

*Short Communication***Recreational Physical Activity and Risk of Prostate Cancer in a Large Cohort of U.S. Men**

Alpa V. Patel, Carmen Rodriguez, Eric J. Jacobs, Laura Solomon, Michael J. Thun, and Eugenia E. Calle

Department of Epidemiology and Surveillance Research, American Cancer Society, Atlanta, Georgia

**Abstract**

Physical activity has been proposed as a modifiable risk factor for prostate cancer because of its potential effects on circulating hormones such as testosterone and insulin. We examined the association of various measures of physical activity with prostate cancer risk among men in the American Cancer Society Cancer Prevention Study II Nutrition Cohort, a large prospective study of U.S. adults. Information on recreational physical activity was obtained from a self-administered questionnaire completed at cohort enrollment in 1992/1993, as well as from a questionnaire completed as part of an earlier study in 1982. During the 9-year prospective follow-up, 5,503 incident prostate cancer cases were identified among 72,174 men who were cancer-free at enrollment. Cox proportional hazards modeling was used to compute hazard rate ratios (RR) for measures of recreational physical activity and to adjust for potential confounding factors. We observed no difference in risk of prostate cancer between men who engaged in the highest

level of recreational physical activity (>35 metabolic equivalent-hours/wk) and those who reported no recreational physical activity at baseline (RR, 0.90; 95% confidence interval, 0.78-1.04; *P* for trend = 0.31). We also did not observe an association between prostate cancer and recalled physical activity at age 40 or exercise reported in 1982. However, the incidence of aggressive prostate cancer was inversely associated with >35 metabolic equivalent-hours/wk of recreational physical activity compared with that in men who reported no recreational physical activity (RR, 0.69; 95% confidence interval, 0.52-0.92; *P* for trend = 0.06). Our findings are consistent with most previous studies that found no association between recreational physical activity and overall prostate cancer risk but suggest physical activity may be associated with reduced risk of aggressive prostate cancer. (Cancer Epidemiol Biomarkers Prev 2005;14(1):275-9)

**Introduction**

Prostate cancer is the leading cause of cancer incidence and the second leading cause of cancer mortality in U.S. men (1). Age, race, family history, and possibly lycopene intake are the only established risk factors for prostate cancer; of these, only lycopene intake is modifiable (2). Physical activity, because it can decrease circulating levels of sex hormones and insulin that promote the proliferation of prostate cells, has been proposed as another modifiable prostate cancer risk factor (3, 4).

Epidemiologic studies on the association between physical activity and prostate cancer are inconclusive. Four (5-8) of 18 observational studies (5-22) suggest that physical activity may reduce prostate cancer risk but the majority do not. Two studies report that the inverse association is limited to more vigorous physical activity and/or to aggressive prostate cancer. A high level of vigorous physical activity was associated with lower risk of metastatic prostate cancer in a large prospective study of U.S. men [rate ratio (RR), 0.46; 95% confidence interval (95% CI), 0.24-0.89], but no association was seen between total physical activity and all or metastatic prostate cancer (6). Similarly, a high level of vigorous physical activity was associated with lower prostate cancer risk in a Canadian case-control study (RR, 0.70; 95% CI, 0.54-0.92; ref. 8). Recreational physical activity also was inversely associated with prostate

cancer risk among men attending a screening center in Norway (RR, 0.80; 95% CI, 0.62-1.00; ref. 5) and in a cohort of middle-aged British men (RR, 0.25; 95% CI, 0.06-0.99; ref. 7).

It remains unclear whether recreational physical activity is associated with prostate cancer risk and whether the association varies by type, dose (e.g., frequency, duration, intensity) or time period in life of physical activity or the stage at prostate cancer diagnosis. Therefore, we examined the association between various measures of physical activity and prostate cancer risk among men in the American Cancer Society Cancer Prevention Study II (CPS-II) Nutrition Cohort, a large prospective study in the United States.

