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Research Article

Cancer Epidemiology, Biomarkers & Prevention

Physical Activity and Cancer Incidence in Alberta's Tomorrow Project: Results from a Prospective Cohort of 26,538 Participants

Amanda M. Barberio[1], Christine M. Friedenreich[1,2], Brigid M. Lynch[3,4,5], Kristin L. Campbell[6], Paul Arora[7], and Darren R. Brenner[1,2]

Abstract

Background: Physical activity (PA) has been associated with lower risks of several cancers. We examined the association between total and domain-specific PA and risk of all and site-specific cancer risk.

Methods: We analyzed baseline data from Alberta's Tomorrow Project. Specifically, adults ages 35–69 years who completed the Past Year Total Physical Activity Questionnaire were included ($n = 26{,}538$). For each activity, participants reported the type, duration, and intensity of PA. Total, recreational, and occupational PA metabolic equivalent hours/week were divided into quartiles. Incident cancer cases up to December 2016 were identified via linkage to the Alberta Cancer Registry. The associations of PA on cancer risk were examined using Cox proportional hazards models.

Results: A total of 2,186 participants (8.24%) developed cancer during follow-up from 2001 to 2016. We observed a significant inverse association between total PA and all-cancer incidence in the multivariate-adjusted model [$HR_{Q4vQ1} = 0.87$; 95% confidence interval (CI): 0.76–0.99] that remained significant in the latency multivariate-adjusted model. Higher recreational PA was associated with a risk decrease for all-cancer in the latency multivariate-adjusted model (HR = 0.84; 95% CI: 0.74–0.96), and showed a linear inverse association with breast cancer. While none of the HR estimates for quartiles of occupational PA and all-cancer reached statistical significance, the model P_{trend} was marginally significant in the latency multivariate-adjusted model ($P = 0.06$).

Conclusions: In this cohort of Albertans, higher total PA and recreational PA appears to convey modest protection against the development of all-cancer.

Impact: Public health and cancer prevention efforts should focus on encouraging population-level increases in PA. *Cancer Epidemiol Biomarkers Prev; 27(8); 945–54. ©2018 AACR.*

Introduction

Physical activity (PA) is integral for the prevention of many noncommunicable diseases, such as type II diabetes and cardiovascular diseases (1). Over the past three decades, a considerable body of epidemiologic evidence has accumulated to suggest that regular PA helps to reduce the risk of certain types of cancer (2). Specifically, recent systematic reviews and meta-analyses provide strong evidence that greater PA is associated with a lower risk of breast cancer (3–6), colon cancer (3, 7–9), endometrial cancer (3, 10, 11) and adenocarcinoma of the esophagus (12–14), and moderate evidence that greater PA is associated with a lower risk of lung cancer (3, 15–18). For breast and colon cancers, strong evidence of dose–response relationship exists, such that increasing the duration and/or intensity of PA results in greater reductions in cancer risk (3–6, 19). In 2016, the Physical Activity Collaboration of the National Cancer Institute Cohort Consortium published a pooled analysis of data from 12 prospective cohort studies, involving 1.44 million adults from the United States and Europe. This analysis found that leisure time PA decreased the risk of 13 different cancer types: esophageal adenocarcinoma, liver, lung, kidney, gastric cardia, endometrial, myeloid leukemia, myeloma, colon, head and neck, rectal, bladder, and breast. Estimated risk reductions ranged from 42% [95% confidence interval (CI): 0.37–0.89] for esophageal adenocarcinoma to 10% (95% CI: 0.87–0.93) for breast cancer, with seven sites (esophageal adenocarcinoma, liver, lung, kidney, gastric cardia, endometrial, and myeloid leukemia) associated with a risk reduction of at least 20% (20).

The Canadian Society for Exercise Physiology (21) recommends that healthy adults (ages 18–64 years) accumulate at least 150 minutes of moderate- to vigorous-intensity PA per week to achieve health benefits, including reducing the risk of certain types of cancer. While PA promotion efforts have historically

[1]Department of Cancer Epidemiology and Prevention Research, CancerControl Alberta, Alberta Health Services, Calgary, Alberta, Canada. [2]Departments of Oncology and Community Health Sciences, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada. [3]Cancer Epidemiology and Intelligence Division, Cancer Council Victoria, Melbourne, Victoria, Australia. [4]Centre for Epidemiology and Biostatistics, Melbourne School of Population and Global Health, The University of Melbourne, Melbourne, Victoria, Australia. [5]Physical Activity Laboratory, Baker Heart and Diabetes Institute, Melbourne, Victoria, Australia. [6]Department of Physical Therapy, Faculty of Kinesiology, University of British Columbia, Vancouver, British Columbia, Canada. [7]Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario, Canada

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Corresponding Author: Darren R. Brenner, Departments of Oncology and Community Health Sciences, Cumming School of Medicine, University of Calgary Address: Department of Cancer Epidemiology and Prevention Research CancerControl Alberta—Alberta Health Services Holy Cross Centre, Room 514 Box ACB, 2210 2nd St SW Calgary, Alberta T2S 3C3. Phone: 587-439-6177; Fax: 403-476-2654; E-mail: darren.brenner@ucalgary.ca

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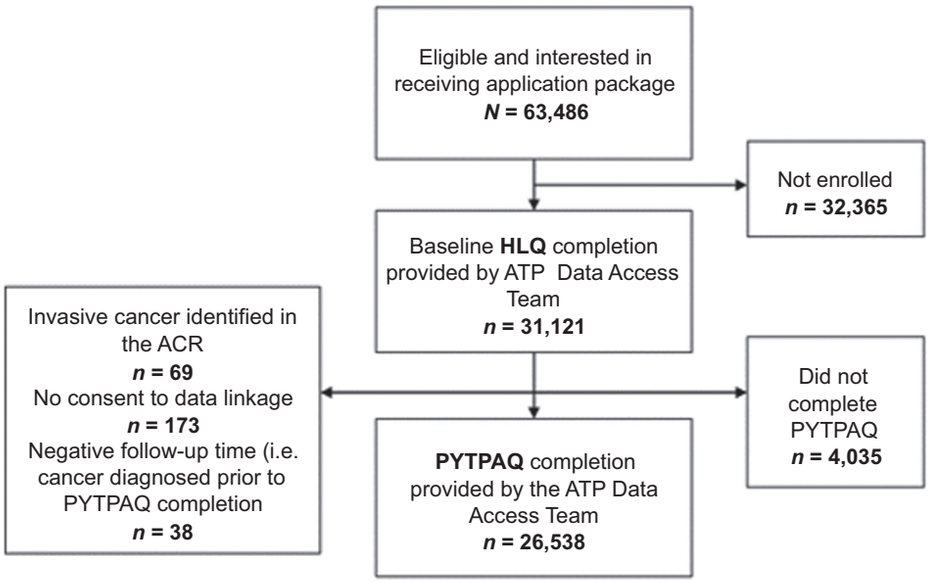

Figure 1.
Recruitment, enrollment, and analytic sample selection flow diagram in Alberta's Tomorrow Project, resulting in an analytic sample of 26,538 participants.

emphasized increasing recreational PA, other domains of PA including occupational (employment and volunteer activities), household (housework, childcare, yard-work activities), and transportation (walking or cycling to and from employment and volunteer activities) represent important potential contributors to overall energy expenditure. A recent study examined domain-specific hours of activity among Albertans enrolled in a prospective cohort study, and found that occupational and household activities were the greatest contributors to overall energy expenditure, while levels of leisure time activities were relatively low (22). Accordingly, it is pertinent to examine different domains of PA, in addition to total PA, when investigating the associations between PA and cancer incidence.

