

# Prostate Cancer Risk in Relation to Anthropometry and Physical Activity: The National Health and Nutrition Examination Survey I Epidemiological Follow-Up Study

Geraldine Clarke and Alice S. Whittemore<sup>1</sup>

Department of Health Research and Policy, Stanford University School of Medicine, Stanford, California 94305-5405

## Abstract

**We studied the relationship of prostate cancer to anthropometry and self-reported physical activity among 5377 African-American and Caucasian participants in the National Health and Nutrition Examination Survey I cohort. The cohort was first examined between 1971 and 1975 and then followed prospectively through the Epidemiologic Follow-up Study in 1982–1984, 1986, 1987, and 1992. Men who reported low levels of nonrecreational physical activity had increased risk of prostate cancer compared with very active men. These findings were unchanged after adjustment for potential confounders and were stronger for African-Americans (relative risk, 3.7; 95% confidence interval, 1.7–8.4) than for Caucasians (relative risk, 1.7; confidence interval, 0.8–2.3). Lower levels of recreational activity were weakly associated with increased prostate cancer risk among African-Americans but not among Caucasians. Prostate cancer risk was unrelated to a variety of anthropometric variables. These results suggest that inactive men are at increased risk of prostate cancer.**

## Introduction

Cancer of the prostate is the most common noncutaneous malignancy and the second leading cause of cancer death among men (1). Both incidence and mortality from prostate cancer increase with age and at all ages are higher for African-American men than for Caucasian men. The only established risk factors for prostate cancer are age, race, and a positive family history (2).

Evidence suggests that endogenous androgens are likely to play a fundamental role in prostate carcinogenesis (3). Antitestosterone therapy is the recommended treatment for metastatic carcinoma of the prostate (4). It has been observed that men with prostate cancer have higher levels of endogenous testosterone than healthy men (5, 6), and higher levels of testosterone have been found in tumor tissue than in normal tissue or tissue from men with benign prostatic hyperplasia (7–9). African-

American men have serum testosterone levels 15% higher than Caucasian men, which has been hypothesized to account almost entirely for the increased incidence and mortality of prostate cancer observed in African-American men as compared with Caucasian men (10). Studies show that trained athletes may have lower basal levels of circulating testosterone than nonathletes (11–15). Temporary reductions of testosterone have also been noted immediately after exercise (11, 16, 17). In summary, it is reasonable to suppose that reductions in testosterone through exercise may protect against prostate cancer.

Obesity is also associated with modulation of the endocrine system, including increasing serum estrogen and decreasing testosterone levels (18). Because, as outlined above and in Ref. 19, this hormonal pattern may decrease the risk of prostate cancer, we might expect to see a lower risk of prostate cancer among obese men. BMI,<sup>2</sup> defined as weight in kilograms divided by the square of height in meters, is frequently used as a measure of obesity (20, 21), but studies have shown an inconsistent association between BMI and the risk of prostate cancer (2). In fact, BMI is correlated with both lean body mass as well as fat body mass (22). A prospective study by Severson *et al.* (23) indicated that a direct association between BMI and the risk of prostate cancer was attributable to the lean-body component present in the BMI, which suggests that BMI may not be an unconfounded measure of obesity. Skinfold measurements provide an alternative estimate of adiposity (24).

Various studies have suggested plausible biological mechanisms for the roles of dietary factors in the etiology of prostate cancer (25, 26). However, the dietary assessment of individuals or populations poses many difficulties in epidemiological studies (27, 28). Anthropometric variables such as height and weight can be measured with greater reproducibility than dietary information and partially reflect dietary practices.

In light of the above, recent data from the National Center for Health Statistics provided an opportunity to examine prospectively in a large cohort of United States men the role of a variety of anthropometric measurements as well as self-reported physical activity levels in the subsequent development of prostate cancer.

## Materials and Methods

The NHEFS is a prospective cohort study generated from the original NHANES I and its Augmentation Survey. NHANES I and its Augmentation Survey were conducted from 1971 to 1975 in a sample of the civilian noninstitutionalized population of the United States (29, 30). These surveys provided cross-

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<sup>1</sup> To whom requests for reprints should be addressed, at Department of Health Research and Policy, Redwood Building Room T204, Stanford University School of Medicine, Stanford, CA 94305-5402.