**Methods**

**Study Population.** Men in this analysis were drawn from the 86,404 male participants in the CPS-II Nutrition Cohort, which was established by the American Cancer Society in 1992 as a subgroup of the larger 1982 CPS-II baseline cohort (23). Most participants were ages 50 to 74 years at enrollment in 1992. At baseline, they completed a 10-page self-administered questionnaire that included questions on demographic, medical, behavioral, environmental, and dietary factors. Follow-up questionnaires were sent to cohort members in 1997 to 1998, 1999 to 2000, and 2001 to 2002 to update exposure information and to ascertain newly diagnosed cancers. Questionnaire response rates among living cohort members are at least 90%.

We excluded from the analyses men who were lost to follow-up from 1992 to 2001 (*n* = 3,431), who reported prevalent cancer (except nonmelanoma skin cancer) at baseline (*n* = 9,004), or who did not complete the section on recreational

Received 5/13/04; revised 7/7/04; accepted 7/20/04.

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked advertisement in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

**Requests for reprints:** Alpa V. Patel, Epidemiology and Surveillance Research, American Cancer Society, National Home Office, 1599 Clifton Road Northeast, Atlanta, GA 30329-4251. Phone: 404-329-7726; Fax: 1-404-327-6450. E-mail: Alpa.Patel@cancer.org  
Copyright © 2005 American Association for Cancer Research.

physical activity at baseline ( $n = 1,122$ ). We also excluded reported cases of prostate cancer that could not be verified through medical or cancer registry records ( $n = 623$ ), and stage I prostate cancer cases ( $n = 50$ ). After all exclusions, the final analytic cohort consisted of 72,174 men with a mean age at study entry of 63.9 ( $\pm 6.1$  SD) years.

**Case Ascertainment.** A total of 5,503 verified incident cases of fatal and nonfatal prostate cancer diagnosed between the date of enrollment and August 31, 2001 were included in this analysis. Of these, 5,290 cases were identified initially by self-report on a follow-up questionnaire and subsequently verified from medical records ( $n = 4,361$ ) or linkage with state cancer registries ( $n = 929$ ). A small number ( $n = 110$ ) of incident prostate cancer cases also were identified during confirmation of another reported cancer diagnosis. Incident cases ( $n = 103$ ) were identified as interval deaths through automated linkage of the entire cohort with the National Death Index (24). For these cases, prostate cancer was listed as the primary cause of death (International Classification of Diseases, Ninth Revision, codes 185.0-185.9; Tenth Revision, codes C61.0-C61.9; refs. 25, 26) during the interval between the date of enrollment and December 31, 2000. For 72 interval deaths, additional information was obtained through linkage with state cancer registries. We further classified prostate cancer cases as "nonaggressive" ( $n = 4,160$ ) or "aggressive" ( $n = 1,343$ ) based on information from the medical or registry records. Aggressive prostate cancers were defined as (a) cases diagnosed at stages III and IV or Gleason Score of 8 or higher or grades 3 to 4 on medical records, (b) cases verified by a state cancer registry and classified as regional or distant, or (c) prostate cancer deaths.

**Physical Activity Measures.** Baseline recreational physical activity information was collected using the question "During the past year, what was the average time per week you spent at the following kinds of activities: walking, jogging/running, lap swimming, tennis or racquetball, bicycling or stationary biking, aerobics/calisthenics, and dancing?" Response to each activity included "none," "1 to 3 hours per week," "4 to 6 hours per week," or ">7 hours per week." Summary metabolic equivalent (MET)-hours/wk were calculated for each participant. A MET is the ratio of metabolic rate during a specific activity to resting metabolic rate (27). Due to the older age of this population, the summary MET score for each participant was calculated by multiplying the lowest number of hours within each category times the moderate intensity MET score for each activity according to the Compendium of Physical Activities (27) to provide conservatively estimated summary measures. The MET scores for various activities were (27) 3.5 for walking, 7.0 for jogging/running, 7.0 for lap swimming, 6.0 for tennis or racquetball, 4.0 for bicycling/stationary biking, 4.5 for aerobics/calisthenics, and 3.5 for dancing.

