Published in final edited form as:
Int J Cancer. 2014 July 15; 135(2): 423–431. doi:10.1002/ijc.28659.

Physical activity and cancer-specific mortality in the NIH-AARP Diet and Health Study cohort

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Abstract

Higher physical activity levels have been associated with a lower risk of developing various cancers and all-cancer mortality, but the impact of pre-diagnosis physical activity on cancer-specific death has not been fully characterized. In the prospective National Institutes of Health-AARP Diet and Health Study with 293,511 men and women, we studied pre-diagnosis moderate to vigorous intensity leisure time physical activity (MVPA) in the past 10 years and cancer-specific mortality. Over a median 12.1 years we observed 15,001 cancer deaths. Using Cox proportional hazards regression, we estimated hazard ratios (HRs) and 95% confidence intervals (CIs) for MVPA with cancer mortality overall and by 20 specific cancer sites, adjusting for relevant risk factors. Compared to participants reporting never/rare MVPA, those reporting >7 hours/week MVPA had a lower risk of total cancer mortality (HR=0.89, 95% CI 0.84–0.94; p-trend<.001). When analyzed by cancer site-specific deaths, comparing those reporting >7 hours/week of MVPA to those reporting never/rare MVPA, we observed a lower risk of death from colon (HR=0.70; 95% CI 0.57–0.85; p-trend<.001), liver (0.71; 0.52–0.98; p-trend=.012) and lung cancer (0.84; 0.77–0.92; p-trend<.001) and a significant p-trend for non-Hodgkins lymphoma (0.80; 0.62–1.04; p-trend=.017). An unexpected increased mortality p-trend with increasing MVPA was observed for death from kidney cancer (1.42; 0.98–2.03; p-trend=.016). Our findings suggest that higher pre-diagnosis leisure time physical activity is associated with lower risk of overall cancer mortality and mortality from multiple cancer sites. Future studies should confirm observed associations and further explore timing of physical activity and underlying biological mechanisms.

Keywords

physical activity; cancer; mortality

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Introduction

A recent Annual Report to the Nation reported that more than 1/3 of U.S. men and women were considered to be physically inactive and that over half did not meet physical activity recommendations of 150 minutes of moderate to vigorous intensity activity each week[1]. Physical activity has been related to lower cancer incidence for the breast, colon and endometrium[2], and has also been associated with disease severity, recurrence and survival, particularly for breast and colorectal cancer[3–4]. Existing studies on physical activity and mortality have shown an association between physical activity and lower risk of all cause[5–6] and overall cancer mortality[7–9], but the effect of leisure time physical activity on mortality from individual cancer sites has not been fully characterized.

We hypothesized that moderate to vigorous intensity leisure time physical activity (MVPA) would be inversely related to overall cancer death, and that examination of physical activity in relation to specific cancer sites would generate hypotheses for future research. While physical activity and overall mortality have previously been examined in the National Institutes of Health (NIH)-AARP Diet and Health Study[10–11], the large, prospective nature and extended follow-up time in this cohort of men and women allowed for additional exploration of individual cancer sites. We thus analyzed pre-diagnosis physical activity and cancer-specific deaths in the NIH-AARP cohort to augment the paucity of evidence on physical activity and cancer mortality.

Methods

Study Population

The NIH-AARP Diet and Health Study has been previously described[12]. Briefly, the NIH-AARP cohort included 566,398 AARP members (aged 50–71 years) who completed a mailed baseline questionnaire in 1995–1996. In 1996–1997 an additional risk factor questionnaire (RFQ) including additional questions about participation in physical activity was mailed to participants who did not have self-reported cancer of the colon, breast or prostate at the time of the baseline questionnaire (response rate=67%). Participants resided in six states (California, Florida, Pennsylvania, New Jersey, North Carolina, or Louisiana) or two metropolitan areas (Atlanta, Georgia or Detroit, Michigan). Of the 334,905 men and women who completed the baseline and risk factor questionnaires we excluded those whose questionnaires were completed by proxy (n=10,383), those diagnosed with cancer before collection of physical activity data (n=18,810), those with self-reported poor health (n=4,382), those who moved out of the study area or died at or before processing of the questionnaires (n=23) and individuals with missing information on physical activity (n=7,796). After exclusions, 293,511 participants were included in this analysis. The NIH-AARP Diet and Health study was approved by the Special Studies Institutional Review Board of the U.S. National Cancer Institute, and all participants gave informed consent by virtue of completing and returning the questionnaire.

