Physical Activity and the Risk of Prostate Cancer in The Netherlands Cohort Study, Results after 9.3 Years of Follow-up

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Abstract

Background: **The aim of the current study was to evaluate the relation between physical activity and prostate cancer risk with specific emphasis on interaction with body mass index (BMI) and baseline energy intake.**
Methods: **The association between prostate cancer and physical activity was evaluated in the Netherlands Cohort Study, conducted among 58,279 men ages 55 to 69 years at entry. Information regarding baseline nonoccupational physical activity, history of sports participation, and occupational physical activity was collected with a questionnaire in 1986. After 9.3 years, 1,386 incident prostate cancer cases were available for case-cohort analyses. Multivariate incidence rate ratios (RR) and corresponding 95% confidence intervals (95% CI) were calculated using Cox regression analyses.**
Results: **Neither baseline nonoccupational physical activity (RR, 1.01; 95% CI, 0.81-1.25 for >90 versus <30 minutes per day), history of sports participation (RR, 1.04; 95% CI, 0.90-1.22 for ever versus never participated), nor occupational physical activity (RR, 0.91; 95% CI, 0.70-1.18 for >12 versus <8 KJ/min energy expenditure in the longest held job) showed an inverse relation with prostate cancer risk. We found an increased risk of prostate cancer for men who were physically active for >1 hour per day in obese men (BMI > 30) and men with a high baseline energy intake.**
Discussion: **The results of this current study do not support the hypothesis that physical activity protects against prostate cancer in men.** (Cancer Epidemiol Biomarkers Prev 2005;14(6):1490–5)

Introduction

Although prostate cancer is the second most commonly diagnosed cancer among men in the European Union (1) and in the Netherlands (2), today, only few etiologic determinants for prostate cancer have been identified, including dietary habits (3, 4), race (5-7), family history (8), and genetic factors (9, 10). Only few of these postulated determinants have been confirmed consistently in epidemiologic studies and many are not suitable for primary prevention because these cannot be modified through, e.g., health education programs. A potential interesting and modifiable determinant for prostate cancer is physical activity (11).

Several hypotheses have been proposed to explain the influence of physical activity on prostate cancer, including alteration in endogenous hormones, energy balance, immune function, and antioxidant defense mechanisms. Physical activity increases production of sex hormone binding globulin, which results in low free testosterone levels that may alter prostate cancer risk (12, 13). Second, physical activity may enhance the immune system by improving the capacity and numbers of natural killer cells (14-16). Finally, acute exercise may promote free radical production, whereas chronic exercise improves free radical defenses by up-regulating the levels of antioxidants (16-18).

The association between physical activity and prostate cancer risk has been inconsistent across the previously conducted epidemiologic studies and it is not yet known what the magnitude of the effect is. In addition, it is not known what intensity, duration, and frequency of activity are required for a reduction in prostate cancer risk.

Therefore, we conducted this study to evaluate the relation between physical activity and prostate cancer risk in an ongoing prospective cohort study in the Netherlands. Furthermore, we were interested in the possible interaction with other aspects of energy balance, such as body mass index (BMI) and baseline energy intake.

Materials and Methods

Cohort. We will only briefly outline the design of the Netherlands Cohort Study (NLCS) because this has been reported in detail elsewhere (19). The NLCS was initiated in September 1986 and includes 58,279 men ages 55 to 69 years at the beginning of the study. The study population originated from 204 municipal registries throughout the country. All cohort members completed a mailed, self-administered questionnaire on risk factors for cancer, including baseline nonoccupational physical activity, history of sports participation, and occupational history.

For reasons of efficiency in data processing and analysis, the case-cohort approach (20, 21) was used. In a case-cohort approach, cases are derived from the entire cohort (providing numerator information for calculation of cancer incidence rates), whereas accumulated person-years at risk in the total cohort are estimated using a random subcohort sample (providing denominator information for the rates). The subcohort (n = 2,411 men) was sampled directly after identification of all cohort members and has been followed up biennially for vital status information.

Follow-up. Follow-up for incidence of prostate cancer was established by computerized record linkage with all nine

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cancer registries in the Netherlands and with the Dutch national data base of pathology reports (PALGA; ref. 22). Only two subcohort members were lost to follow-up and completeness of follow-up of cancer has been estimated to be at least 96% (23). The present analysis is restricted to cancer incidence in 9.3 years of follow-up, up to December 1995. After excluding prevalent cases (except for epithelial skin tumors), a total of 2,335 subcohort men and 1,386 incident, microscopically or histologically confirmed, primary prostate cancer cases were available for analyses.