The baseline questionnaire also asked participants to recall physical activity at age 40 using the question, "At age 40, what was the average time per week you spent at the following kinds of activities: walking, jogging/running, lap swimming, tennis or racquetball, bicycling or stationary biking, aerobics/calisthenics, and dancing?" A summary MET score at age 40 was created using the same method described above. Recreational physical activity at baseline and age 40 were categorized in MET-hours/wk as none, >0 to 7, >7 to 14, >14 to 21, >21 to 28, >28 to 35, or >35. Another measure of past physical activity was obtained from a questionnaire completed in 1982, when participants in the CPS-II Nutrition Cohort were enrolled in the large CPS-II mortality study. The 1982 questionnaire asked "How much exercise do you get (work or play): none, slight, moderate, heavy?" Physical activity in 1982 was categorized as none, slight, moderate, or heavy. Physical activity at age 40 (as recalled in 1992) and activity reported in 1982 were examined together with baseline 1992 exposure information to assess whether risk of prostate cancer was reduced among men who consistently reported being physically active.

**Statistical Analysis.** We used Cox proportional hazards modeling (28) to calculate hazards RR and corresponding 95% CI to examine the relationship between measures of recreational physical activity and prostate cancer. For each physical activity exposure variable, we assessed risk in two models, one adjusted only for age and race, and the other adjusted for age, race, and other potential confounding factors. All Cox models were stratified on exact year of age at enrollment and race (white, black, and other). Potential confounders included in the multivariate models were body mass index (weight in kg/height in  $m^2$ ; <22.0, 22.0 to <25.0, 25.0 to <27.0, 27.0 to <30.0, 30.0 to <35.0,  $\geq 35.0$ , and missing), weight change from age 18 to 1992 (>5 lb. loss, 5 loss to 5 gain, 6-10 gain, 11-15 gain, 16-20 gain, 21-25 gain, 36-30 gain, 31-35 gain, 36-40 gain, 41-45 gain, 46-50 gain, >50 gain, and missing), personal history of diabetes (no, < 10 or  $\geq 10$  years since diagnosis), long-term multivitamin use (nonuser, occasional use, past regular use, recent regular use, long-term regular use, and missing), daily caloric intake (quartiles), daily calcium intake (quartiles), daily lycopene intake (quartiles), weekly servings of red meat (quartiles), and family history of prostate cancer (yes and no). Information on history of prostate-specific antigen (PSA) testing was first collected in the 1997 questionnaire and was included in multivariate models as a time dependent covariate starting in 1997. We also examined the relationship between recreational physical activity and prostate cancer separately for nonaggressive and aggressive disease.

Trend tests for baseline and age 40 physical activity models were calculated by assigning the median MET value within each category to that category. Trend tests for physical activity in 1982 were obtained by using an ordinal variable corresponding with each level of physical activity. To test whether any of the potential confounders described above modified the association between recreational physical activity and prostate cancer risk, we constructed multiplicative interaction terms with all other risk factors. Due to small numbers in some strata, categories of potential effect modifiers were sometimes collapsed. Statistical interaction was assessed in multivariate models using the likelihood ratio test and a  $P < 0.05$  was considered statistically significant (29).

## Results

Approximately 12% ( $n = 8,881$ ) of men reported no recreational physical activity at baseline (Table 1). Among physically active men (defined as those reporting any recreational physical activity at baseline), the median MET expenditure was 14.0 MET-hour/wk, corresponding to ~4 hours of moderately paced walking per week. Physically active men, regardless of level of MET expenditure, engaged primarily in activities judged to be of low intensity (walking, biking, aerobics/calisthenics, or dancing) rather than moderate or high intensity (jogging/running, swimming, or tennis/racquetball). Physically active men were more likely to be lean and less likely to have gained weight since age 18 years. Physically active men also were more likely to have no history of diabetes, use multivitamins, have higher daily intake of calcium and lycopene, and eat fewer servings of red meat (Table 1). The age-adjusted percentage of men reporting PSA testing on the 1997 and/or the 1999 questionnaire was higher among active (81.3%) than inactive men (70.5%).