Mortality Ascertainment

Participants were followed for address changes using the U.S. Postal Service's National Change of Address database, and vital status was ascertained periodically by linkage to the Social Security Administration Death Master File and the National Death Index Plus through 12/31/2008. To classify deaths due to specific cancers we used ICD-9 (1995–1998) and ICD-10 (1999–2008) codes and considered individual cancer sites where there were more than 50 deaths. Mortality follow-up in this study is estimated to be more than 93% complete[13–14].

Exposure Assessment

The baseline questionnaire (1995–1996) queried about demographic characteristics, diet, reproductive and medical history, and lifestyle. The physical activity questions on the subsequent RFQ (1996–1997) predominantly assessed recreational and leisure time activities performed in the last ten years. Examples of activities include tennis, golf, biking, swimming, heavy gardening, fast walking or dancing, aerobics and jogging. Participants reported categorical duration of activities (never, rarely, <1 hr/week, 1–3 hr/week, 4–7 hr/week, and >7 hr/week). The NIH-AARP physical activity questionnaire has not been validated directly, but has demonstrated expected inverse associations with all-cause mortality[10] and for incident cases of breast, colon and endometrial cancers in this cohort[15–17].

Statistical Analysis

Hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated using Cox proportional hazards regression models with age as the underlying time metric in SAS version 9.2 (SAS Institute Inc, Cary, NC). Follow-up started at physical activity questionnaire completion and ended at death or the end of follow-up, whichever occurred first. MVPA was categorized into never/rarely (reference), <1 hr/week, 1–3 hr/week, 4–7 hr/week, and >7 hr/week.

We explored all variables in Table 1 as potential confounders and retained factors that changed modeled estimates of overall cancer mortality by > 10%, or that are supported in previous literature as associated with cancer mortality. BMI was calculated as kg/m^2 using baseline self-reported height and weight. Physical activity HR estimates were modeled with and without adjustment for BMI to address the possibility that BMI is in the causal pathway between physical activity and mortality. Although including BMI in models did not significantly change estimates, we included BMI in final models to eliminate concerns that the association between MVPA and cancer mortality is explained by BMI. We adjusted for cancer screening in the three years prior to questionnaire in analyses of breast and colon cancer-specific deaths. We did not adjust for prostate cancer screening because the U.S. randomized clinical trial found no association between screening and mortality for this cancer[18]. In analyses of female cancers (breast, endometrial, ovarian), we also adjusted for menopausal hormone therapy use (ever/never) and age at menarche (<12 years old, 12+ years old). We also performed analyses using a 31-level detailed smoking variable to see if our estimates were altered. MVPA estimates did not change substantially with the detailed smoking categories.

The final models thus included adjustment for sex, race (non-Hispanic white, African American, other), body mass index (BMI) (15-<18.5 kg/m^2, 18.5-<25, 25-<30, 30-<35, 35+), smoking (never, quit >10 years before, quit 5–9 years before, quit 1–4 years before, quit <1 year prior or current smoker ≤20 cigarettes per day, quit <1 year prior or current smoker >20 cigarettes per day), alcohol intake (0, 0<-<3, and 3+ drinks/day), Healthy Eating Index-2010 (HEI-2010) score, energy intake, married or living as married (yes/no), and history of diabetes (yes/no). Tests for linear trend were performed coding MVPA categories in an ordinal fashion.

To maintain power in stratified analyses we created a continuous MVPA measure by assigning the average number of hours per week to each category of physical activity and treated that parameter as continuous variable. To assess effect modification and to detect potential residual confounding by smoking we performed stratified analyses of the association between physical activity and cancer death. We also created an interaction term as the product of continuous MVPA and smoking level, and entered the interaction term into the fully adjusted models, using the Wald test to evaluate the statistical significance of multiplicative interaction.

Because previous studies have shown joint associations of physical activity and BMI on both cancer risk and mortality, we also created models to examine a joint measure of physical activity and obesity. In a dichotomous measure “inactive” individuals included those who reported never/rare MVPA and “active” individuals included those who reported <1–7+ hours per week. Individuals with a BMI <30 kg/m^2 were characterized as “non-obese” and individuals with a BMI ≥30 were characterized as “obese”.

