-related negative outcomes were reported in the medical community. People with alcohol use disorder appeared to have higher incidence of alcohol-related cancers, diabetes, ischemic heart disease compared with those without (Leong, et al. 2022). Excessive alcohol consumption is a risk factor for the development of alcohol-related diabetes (Yessoufou, et al. 2005), cancer in later life (Bassett, et al. 2022), and head-and-neck cancers (Marziliano, et al. 2020). Persons with alcohol-related liver disease are at an elevated cancer risk compared with the general population (Hagström, et al. 2022). In practice, strategies to limit alcohol consumption could potentially reduce the cancer burden (Young, et al. 2018).

These findings regarding the relationship between physical activity and alcohol use were consistent with the early analyses. For example, a study documented the potential of physical activity to attenuate the effects of alcohol-related cancer mortality. Physical activity could minimize alcohol-related cancer risk (Feng, et al. 2020), improve perceived health status (Ko, et al. 2018), and prevented certain cancers (Parada, et al. 2020). A physically active lifestyle has a benefit in socioculturally diverse endometrial cancer survivors (Rossi, et al. 2017). A higher preoperative level of physical activity helped a faster physical recovery among the patients 3 weeks post breast cancer surgery, while the physically recovered effect diminished after 6 weeks (Nilsson, et al. 2016). Among breast cancer survivors, active women engaging in greater amounts of moderate and vigorous activity reported better physical activity-related quality of life than inactive women (Benton, et al. 2019). The health benefits of physical exercises depended on energy expenditure per week (Drygas, et al. 2000).

Some physical activity interventions were confirmed to be feasible and acceptable to attenuate the chronic pain (Fanning, et al. 2022). Two investigations concluded physical activity had

important impact on disability in people with chronic low back pain (Verbunt, et al. 2005; Alzahrani, et al. 2019). The attenuating effects of physical activity on anxiety were reported to be varied by levels of physical activity (Frontini, et al. 2021). Patients with fluid overload states are likely to benefit the most from physical exercise in terms of potentially in terms of obstructive sleep apnea severity (Mirrakhimov, 2013). There is large variability in the effect of physical activity on pain during migraine attacks that can be accounted for by individual differences. For a minority of participants, physical activity consistently contributed to pain worsening (Farris, et al. 2018). Physical-activity-related injury was risk factors for complain of anxiety (Yu, et al. 2022). There were associations between intensity of pain and physical activity levels (Connaughton, et al. 2014).

This study provided evidence to support moderating effect of multiple cancers on physical exercise and alcohol conditions on poor health among cancer patients. There was a high likelihood of the occurrence of multiple cancers (Seegobin, et al. 2018). Theoretically, multiple cancers competed for new blood supply for growth and progression (Wodarz & Anton-Culver, 2005). A study highlighted the increase adoption of healthier behaviors in survivors of multiple cancers (Burris & Andrykowski, 2011).

Wide 95% CIs of average night sleep hours indicated abnormal sleep hours have no definitely relationships with benefits of physical activity and disadvantages of alcohol conditions. The findings in this study indicated there was a complex relationship between sleep duration and cancer development. This can be explained by some paradoxical early findings. For example, abnormal sleep hours were associated with subsequent cancer development (Fukui, et al. 2022), increased breast (Wang, et al. 2015) and lung (Luoju, et al. 2014) cancer risk and cancer mortality (Wong, et al. 2017; Wilunda, et al. 2022; Xiao, et al. 2017). But another study indicated abnormal sleep hours does influence prognosis among early-stage breast cancer survivors (Marinac, et al. 2017). Long sleep duration increased risks of estrogen-mediated cancers (Hurley, et al. 2015), lung cancer (Peeri, et al. 2022), liver cancer (Royse, et al. 2017), colorectal cancer (Lin, et al. 2018), and the risk of cancer mortality (Tao, et al. 2021; Ma, et al. 2016; Stone, et al. 2019; Khan, et al. 2018). Paradoxically, a systematic review and meta-analysis indicated that long sleep may have a potential protective effect on prostate cancer incidence (Liu, et al. 2020). Short sleep duration was associated with adverse health conditions (Lubas, et al. 2021), affected later stages of prostate carcinogenesis (Gapstur, et al. 2014), increased risk of incident breast cancer (Cao, et al. 2019; Xiao, et al. 2016; Lu, et al. 2017; Khawaja, et al. 2013). However, sleep duration was confirmed to be no significant dose-response relationship with breast cancer risk (Wong, et al. 2021; Qian, et al. 2015; Yang, et al. 2014) in some studies. There existed a curvilinear relationship between sleep duration and mortality in advanced cancer patients (Collins, et al. 2017). A categorical meta-analysis indicated that short sleep duration increased cancer risk in Asians and long sleep duration increased the risk of colorectal cancer (Chen, et al. 2018). Sleep changes among breast cancer survivors were likely to be caused by chemotherapy, diagnosis, and fatigue (Alfano, et al. 2011).

Long sleep duration was likely to increase risk of developing colorectal cancer (Lu, et al. 2013; Zhang, et al. 2013; Jiao, et al.

2013). An observational study concluded associations of short or long sleep duration with many cancer risks (Gu, et al. 2016) and cancer mortality (Li, et al. 2019). But, some other studies did not provide evidence of an association between sleep duration and cancer risk (Girschik, et al. 2013; Wu, et al. 2013; Sturgeon, et al. 2012). Likewise, another study indicated that sleep duration had no effect on breast cancer risk (Qin, et al. 2014). A study indicated short sleep might be a risky factor for self-reported diabetes and long sleep duration may reduce the likelihood of self-reported diabetes among cancer survivors (Seixas, et al. 2018).

Associations of physical exercise with fair/poor SRH can be explained by several studies. Biologically, physical activity impacted body composition (Gil-Herrero, et al. 2022), had potent anticancer properties (Papadopetraki, et al. 2022), and preserved bone health (Cagliari, et al. 2022). Physical exercise was confirmed to improve the functioning satisfaction (Spreafico, et al. 2021) and clinical parameters (Baumann, et al. 2018). Engagement in regular physical exercise might be primarily responsible for reduction in all-cause mortality (Ratjen, et al. 2017) and improve the health status of older frail patients receiving chemotherapy (Olsen, et al. 2023).