No association was observed between the level of recreational physical activity at baseline and the overall risk of prostate cancer in this study (Table 2). Men in the highest category of recreational physical activity (>35.0 MET-hour/wk) had 10% lower risk of prostate cancer (RR, 0.90; 95% CI, 0.78-1.04) than men who reported no physical activity at baseline (Table 2). The test for trend was not statistically significant

**Table 1. Selected characteristics in relation to baseline recreational physical activity MET expenditure among 72,174 men in the CPS-II Nutrition Cohort, 1992 to 2001**

Characteristic	Recreational leisure time activity MET expenditure				
	None	>0-7	>7-21	>21-35	>35
No. participants (%)	8,881 (12.3)	21,611 (29.9)	24,962 (34.6)	12,666 (17.6)	4,054 (5.6)
Median MET-h/wk	0	3.5	14.0	24.5	45.5
Low-intensity activity hours* (%)	N/A	97.0	91.5	89.2	65.9
Age at baseline (mean ± SE)	63.5 ± 0.07	63.7 ± 0.04	64.1 ± 0.04	64.4 ± 0.05	63.9 ± 0.09
BMI (weight kg/height m <sup>2</sup> , mean ± SE)	27.2 ± 0.04	26.8 ± 0.02	26.2 ± 0.02	26.0 ± 0.03	25.5 ± 0.06
Weight change (lbs., age 18 to 1992, mean ± SE)	37.3 ± 0.27	35.2 ± 0.17	30.6 ± 0.16	29.0 ± 0.23	23.6 ± 0.40
Personal history of diabetes (%)	10.7	9.7	8.3	8.3	6.5
Long-term multivitamin use (%)	7.6	10.4	12.3	11.7	14.7
Daily caloric intake (kcal, mean ± SE)	1,903.6 ± 6.9	1,781.7 ± 4.4	1,759.7 ± 4.0	1,851.2 ± 5.7	1,824.4 ± 10.0
Daily calcium intake (mg, mean ± SE)	819.1 ± 4.6	873.3 ± 2.9	914.6 ± 2.7	905.5 ± 3.9	970.5 ± 6.8
Daily lycopene intake (µg, mean ± SE)	4,030.6 ± 36.3	4,488.6 ± 23.1	4,946.9 ± 21.4	4,956.0 ± 30.2	5,653.3 ± 53.0
Servings of red meat/wk (mean ± SE)	6.7 ± 0.05	5.7 ± 0.03	5.1 ± 0.03	5.4 ± 0.04	4.5 ± 0.07
Family history of prostate cancer (%)	10.2	10.5	10.7	10.6	10.5

NOTE: All values (except age and median MET-hours) are standardized to the age distribution of the study population.

\*% Total activity hours that are low intensity (walking, biking, dancing, or aerobics).

with ( $P$  for trend = 0.31) or without ( $P$  for trend = 0.53) inclusion of men who reported no recreational physical activity. Similarly, no association was seen between moderate/high intensity activity (jogging/running, swimming, and tennis/racquetball) physical activity and prostate cancer risk (data not shown).

Men reporting any level of recreational physical activity had lower rates of aggressive prostate cancer compared with men

who reported no physical activity (Table 3). Physical activity of  $\geq 35$  MET-hours/wk was associated with a 31% lower risk of aggressive prostate cancer at diagnosis (RR, 0.69; 95% CI, 0.52-0.92;  $P$  for trend = 0.06; Table 3); however, no statistically significant dose response was seen with increasing level of physical activity and the incidence of aggressive prostate cancer when the analysis was restricted to active men ( $P$  for trend = 0.57).

