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Changes in physical activity and diabetes risk after cancer diagnosis: a nationwide cohort study

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Abstract

Purpose Physical activity has the potential to reduce the risk of diabetes after cancer diagnosis. However, current evidence supporting its effects is limited. This study aims to examine the associations between changes in physical activity and subsequent risk of diabetes among cancer survivors.

Methods A total of 264,250 cancer survivors (mean age 56.7 (12.5) years, 44.2% males) without a prior history of diabetes were assessed for adherence to physical activity both before and after their diagnosis. The primary outcome was incident diabetes. The Fine-Gray proportional sub-distribution hazards model was used to calculate sub-distribution hazard ratios (sHRs) and 95% confidence intervals (CIs) for diabetes risk, considering death as a competing risk.

Results Over a follow-up of 1,065,802 person-years, maintaining regular physical activity from pre-diagnosis was associated with a 10% reduced risk of diabetes after cancer diagnosis (sHR 0.90, 95% CI 0.85–0.96), considering traditional diabetes risk factors, sociodemographics, and primary cancer sites. Cancer survivors who became active and inactive after their cancer diagnosis exhibited a marginally decreased risk of diabetes (sHR 0.98, 95% CI 0.93–1.03; sHR 0.97, 95% CI 0.92–1.03). The strength and direction of the association varied depending on the primary site of cancer.

Conclusions Regular physical activity starting before a cancer diagnosis is associated with a lower risk of diabetes following the diagnosis, independent of established diabetes risk factors.

Implications for Cancer Survivors The study underscores the importance of engaging in sufficient physical activity to mitigate the risk of diabetes in cancer survivors.

Keywords Cancer survivor · Physical activity · Diabetes · Competing risk

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Abbreviations

sHR	Sub-distribution hazard ratio
CI	Confidence interval
NHIS	National Health Insurance Service
SD	Standard deviation

Introduction

Cancer and diabetes are two of the most significant health challenges globally, with both conditions exhibiting rapid increases in incidence, affecting global morbidity and mortality [1, 2]. The relationship between the two is complex, with evidence suggesting a bidirectional association. People with cancer are at an increased risk of diabetes [3–5], primarily due to the metabolic dysregulation driven by cancer and the consequences of cancer treatments [6–8]. Conversely, insulin resistance and elevated insulin levels promote tumor growth and impede programmed cell death [9, 10]. Importantly, this association is not just a concurrent health issue: diabetes in cancer survivors is linked with increased mortality rates compared to survivors without diabetes [11–13]. Moreover, for cancer patients, diabetes is associated with increased medical complications [14], a greater incidence of hospitalization [15], and lower health-related quality of life [16]. Thus, it is imperative to identify and manage modifiable risk factors for diabetes to mitigate the risk in this population.

Physical activity is beneficial to protect against the onset of diabetes. Observational studies [17–20] and randomized controlled trials [21–24] consistently demonstrate an inverse association between physical activity and the incidence of diabetes in the general population, underscoring the significance of physical activity as a key modifiable risk factor for diabetes. Nonetheless, no current research has examined the impact of physical activity on diabetes risk after a cancer diagnosis. While considerable evidence supports the benefits of physical activity for survival outcomes [25–29], its specific role in diabetes risk reduction among cancer survivors remains underexplored. Moreover, adherence to recommended physical activity level is notably low among cancer patients, with a substantial drop during and after treatment [30], despite guidelines promoting exercise for improved health outcomes [31, 32].

To bridge this knowledge gap, our nationwide study utilizes data from the Korean National Health Insurance Service (NHIS) to explore the association between changes in physical activity and the subsequent risk of diabetes among cancer survivors from various primary sites. We focus on the relationships between physical activity alteration before and after a cancer diagnosis with diabetes risk in this population.

Materials and methods

Database source

The NHIS operates as the sole insurance provider in Korea, delivering medical coverage to roughly 97% of the Korean population. It also oversees the provision of medical aid to those in the lowest income bracket.

The NHIS provides general health screening to all individuals aged 40 and above and employees of any age, who are eligible to participate in the national general health screening program at least once every 2 years at medical institutions throughout Korea [33]. The program includes anthropometric measurements, social and medical history questionnaires, and laboratory tests. A standardized questionnaire collects medical history and lifestyle behaviors such as smoking, alcohol consumption, and physical activity. Notably, the medical treatment database, which catalogs medical bills submitted by healthcare providers for reimbursement, can be cross-referenced with the health examination database. Therefore, the NHIS curates a wide-ranging health information dataset that spans the entire Korean population and that frequently has been utilized in epidemiological studies in Korea [34–36].

Study population

We identified a total of 351,767 individuals who were newly diagnosed with cancer between January 1, 2010, and December 31, 2016. All of these individuals participated in general health screening examinations within a 2-year period before and after their cancer diagnosis. We excluded 7794 individuals with missing or erroneous values in these examinations. We further excluded subjects aged < 20 ($n = 3$) and those with prior history of type 1 diabetes ($n = 15{,}430$), fasting plasma glucose level ≥ 126 mg/dL in general health screenings, or any history of type 2 diabetes ($n = 57{,}620$). After excluding incident diabetes within 1 year after cancer diagnosis ($n = 6670$), a total of 264,250 cancer survivors were identified and included in our analyses (Fig. 1).

Cancer adjudication

A cancer diagnosis was established if a patient's record contained both an International Classification of Diseases, Tenth Revision (ICD-10) code starting with "C" and a specific insurance claim code for cancer (V193). According to the policies of the NHIS, cancer patients are responsible for only 5% of their total medical expenses for cancer-related treatments, utilizing a unique co-payment reduction code (V193), which mandates a medical certificate from a

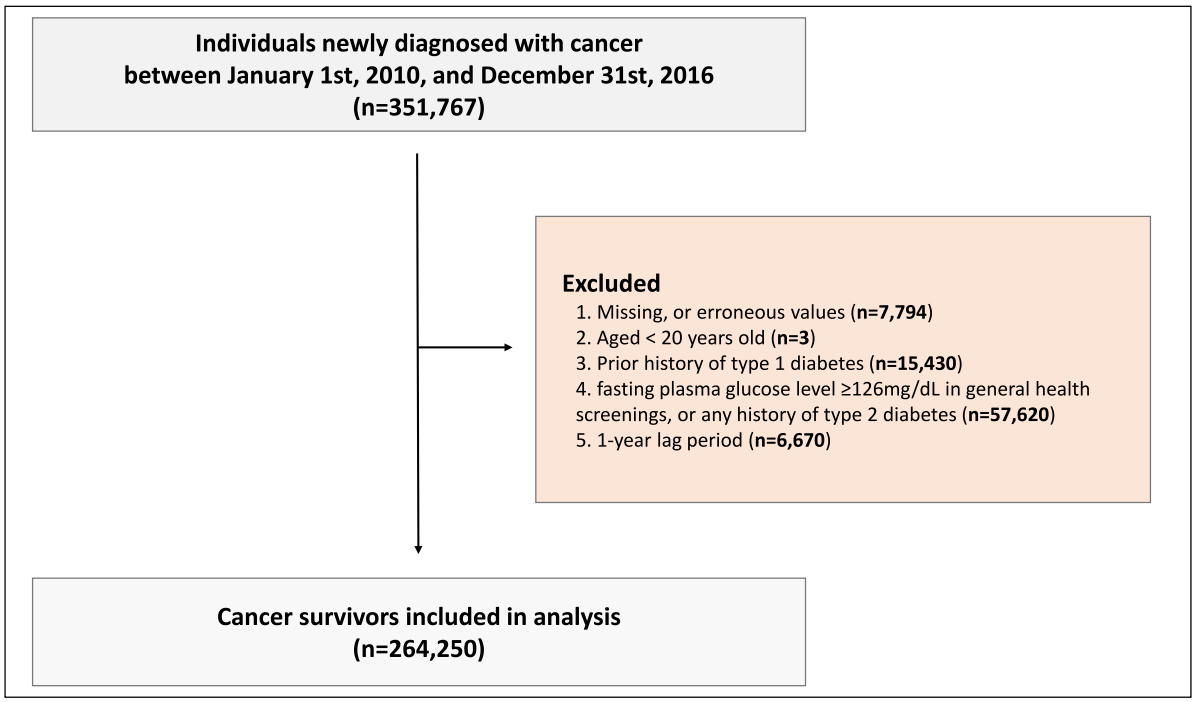

Fig. 1 Flowchart of the study population

physician. Therefore, the reliability of cancer diagnoses in this study is high, with a 97.9% sensitivity and 91.5% positive predictive value [37]. This method has been employed in prior studies [38, 39].