Despite the increase in research on the association between PA and cancer risk, few cohort studies have examined the associations between total and domain-specific PA and cancer risk. In this study, we utilize PA data from Alberta's Tomorrow Project (ATP). Our two main objectives are: (i) to examine the associations between total PA and the risk of all-cancer and site-specific cancers, and (ii) to examine the associations between domain-specific PA and the risk of all-cancer and site-specific cancers.

Materials and Methods

Data source

We examined data from ATP, a prospective cohort of adults in the province of Alberta, Canada. Full details regarding the recruitment and enrollment for phase I of ATP have been described elsewhere (23). Briefly, commencing in the year 2000, males and females between the ages of 35 and 69 years with no previous history of malignant cancer were recruited through eight waves of telephone-based random digit dialing. A total of 63,496 Alberta residents were eligible and interested in receiving an application package. Of these individuals, 31,121 were enrolled in ATP upon providing written consent and returning the Health and Lifestyle Questionnaire (HLQ) that captured detailed information on sociodemographic characteristics, anthropometric measurements, personal and family health history, and some lifestyle factors. Twelve weeks later, enrolled participants were mailed the Canadian Diet History Questionnaire-I and the Past Year Total Physical Activity Questionnaire (PYTPAQ). This analysis includes participants who completed the PYTPAQ and consented to having their data linked with administrative databases (Fig. 1).

Ethical approval for recruitment and data collection for ATP was approved by the former Alberta Cancer Board Research Ethics Committee and the University of Calgary Conjoint Health Research Ethics Board. The present study was conducted following ethical approval from the Health Research Ethics Board of Alberta—Cancer Committee.

Physical activity assessment

The accelerometer-validated PYTPAQ (24) was used to estimate a study participant's total energy expenditure at baseline from PA during the preceding 12 month period. The PYTPAQ captures PA performed in four different domains: (i) employment and volunteer activities, (ii) transportation-related activities, (iii) household activities, and (iv) recreational activities. Within each domain, participants self-reported the type of activity they engaged in (e.g. walking, biking, shoveling, etc.) as well as the frequency of the activity (months/year, days/week), duration of the activity (hours/day), and their perceived physical intensity level (PIL) on a four-point scale [1 = sedentary (activities done mainly sitting); 2 = light (activities mainly done standing that do not increase heart rate); 3 = moderate (activities that cause an increase in heart rate and light sweating); 4 = heavy (activities that cause a substantial increase in heart rate and heavy sweating)]. However, participants were asked not to include activities that were done mainly sitting down for the transportation, household, and recreation domains.

To assist study participants, examples of activities within each domain as well examples of how to complete each section of the questionnaire were provided. Participants were also instructed not to "double-count" their hours of PA and ensure that their total PA hours did not exceed their number of waking hours. Extreme

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values of PA were flagged and resolved via telephone follow-up with the participant.

Self-reported descriptions of activities were used to assign standard metabolic equivalents of task (MET) values according to the Compendium of Physical Activities (25, 26); however, assigned MET values could be adjusted up upward or downward based on the PIL reported by the participant (24). The total hours per week spent in each activity were multiplied by the METs assigned to the activity to determine the MET-hours per week for each broad domain of activity. Total metabolic output per week was derived by summing the four separate MET-hours per week from each domain.

Because of the skewed distributions of PA data, continuous MET-hours per week for total PA, occupational PA, household PA, and recreational PA were categorized into quartiles. As approximately 82% of our sample had a value of 0 MET-hours per week for transportation PA, we do not present results for transportation PA and cancer risk.

Cancer registry linkage

Incident, primary cancers (with the exception of nonmelanoma skin cancers) were identified through data linkage with the Alberta Cancer Registry (ACR) using participants' Personal Health Numbers up to December 2016. The coding of new cancer cases by site is based on the International Classification of Diseases for Oncology, Third Edition (27). The ACR has met the "Gold Standard" for Registry Certification under the North American Association of Central Registries from 2002 to 2013 (ratings for 2014–2016 have not yet been assigned), indicating that cancer case ascertainment was $\geq$95% (28).

We considered all incident cancer cases identified through data linkage with the ACR, as well as eight site-specific cancers with greater than 100 incident cases: breast, colon (includes cancers of the colon and rectosigmoid junction), prostate, lung, endometrial, non-Hodgkin lymphoma, leukemia, and hematologic cancers (includes Hodgkin lymphoma, non-Hodgkin lymphoma, leukemia, multiple myeloma and plasmacytoma, and other hematopoeitic and reticuloendothelioma cancers).

Covariates

We adjusted for several covariates on the basis of known associations both with PA and cancer. Adjusted models included age, sex, ethnicity (white/other), marital status (married or living with someone/divorced, separated, or widowed/single, never married), highest level of education (high school or less/some post-high school education/post-high school certificate or degree), total household income ($0 to $49,999/$50,000–$99,999/$\geq$$100,000), geographical area of residence (urban/rural), smoking status (current/former/never), mean alcohol intake (grams of ethanol per day), mean energy intake (kilocalories per day), self-reported body mass index (BMI; kg/m^2), history of a cardiovascular condition (yes/no), history of a respiratory condition (yes/no), and family history of cancer (yes/no). For female-only cancers (breast and endometrial), menopausal status (premenopause/postmenopause) was included in adjusted models. Pack-years of cigarette smoking and mean fibre intake (grams per day) were included in adjusted lung and colon cancer models, respectively. We also included a dichotomous (yes/no) variable for indicating ever having cancer screening tests in adjusted models for breast cancer (physical breast exam and/or mammogram), colon cancer (blood stool test and/or sigmoidoscopy or colonoscopy), and prostate cancer (digital rectal exam and/or prostate-specific antigen test). Finally, we mutually adjusted for each type of PA in each model to examine for independence of effects. For example, in models examining recreational PA and cancer incidence, in addition to adjusting for the relevant aforementioned covariates, we adjusted for quartiles of occupational PA, quartiles of household PA, and groups of transportation PA (none/some/high; the "some" and "high" groups were created by evenly splitting the participants who had a value greater than 0 MET-hours per week for transportation PA).

Statistical analyses

Participants' follow-up time was calculated from their entry into the study (based on their exact age at PYTPAQ completion) to their date of cancer diagnosis (based on their exact age when their incident, first-site cancer was diagnosed), or to the end of follow-up for the current study (based on their exact age at the time of data linkage with ACR in December 2016). Accordingly, each participant contributed person-time from their completion of the PYTPAQ to their diagnosis of cancer or, to the end of follow-up in December 2016, whichever came first.