<sup>2</sup> The abbreviations used are: BMI, body mass index; NHEFS, National Health Examination Follow-up Survey; NHANES, National Health and Nutrition Examination Survey; RR, relative risk; CI, (95%) confidence interval.

sectional information on demographic, nutritional, biochemical, clinical, anthropometric, and medical history variables. Certain population groups were oversampled: children 1–5 years, women 20–44 years, elderly  $\geq 65$  years, and low-income individuals. The NHEFS cohort includes all of the participants ( $n = 14,407$ ; male  $n = 5,810$ ) ages 25–75 years at the time of the NHANES I and its Augmentation Survey. These subjects were traced and interviewed again for the NHEFS in 1982–1984, 1986, 1987, and 1992. Of the 5,810 men in this cohort, 4,915 (85%) were Caucasian and 824 (14%) were African-American.

The National Center for Health Statistics provides computerized public-use NHEFS data files that list self reports of physician-diagnosed cancer as well as confirmed overnight hospitalizations and mortality by International Classification of Disease (ICD) codes. Only invasive prostate cancer diagnoses (ICD 185) identified through either hospital or nursing home records or through death certificates were used in this analysis. Nine self-reported cases without confirmation were grouped with noncases for analyses.

A total of 214 prostate cancer cases were identified through hospital records or death certificates or both. For the 193 cases identified through hospital records, the date of the first admission for which prostate cancer was listed on the discharge diagnosis was considered the incidence date. The date of death was regarded as the incidence date in the 21 cases for which only death certificate information was available.

We removed 71 men of races other than African-American or Caucasian because men of all other races combined comprised only 1% of the cohort. We also excluded 256 men who were lost to follow-up either through the inability to trace them or their refusal to participate. All of the 256 men were lost before the start of the study period of follow-up and, furthermore, are not known to have died; *i.e.*, no death certificates have been found. We removed an additional 98 men with a prior history of malignancy and another 5 individuals with indications of only “possible invasive prostate cancer” on any of their health care records. Two men with indications of prostate cancer on hospital records occurring within 1 year of the baseline exam and one man with prostate cancer listed as a cause of death occurring within 1 year of the baseline exam were also excluded. After all of the exclusions, the final analytic cohort consisted of 5377 men (including 201 cases) who were followed for an average of 14.7 years.

Measurements of height, weight, elbow width, upper-arm girth, and subscapular and triceps skinfold thickness were made at baseline by two trained technicians using standardized state-of-the-art techniques (31). Weight was measured to the nearest 10 g, height and elbow width to the nearest millimeter, and skinfolds to the nearest one-half of a millimeter. Area  $A$  of muscle in the upper arm (in units of  $\text{mm}^2$ ) was calculated as

$$A = \frac{(G - \pi T)^2}{4\pi} - 10 \quad (\text{A})$$

where  $G$  denotes upper arm girth in mm and  $T$  denotes triceps skinfold thickness in mm, according to the equations of Heymsfield *et al.* (32). Area  $F$  of fat in the upper arm was calculated as

$$F = \frac{G^2}{4\pi} - A \quad (\text{B})$$

according to the equations of Frisancho (33). Lean body mass  $L$ , an estimate of body components that are not adipose, was calculated as

$$L = \frac{2.447 - 0.09516x + 0.1074h + 0.3362w}{0.732} \quad (\text{C})$$

according to the equations of Watson *et al.* (34) and Sheng and Huggins (35). Here  $x$  denotes age in years,  $h$  denotes height in cm, and  $w$  denotes weight in kg.

Two questions concerning physical activity were asked at the time of the NHANES I interview. The first, relating to nonrecreational activity, was: “In your usual day, aside from recreation, are you physically very active, moderately active, or quite inactive?”. Answers allowed were “very active,” “moderately active,” or “quite inactive.” The second question, relating to recreational activity, was: “Do you get much exercise in things you do for recreation (sports, or hiking, or anything like that), or hardly any exercise, or in between?”. Answers allowed were “much exercise,” “moderate exercise,” or “little or no exercise.”

Information about possible prostate cancer risk factors including age, race, education, and alcohol use was obtained at baseline. Family history of prostate cancer, defined as reported occurrence of the disease in first-degree relatives, was obtained at the first follow-up interview in 1984 and, therefore, was unknown for a subset of men either dead or not interviewed at this interview. Information regarding benign prostate disease was not available.