## Implications for public health

Findings from the current study have public health implications. This study highlighted physical exercise and socioeconomic factors. According to the findings from this study, cancer patients choose feasible and appropriate intensity and level and time of physical exercise. The medical treatment system prioritized the cancer patients with higher education, high income, and non-Hispanic white race.

## Limitations

First, this cross-sectional survey was implemented by the National Cancer Institute in the United States of America. Thus, the causality of interest could not be determined. Moreover, the associations established in this study need be confirmed in other countries. Secondly, the intensity of physical exercise was not scientifically documented in this study. Till now, medical community was uncertain about what type of exercise was most fit for breast cancer patient undergoing anthracycline treatment (Tranchita, et al. 2022). Feasible exercise programs for cancer patients should take frailty, accessibility, and personal abilities into account (Agasi-Idenburg, et al. 2020). Finally, the treatment stages of the cancer patients were not depicted in the dataset. Thus, it was difficult to determine the most beneficial timing to starting exercise and alcohol content to decrease the myriad of treatment side effects experienced.

## Future directions

In the future, minute-level time data were recommended rather than hour-level time. Due to wide confidence intervals, the associations of short or long sleep duration with disadvantages of alcohol conditions and benefits of physical activity were not accurate, credible, and robust. Similarly, the associations of long sleep duration with disadvantages of alcohol conditions and benefits of physical activity were not accurate. Regarding causality establishment, long-term randomized controlled



trials and panel studies are needed to elucidate the mechanism underlying the associations of interest.

## Conclusions

Abnormal sleep, insufficient activity, and alcoholic were harmful among these cancer patients. Global benefits of physical activity and socioeconomic factors can improve health status among the cancer patients. Some feasible interventions to control alcohol consumption need to implement in the targeted cancer patients.

## References

- Agasi-Idenburg, C. S., Zuilen, M. K., Westerman, M. J., Punt, C. J. A., Aaronson, N. K., & Stuiver, M. M. (2020). "I am busy surviving" - Views about physical exercise in older adults scheduled for colorectal cancer surgery. *Journal of geriatric oncology*, 11(3), 444-450. <https://doi.org/10.1016/j.jgo.2019.05.001>
- Alfano, C. M., Lichstein, K. L., Vander Wal, G. S., Smith, A. W., Reeve, B. B., McTiernan, A., Bernstein, L., Baumgartner, K. B., & Ballard-Barbash, R. (2011). Sleep duration change across breast cancer survivorship: associations with symptoms and health-related quality of life. *Breast cancer research and treatment*, 130(1), 243-254. <https://doi.org/10.1007/s10549-011-1530-2>
- Alzahrani, H., Mackey, M., Stamatakis, E., Pinheiro, M. B., Wicks, M., & Shirley, D. (2019). The effectiveness of incidental physical activity interventions compared to other interventions in the management of people with low back pain: A systematic review and meta-analysis of randomised controlled trials. *Physical therapy in sport: official journal of the Association of Chartered Physiotherapists in Sports Medicine*, 36, 34-42. <https://doi.org/10.1016/j.ptsp.2018.12.008>
- Bassett, J. K., MacInnis, R. J., Yang, Y., Hodge, A. M., Lynch, B. M., English, D. R., Giles, G. G., Milne, R. L., & Jayasekara, H. (2022). Alcohol intake trajectories during the life course and risk of alcohol-related cancer: A prospective cohort study. *International journal of cancer*, 151(1), 56-66. <https://doi.org/10.1002/ijc.33973>
- Batchelor, S., Lunnay, B., Macdonald, S., & Ward, P. R. (2023). Extending the sociology of candidacy: Bourdieu's relational social class and mid-life women's perceptions of alcohol-related breast cancer risk. *Sociology of health & illness*, 10.1111/1467-9566.13644. Advance online publication. <https://doi.org/10.1111/1467-9566.13644>