**Table 2. RRs for recreational leisure time physical activity at various times during a man's lifetime and prostate cancer, CPS-II Nutrition Cohort, 1992 to 2001**

	No. cases/person-years	RR* (95% CI)	RR† (95% CI)
MET-h/wk in 1992‡			
None	624/64,652	1.00 (reference)	1.00 (reference)
>0-7	1,577/163,315	0.98 (0.89-1.07)	0.95 (0.87-1.05)
>7-14	1491/142,298	1.04 (0.95-1.14)	1.00 (0.91-1.09)
>14-21	553/48,431	1.13 (1.01-1.27)	1.07 (0.95-1.20)
>21-28	657/69,505	0.93 (0.83-1.03)	0.89 (0.79-0.99)
>28-35	297/27,203	1.08 (0.94-1.24)	1.02 (0.89-1.18)
>35	304/31,437	0.96 (0.84-1.11)	0.90 (0.78-1.04), $P^{\S}$ for trend = 0.31
MET-h/wk at age 40			
None	870/90,934	1.00 (reference)	1.00 (reference)
>0-7	1,418/137,082	1.09 (1.00-1.18)	1.07 (0.98-1.16)
>7-14	1,059/103,255	1.08 (0.99-1.18)	1.06 (0.97-1.16)
>14-21	448/45,049	1.04 (0.93-1.17)	1.01 (0.90-1.14)
>21-28	762/75,869	1.01 (0.91-1.11)	1.00 (0.91-1.10)
>28-35	323/29,767	1.12 (0.98-1.27)	1.09 (0.96-1.24)
>35	541/57,685	0.99 (0.89-1.10)	0.96 (0.86-1.07), $P^{\S}$ for trend = 0.15
Exercise in 1982¶			
None	97/8,383	1.00 (reference)	1.00 (reference)
Slight	1,261/133,563	0.82 (0.66-1.00)	0.80 (0.65-0.98)
Moderate	3,424/336,119	0.84 (0.69-1.03)	0.81 (0.66-0.99)
Heavy	678/64,956	0.89 (0.72-1.10)	0.85 (0.69-1.05) $P^{\S}$ for trend = 0.72

\*Age- and/or race-adjusted RR and corresponding 95% CI.

†Multivariate-adjusted RR and 95% CI adjusted for: age, race, BMI in 1992, weight change from age 18 to 1992, personal history of diabetes, long-term multivitamin use, daily caloric intake in 1992, daily calcium intake in 1992, daily lycopene intake in 1992, weekly servings of red meat in 1992, family history of prostate cancer, and personal history of PSA testing.

‡MET-hours/wk based on the following activities reported at baseline in 1992: walking, jogging/running, bicycling, swimming, aerobics/calisthenics, tennis/racquetball, and dancing.

§Trend tests conducted in multivariate models.

||MET-hours/wk calculated same as above based on recall on 1992 survey of activity at age 40 [1001 men (82 cases) excluded for missing information].

¶Physical activity reported on 1982 CPS-II survey as "how much exercise do you get?": none, slight, moderate, or heavy [513 men (43 cases) excluded for missing information].

**Table 3. Rate ratios for baseline recreational leisure time physical activity and risk of nonaggressive and aggressive prostate cancer, CPS-II Nutrition Cohort, 1992 to 2001**