For all-cancer and site-specific cancer risk, Cox proportional hazards models were used to estimate the age-adjusted and multivariate-adjusted HR between quartiles of PA (lowest PA quartile as the reference group) and 95% confidence intervals (95% CI) of cancer incidence for each domain of PA. An exception was made for transportation PA such that HRs for site-specific cancer risks were not generated because of low statistical power. For multivariate adjusted models, we ran correlation matrices of coefficients to ensure that there was no evidence of multicollinearity among covariates, including education and income. We conducted sensitivity analyses where incident cancers occurring less than two years after baseline data collection were excluded to minimize the potential of reverse causation (i.e., a participant's PA being lowered by an existing, yet undiagnosed cancer). In additional analyses, we ran the analyses of domain-specific PA and cancer risk without mutual adjustment for each type of PA in each model and the results were unchanged.

We considered how the association between PA and cancer risk may differ between certain population subgroups. Specifically, we examined potential effect modification by the following variables: BMI (<30 kg/m^2/$\geq$30 kg/m^2) for total PA and all-cancer risk, menopausal status (premenopause/postmenopause) for total PA and female-only cancer risk, and smoking status (current/former/never) for total PA and all cancer risk as well as total PA and lung cancer risk. Stata software (version 14.2) was used for all analyses (29).

Results

The analytic study population included 26,538 participants (9,999 males and 16,539 females) who completed the PYTPAQ, had no previous cancer diagnosis in the ACR and consented to data linkage yielding a total of 285,787 person-years of follow-up. Of these, a total of 2,186 participants (925 males and 1,261 females) developed cancer during the study follow-up period, which was a mean of 6.6 years for cancer cases and 11.1 years for noncancer cases. Although a total of 4,303 participants who completed the HLQ did not complete the PYTPAQ, the percentage of these individuals who developed cancer was similar to the percentage of individuals who

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Table 1. Descriptive statistics for Alberta's Tomorrow Project study population who completed the Past Year Total Physical Activity Questionnaire and consented to data linkage, $n = 26{,}538$

	Male cancer cases ($n = 925$)	**Male noncancer ($n = 9{,}074$)**	**Female cancer cases ($n = 1{,}261$)**	**Females noncancer ($n = 15{,}278$)**
Follow-up time (years)	6.6 (3.8)	11.3 (2.5)	6.6 (3.7)	11.1 (2.5)
Total PA (MET-hrs/wk)	151.1 (75.1)	173.6 (74.8)	145.3 (68.5)	157.3 (65.1)
Occupational PA (MET-hrs/wk)	90.8 (72.9)	112.1 (70.0)	58.1 (56.8)	67.2 (53.4)
Recreational PA (MET-hrs/wk)	26.6 (26.9)	27.9 (27.3)	20.6 (20.6)	23.5 (23.4)
Household PA (MET-hrs/wk)	33.2 (28.5)	32.5 (28.4)	66.0 (44.5)	65.8 (42.9)
Transportation PA (MET-hrs/wk)	0.6 (2.8)	1.2 (4.9)	0.6 (2.4)	0.7 (2.7)
Age (years)	57.8 (8.2)	50.7 (9.0)	55.9 (9.0)	50.8 (9.1)
Self-reported measured BMI (kg/m^2)	28.9 (4.8)	28.0 (4.4)	28.3 (6.3)	27.2 (5.9)
BMI <30 kg/m^2	65.7% ($n = 608$)	72.9% ($n = 6{,}614$)	67.2% ($n = 847$)	74.3% ($n = 11{,}357$)
BMI ≥30 kg/m^2	34.3% ($n = 317$)	27.1% ($n = 2{,}460$)	32.8% ($n = 414$)	25.7% ($n = 3{,}921$)
Mean daily energy intake (kcal)	2,154.8 (1,023.6)	2,244.9 (1,019.1)	1,592.0 (647.6)	1,643.5 (668.2)
Mean daily fibre intake (g)	20.0 (9.3)	20.7 (9.8)	17.7 (8.2)	18.4 (8.8)
Mean daily alcohol intake (g)	17.5 (41.1)	16.6 (45.2)	6.0 (14.1)	6.5 (19.8)
Marital status				
Married or living with someone	83.7% ($n = 774$)	83.3% ($n = 7{,}556$)	72.2% ($n = 910$)	76.4 ($n = 11{,}667$)
Divorced, separated, or widowed	11.0% ($n = 102$)	10.2% ($n = 928$)	21.8% ($n = 275$)	18.3% ($n = 2{,}803$)
Single	5.3% ($n = 49$)	6.5% ($n = 589$)	6.0% ($n = 75$)	5.3% ($n = 807$)
Education				
High school or less	32.4% ($n = 300$)	24.2% ($n = 2{,}201$)	34.5% ($n = 435$)	29.5% ($n = 4{,}509$)
Some post-high school	18.6% ($n = 172$)	18.3% ($n = 1{,}660$)	22.8% ($n = 288$)	21.9% ($n = 3{,}341$)
Post–high school certificate or degree	49.0% ($n = 453$)	57.5% ($n = 5{,}212$)	42.7% ($n = 538$)	48.6% ($n = 7{,}427$)
Total household income				
$0–$49,999	33.5% ($n = 304$)	23.3% ($n = 2{,}083$)	46.7% ($n = 570$)	35.3% ($n = 5{,}238$)
$50,000–$99,999	44.0% ($n = 399$)	45.1% ($n = 4{,}037$)	37.8% ($n = 461$)	40.2% ($n = 5{,}973$)
≥$100,000	22.5% ($n = 204$)	31.6% ($n = 2{,}830$)	15.5% ($n = 189$)	24.5% ($n = 3{,}632$)
Urban/rural status				
Urban	74.7% ($n = 691$)	77.8% ($n = 7{,}053$)	73.0% ($n = 920$)	76.1% ($n = 11{,}613$)
Rural	25.3% ($n = 234$)	22.2% ($n = 2{,}011$)	27.0% ($n = 340$)	23.9% ($n = 3{,}648$)
Smoking status				
Never	32.4% ($n = 300$)	42.9% ($n = 3{,}888$)	39.7% ($n = 500$)	47.0% ($n = 7{,}179$)
Former	47.0% ($n = 435$)	39.3% ($n = 3{,}565$)	36.9% ($n = 465$)	36.3% ($n = 5{,}537$)
Current	20.5% ($n = 190$)	17.8% ($n = 1{,}616$)	23.4% ($n = 295$)	16.7% ($n = 2,\ 550$)
Pack-years of smoking	16.1 (19.2)	10.3 (15.0)	12.4 (16.6)	7.5 (12.3)
Self-reported history of a cardiovascular condition				
No	45.3% ($n = 419$)	56.6% ($n = 5{,}133$)	53.2% ($n = 671$)	63.0% ($n = 9{,}628$)
Yes	54.7% ($n = 505$)	43.4% ($n = 3{,}939$)	46.8% ($n = 590$)	37.0% ($n = 5{,}644$)
Self-reported history of a respiratory condition				
No	94.9% ($n = 877$)	96.9% ($n = 8{,}785$)	94.6% ($n = 1{,}193$)	95.9% ($n = 14{,}646$)
Yes	5.1% ($n = 47$)	3.1% ($n = 283$)	5.4% ($n = 68$)	4.1% ($n = 625$)
Self-reported family history of cancer				
No	42.6% ($n = 394$)	49.9% ($n = 4{,}525$)	38.9% ($n = 490$)	45.8% ($n = 6{,}999$)
Yes	57.4% ($n = 545$)	50.1% ($n = 4{,}549$)	61.1% ($n = 771$)	54.2% ($n = 8{,}279$)
Self-reported colon cancer screening				
No	53.8% ($n = 498$)	60.3% ($n = 5{,}469$)	50.9% (642)	57.4% ($n = 8{,}765$)
Yes	46.2% ($n = 427$)	39.7% ($n = 3{,}605$)	49.1% ($n = 619$)	42.6% ($n = 6{,}513$)
Self-reported prostate cancer screening				
No	12.0% ($n = 111$)	25.2% ($n = 2{,}290$)	N/A	N/A
Yes	88.0% ($n = 814$)	74.8% ($n = 6{,}783$)	N/A	N/A
Self-reported breast cancer screening				
No	N/A	N/A	1.5% ($n = 19$)	2.5% ($n = 385$)
Yes	N/A	N/A	98.5% ($n = 1{,}242$)	97.5% ($n = 14{,}891$)
Menopausal status				
Premenopausal	N/A	N/A	31.8% ($n = 401$)	52.6% ($n = 8{,}028$)
Postmenopausal	N/A	N/A	68.2% ($n = 860$)	47.4% ($n = 7{,}249$)