- Baumann, F. T., Reike, A., Reimer, V., Schumann, M., Hallek, M., Taafe, D. R., Newton, R. U., & Galvao, D. A. (2018). Effects of physical exercise on breast cancer-related secondary lymphedema: a systematic review. *Breast cancer research and treatment*, 170(1), 1-13. <https://doi.org/10.1007/s10549-018-4725-y>
- Belloni, S., Arrigoni, C., & Caruso, R. (2021). Effects from physical exercise on reduced cancer-related fatigue: a systematic review of systematic reviews and meta-analysis. *Acta oncologica (Stockholm, Sweden)*, 60(12), 1678-1687. <https://doi.org/10.1080/0284186X.2021.1962543>
- Benton, M. J., Schlairet, M. C., & Graham, H. L. (2019). Physical activity-related quality of life in breast cancer survivors compared to healthy women. *European journal of cancer care*, 28(6), e13142. <https://doi.org/10.1111/ecc.13142>
- Burris, J. L., & Andrykowski, M. A. (2011). Physical and mental health status and health behaviors of survivors of multiple cancers: a national, population-based study. *Annals of behavioral medicine: a publication of the Society of Behavioral Medicine*, 42(3), 304-312. <https://doi.org/10.1007/s12160-011-9290-0>
- Cagliari, M., Bressi, B., Bassi, M. C., Fugazzaro, S., Prati, G., Iotti, C., & Costi, S. (2022). Feasibility and Safety of Physical Exercise to Preserve Bone Health in Men With Prostate Cancer Receiving Androgen Deprivation Therapy: A Systematic Review. *Physical therapy*, 102(3), pzab288. <https://doi.org/10.1093/ptj/pzab288>
- Cao, J., Eshak, E. S., Liu, K., Muraki, I., Cui, R., Iso, H., Tamakoshi, A., & JACC Study Group (2019). Sleep duration and risk of breast cancer: The JACC Study. *Breast cancer research and treatment*, 174(1), 219-225. <https://doi.org/10.1007/s10549-018-4995-4>
- Chen, Y., Tan, F., Wei, L., Li, X., Lyu, Z., Feng, X., Wen, Y., Guo, L., He, J., Dai, M., & Li, N. (2018). Sleep duration and the risk of cancer: a systematic review and meta-analysis including dose-response relationship. *BMC cancer*, 18(1), 1149. <https://doi.org/10.1186/s12885-018-5025-y>
- Chen, H. M., Tsai, C. M., Wu, Y. C., Lin, K. C., & Lin, C. C. (2015). Randomised controlled trial on the effectiveness of home-based walking exercise on anxiety, depression and cancer-related symptoms in patients with lung cancer. *British journal of cancer*, 112(3), 438-445. <https://doi.org/10.1038/bjc.2014.612>
- Chen, X., Wei, Q., Jing, R., & Fan, Y. (2021). Effects of music therapy on cancer-related fatigue, anxiety, and depression in patients with digestive tumors: A protocol for systematic review and meta-analysis. *Medicine*, 100(22), e25681. <https://doi.org/10.1097/MD.00000000000025681>
- Christensen, A. S. P., Meyer, M. K. H., Dalum, P., & Krarup, A. F. (2019). Can a mass media campaign raise awareness of alcohol as a risk factor for cancer and public support for alcohol related policies?. *Preventive medicine*, 126, 105722. <https://doi.org/10.1016/j.ypmed.2019.05.010>
- Collins, K. P., Geller, D. A., Antoni, M., Donnell, D. M., Tsung, A., Marsh, J. W., Burke, L., Penedo, F., Terhorst, L., Kamarck, T. W., Greene, A., Buysse, D. J., & Steel, J. L. (2017). Sleep duration is associated with survival in advanced cancer patients. *Sleep medicine*, 32, 208-212. <https://doi.org/10.1016/j.sleep.2016.06.041>
- Connaughton, J., Patman, S., & Pardoe, C. (2014). Are there associations among physical activity, fatigue, sleep quality and pain in people with mental illness? A pilot study. *Journal of psychiatric and mental health nursing*, 21(8), 738-745. <https://doi.org/10.1111/jpm.12122>
- Cui, M., Li, F., Gang, X., Gao, Y., Xiao, X., Wang, G., Liu, Y., & Wang, G. (2023). Association of alcohol consumption with all-cause mortality, new-onset stroke, and coronary heart disease in patients with abnormal glucose metabolism-Findings from a 10-year follow-up of the REACTION study. *Journal of diabetes*, 15(4), 289-298. <https://doi.org/10.1111/1753-0407.13371>
- Dam, M. K., Hvidtfeldt, U. A., Tjønneland, A., Overvad, K., Grønbaek, M., & Tolstrup, J. S. (2016). Five year change in alcohol intake and risk of breast cancer and coronary heart