In additional analyses, we stratified by sex and age at questionnaire completion (<55, 55–<60, 60–<65, and 65+ years old), and performed Wald tests for interaction. HR estimates are presented by cancer site for men and women combined because stratification by sex did not show substantial differences and marginal multiplicative interaction by sex as indicated by the Wald test was observed only for oral cancer deaths (p=0.05). We also assessed robustness of estimates by restricting analyses to individuals without heart disease, diabetes, and emphysema at baseline. Additionally, we performed analyses limiting the population to those with a BMI >15 and ≤50 kg/m^2 to test whether estimates were influenced by outliers. We also ran models excluding individuals who were diagnosed within two years of completing the physical activity questionnaire to test whether latent disease affected our mortality risk estimates. The proportional hazards assumption, which was evaluated by modeling interaction terms of the main exposure trend with follow up time, was met using the Wald test. All statistical tests were two-sided, with p-values<0.05 considered significant. We report results as significant where the p-trend test shows statistical significance, and present the comparison of highest to lowest categories to show the estimated magnitude of effect at the highest reported activity levels.

Results

Our analytic cohort included 293,511 participants (171,666 men and 121,845 women). The median time from MVPA assessment to cancer diagnosis was 5.2 years (range 0–13.2).

Over a median 12.1 years, we observed 15,001 cancer deaths. Population characteristics are presented in Table 1. Compared to those reporting never/rare physical activity, those who reported higher levels of physical activity had a lower BMI and a healthier diet as scored by the HEI-2010. Active individuals were also more likely to be married or living as married, report regular multivitamin use, and were less likely to report diabetes and smoking at baseline. Active women were less likely to report menarche at age<12 years.

We found a reduction in risk for overall cancer mortality with increasing MVPA (p-trend=<.001), which reached statistical significance for those reporting greater than one hour per week of MVPA. Compared to those reporting never/rare MVPA, we observed a 7% lower risk for those reporting 1–3 MVPA h/wk (HR=0.93; 95% CI 0.88–0.98), a 10% lower risk for those reporting 4–7 h/wk (0.90; 0.85–0.95), and a 11% lower risk for those reporting >7 h/wk of MVPA (0.89; 0.84–0.94) (Table 2). Estimates for MVPA and cancer-specific mortality are presented in Table 2 by strongest inverse to strongest positive point estimates in the highest category of MVPA. We observed statistically significant inverse trends with higher MVPA for deaths due to cancers of the colon (HR=0.70; 95% CI 0.57–0.85, p-trend=<.001), liver (0.71; 0.52–0.98, p-trend=0.012), lung (0.84; 0.77–0.92, p-trend=<.001) and non-Hodgkins lymphoma (0.80; 0.62–1.04, p-trend=0.017). In sensitivity analysis, excluding those diagnosed within two years of the MVPA questionnaire, the trend became non-significant for non-Hodgkins lymphoma (0.86; 0.62–1.19, p-trend=0.176) (Supplemental Table 1). No statistically significant trends were observed for lymphocytic leukemia, oral cavity and pharynx, esophagus, myeloma, myeloid/monocytic leukemia, stomach, ovarian, prostate, bladder, breast, brain, pancreas or rectum cancer deaths. We observed an unexpected statistically significant positive trend between MVPA and mortality from kidney cancer (1.42; 0.98–2.03, p-trend=0.016), which remained significant in the analyses excluding individuals diagnosed within two years of MVPA assessment (1.67; 1.04–2.70, p-trend=0.013) (Supplemental Table 1).

To explore the possibility of effect modification by smoking, in Table 3 we present analyses stratified by smoking status for MVPA and cancer death overall and by cancer site. Multiplicative interaction was not observed for any of the cancer sites (all p-interactions<0.05) except for ovarian cancer death (p=0.022). Still, stratified ovarian cancer death hazard ratios were not statistically significant for never (1.04; 0.99–1.09) or ever (0.96; 0.92–1.01) smokers.

Joint associations for physical activity and BMI with all cancer mortality are presented in Table 4. Compared to the reference group of those who were active (reported more than never/rare MVPA) and non-obese (BMI<30 kg/m^2), we found an increased risk of cancer mortality for those who were inactive and non-obese, (HR=1.12; 95% CI 1.06–1.18) active and obese (1.16; 1.11–1.21), and inactive and obese (1.22; 1.13–1.32). Individuals who were obese, whether active or inactive, showed a 39% to over two-fold statistically significant increased risk of death due to cancers of the colon, liver, breast and endometrium compared to those who were active and non-obese.

Restricting analyses to individuals without heart disease, diabetes, and emphysema did not change results (data not shown). Excluding individuals with a BMI <15 kg/m^2 or >50 also

did not affect associations (data not shown). Stratification by age at questionnaire completion suggested stronger associations among older participants, but multiplicative interaction terms were not significant (data not shown).