Physical Activity. The collected data on physical activity and other risk factors from subcohort and prostate cancer cases were key entered twice by research assistants who were blinded with respect to subcohort/case status to minimize observer bias in coding and interpretation of the data.

Baseline Nonoccupational Physical Activity. Assessment of baseline nonoccupational physical activity was based on two questions. The first question was ''How many minutes do you spend on average per day walking or cycling to your work, to go shopping or to take out your dog?'' The subjects could fill in the number of minutes per day they spent on these activities. The total time spent per day on these activities were categorized (<30, 30-60, 60-90, or >90 minutes per day). The second question was ''How many hours of your leisure time do you spend on average per week on the following activities: gardening/doing odd jobs, cycling/walking (other than in first question), and sports/exercise.'' Possible answers were never, <1, 1-2, or >2 h/wk. We added up the times spent on these activities to obtain an overall measure (in minutes per day). The subjects who engaged in a sport at baseline could also fill in the type of sport played. Baseline nonoccupational physical activity was calculated by adding up the number of minutes spent per day on biking/walking, shopping, and walking the dog and the number of hours spent per week on gardening/doing odd jobs, cycling/walking, and sports/exercise.

History of Sports Participation. Past sports activity was assessed by asking about the men's history of sports participation. For each type of sport, we recorded the number of hours per week spent on that sport, and the years in which the participant had engaged in the sport. A maximum of three sports could be mentioned. We first dichotomized the respondents as never/ever playing a sport. The total duration of sports activities in years was calculated by adding up the duration of all episodes of participation in a sport (accounting for any overlap between sports). The total numbers of hours per week that they had participated in each sport were also added up.

Occupational Physical Activity. Subjects were asked for the history of their last five occupations, with respect to job title and duration. In total, five jobs could be mentioned. We used information about the longest job ever held as well as information about the last occupation as indicators for the lifetime physical activity at work. Assessment of physical activity at work was based on job title. Two different measures of occupational physical activity have been used: (a) sitting time (hours per day) and (b) energy expenditure (kJ/min). The first measure was divided into three groups: low activity (>6 working hours per day spent sitting), moderate activity (2-6 hours per day sitting), and high activity (<2 working hours per day sitting). The second measure was based on a rating system developed by Hettinger et al. (24). Low activity included work with energy expenditure of <8 kJ/min, moderate activity was defined as energy expenditure between 8 and 12 kJ/min, and high activity corresponded to an activity level of >12 kJ/min.

Data Analysis. Previous analyses on prostate cancer in the NLCS revealed that age (years), alcohol intake from wine (g ethanol/d), BMI (kg/m^2), energy intake (kcal/d), family history (no/yes), and level of education (low, medium, and high) were risk factors of prostate cancer within the NLCS (4, 8, 25-27). These covariates were considered potential confounders in the current analysis. Their association with physical activity has been studied in the subcohort. When investigating specific nonoccupational physical activities, one activity has been adjusted by the other (Table 2).

Incidence rate ratios (RR) and corresponding 95% confidence intervals (95% CI) for prostate cancer were estimated in age-adjusted and multivariable case-cohort analyses using the Cox proportional hazards model (28) processed with the Stata statistical software package (29). SEs were estimated using the robust Huber-White sandwich estimator to account for additional variance introduced by sampling from the cohort (30). The proportional hazards assumption was tested using the scaled Schoenfeld residuals (31). Tests for dose-response trends in risk of prostate cancer were assessed by fitting ordinal exposure variables as continuous terms. Two-sided *P*s are reported throughout the article.

Subgroup analyses conditional on categories of BMI and tertiles of energy intake were done to evaluate interaction with physical activity.

Statistical tests for interaction were based on Wald statistics of the product term of these strata identifiers and baseline nonoccupational physical activity. Advanced prostate cancer

Table 1. Means and distributions of potential confounders according to levels of total baseline nonoccupational physical activity, history of sports participation, and occupational physical activity in the NLCS, 1986-1995 (subcohort men, *n* = 2,335)