Ascertainment of physical activity changes

Information regarding physical activity was gathered through general health screenings before and after a cancer diagnosis using the modified International Physical Activity Questionnaire (IPAQ) [40]. Participants self-reported how many days during the preceding week they participated in light, moderate, or vigorous physical activity. The questionnaire provided an example of moderate physical activity, such as carrying light items, cycling at a steady place, or playing doubles tennis, and examples of vigorous activities that included heavy lifting, digging, aerobic exercises, or rapid cycling.

For this study, participants were categorized as either being adherent to physical activity, defined as engaging in a minimum of 30 min of moderate-intensity activity at least 5 days a week or at least 20 min of high-intensity activity at least 3 days a week, or non-adherent to physical activity [31]. Employing guideline adherence as the basis for classification provides a more precise evaluation of the influence of recommended physical activity levels on diabetes risk among cancer survivors [19], compared to quantifying physical activity in metabolic equivalent of task (MET) hours, as MET-based analysis is not feasible in our study setting with survey questionnaire. Four groups were constructed based on changes in physical activity status with respect to cancer diagnosis: remained inactive, became inactive, became active, and remained active.

Study outcome: diabetes

The primary outcome of this study was the incidence of newly diagnosed diabetes. Diabetes was defined by ICD-10 codes ranging from E11.x to E14.x, accompanied by the use of antidiabetic medications or a fasting glucose level of 126 mg/dL or higher. The cohort was followed from 1 year after the date of the post-cancer diagnosis general health screening examination to the date of incident diabetes, censored date, death, or the end of the study period (December 31, 2019), whichever came first. This approach was selected to exclude cases of pre-existing diabetes or temporary diabetes induced by cancer treatments (e.g., steroid use) and to allow a sufficient observation period post-treatment for the potential development of diabetes [41].

Covariates

Covariates were assessed at the post-diagnosis health screening examination. Age and income were recorded. Anthropometric measures were collected from general screening examinations. Obesity was defined following the

Asian-Pacific criteria, with a body mass index (BMI) ≥ 25 kg/m^2 considered obese [42]. BMI was calculated as weight in kilograms divided by the height in meters squared (kg/m^2). Participants' comorbidities were identified based on laboratory measures, claims, and prescription information prior to the index date as follows: hypertension (ICD-10 codes (I10.x-I13.x and I15.x), use of antihypertensive medication, or blood pressure ≥ 140/90 mmHg), dyslipidemia (ICD-10 code E78.x with lipid-lowering medication or total cholesterol ≥ 240 mg/dL), and chronic kidney disease (CKD; glomerular filtration rate < 60 mL/min/1.73 m^2 as estimated by the Modification of Diet in Renal Disease equation). Information on smoking (current/no) and alcohol consumption (yes/no) was obtained from the general health screening after cancer diagnosis.

Statistical analyses

General characteristics are presented as means and standard deviations for continuous variables and as counts and percentages for categorical variables. To examine the significance of differences in proportions or means across four groups, chi-square tests were employed for categorical variables and one-way analysis of variance tests for continuous variables. The Fine-Gray proportional sub-distribution hazards model was used to calculate sub-distribution hazard ratios (sHRs) and 95% confidence intervals (CIs) for diabetes risk with death as a competing risk [43]. The proportional hazards assumption was assessed using Schoenfeld's residuals, and no specific departure was observed. The reference group was "remained inactive," and sHRs and 95% CIs were calculated for each group relative to the reference group. sHRs were obtained through a multi-step adjustment process. In the first model (Model 1), HRs were unadjusted. We identified potential confounders in the multivariable-adjusted models a priori based on a literature review [44]. Model 2 incorporated age, sex, income, smoking, alcohol consumption, obesity, hypertension, dyslipidemia, and CKD. In the final step (Model 3), we further adjusted for primary site of cancer. Subgroup analysis by primary site of cancer was performed using Model 2. Stratified analyses were conducted based on age, sex, and obesity-related cancer to identify interactions between changes in physical activity and diabetes risk. The definition of "obesity-related cancer" was followed to the International Agency for Research on Cancer (IARC) working group (Supplemental Table 1) [45]. Regarding breast cancer, we defined postmenopausal breast cancer as occurring at age 50 or older, considering the average age of menopause in Korea [46]. This definition was used because our current cohort data did not include information on menopausal status. Statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA). *P* values provided are two-sided, and the level of significance was set to 0.05.

Ethics statement

This study was approved by the Institutional Review Board of Soongsil University (No. SSU-202303-HR-465–1). Anonymized and de-identified information was used for analyses, and informed consent was not required. The database is open to all researchers whose study protocols are approved by the official review committee.

Results

The cohort comprised 264,250 cancer survivors, with a mean age of 56.7 (12.5) years and 44.2% males. Among these survivors, 62.6% consistently remained inactive, while 9.8% consistently remained active. While 16.4% became active post-diagnosis, 11.2% became inactive post-diagnosis (Table 1). The "became inactive" group was the oldest, and the "became active" group was the youngest. Variations in waist circumference and the prevalence of obesity, current smoking, alcohol consumption, hypertension, dyslipidemia, and CKD among four groups were reported (all $P < 0.001$). However, these variations were considered clinically minimal.

Among primary sites of cancer, distinct patterns were observed in physical activity change patterns. Most cervical (70.5%), corpus uteri (64.9%), and skin cancer (68.6%) patients remained inactive. Notable shifts from inactive to active were observed in breast (23.4%), ovarian (20.3%), and Hodgkin's lymphoma (21.3%) cases. A decrease in activity level was significant in prostate cancer (14.3%), whereas sustained physical activity was most common in thyroid (8.5%), testicular (9.8%), and corpus uteri cancer (8.2%) survivors.

Associations of physical activity change with diabetes risk after cancer diagnosis

During a mean follow-up period of 4.0 (2.0) years with 1,065,802 person-years, we observed 12,196 new cases of diabetes among cancer survivors (Table 2). In the sociodemographic-, traditional diabetes risk factor-, and primary site of cancer-adjusted model (Model 3), survivors with persistent physical activity had a 10% decreased risk of diabetes (sHR 0.90, 95% CI 0.85–0.96). Cancer survivors who became active or inactive after cancer diagnosis showed a slightly decreased risk of diabetes (sHR 0.98, 95% CI 0.93–1.03; sHR 0.97, 95% CI 0.92–1.03, respectively). Kaplan–Meier curves showing the estimated incidence probability of diabetes over time are presented in Fig. 2.

Table 1 Baseline characteristics of the study population according to physical activity change