- disease among postmenopausal women: prospective cohort study. *BMJ (Clinical research ed.)*, 353, i2314. <https://doi.org/10.1136/bmj.i2314>.
- Drygas, W., Kostka, T., Jegier, A., & Kuński, H. (2000). Long-term effects of different physical activity levels on coronary heart disease risk factors in middle-aged men. *International journal of sports medicine*, 21(4), 235–241. <https://doi.org/10.1055/s-2000-309>
  - de Sousa, D. E., de Carli, M. N., Fernandes, R. C., Trindade, D. B., Laviano, A., Pichard, C., & Pimentel, G. D. (2020). Are depression and anxiety disorders associated with adductor pollicis muscle thickness, sleep duration, and protein intake in cancer patients?. *Experimental gerontology*, 130, 110803. <https://doi.org/10.1016/j.exger.2019.110803>
  - Dean R. (2022). Can improving quality of sleep reduce the symptoms of cancer-related fatigue in adults?: A systematic review. *European journal of cancer care*, 31(4), e13597. <https://doi.org/10.1111/ecc.13597>
  - Du, Q., Xiao, R. D., Luo, R. G., Xie, J. B., Su, Z. D., & Wang, Y. (2022). Construction of long non-coding RNA- and microRNA-mediated competing endogenous RNA networks in alcohol-related esophageal cancer. *PloS one*, 17(6), e0269742. <https://doi.org/10.1371/journal.pone.0269742>
  - Eisen, T., Kooijstra, E. M., Groeneweg, R., Verseveld, M., & Hidding, J. (2021). The Needs and Experiences of Patients on Pain Education and the Clinical Reasoning of Physical Therapists Regarding Cancer-Related Pain. A Qualitative Study. *Frontiers in pain research (Lausanne, Switzerland)*, 2, 675302. <https://doi.org/10.3389/fpain.2021.675302>
  - Fanning, J., Brooks, A. K., Ford, S., Robison, J. T., Irby, M. B., & Rejeski, W. J. (2022). A remote group-mediated daylong physical activity intervention for older adults with chronic pain: Results of the MORPH-II randomized pilot trial. *Frontiers in digital health*, 4, 1040867. <https://doi.org/10.3389/fdgth.2022.1040867>
  - Farris, S. G., Thomas, J. G., Abrantes, A. M., Lipton, R. B., Pavlovic, J., Smitherman, T. A., Irby, M. B., Penzien, D. B., Roth, J., O'Leary, K. C., & Bond, D. S. (2018). Pain worsening with physical activity during migraine attacks in women with overweight/obesity: A prospective evaluation of frequency, consistency, and correlates. *Cephalalgia: an international journal of headache*, 38(11), 1707–1715. <https://doi.org/10.1177/0333102417747231>
  - Feng, Y., Powell, L., Vassallo, A. J., Hamer, M., & Stamatakis, E. (2020). Does adequate physical activity attenuate the associations of alcohol and alcohol-related cancer mortality? A pooled study of 54,686 British adults. *International journal of cancer*, 147(10), 2754–2763. <https://doi.org/10.1002/ijc.33052>
  - Frontini, R., Rebelo-Gonçalves, R., Amaro, N., Salvador, R., Matos, R., Morouço, P., & Antunes, R. (2021). The Relationship Between Anxiety Levels, Sleep, and Physical Activity During COVID-19 Lockdown: An Exploratory Study. *Frontiers in psychology*, 12, 659599. <https://doi.org/10.3389/fpsyg.2021.659599>
  - Fukui, S., Shimbo, T., & Kobayashi, D. (2022). Both increased and decreased sleep duration over time are associated with subsequent cancer development. *Sleep & breathing = Schlaf & Atmung*, 26(4), 2035–2043. <https://doi.org/10.1007/s11325-021-02517-7>
  - Gapstur, S. M., Diver, W. R., Stevens, V. L., Carter, B. D., Teras, L. R., & Jacobs, E. J. (2014). Work schedule, sleep duration, insomnia, and risk of fatal prostate cancer. *American journal of preventive medicine*, 46(3 Suppl 1), S26–S33. <https://doi.org/10.1016/j.amepre.2013.10.033>
  - Gil-Herrero, L., Pollán, M., Martín, M., López-Tarruella, S., Castellanos, M., & Casla-Barrio, S. (2022). The importance of physical exercise in cardiovascular fitness in breast cancer survivors. A cross-sectional study: women in Motion 2.0. *Supportive care in cancer: official journal of the Multinational Association of Supportive Care in Cancer*, 30(8), 6745–6754. <https://doi.org/10.1007/s00520-022-06993-9>
  - Girschik, J., Heyworth, J., & Fritschi, L. (2013). Self-reported sleep duration, sleep quality, and breast cancer risk in a population-based case-control study. *American journal of epidemiology*, 177(4), 316–327. <https://doi.org/10.1093/aje/kws422>
  - Gu, F., Xiao, Q., Chu, L. W., Yu, K., Matthews, C. E., Hsing, A. W., & Caporaso, N. E. (2016). Sleep Duration and Cancer in the NIH-AARP Diet and Health Study Cohort. *PloS one*, 11(9), e0161561. <https://doi.org/10.1371/journal.pone.0161561>
  - Hagström, H., Thiele, M., Sharma, R., Simon, T. G., Roelstraete, B., Söderling, J., & Ludvigsson, J. F. (2022). Risk of Cancer in Biopsy-Proven Alcohol-Related Liver Disease: A Population-Based Cohort Study of 3410 Persons. *Clinical gastroenterology and hepatology: the official clinical practice journal of the American Gastroenterological Association*, 20(4), 918–929.e8. <https://doi.org/10.1016/j.cgh.2021.01.005>
  - Han, J. K., & Kim, G. (2021). Role of physical exercise in modulating the insulin-like growth factor system for improving breast cancer outcomes: A meta-analysis. *Experimental gerontology*, 152, 111435. <https://doi.org/10.1016/j.exger.2021.111435>
  - Hurley, S., Goldberg, D., Bernstein, L., & Reynolds, P. (2015). Sleep duration and cancer risk in women. *Cancer causes & control: CCC*, 26(7), 1037–1045. <https://doi.org/10.1007/s10552-015-0579-3>
  - Ishihara, M., Imano, H., Muraki, I., Yamagishi, K., Maruyama, K., Hayama-Terada, M., Tanaka, M., Yasuoka, M., Kihara, T., Kiyama, M., Okada, T., Takada, M., Shimizu, Y., Sobue, T., & Iso, H. (2023). Relationships of habitual daily alcohol consumption with all-day and time-specific average glucose levels among non-diabetic population samples. *Environmental health and preventive medicine*, 28, 20. <https://doi.org/10.1265/ehpm.22-00215>
  - Jiao, L., Duan, Z., Sangi-Haghpeykar, H., Hale, L., White, D. L., & El-Serag, H. B. (2013). Sleep duration and incidence of colorectal cancer in postmenopausal women. *British journal of cancer*, 108(1), 213–221. <https://doi.org/10.1038/bjc.2012.561>
  - Jee, Y. H., Lee, S. J., Jung, K. J., & Jee, S. H. (2016). Alcohol Intake and Serum Glucose Levels from the Perspective of a Mendelian Randomization Design: The KCPS-II Biobank. *PloS one*, 11(9), e0162930. <https://doi.org/10.1371/journal.pone.0162930>
  - Jung, J. Y., Chon, H. J., Choi, Y. J., Yeon, S. E., Choi, S. Y., & Lee, K. H. (2022). A prospective, multicenter, open-label study of the clinical efficacy of tapentadol extended-release in the treatment of cancer-related pain and improvement in