Discussion

In our study population higher MVPA before diagnosis was independently associated with a reduced risk of total cancer mortality. The observed inverse association was primarily driven by lower risks for death from cancers of the colon, liver, and lung and non-Hodgkins lymphoma. Analyses of the joint effects of BMI and MVPA suggested lower risks of cancer death for active, non-obese individuals for various cancer sites.

Few studies report on physical activity and cancer mortality. A previous study in this cohort with less follow up and fewer deaths found that those reporting >7 hours of MVPA each week had an a 17% lower risk of cancer mortality (0.83; 0.74–0.93) compared to individuals reporting no MVPA[19]. In a large Taiwanese cohort researchers found a lower overall cancer mortality risk (0.83; 0.77–0.90) comparing those with higher leisure time physical activity (~20 metabolic equivalent hrs/wk) to inactive individuals[20]. In this Taiwanese study significant inverse associations were observed for deaths due to colon and rectum cancer, liver cancer, and lung cancer, while the association was not significant for breast cancer mortality. Another study using a treadmill test to assess fitness and a questionnaire to report physical activity levels showed that fitness and reported physical activity each were associated with lower overall cancer mortality among men, while among women there was a suggested but not significant association[21]. However, that study[21] had a small number of female deaths due to cancer (n=44), possibly contributing to the lack of statistically significant findings.

In this cohort previous physical activity analyses focused largely on cancer incidence, reporting inverse associations for liver, renal cell, breast, endometrial and colon cancers[17, 22–25]. Another study in this cohort on the joint effects of physical activity and adiposity on all-cause mortality also showed independent effects of each on mortality risk[11]. Our finding on the joint association between physical activity and body mass index with all-cancer mortality adds to the published literature in this cohort and is consistent with a previous publication in a large cohort of women reporting independent and joint effects of physical activity and BMI on reduced all-cancer mortality risk[8].

To our knowledge, previous studies have not comprehensively reported on physical activity and risk of death from individual cancers. A growing body of energy balance survivorship literature was summarized in a recent review of 27 observational studies on physical activity among cancer survivors, reporting that physical activity was associated with lower rates of all-cause mortality and cancer-specific mortality for breast and colon cancers[4]. A recent forum on obesity, energy balance and cancer survival also highlighted protective effects among those who were normal weight and active for breast and colon cancer-specific mortality among survivors[26]. Our observed inverse association between physical activity and colon cancer mortality is consistent with these findings. A study in the Women's Health Initiative reported an association between pre-diagnosis moderate intensity activity and

breast cancer death[27], but similar to our findings, other studies have shown no association between pre-diagnosis physical activity and breast cancer death[20, 28–29]. These conflicting findings could be due to differences in physical activity questionnaires, differences in time periods from measurement to diagnosis and follow up time, or differences in study populations, such as the age at diagnosis or the percentage who reported menopausal hormone therapy usage. Literature on physical activity and mortality from other specific cancer sites is limited, although the above mentioned review summarized limited evidence of an inverse association for prostate cancer mortality and no association for ovarian cancer mortality[4]. Also, a previous study on pre-diagnosis physical activity and endometrial cancer mortality in this cohort also showed no association[30]. Our observed positive association between MVPA and kidney cancer death contrasts with previous findings on MVPA cancer incidence in this cohort, which showed an inverse association between physical activity and renal cancer, which accounts for about 80% of kidney cancers[25]. However, other prospective cohort studies have shown no association between physical activity and renal cancer risk[31–33] and both risk factors and potential mechanisms related to physical activity may be different for incidence than for cancer mortality. A recent meta-analysis showed protective associations between leisure-time physical activity and lung cancer risk[34], and the high fatality of lung cancer may translate into similarities between risk factors for incidence and mortality. Published findings on physical activity and liver cancer are limited, although a previous analysis in this cohort showed an inverse association between physical activity and risk of developing liver cancer[22].

Mechanisms explaining the association between physical activity and mortality have been more widely studied in relation to cancer incidence. Review papers on mechanisms by which physical activity may affect cancer risk cite metabolic effects of high physical activity including lower body mass index, lower circulating sex hormones and insulin levels, and possibly effects on inflammation or the immune system[35–36]. These proposed mechanisms likely differ by specific cancer site. Some exercise intervention studies among survivors show improvements in circulating insulin levels and biomarkers related to cancer progression and recurrence[37–38]. It is also possible that individuals who are active before diagnosis might have healthful habits (e.g. exercise) that are easier to maintain after diagnosis.