	Total ($n=264,250$)	Remained inactive ($n=165,300$)	Became inactive ($n=29,602$)	Became active ($n=43,438$)	Remained active ($n=25,910$)	*P* value
Age at baseline, years	56.7 ± 12.5	56.4 ± 13.0	58.5 ± 12.0	56.0 ± 11.5	58.0 ± 11.1	< .001
Sex, male	116,662 (44.2)	68,881 (41.7)	14,332 (48.4)	19,304 (44.4)	14,145 (54.6)	< .001
Income status, low	45,182 (17.1)	28,711 (17.4)	5178 (17.5)	7291 (16.8)	4002 (15.5)	< .001
BMI (kg/m^2)	23.6 ± 3.2	23.6 ± 3.2	23.7 ± 3.1	23.5 ± 3.0	23.7 ± 2.9	< .001
WC (cm)	80.1 ± 9.0	80.1 ± 9.2	80.7 ± 8.9	79.5 ± 8.8	80.5 ± 8.6	< .001
Obesity, yes	81,297 (30.8)	51,169 (31.0)	9500 (32.1)	12,543 (28.9)	8085 (31.2)	< .001
Smoking, yes	18,889 (7.2)	13,051 (7.9)	1984 (6.7)	2410 (5.6)	1444 (5.6)	< .001
Alcohol, yes	58,115 (22.0)	36,535 (22.1)	6491 (21.9)	8617 (19.8)	6472 (25.0)	< .001
Hypertension, yes	90,462 (34.2)	55,597 (33.6)	11,180 (37.8)	14,217 (32.7)	9468 (36.5)	< .001
Dyslipidemia, yes	62,764 (23.8)	39,025 (23.6)	7507 (25.4)	9838 (22.7)	6394 (24.7)	< .001
CKD, yes	15,355 (5.8)	9778 (5.9)	1875 (6.3)	2183 (5.0)	1519 (5.9)	< .001
Height (cm)	161.8 ± 8.4	161.3 ± 8.5	162.0 ± 8.2	162.1 ± 8.2	163.4 ± 8.0	< .001
Weight (kg)	61.9 ± 10.7	61.6 ± 10.8	62.5 ± 10.6	61.9 ± 10.4	63.6 ± 10.3	< .001
SBP, mmHg	121.6 ± 14.5	121.4 ± 14.6	122.4 ± 14.4	121.0 ± 14.2	122.5 ± 14.1	< .001
DBP, mmHg	75.3 ± 9.6	75.2 ± 9.6	75.5 ± 9.5	75.0 ± 9.5	75.6 ± 9.3	< .001
Fasting glucose, mg/dL	94.5 ± 10.7	94.4 ± 10.7	95.1 ± 10.7	94.3 ± 10.6	95.2 ± 10.7	< .001
Total cholesterol, mg/dL	190.6 ± 37.0	191.0 ± 37.3	190.8 ± 37.1	189.3 ± 36.6	189.8 ± 36.1	< .001
eGFR	90.7 ± 41.8	90.9 ± 40.8	89.8 ± 42.7	91.4 ± 43.2	89.6 ± 43.9	< .001
Cancer type		62.5%	11.2%	16.4%	9.8%	
Biliary	2012 (0.8)	1200 (59.6)	247 (12.3)	339 (16.8)	226 (11.2)	
Bladder	6188 (2.3)	3795 (61.3)	804 (13.0)	939 (15.2)	650 (10.5)	
Breast	29,035 (11.0)	16,719 (57.6)	2773 (9.5)	6789 (23.4)	2754 (9.5)	
Cervix	5044 (1.9)	3556 (70.5)	500 (9.9)	684 (13.6)	304 (6.0)	
Colorectum	29,394 (11.1)	17,792 (60.5)	3375 (11.5)	5084 (17.3)	3143 (10.7)	
Corpus uteri	3073 (1.2)	1996 (64.9)	305 (9.9)	519 (16.9)	253 (8.2)	
Esophagus	1017 (0.4)	592 (58.2)	131 (12.9)	179 (17.6)	115 (11.3)	
Hodgkin	178 (0.1)	99 (55.6)	18 (10.1)	38 (21.3)	23 (12.9)	
Kidney	6118 (2.3)	3778 (61.7)	701 (11.5)	966 (15.8)	673 (11.0)	
Larynx	1,309 (0.5)	805 (61.5)	161 (12.3)	200 (15.3)	143 (10.9)	
Leukemia	1507 (0.6)	944 (62.6)	188 (12.5)	249 (16.5)	126 (8.4)	
Liver	8123 (3.1)	4865 (59.9)	980 (12.1)	1410 (17.4)	868 (10.7)	
Lung	10,888 (4.1)	6458 (59.3)	1256 (11.5)	2027 (18.6)	1147 (10.5)	
Lymphoma	3467 (1.3)	2113 (60.9)	420 (12.1)	588 (17.0)	346 (10.0)	
Multiple myeloma	692 (0.3)	425 (61.4)	88 (12.7)	119 (17.2)	60 (8.7)	
Nerves	2148 (0.8)	1462 (68.1)	227 (10.6)	303 (14.1)	156 (7.3)	
Oral cavity	2804 (1.1)	1711 (61.0)	380 (13.5)	420 (15.0)	293 (10.4)	
Ovary	2108 (0.8)	1289 (61.2)	213 (10.1)	428 (20.3)	178 (8.4)	
Pancreas	577 (0.2)	366 (63.4)	58 (10.1)	99 (17.2)	54 (9.4)	
Prostate	16,068 (6.1)	8947 (55.7)	2300 (14.3)	2549 (15.9)	2272 (14.1)	
Skin	7,221 (2.7)	4953 (68.6)	846 (11.7)	817 (11.3)	605 (8.4)	
Stomach	32,693 (12.4)	20,020 (61.2)	3851 (11.8)	5307 (16.2)	3515 (10.7)	
Testis	397 (0.2)	263 (66.2)	41 (10.3)	54 (13.6)	39 (9.8)	
Thyroid	83,541 (31.6)	55,669 (66.7)	8,731 (10.5)	12,033 (14.4)	7108 (8.5)	
Others	8648 (3.3)	5483 (63.4)	1008 (11.6)	1298 (15.0)	859 (9.9)	

Four groups were constructed based on changes in physical activity status with respect to cancer diagnosis: remained inactive, became inactive, became active, and remained active. For this study, participants were categorized as either being adherent to physical activity, defined as engaging in a minimum of 30 min of moderate-intensity activity at least 5 days a week or at least 20 min of high-intensity activity at least 3 days a week, or non-adherent to physical activity

BMI, body mass index; *WC*, waist circumference; *CKD*, chronic kidney disease; *SBP*, systolic blood pressure; *DBP*, diastolic blood pressure; *eGFR*, estimated glomerular filtration rate

Table 2 Association of physical activity change with diabetes risk after cancer diagnosis

	Subjects (*N*)	Event (*n*)	Duration	IR per 1000 person-years	Model 1 (crude) HR (95% CI)	Model 2 sHR (95% CI)	Model 3 sHR (95% CI)
Remained inactive	165,300	7724	669,244.1	11.54	1 (Ref.)	1 (Ref.)	1 (Ref.)
Became inactive	29,602	1451	119,055.1	12.19	1.06 (1.00–1.12)	0.97 (0.92–1.03)	0.97 (0.92–1.03)
Became active	43,438	1898	174,472.4	10.88	0.95 (0.90–1.00)	0.98 (0.94–1.04)	0.98 (0.93–1.03)
Remained active	25,910	1123	103,030.6	10.90	0.96 (0.90–1.02)	0.90 (0.85–0.96)	**0.90 (0.85–0.96)**

IR, incidence rate; *sHR*, sub-distribution hazard ratio; *CI*, confidence interval

Significant values are highlighted with bold text

Model 2: adjusted for age, sex, income, smoking, alcohol consumption, obesity, hypertension, dyslipidemia, and chronic kidney disease