Characteristics	Baseline nonoccupational physical activity (min/d)				History of sports participation		Occupational physical activity (energy expenditure in longest held job), kJ/min		
	<30	30-60	61-90	>90	No	Yes	<8	8-12	>12
Mean age (y)	61.50	61.22	60.82	61.67	61.50	61.22	61.12	61.55	61.22
Mean alcohol intake (g/d)*	3.67	4.01	4.64	3.76	3.03	4.84	5.41	2.69	1.96
Mean BMI (kg/m^2)	25.34	24.86	25.02	24.87	24.96	25.00	24.74	25.13	25.28
Mean energy intake (kcal/d)	2,069	2,135	2,169	2,197	2,135	2,154	2,139	2,118	2,262
Family history (%)									
No	97.09	97.88	97.86	98.20	98.22	97.28	96.71	98.53	98.80
Yes	2.91	2.12	2.14	1.80	1.78	2.72	3.29	1.47	1.20
Level of education (%)									
Low	54.40	42.31	40.10	52.79	57.85	38.38	25.78	66.30	80.91
Medium	30.02	35.04	38.66	33.52	29.60	38.63	43.23	29.10	17.88
High	15.58	22.65	21.24	13.69	12.56	22.99	30.99	4.60	1.21

*g ethanol intake/d from wine.

Table 2. Age-adjusted and multivariable RRs of prostate cancer according to baseline nonoccupational physical activity: the NLCS, 1986-1995

	Cases	PY	RR*	RR	L 95% CI	H 95% CI	P_{trend}
Total nonoccupational physical activity (min/d)							
<30	245	5,014	1.00†	1.00†			0.67‡
30-60	417	8,542	1.01	0.99‡	0.79‡	1.23‡	
61-90	269	5,061	1.19	1.19‡	0.94‡	1.52‡	
>90	421	8,417	0.99	1.01‡	0.81‡	1.25‡	
Daily biking/walking (min/d)							
<10	493	9,462	1.00†	1.00†			0.50§
10-30	277	5,992	1.00	0.92§	0.75§	1.14§	
31-60	332	6,170	1.13	1.13§	0.93§	1.38§	
>60	250	5,409	0.83	0.85§	0.69§	1.05§	
Gardening/doing odd jobs (h/wk)							
<1	403	8,080	1.00†	1.00†			0.90∥
1-2	288	5,669	1.13	1.08∥	0.88∥	1.34∥	
>2	664	13,308	1.01	1.00∥	0.84∥	1.19∥	
Sports/gymnastics (h/wk)							
<1	1,104	22,438	1.00†	1.00†			0.30¶
1-2	143	2,389	1.35	1.30¶	1.01¶	1.67¶	
>2	108	2,229	1.06	1.04¶	0.79¶	1.36¶	

*Age-adjusted.
†Reference category.
‡Multivariable analysis adjusted for age (y), alcohol intake from wine (g ethanol/d), BMI (kg/m^2), energy intake (kcal/d), family history (no/yes), level of education (low, medium, and high).
§Multivariable analysis adjusted for age (y), alcohol intake from wine (g ethanol/d), BMI (kg/m^2), energy intake (kcal/d), family history (no/yes), level of education (low, medium, and high), gardening/doing odd jobs (<1, 1-2, >2 h/wk), and sport/gymnastics (<1, 1-2, >2 h/wk).
∥Multivariable analysis adjusted for age (y), alcohol intake from wine (g ethanol/d), BMI (kg/m^2), energy intake (kcal/d), family history (no/yes), level of education (low, medium, and high), daily biking/walking (<10, 10-30, 31-60, >60 min/d), and sport/gymnastics (<1, 1-2, >2 h/wk).
¶Multivariable analysis adjusted for age (y), alcohol intake from wine (g ethanol/d), BMI (kg/m^2), energy intake (kcal/d), family history (no/yes), level of education (low, medium, and high), biking/walking (<10, 10-30, 31-60, >60 min/d), and gardening/doing odd jobs (<1, 1-2, >2 h/wk).

cases (T3-4, M0 and T0-4, M1) were evaluated separately from localized cases (T0-2, M0) to test the hypothesis that physical activity is more strongly inversely related to advanced prostate tumors.

Results

Table 1 presents the overall means of the continuous potential confounders and distributions of categorical variables stratified by baseline nonoccupational physical activity, history of sports participation, and occupational physical activity among subcohort men. Neither age, alcohol intake, BMI, nor energy intake was differently distributed across the different categories of physical activity. Men with a positive family history of prostate cancer seemed less active at baseline or during their longest held occupation, although they have engaged in sports more frequently in the past compared with men without a positive family history. In the past, men with a lower level of education seemed to have participated less in sports but were occupationally more active compared with men with higher levels of education, although at baseline, no differences in nonoccupational physical activity could be found (Table 1).