Strengths of our study include the large, prospective nature of the cohort and sufficient follow-up time. Other strengths include the objective endpoint (mortality) as well as a comprehensive range of cancer deaths, allowing examination of site-specific cancers. Detailed covariate information allowed us to examine effect modification by other risk factors such as BMI, smoking and diabetes.

Limitations of our study include measurement errors associated with self-report of physical activity. Although we had only a single measure of physical activity, we asked about physical activity in the past 10 years, attempting to reflect individuals' usual activity levels over time. Also, we lacked information on physical activity levels after cancer diagnosis, which may differ from pre-diagnosis levels. We adjusted for known confounders but we cannot eliminate the possibility that results were influenced by other lifestyle factors associated with physical activity, including better health maintenance and health insurance

coverage. Lastly, we cannot rule out a possibility of observing associations by chance due to multiple comparisons.

Notably, the inverse association between MVPA and cancer mortality risk became significant with one hour or more of physical activity per week, and the magnitude of the protective association increased only slightly with more MVPA, as shown by similar point estimates in the higher MVPA categories. This exploratory analysis was the first to examine MVPA and site-specific cancer mortality, and was intended to generate new hypotheses. In particular, inverse associations observed with MVPA and deaths from colon, liver and lung cancers should be further explored. The observed positive association with kidney cancer death also merits investigation. In addition, future research should isolate associations with moderate versus vigorous activities, post-diagnosis physical activity, and whether changes in activity levels from pre to post-diagnosis affect cancer-specific mortality.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

List of abbreviations

BMI	Body mass index
CI	Confidence Interval
HEI	Healthy Eating Index
HR	Hazard Ratio
MVPA	Moderate to vigorous physical activity
NIH	National Institutes of Health
RFQ	Risk factor questionnaire

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Novelty and impact

Despite evidence that physical activity reduces risk of multiple chronic diseases including cancer, 1/3 of the U.S. population is inactive. This study comprehensively explores associations between pre-diagnosis physical activity and cancer mortality, finding inverse trends for physical activity and cancer mortality overall and for death from cancers of the colon, liver, lung, and non-Hodgkins lymphoma.

Int J Cancer. Author manuscript; available in PMC 2015 July 15.

Table 1

Baseline characteristics in the NIH-AARP Diet and Health study population by level of moderate to vigorous-intensity physical activity (MVPA) (N=293,511)

Frequency of MVPA (h/wk)	**Never/rare**	**<1**	**1–3**	**4–7**	**>7**
Cancer Deaths/Total participants	2,524/41,165	1,659/31,095	3,756/74,502	3,636/76,049	3,426/70,700
Age at MVPA assessment, years	62.8	62.4	62.6	62.8	63.2
Sex, %					
Women	41.7	41.8	41.8	41.3	41.3
Body mass index, kg/m^2	28.4	27.9	27.1	26.4	25.9
Education, %					
<High school/ high school graduate	28.5	23.6	21.0	20.5	24.1
Post high school/ some college	32.9	34.4	33.8	32.5	33.0
College or graduate degree	36.1	39.7	42.9	44.7	40.3
Race/ethnicity, %					
Non-Hispanic White	90.4	91.4	92.8	93.6	93.7
African American	4.7	4.1	3.3	2.6	2.4
Other	3.7	3.4	2.8	2.8	2.9
Married or living as married, %	63.4	67.2	68.3	69.9	70.1
Television or video watching ≤2 h/d, %	28.3	33.2	35.8	38.6	37.9
Self-reported diabetes, %	12.6	9.6	8.2	6.8	6.1
Family history of cancer, %	52.4	52.8	53.3	53.4	54.3
Daily aspirin use, %	26.0	24.4	24.5	24.9	25.4
Daily ibuprofen use, %	11.8	10.1	10.0	9.5	9.8
Smoke, %					
Never	33.7	35.6	36.4	36.5	36.6
Former	48.0	48.3	49.3	50.8	50.8
Current	14.8	12.9	11.2	9.6	9.2
Total energy intake, kcal/d	1845	1810	1805	1823	1931
Healthy Eating Index-2010 score	62.8	64.7	66.2	67.7	68.1
Red meat intake, grams/1000 kcal/day	37.0	36.6	34.8	32.5	31.4
Alcohol intake, g/d	13.7	12.9	12.5	12.9	14.1

Frequency of MVPA (h/wk)	Never/rare	<1	1–3	4–7	>7
Coffee intake, g/d	769.0	774.9	766.1	767.3	767.6
Multivitamin use, %	51.5	54.7	56.4	57.6	57.3
Age at menarche<12 years[a], %	51.5	50.0	49.0	47.7	46.8
Ever MHT use[a], %	21.0	22.4	23.0	23.5	22.5

[a]Measured only among women

Int J Cancer. Author manuscript; available in PMC 2015 July 15.