Anthropometric variables (including estimates of arm muscle area, arm fat area and lean body mass) were divided into quartiles based on their distribution in the entire cohort. Activity variables were divided according to categories of response at interview. Education was split according to whether individuals were educated up to and including high school or more than high school. Adjusted RRs of prostate cancer according to levels of these variables were estimated from relative hazards obtained from Cox proportional hazards models. Models were adjusted for age (modeled as a continuous variable) and potential confounders as appropriate and were stratified by race (classed as either Caucasian or African-American). We did not adjust for total calories because this information is available only for a subset of participants. One thousand three hundred thirty-two men did not complete a dietary questionnaire, and an additional 30 men had unknown values of this variable. Variables in their continuous form were used in likelihood ratio tests to evaluate linear trends. Analyses were performed with the COXPH procedure available in the S-PLUS statistical package (36).

## Results

Table 1 presents descriptive characteristics of participants by ethnicity and case status. On the basis of a comparison of Caucasian and African-American noncases, African-Americans tended to be older, less well educated, and less recreationally active and to drink less than Caucasians. For both African-Americans and Caucasians, cases were more likely to be older and less well educated and to drink slightly less than noncases. 23.4% of cases were African-American, whereas only 13.7% of noncases were African-American, which indicates that African-Americans were more likely to be cases than Caucasians were. Caucasian cases were more likely to have a family history of prostate cancer than Caucasian noncases, whereas for African-Americans, there are too few numbers for evaluation. African-

Table 1 Distribution of potential prostate cancer risk factors at baseline interview across cases and noncases within race

Characteristic	Caucasians		African Americans	
	Cases <i>n</i> = 154	Noncases <i>n</i> = 4468	Cases <i>n</i> = 47	Noncases <i>n</i> = 708
Age (yr)	n (%)	n (%)	n (%)	n (%)
<50	7 (4.5)	2044 (45.7)	1 (2.1)	286 (40.4)
50–59	39 (25.3)	787 (17.6)	7 (14.9)	121 (17.1)
60–69	74 (48.1)	1080 (24.2)	29 (61.7)	189 (26.7)
≥70	34 (22.1)	557 (12.5)	10 (21.3)	112 (15.8)
Total <sup>a</sup>	154	4468	47	708
Education				
High school or less	132 (85.7)	3206 (72.3)	45 (95.7)	618 (89.0)
More than high school	22 (14.3)	1229 (27.7)	2 (4.3)	76 (11.0)
Total	154	4435	47	694
Nonrecreational activity				
Very active	68 (44.2)	1983 (44.4)	15 (31.9)	343 (48.4)
Moderately active	69 (44.8)	1987 (44.5)	22 (46.8)	288 (40.7)
Inactive	17 (11.0)	494 (11.1)	10 (21.3)	77 (10.9)
Total	154	4464	47	708
Recreational activity				
Much	36 (23.4)	1088 (24.4)	3 (6.4)	129 (18.2)
Moderate	61 (39.6)	1821 (40.8)	16 (34.0)	218 (30.8)
Little or none	57 (37.0)	1554 (34.8)	28 (59.5)	361 (51.0)
Total	154	4463	47	708
Alcohol frequency				
Some	113 (73.4)	3536 (79.3)	23 (48.9)	519 (73.3)
None <sup>b</sup>	41 (26.6)	921 (20.7)	24 (51.1)	189 (26.7)
Total	154	4457	47	708
Family history of prostate cancer				
No	144 (94.1)	4304 (98.0)	44 (100.0)	684 (99.7)
Yes	9 (5.9)	87 (2.0)	0 (0.0)	2 (.28)
Total	153	4391	44	686

<sup>a</sup> Without missing values.

<sup>b</sup> Answered “no” to having consumed alcohol in the previous year.