	No. cases/person-years	RR* (95% CI)
Nonaggressive prostate cancer <sup>†</sup>		
MET-h/wk in 1992 <sup>‡</sup>		
None	440/63,885	1.00 (reference)
>0-7	1,205/161,811	1.02 (0.92-1.14)
>7-21	1,549/188,800	1.07 (0.96-1.20)
>21-35	728/95,816	0.99 (0.88-1.11)
>35	238/31,182	0.98 (0.84-1.16), <i>P</i> for trend = 0.57
Aggressive prostate cancer <sup>†</sup>		
MET-h/wk in 1992 <sup>‡</sup>		
None	184/62,782	1.00 (reference)
>0-7	372/157,940	0.79 (0.66-0.94)
>7-21	495/183,771	0.87 (0.73-1.04)
>21-35	226/93,473	0.77 (0.63-0.94)
>35	66/30,327	0.69 (0.52-0.92), <i>P</i> for trend = 0.06

\*Multivariate-adjusted RR and 95% CI adjusted for age, race, BMI in 1992, weight change from age 18 to 1992, personal history of diabetes, long-term multivitamin use, daily caloric intake in 1992, daily calcium intake in 1992, daily lycopene intake in 1992, weekly servings of red meat in 1992, family history of prostate cancer, and personal history of PSA testing.

<sup>†</sup>Aggressive prostate cancers included cases (a) verified by medical records with stages III and IV at diagnosis, Gleason score of 8 or higher or grades 3 to 4, (b) cases verified by the state cancer registry and classified as regional or distant, and (c) prostate cancer deaths.

<sup>‡</sup>MET-hours/wk based on the following activities reported at baseline in 1992: walking, jogging/running, bicycling, swimming, aerobics/calisthenics, tennis/racquetball, and dancing.

We also examined the association of prostate cancer risk with physical activity at age 40 as recalled at baseline and with reported exercise levels in 1982 (Table 2). Neither physical activity at age 40 (RR, 0.96; 95% CI, 0.86-1.07 for >35 METs versus none; *P* for trend = 0.15) nor exercise reported in 1982 (RR, 0.85; 95% CI, 0.69-1.05 for heavy versus no exercise; *P* for trend = 0.72) were associated with risk of prostate cancer. Furthermore, being physically active across multiple time points was not associated with risk of total prostate cancer (data not shown). There were no statistically significant interactions between baseline recreational physical activity levels and any of the other potential risk factors included in this analysis (data not shown).

To assess whether PSA testing might confound the relationship between physical activity and prostate cancer risk, we conducted a sensitivity analysis starting follow-up in 1997 when information on PSA testing was first collected. During this follow-up period, physical activity (>35 MET-hours/wk) was not associated with risk of total prostate cancer (RR, 0.94; 95% CI, 0.76-1.17; *P* for trend = 0.32), but physical activity (>35 MET-hours/wk) was associated with risk of aggressive prostate cancer (RR, 0.51; 95% CI, 0.30-0.87; *P* for trend = 0.05; among active men, *P* for trend = 0.17).

## Discussion

In this cohort of elderly U.S. men, recreational physical activity was not associated with the overall risk of prostate cancer. No association was observed between past physical activity measures (at age 40 or 10 years before baseline) and prostate cancer risk. These findings are consistent with most previous studies that have examined the relationship between physical activity and prostate cancer risk (9-22). Being physically active, however, was associated with lower rates of aggressive prostate cancer. Similar findings were reported in the only previous study that has examined this relationship in an analysis of physical activity and metastatic prostate cancer (6).

There are several biological reasons why physical activity might inhibit the development of aggressive prostate cancer. First, physical activity may inhibit prostate cancer progression. Physical activity has been consistently associated with decreased levels of circulating insulin, and previous studies

have also observed, albeit less consistently, associations between physical activity and circulating levels of insulin-like growth factor-I, insulin-like growth factor binding proteins, and testosterone (30, 31). Two recent reports from prospective studies found that high circulating levels of insulin-like growth factor-I and low levels of IGFBP-3 may be associated with aggressive prostate cancer suggesting that insulin-like growth factor-I acts as a tumor promoter (32, 33).