Baseline Nonoccupational Physical Activity. Baseline nonoccupational physical activity (daily walking, biking combined with gardening/doing odd jobs, and sports) showed no association with prostate cancer risk (Table 2). Age-adjusted and multivariable adjusted analysis showed comparable results. In this and upcoming analyses, the results of multivariable adjusted analyses will be presented. Men who were active for >90 minutes a day had a RR of 1.01 (95% CI, 0.81-1.25; P_{trend} = 0.67) compared with men who were active less than half an hour a day. The several aspects of baseline nonoccupational physical activity showed the following relations: men who walked/biked for >1 hour a day had a RR of 0.85 (95% CI, 0.69-1.05; P_{trend} = 0.50) compared with men who did these activities in <10 minutes a day. Gardening/doing odd jobs and sports participation were also not related to prostate cancer risk. Men who did these activities for >2 hours a week had a RR of 1.00 (95% CI, 0.84-1.19; P_{trend} = 0.90) and RR of 1.04 (95% CI, 0.79-1.36; P_{trend} = 0.30), respectively, compared with men who did these activities of <1 hour a week (Table 2).

History of Sports Participation. Men who reported to have ever engaged in a sport had no reduction in prostate cancer risk compared with men who never played a sport. The corresponding RR was 1.04 (95% CI, 0.90-1.22; Table 3). Sporting frequency (hours sport per week) showed no association with prostate cancer risk. Men who participated <1, 1-2, 2-3, 3-5, and >5 hours per week in sports had RRs of 1.14, 0.95, 1.24, 1.12, and 0.98 (95% CI, 0.81-1.19; P_{trend} = 0.80), respectively, compared with men not participating in sports. The total duration of sports in years showed no relation with prostate cancer. Men who played a sport longer than 40 years had a RR of 1.27 (95% CI, 0.87-1.84) compared with men who have not played sport (Table 3).

Table 3. Age-adjusted and multivariable RRs of prostate cancer according to history of sports participation and occupational physical activity: the NLCS, 1986-1995

	Cases	PY	RR*	RR†	L 95% CI†	H 95% CI†	P_{trend}†
History of sports participation							
Never	666	13,365	1.00‡	1.00‡			0.57
Ever	697	13,827	1.06	1.04	0.90	1.22	
Frequency (h/wk)							0.80
<1	41	860	1.15	1.14	0.73	1.79	
1-2	107	2,259	0.95	0.95	0.72	1.25	
2-3	105	1,949	1.21	1.24	0.93	1.64	
3-5	141	2,762	1.12	1.12	0.87	1.44	
>5	303	5,998	1.01	0.98	0.81	1.19	
Duration (y)							0.23
1-10	257	5,798	0.92	0.93	0.76	1.13	
11-20	202	3,615	1.20	1.17	0.94	1.47	
21-30	102	2,042	1.06	1.04	0.78	1.39	
31-40	57	1,144	1.01	0.99	0.68	1.43	
>40	67	1,028	1.28	1.27	0.87	1.84	
Occupational physical activity							
Longest held job							
Energy expenditure (kJ/min)							0.81
<8	655	13,539	1.00‡	1.00‡			
8-12	318	6,215	1.03	1.14	0.93	1.39	
>12	154	3,618	0.81	0.91	0.70	1.18	
Sitting time (h/d)							0.22
6-8	254	5,709	1.00‡	1.00‡			
2-6	539	10,659	1.12	1.14	0.93	1.40	
<2	334	7,004	1.04	1.16	0.91	1.47	
Last held job							
Energy expenditure (kJ/min)							0.77
<8	712	14,542	1.00‡	1.00‡			
8-12	294	5,983	0.98	1.07	0.88	1.32	
>12	162	3,738	0.82	0.93	0.72	1.20	
Sitting time (h/d)							0.57
6-8	274	6,125	1.00‡	1.00‡			
2-6	584	11,314	1.18	1.20	0.98	1.45	
<2	310	6,823	0.98	1.06	0.83	1.34	

*Age-adjusted.
†Multivariable analysis adjusted for age (y), alcohol intake from wine (g ethanol/d), body mass index (kg/m^2), energy intake (kcal/day), family history (no/yes), level of education (low, medium, and high).
‡Reference category.