Table 2 Unadjusted means of anthropometric variables of prostate cancer cases and noncases, by race at baseline interview

Characteristic	Caucasians		African Americans	
	Cases <i>n</i> = 154	Non-cases <i>n</i> = 4468	Cases <i>n</i> = 47	Non-cases <i>n</i> = 708
Height (m)	1.73	1.74	1.72	1.73
Weight (kg)	76.7	78.1	76.2	76.8
BMI (kg/m <sup>2</sup> )	25.8	25.7	25.8	25.6
Elbow width (cm)	7.3	7.3	7.4	7.3
Right subscapular skinfold (mm)	16.0	16.4	16.0	16.2
Right triceps skinfold (mm)	11.7	12.4	10.5	10.5
Right upper arm girth (cm)	31.0	31.7	32.0	32.1

American cases seem to be more nonrecreationally and recreationally inactive than African-American noncases, whereas nonrecreational and recreational activity does not seem to differ much between Caucasian cases and Caucasian noncases.

Unadjusted means of participants' baseline raw anthropometric measurements are given in Table 2. Triceps skinfold thicknesses for Caucasians seemed to be higher than for African-Americans and among Caucasians seemed to be lower for cases than for noncases. Mean upper arm girths for African-Americans were higher than for Caucasians and, among Caucasians and African-Americans, were slightly lower for cases than for noncases. For all of the other measurements there seemed to be little difference in means between cases and noncases both within and across race.

Estimated RRs for prostate cancer incidence across natural categories of potentially confounding variables are shown in

Table 3. The standard prostate cancer risk factors of race, education, and family history generally showed the expected associations. African-Americans were significantly more at risk for prostate cancer than Caucasians. Education greater than high school was significantly negatively related to prostate cancer incidence. Those with a family history of prostate cancer had a significantly increased risk of disease compared with those without a family history. Alcohol was also examined: The upper quartile of alcohol intake (daily consumption) showed a decreased risk (RR, 0.68), although this was not significant, and neither was a test for trend with increasing intake. Adjustments to RRs for education, and family history did not materially change any of the estimates.

Table 4 presents RRs relating prostate cancer risk to levels of nonrecreational, recreational, and combined activity for Caucasian, African-American, and all study participants. Among Caucasians, there were no statistically significant relationships between prostate cancer risk and decreasing recreational, nonrecreational, or combined activity levels. Stronger effects are seen for African-Americans. African-Americans in the least active categories of nonrecreational and combined activity were significantly more likely to be at increased risk of prostate cancer as compared with African-Americans in the most active of these categories (tests for trend  $P < 0.01$  in both categories). The most nonrecreationally inactive African-Americans were at a 3.60-fold increased risk of prostate cancer as compared with those who were very active. Increased risks with marginal statistical significance are observed for recreational activity alone. Differences in results between African-Americans and Caucasians for nonrecreational and recreational activity were not significant (likelihood ratio tests for an interaction between

Table 3 Prostate cancer risk according to race, educational level, and family history of prostate cancer

	Cases	Person-years	RR <sup>a</sup>	CI <sup>b</sup>	RR <sup>b</sup>	CI
Race						
Caucasian	154	69,044	1.00		1.00	
African-American	47	10,097	1.85	1.33–2.57	1.78	1.25–2.47
Education						
High school or less	177	56,286	1.00		1.00	
More than high school	24	22,204	0.60	0.39–0.93	0.60	0.39–0.93
Family history						
No	188	76,441	1.00		1.00	
Yes	9	1,489	2.08	1.06–4.09	2.12	1.08–4.16

<sup>a</sup> Adjusted for age.<sup>b</sup> Adjusted for age and other variables in Table. Analysis was done on a subset of men with complete information for adjusting factors.

Table 4 Estimated relative risks and confidence intervals for prostate cancer in Caucasian and African-American men, by activity