developed cancer in the analytic study population; 6.41% and 8.24%, respectively.

We examined baseline PA and covariates by sex and cancer status (Table 1). For both male and female study participants, the means for total PA, recreational PA, and occupational PA (in MET-hours per week) were all higher among noncancer cases than cancer cases. Mean household PA was slightly higher among cancer cases than noncancer cases. Occupational PA was the greatest contributor to total PA. Males and females who did not develop cancer during follow-up tended to be younger, more educated, reported a higher total household income, smoked fewer cigarettes, had a lower BMI, and were premenopausal (females only) at baseline than their counterparts who developed cancer.

Table 2 shows the results of the age-adjusted and multivariable-adjusted HRs of cancer incidence by cancer site for total PA in MET-hours per week. A modest, inverse association for the highest quartile (201–535 MET-hours per week) versus the lowest

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Table 2. Cox regression HRs of cancer incidence by cancer site and total PA (MET-hours per week) in quartiles

MET-hours per week	Cases	Age-adjusted HR (95% CI)	Cases	Multivariate-adjusted HR[a] (95% CI)	Cases	Latency multivariate-adjusted HR[b] (95% CI)
All-cancer						
0–113.7	763	1.0 (Ref)	729	1.0 (Ref)	625	1.0 (Ref)
113.8–152.9	500	0.89[c] (0.79–1.00)	487	0.93 (0.83–1.04)	424	0.94 (0.83–1.06)
153.0–201.1	487	0.94 (0.84–1.06)	466	0.96 (0.85–1.08)	398	0.94 (0.83–1.07)
201.2–535.3	436	0.88[c] (0.78–0.99)	425	0.87[c] (0.76–0.99)	372	0.87[c] (0.76–1.00)
P_{trend}		0.08		0.06		0.06
Breast cancer						
0–113.7	149	1.0 (Ref)	141	1.0 (Ref)	123	1.0 (Ref)
113.8–152.9	112	0.85 (0.66–1.09)	110	0.86 (0.67–1.11)	99	0.88 (0.67–1.16)
153.0–201.1	108	0.92 (0.71–1.18)	101	0.90 (0.69–1.17)	89	0.89 (0.67–1.18)
201.2–535.3	83	0.83 (0.63–1.09)	81	0.85 (0.64–1.14)	69	0.82 (0.60–1.12)
P_{trend}		0.25		0.32		0.23
Colon cancer						
0–113.7	78	1.0 (Ref)	74	1.0 (Ref)	64	1.0 (Ref)
113.8–152.9	24	0.43[d] (0.27–0.69)	24	0.47[d] (0.29–0.75)	22	0.50[d] (0.30–0.81)
153.0–201.1	39	0.78 (0.52–1.16)	39	0.82 (0.55–1.24)	34	0.81 (0.52–1.26)
201.2–535.3	40	0.83 (0.55–1.24)	40	0.83 (0.54–1.26)	33	0.76 (0.48–1.20)
P_{trend}		0.51		0.54		0.35
Prostate cancer						
0–113.7	115	1.0 (Ref)	113	1.0 (Ref)	90	1.0 (Ref)
113.8–152.9	78	1.16 (0.86–1.56)	78	1.15 (0.85–1.54)	66	1.19 (0.86–1.65)
153.0–201.1	91	1.32[e] (0.99–1.77)	88	1.27 (0.95–1.71)	76	1.35[e] (0.97–1.86)
201.2–535.3	82	1.08 (0.80–1.46)	79	1.08 (0.79–1.48)	70	1.14 (0.81–1.60)
P_{trend}		0.40		0.44		0.32
Lung cancer						
0–113.7	86	1.0 (Ref)	82	1.0 (Ref)	69	1.0 (Ref)
113.8–152.9	44	0.85 (0.58–1.22)	41	0.95 (0.65–1.39)	35	0.92 (0.61–1.40)
153.0–201.1	32	0.73 (0.48–1.11)	29	0.71 (0.46–1.10)	27	0.82 (0.52–1.30)
201.2–535.3	29	0.73 (0.47–1.14)	29	0.76 (0.48–1.21)	26	0.79 (0.49–1.28)
P_{trend}		0.10		0.12		0.28
Endometrial cancer						
0–113.7	43	1.0 (Ref)	37	1.0 (Ref)	33	1.0 (Ref)
113.8–152.9	41	1.07 (0.69–1.65)	38	1.38 (0.86–2.22)	31	1.22 (0.73–2.03)
153.0–201.1	17	0.50[c] (0.28–0.88)	14	0.62 (0.33–1.18)	13	0.62 (0.32–1.21)
201.2–535.3	16	0.54[c] (0.30–0.98)	15	0.77 (0.41–1.46)	13	0.71 (0.36–1.40)
P_{trend}		0.01		0.15		0.13
Non-Hodgkin lymphoma						
0–113.7	36	1.0 (Ref)	35	1.0 (Ref)	33	1.0 (Ref)
113.8–152.9	18	0.63 (0.35–1.12)	17	0.65 (0.36–1.18)	16	0.65 (0.35–1.21)
153.0–201.1	18	0.67 (0.37–1.20)	18	0.69 (0.38–1.26)	11	0.46[c] (0.22–0.93)
201.2–535.3	21	0.79 (0.45–1.40)	21	0.72 (0.40–1.30)	20	0.73 (0.40–1.36)
P_{trend}		0.39		0.28		0.19
Leukemia						
0–113.7	28	1.0 (Ref)	26	1.0 (Ref)	18	1.0 (Ref)
113.8–152.9	22	1.05 (0.59–1.86)	21	1.09 (0.60–1.97)	20	1.49 (0.77–2.86)
153.0–201.1	21	1.09 (0.61–1.96)	21	1.13 (0.62–2.07)	17	1.32 (0.66–2.63)
201.2–535.3	19	1.01 (0.55–1.87)	19	1.01 (0.53–1.92)	18	1.36 (0.68–2.75)
P_{trend}		0.92		0.92		0.47
Hematologic cancers						
0–113.7	65	1.0 (Ref)	62	1.0 (Ref)	52	1.0 (Ref)
113.8–152.9	41	0.81 (0.54–1.21)	39	0.84 (0.55–1.26)	37	0.95 (0.61–1.6)
153.0–201.1	40	0.85 (0.56–1.28)	40	0.87 (0.58–1.33)	29	0.76 (0.47–1.22)
201.2–535.3	40	0.87 (0.57–1.31)	40	0.82 (0.53–1.26)	38	0.93 (0.59–1.46)
P_{trend}		0.51		0.40		0.52