Model 3: adjusted for variables used in Model 2 and primary site of cancer

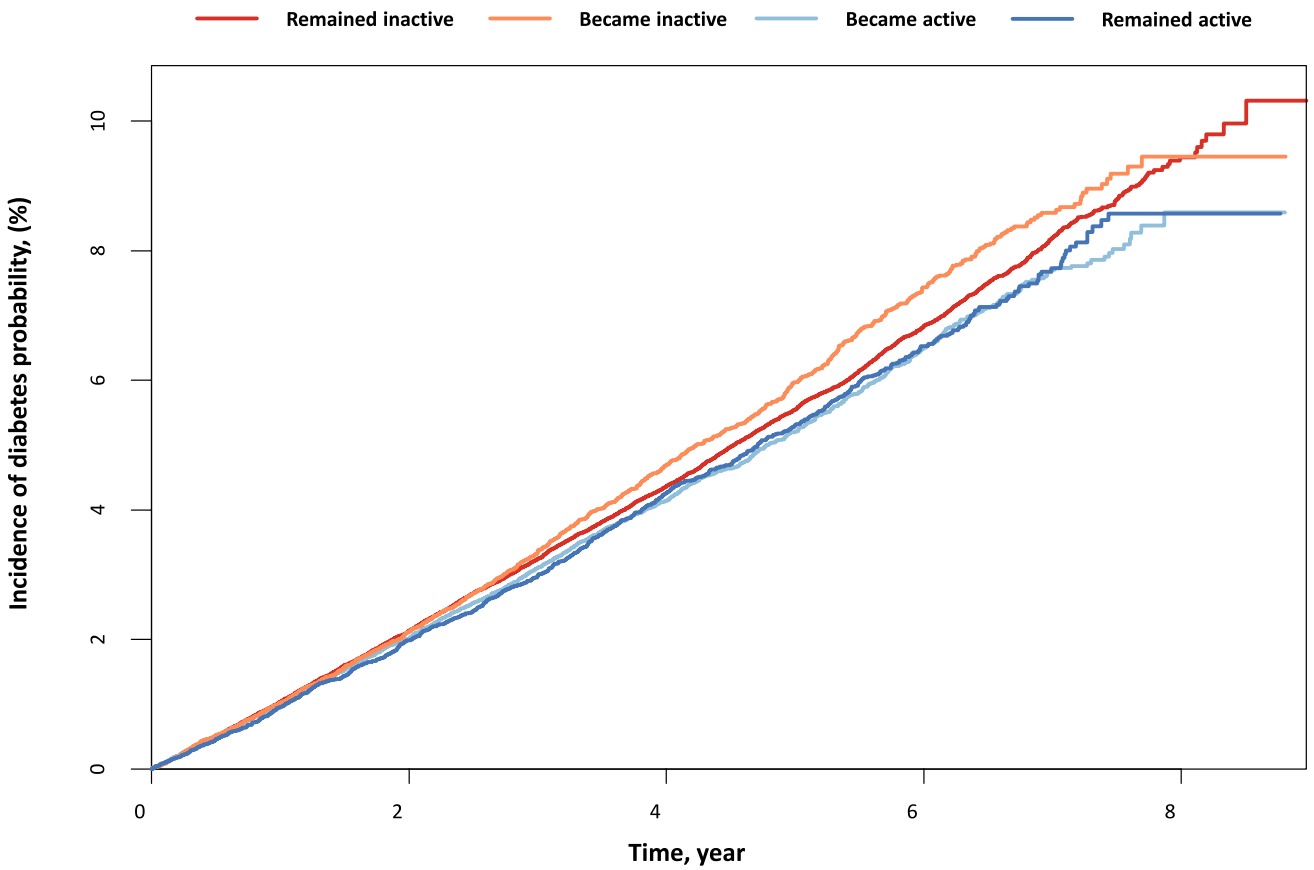

Fig. 2 Estimated incidence probability of diabetes after cancer diagnosis. Kaplan–Meier curves displaying the estimated incidence probability of diabetes by changes in physical activity

Subgroup analyses by primary site of cancer

We examined associations between physical activity changes post-diagnosis and risk of diabetes among various cancer types (Table 3 and Fig. 3). For stomach cancer survivors, initiating physical activity post-diagnosis was associated with a 17% reduced risk of diabetes (sHR 0.83, 95% CI 0.71–0.96), while other activity patterns were only marginally associated with decreased diabetes risk. Similarly, among lymphoma survivors, post-diagnosis activity initiation was correlated with a 46% decrease in diabetes risk (sHR 0.54, 95% CI 0.32–0.91). In breast cancer survivors, a marginal 14% reduction in diabetes risk was observed with post-diagnosis physical activity (sHR 0.86, 95% CI 0.72–1.02), whereas lung cancer survivors showed a marginal 24% decrease in diabetes risk with sustained physical activity (sHR 0.76, 95% CI 0.57–1.01), without

Table 3 Subgroup analyses according to primary cancer site

		Subjects (*N*)	Event (*n*)	Duration	IR per 1000 PYs	Model 1 (crude) sHR (95% CI)	Model 2 sHR (95% CI)
Biliary	Remained inactive	1200	109	3931.7	27.72	1 (Ref.)	1 (Ref.)
	Became inactive	247	24	794.1	30.22	1.12 (0.72–1.73)	1.07 (0.68–1.68)
	Became active	339	25	1097.0	22.79	0.84 (0.54–1.29)	0.81 (0.52–1.25)
	Remained active	226	19	759.2	25.03	0.91 (0.56–1.48)	0.86 (0.53–1.42)
Bladder	Remained inactive	3795	260	14,873.5	17.48	1 (Ref.)	1 (Ref.)
	Became inactive	804	61	3190.8	19.12	1.11 (0.84–1.46)	1.06 (0.80–1.40)
	Became active	939	56	3635.4	15.40	0.90 (0.67–1.20)	0.91 (0.68–1.21)
	Remained active	650	39	2593.3	15.04	0.89 (0.64–1.25)	0.87 (0.62–1.23)
Breast	Remained inactive	16,719	580	63,350.7	9.16	1 (Ref.)	1 (Ref.)
	Became inactive	2773	101	10,528.8	9.59	1.05 (0.85–1.30)	0.96 (0.78–1.19)
	Became active	6789	174	25,648.2	6.78	0.74 (0.63–0.88)	0.86 (0.72–1.02)
	Remained active	2754	83	10,098.6	8.22	0.90 (0.72–1.13)	0.97 (0.77–1.22)
Cervix	Remained inactive	3556	119	14,678.6	8.11	1 (Ref.)	1 (Ref.)
	Became inactive	500	22	2026.3	10.86	1.34 (0.85–2.11)	1.26 (0.79–2.01)
	Became active	684	21	2817.6	7.45	0.91 (0.57–1.45)	0.98 (0.61–1.56)
	Remained active	304	7	1232.6	5.68	0.71 (0.33–1.52)	0.82 (0.38–1.78)
Colorectum	Remained inactive	17,792	993	71,385.5	13.91	1 (Ref.)	1 (Ref.)
	Became inactive	3375	193	13,505.0	14.29	1.03 (0.88–1.20)	0.98 (0.83–1.14)
	Became active	5084	275	20,446.4	13.45	0.97 (0.85–1.11)	1.03 (0.90–1.18)
	Remained active	3143	162	12,783.9	12.67	0.93 (0.78–1.09)	0.93 (0.79–1.11)
Corpus uteri	Remained inactive	1996	90	7807.0	11.53	1 (Ref.)	1 (Ref.)
	Became inactive	305	16	1,154.6	13.86	1.20 (0.70–2.06)	1.27 (0.74–2.17)
	Became active	519	20	2122.2	9.42	0.82 (0.50–1.33)	0.84 (0.51–1.38)
	Remained active	253	11	977.4	11.25	0.99 (0.53–1.85)	1.03 (0.55–1.93)
Esophagus	Remained inactive	592	37	1898.2	19.49	1 (Ref.)	1 (Ref.)
	Became inactive	131	8	476.9	16.77	0.91 (0.42–1.94)	0.98 (0.46–2.12)
	Became active	179	11	575.4	19.12	1.02 (0.52–1.98)	1.05 (0.52–2.09)
	Remained active	115	0	418.4	0	N/A	N/A
Hodgkin	Remained inactive	99	4	385.1	10.39	1 (Ref.)	1 (Ref.)
	Became inactive	18	0	81.2	0	N/A	N/A
	Became active	38	2	152.6	13.11	N/A	N/A
	Remained active	23	2	85.6	N/A	N/A	N/A
Kidney	Remained inactive	3778	210	14,783.8	14.20	1 (Ref.)	1 (Ref.)
	Became inactive	701	42	2827.7	14.85	1.04 (0.74–1.44)	0.91 (0.65–1.26)
	Became active	966	46	3846.6	11.96	0.84 (0.61–1.16)	0.87 (0.63–1.19)
	Remained active	673	37	2588.3	14.30	1.01 (0.71–1.43)	0.95 (0.67–1.36)
Larynx	Remained inactive	805	50	3083.2	16.22	1 (Ref.)	1 (Ref.)
	Became inactive	161	13	623.0	20.87	1.32 (0.72–2.40)	1.34 (0.73–2.47)
	Became active	200	13	798.2	16.29	1.05 (0.57–1.93)	1.15 (0.61–2.14)
	Remained active	143	7	535.7	13.07	0.85 (0.39–1.87)	0.86 (0.39–1.90)
Leukemia	Remained inactive	944	70	3545.0	19.75	1 (Ref.)	1 (Ref.)
	Became inactive	188	11	698.2	15.75	0.79 (0.42–1.48)	0.81 (0.43–1.51)
	Became active	249	14	935.2	14.97	0.76 (0.43–1.34)	0.76 (0.43–1.37)
	Remained active	126	15	449.9	33.34	1.63 (0.93–2.84)	1.47 (0.83–2.62)
Liver	Remained inactive	4865	343	16,515.3	20.77	1 (Ref.)	1 (Ref.)
	Became inactive	980	63	3361.8	18.74	0.91 (0.70–1.19)	0.89 (0.68–1.17)
	Became active	1410	117	4915.5	23.80	1.20 (0.98–1.48)	1.21 (0.98–1.50)
	Remained active	868	47	3103.0	15.15	0.76 (0.56–1.04)	0.76 (0.56–1.03)