	Caucasians				African Americans				Both races			
	Cases	Person-years	RR <sup>a</sup>	CI	Cases	Person-years	RR	CI	Cases	Person-years	RR <sup>b</sup>	CI
Nonrecreational activity (NRA)												
1. Very active	68	32,775	1.00		15	5,390	1.00		83	38,165	1.00	
2. Moderately active	69	29,777	0.93	0.66–1.30	22	3,883	1.74	0.90–3.38	91	33,660	1.06	0.79–1.44
3. Inactive	17	6,434	1.67	0.78–2.28	10	823	3.74	1.66–8.44	27	7,258	1.73	1.12–2.67
<i>P</i> for trend			0.62				<0.01				0.05	
Recreational activity (RA)												
1. Much	36	17,998	1.00		3	1,961	1.00		39	19,959	1.00	
2. Moderate	61	27,666	0.92	0.61–1.39	16	3,241	2.96	0.85–10.23	77	31,907	1.10	0.75–1.61
3. Little or none	57	22,309	0.98	0.64–1.49	28	4,895	3.17	0.96–10.46	85	27,204	1.17	0.80–1.72
<i>P</i> for trend			0.97				0.08				0.41	
Combined activity (NRA, RA)												
(1,1)	27	13,185	1.00		3	1,649	1.00		30	14,834	1.00	
(1,2) or (2,1)	30	14,825	1.09	0.65–1.83	6	1,733	1.75	0.44–7.03	36	16,558	1.15	0.71–1.87
(1,3) or (2,2) or (3,1)	56	25,914	0.94	0.60–1.49	16	3,988	2.08	0.60–7.22	72	29,902	1.07	0.70–1.64
(2,3) or (3,2)	28	10,933	0.97	0.57–1.64	12	2,054	2.66	0.75–9.44	40	12,987	1.15	0.71–1.84
(3,3)	13	4,115	1.35	0.69–2.62	10	672	5.86	1.60–21.47	23	4,788	1.89	1.10–3.27
<i>P</i> for trend			0.80				<0.01				0.10	

<sup>a</sup> Adjusted for age, education, and family history.<sup>b</sup> Adjusted for age, education, family history, and race.

African-Americans and Caucasians with respect to activity levels were  $P = 0.12$  for nonrecreational and  $P = 0.38$  for recreational). Among both races combined, there was a trend of increasing risk with decreasing nonrecreational activity ( $P = 0.05$ ). Those who indulged in little or no recreational activity were at a slightly increased risk of prostate cancer although the risk was not significant, and no dose-response relationship was detected. Activity levels were jointly assessed in relation to risk of prostate cancer and the results shown under “combined activity”: individuals both recreationally and nonrecreationally least active were at a significantly increased risk of prostate cancer. In all of the categories, further adjustment for education and family history did not materially alter any estimates.

RRs across quartiles of anthropometric variables did not indicate any significant associations (data not shown). Risk of prostate cancer was marginally significantly associated with upper arm girth: men in the third quartile of upper arm girth had a 0.65-fold risk of disease (RR, 0.65; CI, 0.42–1.00) as compared with men in the lowest quartile. However, the second and fourth quartiles showed no significant association, the test for trend was not significant, and controlling for the effect of potential confounders removed any significant association between upper arm girth and prostate cancer (RR, 0.67; CI,

0.43–1.03). Men in the middle quartiles of height were at a slightly increased risk of prostate cancer as compared with men in the other quartiles (RR, 1.38 and 1.22 for second and third quartiles, respectively). However, none of the risk estimates associated with height or elbow width were significantly different from unity, and there was no evidence of a trend across quartiles. Adjustment for potential confounders did not substantially change any risk estimates associated with height or elbow width. Neither weight nor skinfold measurements were related in a consistent or significant fashion to the risk of disease. Adjustment for potential confounders did not materially alter any of the risk estimates for weight or skinfold measurements; and no evidence of any dose-response relationship was found for these measurements either before or after controlling for potential confounders. Separate analyses of African-Americans and Caucasians revealed no significant differences.

Similarly, we found no clear or consistent associations between prostate cancer risk and the derived variables BMI, lean body mass, and estimated areas of muscle and fat in the upper arm. There was no evidence of any dose-response relationship for any of these variables. Adjustment for potential confounders, although tending to increase risk estimates by a

small percentage, did not materially change any results. Again, separate analyses of African-Americans and Caucasians did not reveal any significant differences.

## Discussion

Data from this cohort study of 5377 men who were followed for an average of 14.7 years revealed an inverse association between self-reported physical activity levels and subsequent development of prostate cancer, with stronger effects for nonrecreational than recreational activity, and stronger effects for African-Americans than for Caucasians. In contrast, the risk of prostate cancer was unrelated to a variety of anthropometric variables.