[a]Adjusted for: age (continuous), sex (for non–sex-specific cancers), ethnicity (white/other), marital status (married or living with someone/divorced, separated, or widowed/single, never married), highest level of education (high school or less/some post–high school education/post–high school certificate or degree), total household income ($0 to $49,999/$50,000 to $99,999/$\geq$ $100,000), geographical area of residence (urban/rural), smoking status (current/former/never), pack-years of cigarettes (lung cancer only), alcohol consumption (grams of ethanol per day), energy intake (kilocalories per day), fiber intake (grams per day) (colon cancer only), BMI (continuous), history of cardiovascular condition (yes/no), history of respiratory condition (yes/no), family history of cancer (yes/no), menopausal status (premenopause/postmenopause) (breast and endometrial cancers), history of breast cancer screening (yes/no) (breast cancer only), history of colon cancer screening (yes/no) (colon cancer only), and history of prostate cancer screening (yes/no) (prostate cancer only).

[b]Cancers occurring less than 2 years after baseline data collection removed.

[c]$P < 0.05$.

[d]$P < 0.01$.

[e]$P < 0.1$.

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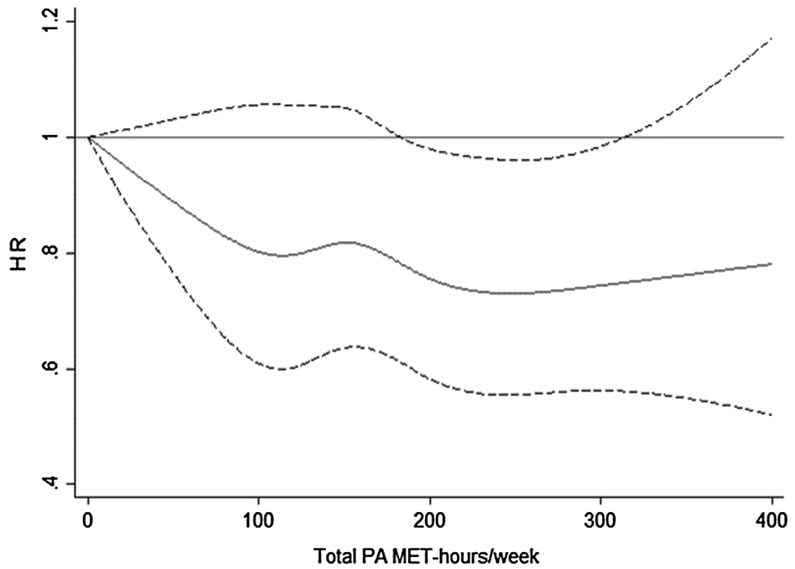

Figure 2.
Effect of total PA on all-cancer risk (2,105 cancer cases) in Alberta's Tomorrow Project ($N = 25,621$) adjusted for covariates. For ease of presentation, those with a total PA of >400 MET-hours/week were excluded. The model was adjusted for: age (continuous), sex, ethnicity (white/other), marital status (married or living with someone/divorced, separated, or widowed/single, never married), highest level of education (high school or less/some post–high school education/post–high school certificate or degree), total household income ($0 to $49,999/$50,000 to $99,999/≥$100,000), geographical area of residence (urban/rural), smoking status (current/former/never), alcohol consumption (grams of ethanol per day), energy intake (kilocalories per day), BMI (continuous), history of cardiovascular condition (yes/no), history of respiratory condition (yes/no), and family history of cancer (yes/no). The HR is represented by the solid line and the 95% CIs by the dashed lines on either side of the solid line. The solid horizontal line at 1 represents the null value for the hazard ratio.

quartile of total PA (0 to 114 MET-hours per week) and all-cancer incidence was observed in the age-adjusted model (HR = 0.88, 95% CI: 0.78–0.99, $P = 0.04$), which was virtually unchanged in the multivariate-adjusted model (HR = 0.87; 95% CI: 0.76–0.99; $P = 0.04$). When cancers occurring less than two years after baseline data collection were removed ($n = 288$), the estimates did not change (HR = 0.87; 95% CI: 0.76–1.00; $P = 0.05$). Figure 2 presents the effect of total PA modeled as a continuous variable on all-cancer risk adjusted for covariates; diminishing returns of total PA on all-cancer risk were observed after 100 MET-hours per week with no apparent benefit after 200 MET-hours per week. Risk reductions of 57% (95% CI, 0.27–0.69) and 53% (95% CI, 0.29–0.75) for colon cancer were observed for the second quartile (114–153 MET-hours per week) versus first quartile (0–114 MET-hours per week) in the age-adjusted and multivariable-adjusted models, respectively. There was no apparent colon cancer risk reduction for the third quartile (153–201 MET-hours per week) versus the lowest quartile (0–114 MET-hours per week), and a more modest risk reduction for the highest quartile (201–535 MET-hours per week) versus the lowest quartile (HR = 0.76; 95% CI: 0.48–1.20) in the latency multivariate-adjusted model. These findings do not support a dose–response effect as none of the colon cancer model P_{trend} values were statistically significant.

Age-adjusted and multivariable-adjusted HRs of cancer incidence by cancer site for quartiles of recreational PA in MET-hours per week are presented in Table 3. Higher recreational PA was associated with an overall decrease in all-cancer risk in the age-adjusted model ($P_{trend} = 0.02$), although the trends in the multivariate-adjusted analysis ($P_{trend} = 0.22$) and the latency multivariate-adjusted model ($P_{trend} = 0.06$) were not statistically significant. Recreational PA was inversely related to lung cancer risk in the age-adjusted model ($P_{trend} < 0.0001$) and latency multivariate-adjusted model ($P_{trend} = 0.05$), and was marginally inversely related to breast cancer risk in the age-adjusted model ($P_{trend} = 0.09$), multivariate-adjusted model ($P_{trend} = 0.06$), and latency multivariate-adjusted model ($P_{trend} = 0.06$). When the effect of total PA modeled as a continuous variable on breast cancer risk (Fig. 3A) and lung cancer risk (Fig. 3A), a decreased risk for breast cancer was observed with increasing recreational PA, whereas the decreased risk of lung cancer peaked at approximately 10 MET-hours per week of recreational PA and remained relatively constant thereafter.