- the quality of life of opioid-naïve or opioid-resistant patients. Supportive care in cancer: official journal of the Multinational Association of Supportive Care in Cancer, 30(7), 6103–6112. <https://doi.org/10.1007/s00520-022-06992-w>
- Khan, H., Kella, D., Kunutsor, S. K., Savonen, K., & Laukkanen, J. A. (2018). Sleep Duration and Risk of Fatal Coronary Heart Disease, Sudden Cardiac Death, Cancer Death, and All-Cause Mortality. The American journal of medicine, 131(12), 1499–1505.e2. <https://doi.org/10.1016/j.amjmed.2018.07.010>
  - Khawaja, A., Rao, S., Li, L., & Thompson, C. L. (2013). Sleep duration and breast cancer phenotype. Journal of cancer epidemiology, 2013, 467927. <https://doi.org/10.1155/2013/467927>
  - Kim, S. Y., Yoo, D. M., Min, C., & Choi, H. G. (2021). Association between Coffee Consumption/Physical Exercise and Gastric, Hepatic, Colon, Breast, Uterine Cervix, Lung, Thyroid, Prostate, and Bladder Cancer. Nutrients, 13(11), 3927. <https://doi.org/10.3390/nu13113927>
  - King, G., Tomz, M., and Wittenberg, J. (2000). Making the most of statistical analyses: improving interpretation and presentation. American Journal of Political Science 44, no. 2 (April): 347–61.
  - Ko, J. M., White, K. S., Kovacs, A. H., Tecson, K. M., Apers, S., Luyckx, K., Thomet, C., Budts, W., Enomoto, J., Sluman, M. A., Wang, J. K., Jackson, J. L., Khairy, P., Cook, S. C., Subramanyan, R., Alday, L., Eriksen, K., Dellborg, M., Berghammer, M., Johansson, B., ... APPROACH-IS consortium and International Society for Adult Congenital Heart Disease (ISACHD) (2018). Physical Activity-Related Drivers of Perceived Health Status in Adults With Congenital Heart Disease. The American journal of cardiology, 122(8), 1437–1442. <https://doi.org/10.1016/j.amjcard.2018.06.056>
  - Kopp, T. I., Jensen, D. M., Ravn-Haren, G., Cohen, A., Sommer, H. M., Dragsted, L. O., Tjønneland, A., Hougaard, D. M., & Vogel, U. (2016). Alcohol-related breast cancer in postmenopausal women - effect of CYP19A1, PPARG and PPARGC1A polymorphisms on female sex-hormone levels and interaction with alcohol consumption and NSAID usage in a nested case-control study and a randomised controlled trial. BMC cancer, 16, 283. <https://doi.org/10.1186/s12885-016-2317-y>
  - Leong, C., Bolton, J. M., Ekuma, O., Prior, H. J., Singal, D., Nepon, J., Konrad, G., Paillé, M., Finlayson, G., & Nickel, N. (2022). Association of alcohol use disorder on alcohol-related cancers, diabetes, ischemic heart disease and death: a population-based, matched cohort study. Addiction (Abingdon, England), 117(2), 368–381. <https://doi.org/10.1111/add.15646>
  - Li, Y., Cai, S., Ling, Y., Mi, S., Fan, C., Zhong, Y., & Shen, Q. (2019). Association between total sleep time and all cancer mortality: non-linear dose-response meta-analysis of cohort studies. Sleep medicine, 60, 211–218. <https://doi.org/10.1016/j.sleep.2019.03.026>
  - Lin, Y., Peng, Y., Liang, B., Zhu, S., Li, L., Jang, F., Huang, X., & Xie, Y. (2018). Associations of dinner-to-bed time, post-dinner walk and sleep duration with colorectal cancer: A case-control study. Medicine, 97(34), e12038. <https://doi.org/10.1097/MD.00000000000012038>
  - Liu, R., Wu, S., Zhang, B., Guo, M., & Zhang, Y. (2020). The association between sleep duration and prostate cancer: A systematic review and meta-analysis. Medicine, 99(28), e21180. <https://doi.org/10.1097/MD.00000000000021180>
  - Lopez-Garzon, M., Cantarero-Villanueva, I., Postigo-Martin, P., González-Santos, Á., Lozano-Lozano, M., & Galiano-Castillo, N. (2022). Can Physical Exercise Prevent Chemotherapy-Induced Peripheral Neuropathy in Patients With Cancer? A Systematic Review and Meta-analysis. Archives of physical medicine and rehabilitation, 103(11), 2197–2208. <https://doi.org/10.1016/j.apmr.2022.02.008>
  - Luojus, M. K., Lehto, S. M., Tolmunen, T., Erkkilä, A. T., & Kauhanen, J. (2014). Sleep duration and incidence of lung cancer in ageing men. BMC public health, 14, 295. <https://doi.org/10.1186/1471-2458-14-295>
  - Lu, C., Sun, H., Huang, J., Yin, S., Hou, W., Zhang, J., Wang, Y., Xu, Y., & Xu, H. (2017). Long-Term Sleep Duration as a Risk Factor for Breast Cancer: Evidence from a Systematic Review and Dose-Response Meta-Analysis. BioMed research international, 2017, 4845059. <https://doi.org/10.1155/2017/4845059>
  - Lu, Y., Tian, N., Yin, J., Shi, Y., & Huang, Z. (2013). Association between sleep duration and cancer risk: a meta-analysis of prospective cohort studies. PloS one, 8(9), e74723. <https://doi.org/10.1371/journal.pone.0074723>
  - Lubas, M. M., Mandrell, B. N., Ness, K. K., Srivastava, D. K., Ehrhardt, M. J., Wang, Z., Hudson, M. M., Robison, L. L., Krull, K. R., & Brinkman, T. M. (2021). Short sleep duration and physical and psychological health outcomes among adult survivors of childhood cancer. Pediatric blood & cancer, 68(7), e28988. <https://doi.org/10.1002/pbc.28988>
  - Ma, Q. Q., Yao, Q., Lin, L., Chen, G. C., & Yu, J. B. (2016). Sleep duration and total cancer mortality: a meta-analysis of prospective studies. Sleep medicine, 27–28, 39–44. <https://doi.org/10.1016/j.sleep.2016.06.036>
  - Marinac, C. R., Nelson, S. H., Flatt, S. W., Natarajan, L., Pierce, J. P., & Patterson, R. E. (2017). Sleep duration and breast cancer prognosis: perspectives from the Women's Healthy Eating and Living Study. Breast cancer research and treatment, 162(3), 581–589. <https://doi.org/10.1007/s10549-017-4140-9>
  - Marziliano, A., Teckie, S., & Diefenbach, M. A. (2020). Alcohol-related head and neck cancer: Summary of the literature. Head & neck, 42(4), 732–738. <https://doi.org/10.1002/hed.26023>
  - McFarland, D. C., Applebaum, A. J., Bengtson, E., Alici, Y., Breitbart, W., Miller, A. H., & Nelson, C. (2022). Potential use of albumin and neutrophil-to-lymphocyte ratio to guide the evaluation and treatment of cancer-related depression and anxiety. Psycho-oncology, 31(2), 306–315. <https://doi.org/10.1002/pon.5811>
  - Medeiros Torres, D., Jorge Koifman, R., & da Silva Santos, S. (2022). Impact on fatigue of different types of physical exercise during adjuvant chemotherapy and radiotherapy in breast cancer: systematic review and meta-analysis. Supportive care in cancer: official journal of the Multinational Association of Supportive Care in Cancer, 30(6), 4651–4662. <https://doi.org/10.1007/s00520-022-06809-w>
  - Menvielle, G., Kunst, A. E., Stirbu, I., Borrell, C., Bopp, M., Regidor, E., Heine Strand, B., Deboosere, P., Lundberg, O.,