Table 2

Associations between moderate to vigorous intensity physical activity (MVPA) and cancer mortality in the NIH-AARP study population (N=293,511)[a]

MVPA (h/wk)	Never/rare		<1		1–3		4–7		>7		
Cancer death	**No. of deaths**	**HR (ref.)**	**No. of deaths**	**HR (95% CI)**	**No. of deaths**	**HR (95% CI)**	**No. of deaths**	**HR (95% CI)**	**No. of deaths**	**HR (95% CI)**	**P trend**
All cancers	2524	1.00	1659	0.95 (0.89–1.01)	3756	0.93 (0.88–0.98)	3636	0.90 (0.85–0.95)	3426	0.89 (0.84–0.94)	<0.001
Individual cancer sites by inverse magnitude of point estimate comparing MVPA >7 h/wk to never/rare MVPA											
Lymphocytic leukemia	20	1.00	14	0.96 (0.48–1.89)	46	1.30 (0.76–2.21)	24	0.65 (0.35–1.19)	24	0.68 (0.37–1.25)	0.058
Colon[b]	198	1.00	109	0.80 (0.63–1.01)	268	0.85 (0.70–1.02)	250	0.79 (0.65–0.96)	211	0.70 (0.57–0.85)	<0.001
Liver	82	1.00	43	0.79 (0.54–1.14)	112	0.90 (0.68–1.21)	78	0.64 (0.47–0.88)	82	0.71 (0.52–0.98)	0.012
Oral cavity and pharynx	38	1.00	20	0.83 (0.48–1.44)	41	0.79 (0.51–1.24)	38	0.76 (0.48–1.21)	36	0.75 (0.47–1.20)	0.217
Non-Hodgkins lymphoma	104	1.00	90	1.19 (0.90–1.58)	137	0.76 (0.58–0.98)	154	0.83 (0.64–1.06)	143	0.80 (0.62–1.04)	0.017
Esophagus	88	1.00	55	0.92 (0.65–1.29)	123	0.91 (0.69–1.20)	127	0.96 (0.73–1.27)	98	0.80 (0.60–1.08)	0.251
Myeloma	61	1.00	34	0.75 (0.49–1.14)	63	0.56 (0.40–0.81)	90	0.77 (0.55–1.07)	93	0.82 (0.59–1.15)	0.579
Lung	923	1.00	522	0.85 (0.76–0.95)	1258	0.92 (0.84–1.00)	1095	0.82 (0.75–0.90)	1073	0.84 (0.77–0.92)	<0.001
Myeloid/monocytic leukemia	54	1.00	50	1.27 (0.86–1.86)	81	0.85 (0.60–1.21)	109	1.10 (0.79–1.54)	82	0.86 (0.60–1.22)	0.346
Stomach	49	1.00	34	1.00 (0.65–1.56)	77	0.99 (0.69–1.42)	76	0.97 (0.67–1.40)	68	0.90 (0.61–1.31)	0.541
Ovarian[c]	61	1.00	41	0.92 (0.62–1.36)	90	0.83 (0.59–1.15)	98	0.87 (0.63–1.21)	97	0.91 (0.65–1.26)	0.623
Prostate	80	1.00	55	0.97 (0.69–1.37)	107	0.79 (0.59–1.06)	145	1.03 (0.78–1.37)	126	0.93 (0.69–1.24)	0.968
Bladder	52	1.00	45	1.25 (0.84–1.86)	82	0.97 (0.68–1.38)	82	0.95 (0.67–1.36)	85	1.03 (0.72–1.46)	0.698
Breast[b,c]	70	1.00	55	1.21 (0.82–1.80)	103	0.92 (0.65–1.29)	99	0.97 (0.68–1.37)	109	1.08 (0.76–1.53)	0.973
Brain	57	1.00	51	1.14 (0.78–1.66)	115	1.03 (0.75–1.42)	107	0.91 (0.65–1.26)	128	1.14 (0.82–1.56)	0.791
Endometrial[c,d]	23	1.00	24	1.52 (0.85–2.69)	27	0.79 (0.45–1.38)	35	1.13 (0.66–1.93)	34	1.21 (0.70–2.08)	0.745
Pancreas	149	1.00	145	1.35 (1.07–1.70)	292	1.14 (0.93–1.39)	338	1.28 (1.05–1.56)	315	1.25 (1.03–1.53)	0.065
Kidney	47	1.00	36	1.10 (0.71–1.70)	85	1.14 (0.80–1.64)	106	1.47 (1.03–2.09)	93	1.42 (0.98–2.03)	0.016
Rectum	18	1.00	16	1.26 (0.64–2.48)	47	1.57 (0.90–2.71)	39	1.27 (0.72–2.25)	48	1.63 (0.93–2.84)	0.150