Supplementary Table S1 presents the results of the age-adjusted and multivariable-adjusted HRs of cancer incidence by cancer site for quartiles of occupational PA in MET-hours per week. An inverse association was noted for occupational PA and all-cancer risk [highest quartile (117–463 MET-hours per week) vs. lowest quartile (0–35 MET-hours per week) in the latency multivariate-adjusted model: HR = 0.89; 95% CI: 0.91–1.19], and the model trends were marginally statistically significant ($P_{trend} = 0.06$). A risk reduction for colon cancer was observed [highest quartile (117–463 MET-hours per week) versus lowest quartile (0–35 MET-hours per week) in the latency multivariate-adjusted model: HR = 0.61; 95% CI: 0.36–1.04] but the model trends were not statistically significant. Participants in the second (35–76 MET-hours per week) and third (76–117 MET-hours per week) quartiles of occupational PA had a statistically significantly reduced risk of developing hematologic cancers (latency multivariate models $HR_{Q2vsQ1} = 0.61$; 95% CI: 0.37–0.99; $HR_{Q3vsQ1} = 0.41$; 95% CI: 0.24–0.71). A positive association was observed for prostate cancer such that greater amounts of occupational PA are associated with a higher risk of prostate cancer in the age-adjusted, multivariate-adjusted, and latency multivariate models although none of the model trends reached statistical significance.

Age-adjusted and multivariable-adjusted HRs of cancer incidence by cancer site for quartiles of household PA in MET-hours per week are presented in Supplementary Table S2. Greater amounts of household PA were associated with an overall decrease in all-cancer risk in the age-adjusted model ($P_{trend} = 0.02$), although the trends in the multivariate-adjusted analysis ($P_{trend} = 0.64$) and statistically the latency multivariate-adjusted model ($P_{trend} = 0.30$) were not statistically significant. For site-specific cancers, no clear associations between greater amounts of household PA and cancer risk were observed in any of the adjusted models.

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Table 3. Cox regression HRs of cancer incidence by cancer site and recreational PA (MET-hours per week) in quartiles

MET-hours per week	Cases	Age-adjusted HR (95% CI)	Cases	Multivariate-adjusted HR[a] (95% CI)	Cases	Latency multivariate-adjusted HR[b] (95% CI)
All-cancer						
0–7.4	643	1.0 (Ref)	621	1.0 (Ref)	542	1.0 (Ref)
7.5–18.0	511	0.81[c] (0.73–0.91)	502	0.85[c] (0.76–0.96)	431	0.84[c] (0.74–0.96)
18.1–34.9	528	0.86[d] (0.77–0.97)	523	0.91 (0.81–1.03)	444	0.90 (0.79–1.02)
35.0–255.3	504	0.86[d] (0.76–0.96)	496	0.91 (0.80–1.03)	402	0.86[d] (0.75–0.98)
P_{trend}		0.02		0.22		0.06
Breast cancer						
0–7.4	134	1.0 (Ref)	128	1.0 (Ref)	113	1.0 (Ref)
7.5–18.0	119	0.86 (0.67–1.11)	116	0.86 (0.67–1.12)	102	0.86[d] (0.66–1.13)
18.1–34.9	112	0.87 (0.68–1.12)	107	0.84 (0.65–1.10)	94	0.84 (0.64–1.12)
35.0–255.3	87	0.78[e] (0.60–1.03)	82	0.75[d] (0.56–1.00)	71	0.73[d] (0.54–1.00)
P_{trend}		0.09		0.06		0.06
Colon cancer						
0–7.4	51	1.0 (Ref)	49	1.0 (Ref)	43	1.0 (Ref)
7.5–18.0	43	0.87 (0.58–1.30)	43	0.94 (0.62–1.43)	38	0.95 (0.61–1.48)
18.1–34.9	57	1.19 (0.81–1.73)	55	1.24 (0.83–1.85)	50	1.28 (0.84–1.96)
35.0–255.3	30	0.65[e] (0.42–1.03)	30	0.71 (0.44–1.14)	22	0.59[e] (0.35–1.02)
P_{trend}		0.27		0.44		0.27
Prostate cancer						
0–7.4	88	1.0 (Ref)	87	1.0 (Ref)	81	1.0 (Ref)
7.5–18.0	68	0.87 (0.63–1.20)	67	0.86 (0.62–1.18)	59	0.79 (0.57–1.12)
18.1–34.9	86	0.98 (0.72–1.31)	84	0.96 (0.70–1.31)	71	0.86 (0.62–1.20)
35.0–255.3	124	1.24 (0.94–1.63)	120	1.28 (0.95–1.72)	91	1.04 (0.76–1.43)
P_{trend}		0.08		0.07		0.68
Lung cancer						
0–7.4	83	1.0 (Ref)	79	1.0 (Ref)	68	1.0 (Ref)
7.5–18.0	31	0.39[c] (0.26–0.59)	29	0.47[c] (0.31–0.73)	27	0.48[c] (0.30–0.75)
18.1–34.9	43	0.57[c] (0.39–0.82)	43	0.83 (0.57–1.22)	36	0.74 (0.49–1.12)
35.0–255.3	34	0.48[c] (0.32–0.72)	30	0.62[d] (0.40–0.98)	26	0.59[d] (0.37–0.95)
P_{trend}		<0.0001		0.09		0.05
Endometrial cancer						
0–7.4	37	1.0 (Ref)	32	1.0 (Ref)	29	1.0 (Ref)
7.5–18.0	36	0.95 (0.60–1.50)	32	1.12 (0.68–1.84)	26	0.99 (0.57–1.69)
18.1–34.9	30	0.85 (0.52–1.37)	27	1.16 (0.68–1.97)	25	1.14 (0.65–1.99)
35.0–255.3	14	0.46[d] (0.25–0.86)	13	0.70 (0.36–1.38)	10	0.56 (0.27–1.20)
P_{trend}		0.02		0.51		0.32
Non-Hodgkin lymphoma						
0–7.4	27	1.0 (Ref)	27	1.0 (Ref)	24	1.0 (Ref)
7.5–18.0	18	0.68 (0.37–1.24)	17	0.69 (0.37–1.28)	16	0.73 (0.38–1.38)
18.1–34.9	27	1.04 (0.61–1.77)	27	1.14 (0.65–1.97)	22	1.02 (0.56–1.85)
35.0–255.3	21	0.83 (0.47–1.47)	20	0.87 (0.47–1.60)	18	0.86 (0.45–1.65)
P_{trend}		0.86		0.98		0.89
Leukemia						
0–7.4	26	1.0 (Ref)	25	1.0 (Ref)	21	1.0 (Ref)
7.5–18.0	19	0.75 (0.41–1.35)	18	0.75 (0.41–1.39)	14	0.69 (0.35–1.36)
18.1–34.9	21	0.84 (0.47–1.49)	21	0.86 (0.47–1.56)	17	0.82 (0.42–1.57)
35.0–255.3	24	1.00 (0.57–1.74)	23	0.93 (0.51–1.69)	21	0.98 (0.51–1.86)
P_{trend}		0.95		0.90		0.95
Hematologic cancers						
0–7.4	54	1.0 (Ref)	53	1.0 (Ref)	46	1.0 (Ref)
7.5–18.0	38	0.72 (0.47–1.09)	36	0.73 (0.47–1.11)	31	0.71 (0.45–1.12)
18.1–34.9	49	0.94 (0.64–1.39)	49	0.99 (0.66–1.45)	40	0.91 (0.59–1.41)
35.0–255.3	45	0.89 (0.60–1.33)	43	0.88 (0.57–1.34)	39	0.89 (0.57–1.40)
P_{trend}		0.86		0.85		0.83