- Leclerc, A., Costa, G., Chastang, J. F., Esnaola, S., Martikainen, P., & Mackenbach, J. P. (2007). Socioeconomic inequalities in alcohol related cancer mortality among men: to what extent do they differ between Western European populations? *International journal of cancer*, 121(3), 649–655. <https://doi.org/10.1002/ijc.22721>
- Merlin, J. S., Khodyakov, D., Arnold, R., Bulls, H. W., Dao, E., Kapo, J., King, C., Meier, D., Paice, J., Ritchie, C., & Liebschutz, J. M. (2021). Expert Panel Consensus on Management of Advanced Cancer-Related Pain in Individuals With Opioid Use Disorder. *JAMA network open*, 4(12), e2139968. <https://doi.org/10.1001/jamanetworkopen.2021.39968>
  - Mirrahimov A. E. (2013). Physical exercise related improvement in obstructive sleep apnea. Look for the rostral fluid shift. *Medical hypotheses*, 80(2), 125–128. <https://doi.org/10.1016/j.mehy.2012.11.007>
  - Navigante, A., Cresta Morgado, P., Daud, M. L., Dos Santos Regis, H., Kolberg, M., Marazzi, C., Lobbe, V., González, A. A., & De Simone, G. (2023). Physical exercise and fatigue in advanced gastrointestinal cancer during chemotherapy. *BMJ supportive & palliative care*, 13(2), 218–227. <https://doi.org/10.1136/bmjspcare-2021-003516>
  - Nilsson, H., Angerås, U., Bock, D., Börjesson, M., Onerup, A., Fagevik Olsen, M., Gellerstedt, M., Haglind, E., & Angenete, E. (2016). Is preoperative physical activity related to post-surgery recovery? A cohort study of patients with breast cancer. *BMJ open*, 6(1), e007997. <https://doi.org/10.1136/bmjopen-2015-007997>
  - Olsen, A. P., Vinther, A., Ragle, A. M., Dolin, T. G., Johansen, J. S., Vistisen, K., Nielsen, D. L., & Lund, C. M. (2023). Physical exercise program to older frail patients receiving chemotherapy for colorectal cancer - feasibility and experiences from the GERICO study. *Journal of geriatric oncology*, 14(1), 101382. <https://doi.org/10.1016/j.jgo.2022.09.011>
  - O'Neill, D., Britton, A., Hannah, M. K., Goldberg, M., Kuh, D., Khaw, K. T., & Bell, S. (2018). Association of longitudinal alcohol consumption trajectories with coronary heart disease: a meta-analysis of six cohort studies using individual participant data. *BMC medicine*, 16(1), 124. <https://doi.org/10.1186/s12916-018-1123-6>
  - Papadopetraki, A., Maridaki, M., Zagouri, F., Dimopoulos, M. A., Koutsilieris, M., & Philippou, A. (2022). Physical Exercise Restrains Cancer Progression through Muscle-Derived Factors. *Cancers*, 14(8), 1892. <https://doi.org/10.3390/cancers14081892>
  - Parada, H., Jr, McDonald, E., Bellettiere, J., Evenson, K. R., LaMonte, M. J., & LaCroix, A. Z. (2020). Associations of accelerometer-measured physical activity and physical activity-related cancer incidence in older women: results from the WHI OPACH Study. *British journal of cancer*, 122(9), 1409–1416. <https://doi.org/10.1038/s41416-020-0753-6>
  - Peeri, N. C., Tao, M. H., Demissie, S., & Nguyen, U. D. T. (2022). Sleep Duration, Chronotype, and Insomnia and the Risk of Lung Cancer: United Kingdom Biobank Cohort. *Cancer epidemiology, biomarkers & prevention: a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology*, 31(4), 766–774. <https://doi.org/10.1158/1055-9965.EPI-21-1093>
  - Polednak A. P. (2007). Secular trend in U.S. black-white disparities in selected alcohol-related cancer incidence rates. *Alcohol and alcoholism (Oxford, Oxfordshire)*, 42(2), 125–130. <https://doi.org/10.1093/alcalc/agl121>
  - Qian, X., Brinton, L. A., Schairer, C., & Matthews, C. E. (2015). Sleep duration and breast cancer risk in the Breast Cancer Detection Demonstration Project follow-up cohort. *British journal of cancer*, 112(3), 567–571. <https://doi.org/10.1038/bjc.2014.600>
  - Qin, Y., Zhou, Y., Zhang, X., Wei, X., & He, J. (2014). Sleep duration and breast cancer risk: a meta-analysis of observational studies. *International journal of cancer*, 134(5), 1166–1173. <https://doi.org/10.1002/ijc.28452>
  - Ratjen, I., Schafmayer, C., di Giuseppe, R., Waniek, S., Plachta-Danielzik, S., Koch, M., Burmeister, G., Nöthlings, U., Hampe, J., Schlesinger, S., & Lieb, W. (2017). Postdiagnostic physical activity, sleep duration, and TV watching and all-cause mortality among long-term colorectal cancer survivors: a prospective cohort study. *BMC cancer*, 17(1), 701. <https://doi.org/10.1186/s12885-017-3697-3>
  - Ren, X., Wang, X., Sun, J., Hui, Z., Lei, S., Wang, C., & Wang, M. (2022). Effects of physical exercise on cognitive function of breast cancer survivors receiving chemotherapy: A systematic review of randomized controlled trials. *Breast (Edinburgh, Scotland)*, 63, 113–122. <https://doi.org/10.1016/j.breast.2022.03.014>
  - Rendeiro, J. A., Rodrigues, C. A. M. P., de Barros Rocha, L., Rocha, R. S. B., da Silva, M. L., & da Costa Cunha, K. (2021). Physical exercise and quality of life in patients with prostate cancer: systematic review and meta-analysis. *Supportive care in cancer: official journal of the Multinational Association of Supportive Care in Cancer*, 29(9), 4911–4919. <https://doi.org/10.1007/s00520-021-06095-y>
  - Rodríguez-Cañamero, S., Cobo-Cuenca, A. I., Carmona-Torres, J. M., Pozuelo-Carrascosa, D. P., Santacruz-Salas, E., Rabanales-Sotos, J. A., Cuesta-Mateos, T., & Laredo-Aguilera, J. A. (2022). Impact of physical exercise in advanced-stage cancer patients: Systematic review and meta-analysis. *Cancer medicine*, 11(19), 3714–3727. <https://doi.org/10.1002/cam4.4746>
  - Rossi, A., Garber, C. E., Kaur, G., Xue, X., Goldberg, G. L., & Nevadunsky, N. S. (2017). Physical activity-related differences in body mass index and patient-reported quality of life in socioculturally diverse endometrial cancer survivors. *Supportive care in cancer: official journal of the Multinational Association of Supportive Care in Cancer*, 25(7), 2169–2177. <https://doi.org/10.1007/s00520-017-3622-y>
  - Royse, K. E., El-Serag, H. B., Chen, L., White, D. L., Hale, L., Sangi-Haghpeykar, H., & Jiao, L. (2017). Sleep Duration and Risk of Liver Cancer in Postmenopausal Women: The Women's Health Initiative Study. *Journal of women's health* (2002), 26(12), 1270–1277. <https://doi.org/10.1089/jwh.2017.6412>
  - Seegobin, K., Staggs, E., Khawaja, R., Maharaj, S., Gautam, S., Smotherman, C., & Rana, F. (2018). Pilot study on the occurrence of multiple cancers following cancer-related therapy at the University of Florida, Jacksonville (2011–