[a] Models are adjusted for sex, BMI (categories), education, race, alcohol (categories of 0, 0<–<3, and 3+ drinks/day), Healthy Eating Index-2010 score, calories, marriage status, diabetes, and smoke level (6 categories describing status and dose)

[b] Additionally adjusted for screening in the three years prior to questionnaire.

[c] Additionally adjusted for hormone therapy use and age at menarche.

[d] Excluded women who reported a hysterectomy.

Table 3

Associations for a one hour increase in moderate to vigorous intensity physical activity (MVPA) per week and cancer mortality in the NIH-AARP study population, stratified by smoking status (N=293,511)[a]

Type of cancer death	Total population		Never smokers		Ever Smokers		P-interaction
	No. of events	HR (95% CI)	No. of events	HR (95% CI)	No. of events	HR (95% CI)	
All cancers	15001	0.99 (0.98–0.99)[b]	3200	0.99 (0.98–1.00)	11,801	0.99 (0.98–0.99)[b]	0.782
Lymphocytic leukemia	128	0.93 (0.88–0.99)[b]	39	0.90 (0.81–1.00)[b]	89	0.95 (0.88–1.02)	0.744
Colon	1036	0.97 (0.95–0.99)[b]	309	0.98 (0.94–1.01)	727	0.96 (0.94–0.98)[b]	0.507
Liver	397	0.96 (0.93–0.99)[b]	118	0.92 (0.87–0.98)[b]	279	0.98 (0.94–1.02)	0.112
Oral cavity and pharynx	173	0.98 (0.93–1.02)	25	0.93 (0.81–1.06)	148	0.98 (0.93–1.04)	0.597
Non-Hodgkins lymphoma	628	0.97 (0.95–1.00)[b]	218	0.96 (0.92–1.01)	410	0.98 (0.95–1.01)	0.606
Esophagus	491	0.98 (0.96–1.01)	62	0.96 (0.89–1.05)	429	0.99 (0.96–1.02)	0.635
Myeloma	341	1.01 (0.97–1.04)	121	1.02 (0.96–1.08)	220	1.00 (0.96–1.05)	0.840
Lung	4871	0.98 (0.98–0.99)[b]	252	1.00 (0.96–1.04)	4619	0.98 (0.97–0.99)[b]	0.454
Myeloid leukemia	376	0.99 (0.95–1.02)	100	0.99 (0.93–1.06)	276	0.98 (0.95–1.02)	0.884
Stomach	304	0.99 (0.95–1.02)	74	0.98 (0.91–1.05)	230	0.99 (0.95–1.04)	0.745
Ovarian[c]	387	1.00 (0.97–1.03)	184	1.04 (0.99–1.09)	203	0.96 (0.92–1.01)	0.022
Prostate	513	1.01 (0.98–1.03)	132	0.98 (0.93–1.04)	381	1.01 (0.98–1.05)	0.258
Bladder	346	0.99 (0.96–1.03)	60	0.94 (0.87–1.03)	286	1.00 (0.97–1.04)	0.433
Breast[c]	436	1.01 (0.98–1.04)	189	0.99 (0.95–1.04)	247	1.02 (0.98–1.06)	0.653
Brain	458	1.01 (0.98–1.04)	166	1.02 (0.97–1.07)	292	1.00 (0.96–1.03)	0.335
Endometrial	146	1.02 (0.97–1.07)	73	1.02 (0.94–1.09)	73	1.02 (0.94–1.09)	0.791
Pancreas	1239	1.02 (1.00–1.03)	370	1.00 (0.96–1.03)	869	1.02 (1.00–1.05)[b]	0.314
Kidney	367	1.04 (1.01–1.08)[b]	99	1.07 (1.00–1.14)[b]	268	1.03 (0.99–1.08)	0.598
Rectum	168	1.03 (0.98–1.08)	49	0.99 (0.91–1.09)	119	1.04 (0.99–1.11)	0.385

[a] Models are adjusted for sex, body mass index, education, race, alcohol intake, Healthy Eating Index-2010 score, calories, marriage status, diabetes and smoking intensity (where appropriate).