Table 3 (continued)

		Subjects (*N*)	Event (*n*)	Duration	IR per 1000 PYs	Model 1 (crude) sHR (95% CI)	Model 2 sHR (95% CI)
Lung	Remained inactive	6458	392	20,687.1	18.95	1 (Ref.)	1 (Ref.)
	Became inactive	1256	70	3939.9	17.77	0.93 (0.72–1.19)	0.91 (0.71–1.17)
	Became active	2027	119	6661.5	17.86	0.96 (0.79–1.18)	1.00 (0.82–1.24)
	Remained active	1147	54	3745.0	14.42	0.79 (0.60–1.05)	0.76 (0.57–1.01)
Lymphoma	Remained inactive	2113	106	8189.8	12.94	1 (Ref.)	1 (Ref.)
	Became inactive	420	22	1642.9	13.39	1.04 (0.66–1.65)	0.99 (0.62–1.57)
	Became active	588	16	2302.6	6.95	0.54 (0.32–0.92)	**0.54 (0.32–0.91)**
	Remained active	346	20	1291.4	15.49	1.22 (0.76–1.97)	1.13 (0.70–1.84)
Multiple myeloma	Remained inactive	425	31	1269.7	24.42	1 (Ref.)	1 (Ref.)
	Became inactive	88	10	243.7	41.03	1.61 (0.79–3.29)	1.71 (0.83–3.50)
	Became active	119	15	384.6	39.00	1.71 (0.92–3.16)	1.84 (0.96–3.54)
	Remained active	60	5	190.6	26.24	1.12 (0.44–2.87)	1.30 (0.50–3.39)
Nerves	Remained inactive	1462	68	5757.9	11.81	1 (Ref.)	1 (Ref.)
	Became inactive	227	20	925.8	21.60	1.85 (1.13–3.03)	**1.67 (1.00–2.78)**
	Became active	303	17	1139.5	14.92	1.26 (0.74–2.14)	1.20 (0.70–2.06)
	Remained active	156	6	673.4	8.91	0.79 (0.34–1.82)	0.74 (0.32–1.71)
Oral cavity	Remained inactive	1711	66	6372.4	10.36	1 (Ref.)	1 (Ref.)
	Became inactive	380	17	1436.9	11.83	1.13 (0.67–1.92)	1.08 (0.64–1.82)
	Became active	420	15	1601.0	9.37	0.90 (0.51–1.59)	0.93 (0.52–1.65)
	Remained active	293	10	1099.3	9.10	0.91 (0.47–1.76)	0.83 (0.42–1.64)
Ovary	Remained inactive	1289	72	4673.2	15.41	1 (Ref.)	1 (Ref.)
	Became inactive	213	9	741.6	12.14	0.78 (0.39–1.56)	0.69 (0.35–1.38)
	Became active	428	20	1525.5	13.11	0.85 (0.52–1.39)	0.93 (0.55–1.56)
	Remained active	178	6	683.4	8.78	0.58 (0.25–1.31)	0.58 (0.25–1.33)
Pancreas	Remained inactive	366	56	1077.6	51.97	1 (Ref.)	1 (Ref.)
	Became inactive	58	7	204.6	34.21	0.71 (0.33–1.52)	0.62 (0.30–1.28)
	Became active	99	16	270.4	59.18	1.10 (0.63–1.92)	1.15 (0.66–2.03)
	Remained active	54	9	154.9	58.12	1.15 (0.57–2.32)	1.16 (0.58–2.33)
Prostate	Remained inactive	8947	571	34,254.3	16.67	1 (Ref.)	1 (Ref.)
	Became inactive	2300	145	8950.4	16.20	0.99 (0.83–1.19)	1.02 (0.85–1.22)
	Became active	2549	184	10,134.9	18.16	1.13 (0.96–1.33)	1.17 (0.99–1.38)
	Remained active	2272	126	8814.6	14.29	0.89 (0.74–1.08)	0.93 (0.77–1.13)
Skin	Remained inactive	4953	266	19,402.8	13.71	1 (Ref.)	1 (Ref.)
	Became inactive	846	41	3285.6	12.48	0.92 (0.66–1.27)	0.89 (0.64–1.25)
	Became active	817	40	3168.2	12.63	0.94 (0.67–1.31)	0.96 (0.69–1.35)
	Remained active	605	36	2256.1	15.96	1.20 (0.85–1.70)	1.29 (0.90–1.83)
Stomach	Remained inactive	20,020	1036	79,334.5	13.06	1 (Ref.)	1 (Ref.)
	Became inactive	3851	201	15,231.7	13.20	1.02 (0.88–1.19)	0.97 (0.84–1.13)
	Became active	5307	217	21,360.4	10.16	0.78 (0.68–0.91)	**0.83 (0.71–0.96)**
	Remained active	3515	167	13,808.8	12.09	0.95 (0.80–1.11)	0.92 (0.78–1.09)
Testis	Remained inactive	263	6	1115.6	5.38	1 (Ref.)	1 (Ref.)
	Became inactive	41	0	189.5	0	N/A	N/A
	Became active	54	2	231.5	N/A	N/A	N/A
	Remained active	39	2	139.9	N/A	N/A	N/A
Thyroid	Remained inactive	55,669	1911	250,862.1	7.62	1 (Ref.)	1 (Ref.)
	Became inactive	8731	308	39,266.4	7.84	1.03 (0.91–1.16)	0.94 (0.84–1.07)
	Became active	12,033	394	54,091.4	7.28	0.96 (0.86–1.07)	0.95 (0.85–1.06)
	Remained active	7108	221	31,446.4	7.03	0.93 (0.81–1.07)	**0.87 (0.75–1.00)**

Table 3 (continued)

		Subjects (*N*)	Event (*n*)	Duration	IR per 1000 PYs	Model 1 (crude) sHR (95% CI)	Model 2 sHR (95% CI)
Others	Remained inactive	5483	278	20,009.5	13.89	1 (Ref.)	1 (Ref.)
	Became inactive	1008	47	3727.7	12.61	0.90 (0.66–1.23)	0.86 (0.63–1.17)
	Became active	1298	69	4,610.6	14.97	1.07 (0.82–1.39)	1.13 (0.87–1.48)
	Remained active	859	32	3101.1	10.32	0.75 (0.52–1.09)	0.76 (0.53–1.10)

IR, incidence rate; *PYs*, person-years; *sHR*, sub-distribution hazard ratio; *CI*, confidence interval

Significant values are highlighted with bold text

Model 2: adjusted for age, sex, income, smoking, alcohol consumption, obesity, hypertension, diabetes mellitus, dyslipidemia, and chronic kidney disease

notable associations in other patterns. A similar trend was observed in survivors of liver and thyroid cancer.

Conversely, for pancreatic cancer survivors, changes in physical activity level post-diagnosis did not correlate with diabetes risk. For survivors of multiple myeloma, an increased risk of diabetes was noted across all three physical activity change patterns. However, the small number of events for survivors of these cancer types precluded any meaningful interpretation.

Stratified analyses according to age, sex, and obesity-related cancer

Stratified analyses showed no significant interactions of age, sex, and obesity-related cancer between changes in physical activity and diabetes risk among cancer survivors (Table 4).

Discussion

To the best of our knowledge, this is the first large-scale cohort study to investigate physical activity changes and risk of diabetes after cancer diagnosis. In our nationwide cohort of 264,250 survivors of cancer across all primary sites, regular physical activity maintained from pre- to post-diagnosis was associated with an overall decreased risk of diabetes. Physical activity either only before or only after cancer diagnosis showed slightly decreased risks of diabetes. The subgroup analyses demonstrated varied associations across cancer types.