Table 4. Multivariable adjusted RRs of prostate cancer according to categories of baseline nonoccupational physical activity (min/d), stratified by baseline BMI, and energy intake: the NLCS, 1986-1995

	Cases	PY	RR	L 95% CI	H 95% CI
Baseline BMI					
Normal (<25 kg/m^2)					
<1 h/d	307	6,573	1.00*,†		
>1 h/d	376	7,241	1.12	0.91	1.38
Overweight (25-30 kg/m^2)					
<1 h/d	305	5,833	1.00*,†		
>1 h/d	287	5,557	1.02	0.82	1.27
Obese (>30 kg/m^2)					
<1 h/d	22	569	1.00*,†		
>1 h/d	18	417	1.63	0.62	4.26
Baseline energy intake					
Tertile 1 (low)					
<1 h/d	261	4,793	1.00*,‡		
>1 h/d	208	4,125	0.91	0.70	1.17
Tertile 2 (median)					
<1 h/d	224	4,612	1.00*,‡		
>1 h/d	267	4,659	1.29	1.00	1.66
Tertile 3 (high)					
<1 h/d	177	4,150	1.00*,‡		
>1 h/d	215	4,694	1.30	0.89	1.91

*Reference category.
†Multivariable analysis adjusted for age (y), alcohol intake from wine (g ethanol/d), energy intake (kcal/d), family history (no/yes), level of education (low, medium, and high).
‡Multivariable analysis adjusted for age (y), alcohol intake from wine (g ethanol/d), BMI (kg/m^2), family history (no/yes), level of education (low, medium, and high).

Occupational Physical Activity. Men with a high energy expenditure (>2 kJ/min) in the longest held job showed no altered risk (RR, 0.91; 95% CI, 0.70-1.18) compared with those with low energy expenditure (<8 kJ/min; Table 3). Comparable results were found for energy expenditure in the last held job. Men with a high energy expenditure (>12 kJ/min) in the last held job showed no altered risk of prostate cancer (RR, 0.93; 95% CI, 0.72-1.20) compared with men with a last held job with low energy expenditure (<8 kJ/min). No relation was found between total number of sitting hours per day in the longest or last held job and prostate cancer risk (Table 3). Combined analyses of both occupational and nonoccupational physical activity did not reveal substantially altered incidence rates in any of the subgroups (results not shown).

Effect in Subgroups. We stratified the data according to baseline BMI and energy intake (Table 4). Although BMI did not seem a statistical significant effect modifier ($P = 0.63$), we found an increased risk of prostate cancer for obese (BMI >30) men being physically active for >1 hour per day (RR, 1.63; 95% CI, 0.62-4.26; Table 4). The number of cases was small in this subgroup; however, a similar but less strong pattern was found after stratification for energy intake, which was a marginally statistically nonsignificant effect modifier ($P = 0.07$). Men in the two highest tertiles of energy intake being active for >1 hour per day also seemed to have increased prostate cancer risk compared with those experiencing lower levels of energy intake. The corresponding RRs were 1.29 (95% CI, 1.00-1.66) and 1.30 (95% CI, 0.89-1.91), respectively, for those in the second and third tertiles of energy intake (Table 4).

Prostate Cancer Stage. Of all prostate cancer cases, 526 were rated to be localized (T0-2, M0) and 453 were rated to be advanced (T3-4, M0 and T0-4, M1). The association between baseline nonoccupational physical activity and prostate cancer seemed comparable for localized and advanced tumors (Table 5).

Discussion

The results of the current study do not support the hypothesis that physical activity protects against prostate cancer in men. Neither baseline nonoccupational physical activity, history of sports participation, nor occupational physical activity showed an inverse relation with prostate cancer risk. We found an increased risk of prostate cancer in the subgroups of obese men (BMI >30) and men with a high baseline energy intake who were physically active for >1 hour a day. The subgroup analyses were, however, based on a small number of cases.

Before discussing the results of the current study in relation with other studies, some remarks concerning the NLCS are relevant. Loss to follow-up is the primary source of potential selection in prospective cohort studies. The prospective nature of a cohort study together with completeness of follow-up, as has been achieved in the current study, reduces the potential for selection bias to a minimum (23). Because we considered the most important potential confounding factors reported in the literature, we believe that only unknown or unmeasured other factors may have caused residual confounding.

Measuring physical activity in epidemiologic studies is difficult, and different methods have been used, which may explain in part the inconsistent results across studies (32). Studies have differed with regard to the period for which physical activity was assessed (e.g., childhood/adolescence and lifetime), the sources of physical activity (e.g., nonoccupational, occupational, or both), various variables of activity (e.g., frequency, intensity, and duration), and the range of physical activity. In this study, the baseline nonoccupational physical activity was measured by several aspects, including gardening/doing odd jobs, biking/walking during leisure time, daily walking and biking (leaving out walking the dog and go shopping), and playing sports/gymnastics (33).