The observed inverse association between physical activity and aggressive prostate cancer could also be due, in part, to confounding by PSA testing. In this study population, a history of PSA testing was slightly more common among physically active than inactive men. PSA testing would, in general, increase the overall incidence of prostate cancer diagnoses but decrease the incidence of tumors we defined as "aggressive." However, our sensitivity analysis that adjusted for history of PSA testing based on follow-up from 1997 found no evidence of confounding by PSA. Finally, chance remains a possible explanation for our finding in the subgroup of men with aggressive prostate cancer.

There are many strengths that should be mentioned including the prospective design, large sample size, and ability to adjust for known or hypothesized risk factors for prostate cancer. A limitation of this study is the assessment of physical activity since summary measures are based on frequency of physical activity with a lack of information of various time periods in life and imputed intensity. The lack of individual information on intensity of these activities increases the potential for misclassification of true energy expenditure. Another limitation is the limited range of recreational physical activities commonly done by our participants. Even among men reporting high levels of recreational physical activity, most engaged primarily in walking.

In summary, our findings are consistent with most previous studies that found no significant association between recreational physical activity and total prostate cancer risk. However, our results support an earlier finding that physical activity may be inversely associated with risk of aggressive prostate cancer. The type, intensity, and frequency of physical activity needed to affect risk remain unknown. Given the large number of men who develop prostate cancer and the paucity of modifiable risk factors, the possible relationship between physical activity and aggressive prostate cancer deserves further study.