By measuring physical activity repeatedly, we observed that sustaining regular physical activity from pre-diagnosis was associated with a 10% reduced risk of diabetes after cancer diagnosis. While previous research has predominantly assessed effects at a single time point, our findings reinforce the role of sustained physical activity on metabolic health, extending its known benefits to reducing the risk of diabetes after a cancer diagnosis. During adjuvant therapy, cancer patients often encounter unintentional weight gain, skeletal muscle loss, and increased insulin resistance [47, 48], which contribute to a higher risk of diabetes. Furthermore, corticosteroid administration during cancer management can cause hyperglycemia and subsequent onset of diabetes [49]. The risk is further exacerbated by the sedentary lifestyles of cancer patients, mostly related to the deconditioning effects of cancer treatment [50–52]. Physical activity plays a crucial role in this context, helping to mitigate these adverse effects by enhancing insulin sensitivity [53, 54], assisting in weight management [55], and promoting lean muscle mass [56], key factors affecting glycemic control.

There was only a slight and not significant risk reduction of diabetes in cancer survivors who became inactive after cancer diagnosis. Compared to survivors who maintained active lifestyles after cancer diagnosis, these inactive individuals appeared to benefit insufficiently from regular physical activity to prevent the development of diabetes. Although no strict formula can predict the precise amount or duration of physical activity necessary to prevent diabetes, long-term consistency is essential. Studies such as the Diabetes Prevention Program (DPP) demonstrated that lifestyle intervention can significantly reduce the risk of type 2 diabetes by 58% over a 3-year period [57], and follow-up studies such as the Diabetes Prevention Program Outcomes Study (DPPOS) have shown that these benefits were sustained over a 10-year period and beyond [58]. Another study, the Finnish Diabetes Prevention Study (DPS), followed participants for a median of 9 years and found that lifestyle intervention reduced the risk of type 2 diabetes by 33% [59]. These findings highlight the critical role of ongoing physical activity in diabetes prevention, a lesson of particular importance for cancer survivors who may deal with metabolic disturbances and deconditioning due to rigorous cancer treatments [50–52]. Therefore, the findings of our study emphasize the importance for cancer survivors to persist with a sufficient level of physical activity they had established prior to their cancer diagnosis as a strategic measure to reduce the heightened risk of diabetes following cancer treatment.

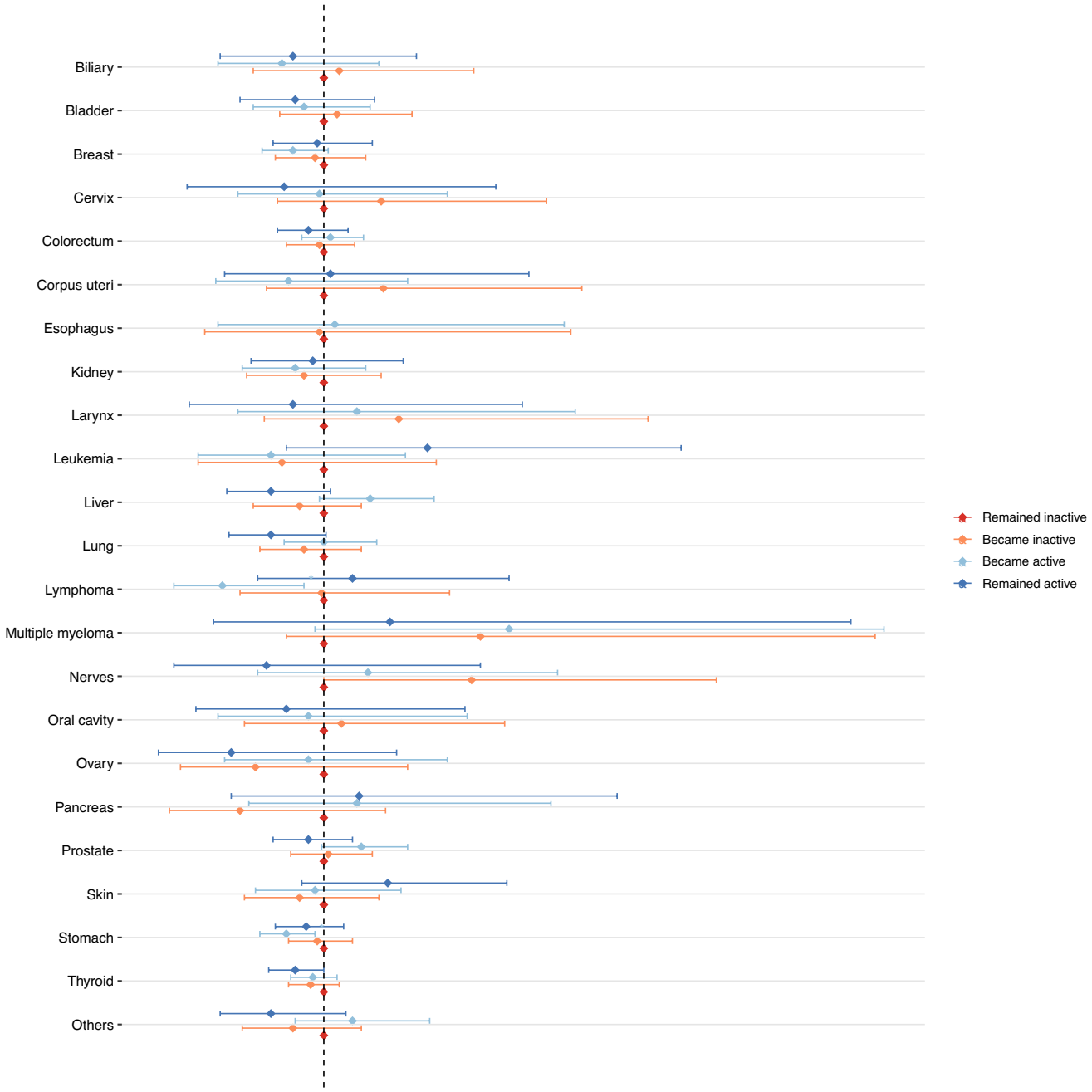

Fig. 3 Sub-distribution hazard ratios (sHRs) and confidence intervals (CIs) of diabetes in various cancer sites

In our study, starting regular physical activity after cancer diagnosis was not associated with a significant reduction in diabetes risk. This subgroup (consisting 16.4% of our cohort) was characterized by the youngest average age and had the lowest prevalence of obesity, hypertension, and dyslipidemia following diagnosis—factors typically associated with lower diabetes risk. In addition, this group had the lowest rates of current smoking and alcohol consumption compared to the other groups in our study. The lack of observed benefit in terms of diabetes risk may be due to the relatively short duration of follow-up or possibly unmeasured confounding variables such as the specifics of exercise regimens (type, intensity, frequency, and timing), steroid use, and the use of immune checkpoint inhibitors. The influence of diet in conjunction with physical activity also warrants consideration, given its significant impact on metabolic health. To affirm the well-established association of physical activity with diabetes risk reduction through improved glycemic control, enhanced insulin sensitivity, and weight management among cancer survivors,