We made use of the history of sports participation as indicator for physical activity in the past. We have no complete overview of all the elements of past physical activity (e.g., gardening and housekeeping activities were not included). Misclassification might play a role in determining the exposure status of the participants early in life. Such misclassification would be nondifferential.

Comparing the results of this large scale prospective cohort study with other cohort studies shows that the results are consistent with some other studies (34-38). These studies also

Table 5. Multivariable adjusted RRs of prostate cancer according to categories of baseline nonoccupational physical activity (min/d) in subgroups of localized (T0-2, M0) and advanced (T3-4, M0 and T0-4, M1) prostate tumors: the NLCS, 1986-1995

	Cases	PY	RR*	L 95% CI	H 95% CI	P_{trend}†
Stage prostate cancer						
Localized (min/d)						
<30	88	3,671	1.00†			0.52
30-60	156	6,186	0.97	0.71	1.33	
61-90	101	3,583	1.22	0.87	1.70	
>90	165	6,130	1.05	0.77	1.42	
Advanced (min/d)						
<30						0.78
30-60	84	3,671	1.00†			
61-90	136	6,186	0.98	0.71	1.36	
>90	88	3,583	1.18	0.83	1.67	

*Multivariable analysis adjusted for age (y), alcohol intake from wine (g ethanol/d), BMI (kg/m^2), energy intake (kcal/d), family history (no/yes), level of education (low, medium, and high).
†Reference category.

found no inverse relation between physical activity and prostate cancer risk. However, other cohort studies showed inverse associations with prostate cancer in general (39, 40) or between very frequent vigorous activity and progressive prostate cancer (34, 38, 41). In addition, one cohort study reported a positive association between physical activity and prostate cancer (42).

A weak age-adjusted inverse relation between occupational physical activity and prostate cancer was found in our study which is consistent with the studies of Hartman et al. (43) and Lund Nilsen et al. (44). However, the analyses may have been confounded because these could not be confirmed in multivariable analyses. Furthermore, occupational physical activity is based on job title in this study, which may not be an accurate marker for the actual level of physical activity, incurred on the job.

Case-control studies show inconsistent results as well. Five studies found an inverse relation between physical activity and prostate cancer risk (45-49), another five found no relation (47, 50-53), and one study found a positive association (54). Odds ratios in these studies varies from 0.6 to 2.2 and the assessment of physical activity varied from recreational activity during puberty, complete lifetime occupational history, and time spent in moderate and vigorous current recreational activities converted to calories. To compare these studies is very difficult (16).

The main aim of the NLCS was to investigate the relationship between diet and the risk of cancer and not specifically aimed at physical activity. An advantage of this large-scale prospective cohort study was the possibility to study interaction among the different aspects of energy balance (physical activity, energy intake, and BMI) and to study subgroup analysis. As the results showed, no interaction was found between baseline nonoccupational physical activity and BMI or baseline energy intake, although in men with a high BMI (>30 kg/m^2), a positive relation was seen between baseline nonoccupational physical activity and prostate cancer risk, independent of baseline energy intake. In addition, men who participated in sports for >40 years showed increased prostate cancer risk. Taking these two observations together (high BMI can also equate to high lean mass, and long-term participation in sports may be the result of or a contributor to greater muscularity), a possible explanation for the positive association that these men were those with greater androgenicity and that this greater androgenicity may have accounted for the modest increase in prostate cancer risk. We also observed a positive association between physical activity and prostate cancer risk among men with a high energy intake. This result was also found in the study of Platz et al. (55). The balance of physical activity and energy intake with body size might play a role in this result (56). Energy intake is determined by basal metabolic rate, activity level, and body size. Highly active men will probably have higher energy intakes compared with inactive people. An imbalance between energy intake and physical activity may yield increased BMI values. In overweight and obese men, multiple physiologic systems are perturbed such as insulin and glucose control and the balance of sex steroids. The specific mechanisms underlying how energy imbalance might affect prostate cancer (reduce or enhance prostate carcinogenesis) are still to be resolved.

Further research should be concentrated on the interrelation of physical activity, energy intake, and body size. Until now, it is unclear in what way and which pattern of energy imbalance will reduce or enhance prostate carcinogenesis (55). Further studies need also to investigate the frequency, intensity, and duration of physical activity as well as the type of activity and period during a man's lifetime when exercise might be beneficial. In addition, the possible biological mechanisms warrant further study.

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