- 2016). Journal of investigative medicine: the official publication of the American Federation for Clinical Research, 66(7), 1050–1054. <https://doi.org/10.1136/jim-2018-000772>
- Seixas, A. A., Gyamfi, L., Newsome, V., Ranger-Murdock, G., Butler, M., Rosenthal, D. M., Zizi, F., Youssef, I., McFarlane, S. I., & Jean-Louis, G. (2018). Moderating effects of sleep duration on diabetes risk among cancer survivors: analysis of the National Health Interview Survey in the USA. *Cancer management and research*, 10, 4575–4580. <https://doi.org/10.2147/CMAR.S177428>
  - Smith, T. O., Pearson, M., Smith, M. J., Fletcher, J., Irving, L., & Lister, S. (2022). Effectiveness of caregiver interventions for people with cancer and non-cancer-related chronic pain: a systematic review and meta-analysis. *British journal of pain*, 16(1), 71–83. <https://doi.org/10.1177/20494637211022771>
  - Soares Falcetta, F., de Araújo Vianna Träsel, H., de Almeida, F. K., Rangel Ribeiro Falcetta, M., Falavigna, M., & Dornelles Rosa, D. (2018). Effects of physical exercise after treatment of early breast cancer: systematic review and meta-analysis. *Breast cancer research and treatment*, 170(3), 455–476. <https://doi.org/10.1007/s10549-018-4786-y>
  - Spreafico, F., Barretta, F., Murelli, M., Chisari, M., Gattuso, G., Terenziani, M., Ferrari, A., Veneroni, L., Meazza, C., & Massimino, M. (2021). Positive Impact of Organized Physical Exercise on Quality of Life and Fatigue in Children and Adolescents With Cancer. *Frontiers in pediatrics*, 9, 627876. <https://doi.org/10.3389/fped.2021.627876>
  - Sturgeon, S. R., Luisi, N., Balasubramanian, R., & Reeves, K. W. (2012). Sleep duration and endometrial cancer risk. *Cancer causes & control: CCC*, 23(4), 547–553. <https://doi.org/10.1007/s10552-012-9912-2>
  - Stone, C. R., Haig, T. R., Fiest, K. M., McNeil, J., Brenner, D. R., & Friedenreich, C. M. (2019). The association between sleep duration and cancer-specific mortality: a systematic review and meta-analysis. *Cancer causes & control: CCC*, 30(5), 501–525. <https://doi.org/10.1007/s10552-019-01156-4>
  - Tao, F., Cao, Z., Jiang, Y., Fan, N., Xu, F., Yang, H., Li, S., Zhang, Y., Zhang, X., Sun, L., & Wang, Y. (2021). Associations of sleep duration and quality with incident cardiovascular disease, cancer, and mortality: a prospective cohort study of 407,500 UK biobank participants. *Sleep medicine*, 81, 401–409. <https://doi.org/10.1016/j.sleep.2021.03.015>
  - Toohey, K., Chapman, M., Rushby, A. M., Urban, K., Ingham, G., & Singh, B. (2023). The effects of physical exercise in the palliative care phase for people with advanced cancer: a systematic review with meta-analysis. *Journal of cancer survivorship: research and practice*, 17(2), 399–415. <https://doi.org/10.1007/s11764-021-01153-0>
  - Tranchita, E., Murri, A., Grazioli, E., Cerulli, C., Emerenziani, G. P., Ceci, R., Caporossi, D., Dimauro, I., & Parisi, A. (2022). The Beneficial Role of Physical Exercise on Anthracyclines Induced Cardiotoxicity in Breast Cancer Patients. *Cancers*, 14(9), 2288. <https://doi.org/10.3390/cancers14092288>
  - Vehmanen, L., Mattson, J., Karademas, E., Oliveira-Maia, A. J., Sousa, B., Pat-Horenczyk, R., Mazzocco, K., Simos, P., Cardoso, F., Pettini, G., Marzorati, C., Kolokotroni, E., Stamatakis, G., Frascquilho, D., & Poikonen-Saksela, P. (2022). Associations between Physical Exercise, Quality of Life, Psychological Symptoms and Treatment Side Effects in Early Breast Cancer. *The breast journal*, 2022, 9921575. <https://doi.org/10.1155/2022/9921575>
  - Verbunt, J. A., Sieben, J. M., Seelen, H. A., Vlaeyen, J. W., Bousema, E. J., van der Heijden, G. J., & Knottnerus, J. A. (2005). Decline in physical activity, disability and pain-related fear in sub-acute low back pain. *European journal of pain* (London, England), 9(4), 417–425. <https://doi.org/10.1016/j.ejpain.2004.09.011>
  - Wang, P., Ren, F. M., Lin, Y., Su, F. X., Jia, W. H., Su, X. F., Tang, L. Y., & Ren, Z. F. (2015). Night-shift work, sleep duration, daytime napping, and breast cancer risk. *Sleep medicine*, 16(4), 462–468. <https://doi.org/10.1016/j.sleep.2014.11.017>
  - Wang, S., Yang, T., Qiang, W., Shen, A., Zhao, Z., Chen, X., Xi, C., Liu, H., & Guo, F. (2021). Effectiveness of physical exercise on the cardiovascular system in breast cancer patients: a systematic review and meta-analysis of randomized controlled trials. *Complementary therapies in clinical practice*, 44, 101426. <https://doi.org/10.1016/j.ctcp.2021.101426>
  - Wiggenraad, F., Bolam, K. A., Mijwel, S., van der Wall, E., Wengström, Y., & Altena, R. (2020). Long-Term Favorable Effects of Physical Exercise on Burdensome Symptoms in the OptiTrain Breast Cancer Randomized Controlled Trial. *Integrative cancer therapies*, 19, 1534735420905003. <https://doi.org/10.1177/1534735420905003>
  - Wilunda, C., Abe, S. K., Svensson, T., Sawada, N., Tsugane, S., Wada, K., Nagata, C., Kimura, T., Tamakoshi, A., Sugawara, Y., Tsuji, I., Ito, H., Kitamura, T., Sakata, R., Mizoue, T., Matsuo, K., Tanaka, K., Lin, Y., Inoue, M., & Research Group for the Development and Evaluation of Cancer Prevention Strategies in Japan (2022). Sleep duration and risk of cancer incidence and mortality: A pooled analysis of six population-based cohorts in Japan. *International journal of cancer*, 151(7), 1068–1080. <https://doi.org/10.1002/ijc.34133>
  - Wodarz, D., & Anton-Culver, H. (2005). Dynamical interactions between multiple cancers. *Cell cycle* (Georgetown, Tex.), 4(6), 764–771. <https://doi.org/10.4161/cc.4.6.1747>
  - Wong, A. T. Y., Heath, A. K., Tong, T. Y. N., Reeves, G. K., Floud, S., Beral, V., & Travis, R. C. (2021). Sleep duration and breast cancer incidence: results from the Million Women Study and meta-analysis of published prospective studies. *Sleep*, 44(2), zsa166. <https://doi.org/10.1093/sleep/zsa166>
  - Wong, J. Y., Bassig, B. A., Vermeulen, R., Hu, W., Ning, B., Seow, W. J., Ji, B. T., Downward, G. S., Katki, H. A., Barone-Adesi, F., Rothman, N., Chapman, R. S., & Lan, Q. (2017). Sleep Duration across the Adult Lifecourse and Risk of Lung Cancer Mortality: A Cohort Study in Xuanwei, China. *Cancer prevention research* (Philadelphia, Pa.), 10(6), 327–336. <https://doi.org/10.1158/1940-6207.CAPR-16-0295>
  - Wu, A. H., Stanczyk, F. Z., Wang, R., Koh, W. P., Yuan, J. M., & Yu, M. C. (2013). Sleep duration, spot urinary 6-sulfatoxymelatonin levels and risk of breast cancer among Chinese women in Singapore. *International journal of cancer*, 132(4), 891–896. <https://doi.org/10.1002/ijc.27653>
  - Wu, I. H. C., Balachandran, D. D., Faiz, S. A., Bashoura, L., Escalante, C. P., & Manzullo, E. F. (2022). Characteristics of Cancer-Related Fatigue and Concomitant Sleep Disturbance in Cancer Patients. *Journal of pain and symptom*