Table 4 Stratified analyses based on age, sex, and obesity-related cancer

		Subjects (*N*)	Event (*n*)	IR per 1000 person-years	Model 1 (crude) HR (95% CI)	Model 2 sHR (95% CI)	Model 3 sHR (95% CI)
Age							
Sex							
Male	Remained inactive	68,881	3957	14.66	1 (Ref.)	1 (Ref.)	1 (Ref.)
	Became inactive	14,332	833	14.85	1.01 (0.94–1.09)	0.94 (0.87–1.01)	0.94 (0.87–1.01)
	Became active	19,304	1058	13.89	0.95 (0.89–1.01)	0.97 (0.91–1.04)	0.96 (0.90–1.03)
	Remained active	14,145	743	13.34	0.91 (0.84–0.99)	0.89 (0.82–0.96)	0.88 (0.82–0.96)
Female	Remained inactive	96,419	3767	9.43	1 (Ref.)	1 (Ref.)	1 (Ref.)
	Became inactive	15,270	618	9.81	1.04 (0.96–1.13)	0.99 (0.91–1.08)	0.99 (0.91–1.08)
	Became active	24,134	840	8.55	0.91 (0.84–0.98)	0.97 (0.90–1.05)	0.96 (0.89–1.04)
	Remained active	11,765	380	8.03	0.85 (0.77–0.95)	0.88 (0.79–0.98)	0.88 (0.79–0.97)
	P-interaction				0.581	0.863	0.834
Obesity-related cancer							
No	Remained inactive	47,464	2,441	178,239.9	13.70	1 (Ref.)	1 (Ref.)
	Became inactive	9064	495	34,070.2	14.53	1.06 (0.96–1.17)	0.98 (0.89–1.08)
	Became active	13,279	612	49,938.7	12.26	0.90 (0.82–0.98)	0.97 (0.89–1.07)
	Remained active	8009	380	29,764.2	12.77	0.93 (0.84–1.04)	0.89 (0.80–0.99)
Yes	Remained inactive	117,836	5283	491,004.3	10.76	1 (Ref.)	1 (Ref.)
	Became inactive	20,538	956	84,984.9	11.25	1.05 (0.98–1.12)	0.95 (0.89–1.02)
	Became active	30,159	1286	124,533.8	10.33	0.96 (0.90–1.02)	0.96 (0.90–1.02)
	Remained active	17,901	743	73,266.3	10.14	0.94 (0.88–1.02)	0.88 (0.81–0.95)
	P-interaction					0.598	0.961

IR, incidence rate; *sHR*, sub-distribution hazard ratio; *CI*, confidence interval

Model 2: adjusted for age, sex, income, smoking, alcohol consumption, obesity, hypertension, dyslipidemia, and chronic kidney disease

Model 3: adjusted for variables used in Model 2 and primary site of cancer

further long-term observational and intervention studies are necessary.

The results of subgroup analysis indicate that the role of physical activity after a cancer diagnosis may differ according to the type of cancer. It is particularly noteworthy that stomach cancer survivors who began exercise after their diagnosis experienced a 17% decrease in the risk of diabetes. For lymphoma survivors, the decrease was even more significant, with a 46% reduction in risk. On the other hand, breast, lung, liver, and thyroid cancer survivors who either maintained or initiated physical activity post-diagnosis exhibited only marginal risk reductions, suggesting that the impact of physical activity on metabolic pathways can vary with the type of cancer. These differences could be attributable to the distinct treatment regimens for each primary site and variations in survivorship durations.

Limitations of our study include an observational study design that prevented causal inference and the measurement of physical activity by self-report questionnaire. The reliance on self-reported physical activity data can introduce recall bias, which could underestimate or overestimate the true association. In addition, the general health screening setting of our cohort could introduce selection bias, as it may not include individuals with severe health conditions. Moreover, the physical activity assessment was limited to two time points. Future studies might benefit from more frequent measurements or the use of pedometers for more accurate tracking. Last, information on cancer stage and treatment was not included in our cohort data.

Conclusions

Our findings suggest that sustaining regular physical activity from pre-diagnosis is associated with a lower risk of diabetes after a cancer diagnosis, independent of established diabetes risk factors. While associations between being physically active either only before or only after a cancer diagnosis and a lower risk of diabetes are suggestive, they are not statistically significant. Future research is warranted to establish clinical practice guidelines.

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Data availability The data will be made available upon request and approval of a proposal by the National Health Insurance Service Database.

Declarations

Consent to participate Anonymized and de-identified information was used for analyses, and informed consent was not required.

Conflict of interest The authors declare no competing interests.

References

1. Collaboration GBoDC. Cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life years for 29 cancer groups from 2010 to 2019: a systematic analysis for the global burden of disease study 2019. JAMA Oncol. 2022;8:420–44.
2. Ong KL, Stafford LK, McLaughlin SA, Boyko EJ, Vollset SE, Smith AE, et al. Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the Global Burden of Disease Study 2021. Lancet. 2023;402:203–34.
3. Sylow L, Grand MK, von Heymann A, Persson F, Siersma V, Kriegbaum M, et al. Incidence of new-onset type 2 diabetes after cancer: a Danish cohort study. Diabetes Care. 2022;45:e105–6.
4. Hwangbo Y, Kang D, Kang M, Kim S, Lee EK, Kim YA, et al. Incidence of diabetes after cancer development: a Korean national cohort study. JAMA Oncol. 2018;4:1099–105.
5. Xiao Y, Wang H, Tang Y, Yan J, Cao L, Chen Z, et al. Increased risk of diabetes in cancer survivors: a pooled analysis of 13 population-based cohort studies. ESMO Open. 2021;6:100218.
6. Honors MA, Kinzig KP. The role of insulin resistance in the development of muscle wasting during cancer cachexia. J Cachexia Sarcopenia Muscle. 2012;3:5–11.
7. Perez A, Jansen-Chaparro S, Saigi I, Bernal-Lopez MR, Miñambres I, Gomez-Huelgas R. Glucocorticoid-induced hyperglycemia. J Diabetes. 2014;6:9–20.
8. Ariaans G, de Jong S, Gietema JA, Lefrandt JD, de Vries EG, Jalving M. Cancer-drug induced insulin resistance: innocent bystander or unusual suspect. Cancer Treat Rev. 2015;41:376–84.
9. Vigneri P, Frasca F, Sciacca L, Pandini G, Vigneri R. Diabetes and cancer. Endocr Relat Cancer. 2009;16:1103–23.
10. Kim DS, Scherer PE. Obesity, diabetes, and increased cancer progression. Diabetes Metab J. 2021;45:799–812.
11. Barone BB, Yeh H-C, Snyder CF, Peairs KS, Stein KB, Derr RL, et al. Long-term all-cause mortality in cancer patients with preexisting diabetes mellitus: a systematic review and meta-analysis. JAMA. 2008;300:2754–64.
12 Campbell PT, Newton CC, Patel AV, Jacobs EJ, Gapstur SM. Diabetes and cause-specific mortality in a prospective cohort of one million U.S. adults. Diabetes Care. 2012;35:1835–44.
13. Tao H, O'Neil A, Choi Y, Wang W, Wang J, Wang Y, et al. Pre- and post-diagnosis diabetes as a risk factor for all-cause and cancer-specific mortality in breast, prostate, and colorectal cancer survivors: a prospective cohort study. Front Endocrinol (Lausanne). 2020;11:60.
14. Srokowski TP, Fang S, Hortobagyi GN, Giordano SH. Impact of diabetes mellitus on complications and outcomes of adjuvant chemotherapy in older patients with breast cancer. J Clin Oncol. 2009;27:2170–6.