[a]Adjusted for: age (continuous), sex (for non–sex-specific cancers), ethnicity (white/other), marital status (married or living with someone/divorced, separated, or widowed/single, never married), highest level of education (high school or less/some post–high school education/post–high school certificate or degree), total household income ($0 to $49,999/$50,000 to $99,999/≥ $100,000), geographical area of residence (urban/rural), smoking status (current/former/never), pack-years of cigarettes (lung cancer only), alcohol consumption (grams of ethanol per day), energy intake (kilocalories per day), fiber intake (grams per day) (colon cancer only), BMI (continuous), history of cardiovascular condition (yes/no), history of respiratory condition (yes/no), family history of cancer (yes/no), menopausal status (premenopause/postmenopause) (breast and endometrial cancers), history of breast cancer screening (yes/no) (breast cancer only), history of colon cancer screening (yes/no) (colon cancer only), history of prostate cancer screening (yes/no) (prostate cancer only), quartiles of occupational PA, quartiles of household PA, and groups of transportation PA.

[b]Cancers occurring less than 2 years after baseline data collection removed.

[c]$P < 0.01$.

[d]$P < 0.05$.

[e]$P < 0.1$.

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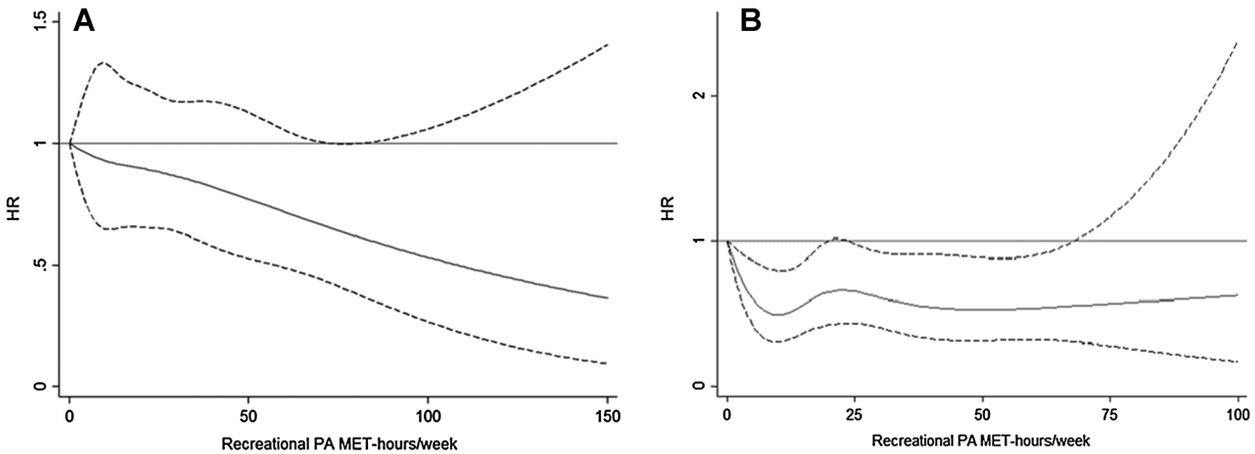

Figure 3.

A, Effect of recreational PA on breast cancer risk (433 cancer cases) in Alberta's Tomorrow Project ($N = 15,887$) adjusted for covariates. For ease of presentation, those with a recreational PA of > 150 MET-hours/week were excluded. **B,** Effect of recreational PA on lung cancer risk (179 cancer cases) in Alberta's Tomorrow Project ($N = 25,246$) adjusted for covariates. For ease of presentation, those with a recreational PA of >100 MET-hours/week were excluded. Models were adjusted for: age (continuous), sex (lung cancer only), ethnicity (white/other), marital status (married or living with someone/divorced, separated, or widowed/single, never married), highest level of education (high school or less/some post–high school education/post–high school certificate or degree), total household income ($0 to $49,999/$50,000 to $99,999/≥ $100,000), geographical area of residence (urban/rural), smoking status (current/former/never), pack-years of cigarettes (lung cancer only), alcohol consumption (grams of ethanol per day), energy intake (kilocalories per day), BMI (continuous), history of cardiovascular condition (yes/no), history of respiratory condition (yes/no), family history of cancer (yes/no), menopausal status (premenopause/postmenopause) (breast cancer only), history of breast cancer screening (yes/no) (breast cancer only), quartiles of occupational PA, quartiles of household PA, and groups of transportation PA. **A** and **B** contain the HRs represented by the solid line and the 95% CIs represented by the dashed lines on either side of the solid line. The solid horizontal line at 1 represents the null value for the HR.

We assessed potential effect modification by smoking status, BMI, and menopausal status for total PA and cancer incidence by performing stratified analyses. In multivariate-adjusted models, a stronger protective effect of total PA on the risk of all-cancer ($P_{trend} = 0.02$) and risk of lung cancer ($P_{trend} = 0.01$) was observed among current smokers than never or former smokers (Supplementary Table S3). The inverse association between total PA and all-cancer risk was marginally stronger among those with a BMI < 30 kg/m^2 ($P_{trend} = 0.06$) than those with a BMI ≥ 30 kg/m^2 ($P_{trend} = 0.33$) in multivariate-adjusted models (Supplementary Table S4). Evidence of effect modification by menopausal status was present for endometrial cancer risk such that the inverse association between total PA and endometrial cancer risk was stronger among postmenopausal females than premenopausal females, although this effect was not observed for breast cancer risk (Supplementary Table S5).

Discussion

In this cohort of Albertans 35–69 years at study enrollment, higher total PA and recreational PA at baseline was associated with modest protection against the development of all-cancer. All-cancer risk reductions of 13% and 14% were observed for participants in the highest quartiles versus lowest quartiles of total PA and recreational PA, respectively. Interestingly, when all-cancer risk was plotted as a function of continuous total PA in MET-hours per week, no additional risk reduction in the incidence of all-cancer was observed beyond 200 MET-hours per week. While none of the individual HR estimates for quartiles of occupational PA and all-cancer incidence reached statistical significance, the model P_{trend} was statistically significant in the multivariate-adjusted model and marginally significant in the latency multivariate-adjusted model. There was no clear association between greater amounts of household PA and the development of all-cancer. Perhaps the risk reduction of all-cancer observed for increasing recreational PA, but not for occupational PA or household PA, is a reflection of the greater fraction of time spent in moderate and vigorous intensity activities in the recreational PA domain. Although recreational PA did not constitute the majority of total energy expenditure in our study population, we observed that 81% recreational PA hours were composed of medium- or high-intensity activities, whereas only 37% of occupational PA hour and 32% of household PA hours were comprised of medium or high intensity activities (Supplementary Fig. S1).