[b] Significant at a p<0.05 level

[c] Additionally adjusted for hormone therapy use and age at menarche.

Table 4

Joint associations between obesity (body mass index 30+ kg/m^2) and moderate to vigorous intensity physical activity (MVPA, <1–7+ h/wk) and cancer mortality in the NIH-AARP study population (N=293,511)[a]

Type of cancer death	Active/ non-obese		Inactive/ non-obese		Active/obese		Inactive/ obese	
	No. of events	HR (ref.)	No. of events	HR (95% CI)	No. of events	HR (95% CI)	No. of events	HR (95% CI)
All cancers	10,001	1.00	1,758	1.12 (1.06–1.18)	2,476	1.16 (1.11–1.21)	766	1.22 (1.13–1.32)
Lymphocytic leukemia	90	1.00	12	0.95 (0.52–1.75)	18	0.97 (0.58–1.63)	8	1.60 (0.77–3.33)
Colon	639	1.00	116	1.22 (1.00–1.49)	199	1.39 (1.18–1.64)	82	2.01 (1.59–2.54)
Liver	231	1.00	41	1.12 (0.80–1.56)	84	1.62 (1.25–2.09)	41	2.64 (1.88–3.72)
Oral cavity and pharynx	112	1.00	32	1.43 (0.96–2.14)	23	0.97 (0.62–1.53)	6	0.73 (0.32–1.67)
Non-Hodgkin's lymphoma	406	1.00	71	1.28 (0.99–1.65)	118	1.35 (1.09–1.66)	33	1.38 (0.96–1.98)
Esophagus	297	1.00	63	1.30 (0.99–1.72)	106	1.63 (1.30–2.04)	25	1.28 (0.85–1.94)
Myeloma	226	1.00	40	1.36 (0.97–1.91)	54	1.14 (0.84–1.54)	21	1.67 (1.06–2.64)
Lung	3347	1.00	701	1.16 (1.06–1.26)	601	0.87 (0.80–0.95)	222	1.01 (0.88–1.16)
Myeloid/monocytic leukemia	262	1.00	31	0.87 (0.60–1.26)	60	1.08 (0.81–1.43)	23	1.55 (1.00–2.38)
Stomach	197	1.00	32	1.05 (0.72–1.53)	58	1.37 (1.01–1.84)	17	1.40 (0.85–2.31)
Ovarian[b]	264	1.00	37	1.05 (0.74–1.48)	62	1.05 (0.79–1.39)	24	1.45 (0.95–2.22)
Prostate	340	1.00	57	1.17 (0.88–1.56)	93	1.45 (1.15–1.82)	23	1.33 (0.87–2.04)
Bladder	235	1.00	35	0.98 (0.68–1.40)	59	1.19 (0.89–1.59)	17	1.20 (0.73–1.98)
Breast[b]	259	1.00	41	1.09 (0.78–1.52)	107	1.73(1.37–2.19)	29	1.58 (1.07–2.35)
Brain	320	1.00	41	1.04 (0.75–1.45)	81	1.22 (0.95–1.56)	16	0.95 (0.57–1.58)
Endometrial[b,c]	73	1.00	11	1.03 (0.55–1.96)	50	2.48 (1.70–3.61)	12	2.04 (1.09–3.82)
Pancreas	880	1.00	115	0.91 (0.74–1.10)	210	1.12 (0.96–1.30)	34	0.64 (0.45–0.91)
Kidney	240	1.00	29	0.81 (0.55–1.19)	80	1.50 (1.16–1.94)	18	1.18 (0.72–1.91)
Rectum	123	1.00	12	0.66 (0.36–1.19)	27	0.99 (0.65–1.50)	6	0.77 (0.34–1.77)

Abbreviations: HR: hazard ratio, CI: confidence interval

[a] Models are adjusted for sex, body mass index (categories), education, race, alcohol (categories of 0, 0<–<3, and 3+ drinks/day), Healthy Eating Index -2010 score, calories, marriage status, diabetes, and smoke level (6 categories describing status and dose)

[b] Additionally adjusted for hormone therapy use and age at menarche

[c] Excluded women who had a hysterectomy.