## References

- American Cancer Society. Cancer facts & figures. Atlanta, GA: American Cancer Society; 2003.
- Gronberg H. Prostate cancer epidemiology. *Lancet* 2003;361:859–64.
- Oliveria SA, Lee IM. Is exercise beneficial in the prevention of prostate cancer? *Sports Medicine* 1997;23:271–8.
- Lee IM, Sesso HD, Chen J, Paffenbarger RS. Does physical activity play a role in the prevention of prostate cancer? *Epidemiologic Reviews* 2001;23:132–7.
- Lund Nilsson TI, Johnsen R, Vatten LJ. Socio-economic and lifestyle factors associated with the risk of prostate cancer. *British Journal of Cancer* 2000;82:1358–63.
- Giovannucci E, Leitzmann M, Spiegelman D, et al. A prospective study of physical activity and prostate cancer in male health professionals. *Cancer Research* 1998;58:5117–22.
- Wannamethee SG, Shaper AG, Walker M. Physical activity and risk of cancer in middle-aged men. *British Journal of Cancer* 2001;85:1311–6.
- Friedenreich CM, McGregor SE, Courneya KS, Angyalfi SJ, Elliott FG. Case-control study of lifetime total physical activity and prostate cancer risk. *American Journal of Epidemiology* 2004;159:740–9.
- Lee IM, Sesso HD, Paffenbarger RS. A prospective cohort study of physical activity and body size in relation to prostate cancer risk (United States). *Cancer Causes and Control* 2001;12:187–93.
- Lacey JV, Deng J, Dosemeci M, et al. Prostate cancer, benign prostatic hyperplasia and physical activity in Shanghai, China. *International Journal of Epidemiology* 2001;30:341–9.
- Cerhan JR, Torner JC, Lynch CF, et al. Association of smoking, body mass, and physical activity with risk of prostate cancer in the Iowa 65+ Rural Health Study (United States). *Cancer Causes and Control* 1997;8:229–38.
- Severson RK, Nomura AMY, Grove JS, Stemmermann GN. A prospective analysis of physical activity and cancer. *American Journal of Epidemiology* 1989;130:522–9.
- Lee IM, Paffenbarger RS, Hsieh C. Physical activity and risk of prostatic cancer among college alumni. *American Journal of Epidemiology* 1992;135:169–79.
- Thune I, Lund E. Physical activity and the risk of prostate and testicular cancer: a cohort study of 53,000 Norwegian men. *Cancer Causes & Control* 1994;5:549–56.
- Hartman TJ, Albanes D, Rautalahti M, et al. Physical activity and prostate cancer in the  $\alpha$ -Tocopherol  $\beta$ -Carotene (ATBC) Cancer Prevention Study (Finland). *Cancer Causes & Control* 1998;9:11–8.
- Clarke G, Whittemore AS. Prostate cancer risk in relation to anthropometry and physical activity: The National Health and Nutrition Examination Survey I Epidemiological Follow-up Survey. *Cancer Epidemiology, Biomarkers & Prevention* 2000;9:875–81.
- Liu S, Lee IM, Linson P, Ajani U, Buring JE, Hennekens CH. A prospective study of physical activity and risk of prostate cancer in US physicians. *International Journal of Epidemiology* 2000;29:29–35.
- Whittemore AS, Kolonel LN, Wu AH, et al. Prostate cancer in relation to diet, physical activity, and body size in Blacks, Whites, and Asians in the United States and Canada. *Journal of the National Cancer Institute* 1995;87:652–61.
- West DW, Slattery ML, Robinson LM, French TK, Mahoney AW. Adult dietary intake and prostate cancer risk in Utah: a case-control study with special emphasis on aggressive tumors. *Cancer Causes & Control* 1991;2:85–94.
- Andersson SO, Baron J, Wolk A, Lindgren C, Bergstrom R, Adami HO. Early life risk factors for prostate cancer: a population-based case-control study in Sweden. *Cancer Epidemiology Biomarkers & Prevention* 1995;4:187–92.
- Sung JFC, Lin RS, Pu Y, Chen Y, Chang HC, Lai M. Risk factors for prostate carcinoma in Taiwan: a case-control study in a Chinese population. *Cancer* 1999;86:484–91.
- Villeneuve PJ, Johnson KC, Kreiger N, Mao Y. The Canadian Cancer Registries Epidemiology Research Group. Risk factors for prostate cancer: results from the Canadian National Enhanced Cancer Surveillance System. *Cancer Causes & Control* 1999;10:355–67.
- Calle EE, Rodriguez C, Jacobs EJ, et al. The American Cancer Society Cancer Prevention Study II Nutrition Cohort-rational, study design, and baseline characteristics. *Cancer* 2002;94:500–11.
- Calle EE, Terrell DD. Utility of the National Death Index for ascertainment of mortality among Cancer Prevention Study II participants. *American Journal of Epidemiology* 1993;137:235–41.
- WHO. International Classification of Diseases Ninth Revision. Manual of the international statistical classification of disease, injuries, and causes of death. 9th rev. ed., vol. 1. Geneva: WHO; 1977.
- WHO. International statistical classification of diseases and related health problems tenth revision. 10th ed., vol. 1. Geneva: WHO; 1992.
- Ainsworth BE, Haskell WL, Leon AS, et al. Compendium of physical activities: classification of energy costs of human physical activities. *Medicine and Science in Sports and Exercise* 1993;25:71–80.
- Cox D. Regression models and life tables. *Journal of the Royal Statistical Society* 1972;34:187–220.
- Kleinbaum G, Kupper L, Morgenstern H. *Epidemiologic research: principles and quantitative methods*. New York: Van Nostrand Reinhold Co; 1982.
- Hackney AC. The male reproductive system and endurance exercise. *Medicine & Science in Sports & Exercise* 1996;28:180–9.
- IARC. IARC Handbooks on Cancer Prevention: weight control and physical activity, Vol. 6. Lyon: IARC. 2002.
- Stattin P, Bylund A, Rinaldi S, et al. Plasma insulin-like growth factor-I, insulin-like growth factor binding proteins, and prostate cancer risk: a prospective study. *Journal of the National Cancer Institute* 2000;92:1910–17.
- Chan JM, Stampfer MJ, Ma J, et al. Insulin-like growth factor-I (IGF-I) and IGF binding protein-3 as predictors of advanced-stage prostate cancer. *Journal of the National Cancer Institute* 2002;94:1099–106.