Risk reductions (53%–57%) for colon cancer were observed for the second quartile versus first quartile of total PA in adjusted models; however, a dose–response effect was not detected. A variety of plausible biological mechanisms have been proposed to explain the association between increased PA and lower colon cancer risk including lower body fatness, especially central adiposity, reduced levels of circulating inflammatory biomarkers, and improved insulin sensitivity (30). For recreational PA, a linear relation between higher amounts of recreational PA and lower breast cancer risk was observed. In addition to the aforementioned biological mechanisms, it is believed that having lower body fat reduces levels of circulating estrogens that have consistently been associated with an increased risk of breast cancer. Among premenopausal women, very high levels of exercise may result in fewer ovulatory cycles, reducing lifetime estrogen exposure (30). For occupational PA, being in the second and third highest PA quartiles, but not the highest PA quartile, was significantly protective against the development of hematologic

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cancers. No associations between household PA and site-specific cancers were observed in adjusted models. Stratified analyses indicated stronger risk reductions for all-cancer and lung cancer with greater amounts total PA among current smokers as well as stronger risk reductions for endometrial cancer with greater amounts of total PA among postmenopausal women.

Some methodologic issues need to be acknowledged when considering the results of our study. First, we made the assumption that participants' self-reported PA at baseline remained constant during the study follow-up period. While PA was assessed twice during the follow-up period via surveys distributed to ATP participants between 2008 and 2015 (in addition to the PYTPAQ administered at baseline), the follow-up PA surveys used a different instrument, the International Physical Activity Questionnaire (IPAQ). The IPAQ captures PA performed over the past 7 days as opposed to the past 12 months (the time frame captured by the PYTPAQ), and importantly, there was limited opportunity to make consistent categories of PA across the PYTPAQ and the IPAQ. Although an individual's PA could change during the follow-up period due to different life events, the possibility of differential changes between cancer cases and noncancer cases is alleviated with the latency analyses. Second, the self-reported nature of PA likely resulted in overestimations of total and domain-specific PA due to social desirability bias, which may have introduced nondifferential misclassification bias. Third, there were small sample sizes for several of the site-specific analyses after dividing PA categories into quartiles and particularly for stratified analyses. These small sample sizes reduced the statistical power to detect an association and thus, the results should be interpreted with caution. We decided to include cancers where more than 100 cases had occurred during the cohort follow-up as these are important prospective data with detailed questionnaire data to be included in the literature. Fourth, although we were able to adjust for several sociodemographic, lifestyle, and health variables, the possibility of residual and unmeasured confounding remains.

Considering these methodologic limitations, we still observed a decreased risk of all-cancer for total PA and recreational PA which is consistent with the findings reported by recent studies. For example, a systematic review and meta-analysis by Liu and colleagues (3) that included 126 studies observed a 10% reduction in total cancer among individuals who engaged in the greatest amount of leisure time PA compared with those who engaged in the lowest amount of leisure time PA. Although other systematic reviews have reported a statistically significant inverse association between all types of PA and breast cancer incidence (5, 6), we did not observe this relation in our study. However, we did observe a reduced risk of breast cancer incidence with increasing amounts of recreational PA, which is consistent with the existing literature (3–6). Interestingly, while there is ample epidemiologic evidence to suggest a dose–response relation between higher PA and lower risk of colon cancer (19), we did not observe this relation in our study for total PA or recreational PA, though a marginally statistically significant trend existed for occupational PA. This lack of association may be attributable to the small number of colon cancer cases and/or not controlling for prolonged time spent sitting. For example, a meta-analysis that aimed to identify the contribution of sedentary time to site-specific cancer risk found that those with highest TV viewing time had a 54% increased risk of colon cancer risk compared with those with the lowest TV viewing time (31). While there is some evidence to suggest a weak relation between greater levels of PA and lower prostate cancer risk (3, 32), we observed that higher amounts of occupational PA were associated with an increased risk of prostate cancer. However, this positive association was not robust to analyses restricted to the 46 cases of prostate cancer that were classified as stage III or IV based on the American Joint Committee on Cancer version 6 collaborative stage guidelines (multivariate model for all stages of prostate cancer: $HR_{Q4vsQ1} = 1.24$; 95% CI: 0.89–1.72 versus multivariate model for stage III and IV prostate cancer: $HR_{Q4vsQ1} = 0.91$; 95% CI: 0.36–2.34). When considering the positive association observed between occupational PA and prostate cancer incidence, we cannot rule out the possibility of confounding by certain chemicals that may be present at higher quantities in occupations expected to have higher levels of PA such as farming and manufacturing. Although a pooled analysis by Moore and colleagues (20) detected strong risk reductions ($\geq$20%) for esophageal adenocarcinoma, cancers of the liver, cancers of the kidney, and gastric cardia, we were unable to examine associations between PA and these types of cancer because of insufficient numbers of incident cases.

Our study has several strengths including: the use of the PYTPAQ, previously shown to be reliable and valid that collected detailed information about total and domain-specific PA; having data on all-cancer from the same cohort; the ability to examine longitudinal relations between PA and cancer incidence given the prospective cohort study design; and minimizing the risk of reverse causation by performing sensitivity analyses that excluded cancers occurring less than 2 years after data collection.

As physical inactivity is a modifiable lifestyle factor that can reduce cancer risk, public health and cancer prevention efforts should focus on encouraging population-level increases in PA to counter the impact of industrialization and technological advancements that have resulted in a reduction in moderate- to vigorous-intensity PA. Future research efforts should integrate multiple assessment time points, to examine how changes in PA over time are related to cancer risk. Another methodologic issue relates to the measurement error and misclassification that arise from the use of self-reported measures. Improving the accuracy of exposure assessment in epidemiologic studies (e.g., by using accelerometry), would help ascertain valid estimates of associations with cancer. Finally, the minimum dose and duration of PA required to confer cancer incidence protection has not been sufficiently investigated and requires further elucidation.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Disclaimer

The views expressed herein represent the views of the author(s) and not of Alberta's Tomorrow Project or any of its funders.

Authors' Contributions

Conception and design: A.M. Barberio, C.M. Friedenreich, K.L. Campbell, D.R. Brenner

Development of methodology: A.M. Barberio, C.M. Friedenreich, P. Arora, D.R. Brenner

Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): D.R. Brenner

Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): A.M. Barberio, C.M. Friedenreich, K.L. Campbell, P. Arora, D.R. Brenner

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Writing, review, and/or revision of the manuscript: A.M. Barberio, C.M. Friedenreich, B.M. Lynch, K.L. Campbell, P. Arora, D.R. Brenner
Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases): A.M. Barberio, D.R. Brenner
Study supervision: C.M. Friedenreich, D.R. Brenner

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