15. Dąbrowski M, Grondecka A. Diabetes as a risk factor of hospitalization in the surgical ward due to cancer in the elderly and middle-aged population. Arch Med Sci. 2017;13:1025–30.
16. Thong MS, van de Poll-Franse L, Hoffman RM, Albertsen PC, Hamilton AS, Stanford JL, Penson DF. Diabetes mellitus and health-related quality of life in prostate cancer: 5-year results from the Prostate Cancer Outcomes Study. BJU Int. 2011;107:1223–31.
17. Smith AD, Crippa A, Woodcock J, Brage S. Physical activity and incident type 2 diabetes mellitus: a systematic review and dose-response meta-analysis of prospective cohort studies. Diabetologia. 2016;59:2527–45.
18. Aune D, Norat T, Leitzmann M, Tonstad S, Vatten LJ. Physical activity and the risk of type 2 diabetes: a systematic review and dose-response meta-analysis. Eur J Epidemiol. 2015;30:529–42.
19. Colberg SR, Sigal RJ, Yardley JE, Riddell MC, Dunstan DW, Dempsey PC, et al. Physical activity/exercise and diabetes: a position statement of the American Diabetes Association. Diabetes Care. 2016;39:2065–79.
20. Kanaley JA, Colberg SR, Corcoran MH, Malin SK, Rodriguez NR, Crespo CJ, et al. Exercise/physical activity in individuals with type 2 diabetes: a consensus statement from the American College of Sports Medicine. Med Sci Sports Exerc. 2022;54:353–68.
21. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, Nathan DM. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med. 2002;346:393–403.
22. Tuomilehto J, Lindström J, Eriksson JG, Valle TT, Hämäläinen H, Ilanne-Parikka P, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med. 2001;344:1343–50.
23. Gillies CL, Abrams KR, Lambert PC, Cooper NJ, Sutton AJ, Hsu RT, Khunti K. Pharmacological and lifestyle interventions to prevent or delay type 2 diabetes in people with impaired glucose tolerance: systematic review and meta-analysis. BMJ. 2007;334:299.
24. Stevens JW, Khunti K, Harvey R, Johnson M, Preston L, Woods HB, et al. Preventing the progression to type 2 diabetes mellitus in adults at high risk: a systematic review and network meta-analysis of lifestyle, pharmacological and surgical interventions. Diabetes Res Clin Pract. 2015;107:320–31.
25. Kenfield SA, Stampfer MJ, Giovannucci E, Chan JM. Physical activity and survival after prostate cancer diagnosis in the health professionals follow-up study. J Clin Oncol. 2011;29:726–32.
26. Schmid D, Leitzmann MF. Association between physical activity and mortality among breast cancer and colorectal cancer survivors: a systematic review and meta-analysis. Ann Oncol. 2014;25:1293–311.
27. Gunnell AS, Joyce S, Tomlin S, Taaffe DR, Cormie P, Newton RU, et al. Physical activity and survival among long-term cancer survivor and non-cancer cohorts. Front Public Health. 2017;5:19.
28. Scott JM, Li N, Liu Q, Yasui Y, Leisenring W, Nathan PC, et al. Association of exercise with mortality in adult survivors of childhood cancer. JAMA Oncol. 2018;4:1352–8.
29. Irwin ML, Smith AW, McTiernan A, Ballard-Barbash R, Cronin K, Gilliland FD, et al. Influence of pre- and postdiagnosis physical activity on mortality in breast cancer survivors: the health, eating, activity, and lifestyle study. J Clin Oncol. 2008;26:3958–64.
30. Pinto BM, Ciccolo JT. Physical activity motivation and cancer survivorship. Recent Results Cancer Res. 2011;186:367–87.
31. Rock CL, Thomson CA, Sullivan KR, Howe CL, Kushi LH, Caan BJ, et al. American Cancer Society nutrition and physical activity guideline for cancer survivors. CA Cancer J Clin. 2022;72:230–62.
32. Campbell KL, Winters-Stone KM, Wiskemann J, May AM, Schwartz AL, Courneya KS, et al. Exercise guidelines for cancer survivors: consensus statement from International Multidisciplinary Roundtable. Med Sci Sports Exerc. 2019;51:2375–90.
33. Shin DW, Cho J, Park JH, Cho B. National general health screening program in Korea: history, current status, and future direction. Precis Future Med. 2022;6:9–31.
34. Lee YH, Han K, Ko SH, Ko KS, Lee KU. Data analytic process of a nationwide population-based study using National Health Information Database established by National Health Insurance Service. Diabetes Metab J. 2016;40:79–82.
35. Cheol Seong S, Kim YY, Khang YH, Heon Park J, Kang HJ, Lee H, et al. Data resource profile: the National Health Information Database of the National Health Insurance Service in South Korea. Int J Epidemiol. 2017;46:799–800.
36 Shin DW, Cho B, Guallar E. Korean National Health Insurance Database. JAMA Intern Med. 2016;176:138.
37. Yang MS, Park M, Back JH, Lee GH, Shin JH, Kim K, et al. Validation of cancer diagnosis based on the National Health Insurance Service Database versus the National Cancer Registry Database in Korea. Cancer Res Treat. 2022;54:352–61.
38. Lee KR, Hwang IC, Han KD, Jung J, Seo MH. Waist circumference and risk of breast cancer in Korean women: a nationwide cohort study. Int J Cancer. 2018;142:1554–9.
39. Park JW, Han K, Shin DW, Yeo Y, Chang JW, Yoo JE, et al. Obesity and breast cancer risk for pre- and postmenopausal women among over 6 million Korean women. Breast Cancer Res Treat. 2021;185:495–506.
40. Craig CL, Marshall AL, Sjöström M, Bauman AE, Booth ML, Ainsworth BE, et al. International Physical Activity Questionnaire: 12-country reliability and validity. Med Sci Sports Exerc. 2003;35:1381–95.
41. Yang K, Liu Z, Thong MSY, Doege D, Arndt V. Higher incidence of diabetes in cancer patients compared to cancer-free population controls: a systematic review and meta-analysis. Cancers (Basel). 2022;14:1808.
42. World Health Organization Regional Office for the Western Pacific. The Asia-Pacific perspective: redefining obesity and its treatment. Sydney : Health Communications Australia; 2000.
43. Fine JP, Gray RJ. A proportional hazards model for the subdistribution of a competing risk. J Am Stat Assoc. 1999;94:496–509.
44. Strain T, Dempsey PC, Wijndaele K, Sharp SJ, Kerrison N, Gonzales TI, et al. Quantifying the relationship between physical activity energy expenditure and incident type 2 diabetes: a prospective cohort study of device-measured activity in 90,096 adults. Diabetes Care. 2023;46:1145–55.
45. Lauby-Secretan B, Scoccianti C, Loomis D, Grosse Y, Bianchini F, Straif K. Body fatness and cancer–viewpoint of the IARC working group. N Engl J Med. 2016;375:794–8.
46. Park CY, Lim JY, Park HY. Age at natural menopause in Koreans: secular trends and influences thereon. Menopause. 2018;25:423–9.
47. Jang MK, Park C, Hong S, Li H, Rhee E, Doorenbos AZ. Skeletal muscle mass change during chemotherapy: a systematic review and meta-analysis. Anticancer Res. 2020;40:2409–18.
48 Dev R, Bruera E, Dalal S. Insulin resistance and body composition in cancer patients. Ann Oncol. 2018;29:ii18–26.
49. Clore JN, Thurby-Hay L. Glucocorticoid-induced hyperglycemia. Endocr Pract. 2009;15:469–74.
50. Bower JE. Cancer-related fatigue–mechanisms, risk factors, and treatments. Nat Rev Clin Oncol. 2014;11:597–609.
51. Cespedes Feliciano EM, Vasan S, Luo J, Binder AM, Chlebowski RT, Quesenberry C, et al. Long-term trajectories of physical function decline in women with and without cancer. JAMA Oncol. 2023;9:395–403.
52. Zullig LL, Sung AD, Khouri MG, Jazowski S, Shah NP, Sitlinger A, et al. Cardiometabolic comorbidities in cancer survivors: JACC: CardioOncology State-of-the-Art Review. JACC CardioOncol. 2022;4:149–65.
53. McTiernan A. Mechanisms linking physical activity with cancer. Nat Rev Cancer. 2008;8:205–11.

54. Kang DW, Lee J, Suh SH, Ligibel J, Courneya KS, Jeon JY. Effects of exercise on insulin, IGF axis, adipocytokines, and inflammatory markers in breast cancer survivors: a systematic review and meta-analysis. Cancer Epidemiol Biomarkers Prev. 2017;26:355–65.
55 Shaw K, Gennat H, O'Rourke P, Del Mar C. Exercise for overweight or obesity. Cochrane Database Syst Rev. 2006;2006:Cd003817.
56. Bann D, Kuh D, Wills AK, Adams J, Brage S, Cooper R. Physical activity across adulthood in relation to fat and lean body mass in early old age: findings from the Medical Research Council National Survey of Health and Development, 1946–2010. Am J Epidemiol. 2014;179:1197–207.
57. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med. 2002;346:393–403.
58. Diabetes Prevention Research Group. Long-term effects of lifestyle intervention or metformin on diabetes development and microvascular complications over 15-year follow-up: the Diabetes Prevention Program Outcomes Study. Lancet Diabetes Endocrinol. 2015;3:866–75.
59. Lindström J, Peltonen M, Eriksson JG, Ilanne-Parikka P, Aunola S, Keinänen-Kiukaanniemi S, et al. Improved lifestyle and decreased diabetes risk over 13 years: long-term follow-up of the randomised Finnish Diabetes Prevention Study (DPS). Diabetologia. 2013;56:284–93.