- management, 63(1), e1–e8. <https://doi.org/10.1016/j.jpainsymman.2021.07.025>
- Wu, X., Qin, F., Zhang, Q., Qiao, J., Qi, Y., & Liu, B. (2022). Immunotherapy improved cancer related pain management in patients with advanced Hepato-Pancreatic Biliary Cancers: A propensity score-matched (PSM) analysis. *Frontiers in oncology*, 12, 914591. <https://doi.org/10.3389/fonc.2022.914591>
  - Xiao, Q., Signorello, L. B., Brinton, L. A., Cohen, S. S., Blot, W. J., & Matthews, C. E. (2016). Sleep duration and breast cancer risk among black and white women. *Sleep medicine*, 20, 25–29. <https://doi.org/10.1016/j.sleep.2015.11.010>
  - Xiao, Q., Arem, H., Pfeiffer, R., & Matthews, C. (2017). Prediagnosis Sleep Duration, Napping, and Mortality Among Colorectal Cancer Survivors in a Large US Cohort. *Sleep*, 40(4), zsx010. <https://doi.org/10.1093/sleep/zsx010>
  - Yang, W. S., Deng, Q., Fan, W. Y., Wang, W. Y., & Wang, X. (2014). Light exposure at night, sleep duration, melatonin, and breast cancer: a dose-response analysis of observational studies. *European journal of cancer prevention: the official journal of the European Cancer Prevention Organisation (ECP)*, 23(4), 269–276. <https://doi.org/10.1097/CEJ.0000000000000030>
  - Yessoufou, A., Moutairou, K., Girard, A., Fatoke, M., Prost, J., Ahissou, H., Djrolo, F., Avode, G., Amoussou-Guenou, D., Hichami, A., & Khan, N. A. (2005). Antioxidant status in alcohol-related diabetes mellitus in Beninese subjects. *Cellular and molecular biology (Noisy-le-Grand, France)*, 51 Suppl, OL849–OL858.
  - Young, S. W., Candido, E., Klein-Geltink, J., & Giesbrecht, N. (2018). Preventing alcohol-related cancer: what if everyone drank within the guidelines?. *Canadian journal of public health = Revue canadienne de sante publique*, 109(1), 70–78. <https://doi.org/10.17269/s41997-018-0033-x>
  - Yu, Y., Yan, W., Yu, J., Xu, Y., Wang, D., & Wang, Y. (2022). Prevalence and Associated Factors of Complaints on Depression, Anxiety, and Stress in University Students: An Extensive Population-Based Survey in China. *Frontiers in psychology*, 13, 842378. <https://doi.org/10.3389/fpsyg.2022.842378>
  - Zhang, X., Giovannucci, E. L., Wu, K., Gao, X., Hu, F., Ogino, S., Schernhammer, E. S., Fuchs, C. S., Redline, S., Willett, W. C., & Ma, J. (2013). Associations of self-reported sleep duration and snoring with colorectal cancer risk in men and women. *Sleep*, 36(5), 681–688. <https://doi.org/10.5665/sleep.2626>
  - Zheng, K., Yu, J., Chen, Z., Zhou, R., Lin, C., Zhang, Y., Huang, Z., Yu, L., Zhao, L., & Wang, Q. (2019). Ethanol promotes alcohol-related colorectal cancer metastasis via the TGF- $\beta$ /RUNX3/Snail axis by inducing TGF- $\beta$ 1 upregulation and RUNX3 cytoplasmic mislocalization. *EBioMedicine*, 50, 224–237. <https://doi.org/10.1016/j.ebiom.2019.11.011>

## Declarations

**Funding:** No specific funding was received for this work.

**Potential competing interests:** No potential competing interests to declare.