These findings are unlikely to be attributable to methodological biases or limitations. Hospital records and death certificate review yielded thorough case ascertainment. This was a prospective study of a representative sample of the United States population. Anthropometric variables were measured prospectively using standard methods under controlled conditions. The observed distributions of height (a relatively fixed biological parameter in adulthood), for example, are comparable to those from other large studies in developed countries (37). The activity data are based on individual estimates and, as such, may be more specific than other well-used classifications (*e.g.*, by job or earlier-life athletic status). Although an effect from the subjective interpretation of the interview questions cannot be excluded, any misclassification should be nondifferential causing risk estimates to be reduced. The validity of the NHANES I self-reported activity classification is supported by both caloric intake data and employment status: Activity level correlated positively with both age-adjusted mean energy intake and energy-not-used-for-resting metabolic rate (energy intake minus predicted resting metabolic rate, a crude estimate of physical activity energy expenditure); nonrecreational activity was positively related to employment status (38).

Previous epidemiological data are inconsistent with respect to the relationship between physical activity and the development of prostate cancer. Two of three population-based case-control studies (39, 40) showed a positive association, whereas the other (41) found no association. Three hospital-based case-control studies (42–44) demonstrated a negative (protective) association. The case-control design has inherent limitations related to the potential for bias in the recall of activity. This is not a limitation in a prospective cohort design, in which activity level is assessed before diagnosis. However, cohort studies also have been inconsistent. Four cohort studies found a positive association (45–48), and five found an inverse association (38, 49–52). Part of the inconsistency may reflect variation in the time period during which physical activity was assessed: four of five cohort studies assessing leisure or recreational activity during adulthood reported an inverse association (38, 49, 51, 52), whereas only one found a positive association (45). All of the cohort studies assessing physical activity during early adulthood (mainly college athletics) found a positive association (46–48). Two cohort studies assessing occupational physical activity during adulthood showed an inverse association (50, 51), whereas one showed a null association (49). Assessment of physical activity at a single point, as in this study, cannot accurately reflect physical activity patterns throughout an individual's life. The use of multiple assessments would increase precision. Lee *et al.* (52) found a stronger inverse association between physical activity and prostate cancer risk when two activity assessments within 10 years were combined.

The present results for physical activity are stronger than the results of Albanes *et al.* (38), who studied the same cohort for the first wave of the NHEFS, and Steenland *et al.* (53), who studied the same cohort for the first two waves of the NHEFS. Both of the studies found suggestions of an inverse association between nonrecreational activity and prostate cancer risk, although their results did not achieve statistical significance (RR, 1.3; CI, 0.7–2.4 and RR, 1.31; CI, 0.76–2.26 for “quite inactive” compared with “very active” for Albanes *et al.* and Steenland *et al.*, respectively). Albanes *et al.* (38) also found a marginally significant inverse association for recreational activity (RR, 1.8; CI, 1.0–3.3) for little or no exercise as compared with much exercise).

We found that the effects of activity on prostate cancer risk were stronger for African-Americans than for Caucasians. These interethnic differences in risk did not achieve statistical significance; this could be a result of low power to detect a difference in risk because of the small number of African-Americans included in the analysis. However, any discrepancies in results for African-Americans and Caucasians are most likely explained by other factors. For example, Whittemore *et al.* (41) found that differences in saturated fat intake might account for 5–10% of African-American-versus-Caucasian difference in prostate cancer incidence and suggested that other environmental factors (diet during adolescence) and nonenvironmental factors (genetically determined hormonal differences) might account for the difference. However, Powell (54) has suggested the possibility of differences in the natural history or disease progression of prostate cancer between African-Americans and Caucasians. Hence, it may be reasonable to suppose that the effects of physical activity may differ between African-Americans and Caucasians. Furthermore, the main role hypothesized for physical activity in prostate carcinogenesis is its effect on testosterone levels. Ross *et al.* (10) found that African-American men had 15% higher levels of circulating testosterone than young Caucasian men. Therefore, if testosterone is a mediator for the role of physical activity, then the effect of physical activity may be more marked in African-Americans than in Caucasians.

Issues concerning the short-term effects of strenuous levels of physical activity on the health of middle-aged and older men might fruitfully be addressed in a large, randomized intervention trial. Although such a trial could confront substantial compliance complications, it would circumvent some of the selection issues inherent in observation studies and provide a needed complement to these studies.

Height and elbow width are indicators of frame size. In these data, neither height nor elbow width emerged as risk factors for prostate cancer. Most of the recent prospective cohort studies (55–57) support a positive relationship between height and prostate cancer although this was not confirmed by a case-control study (58).

We found no appreciable differences in the risk of prostate cancer with increasing BMI. Two cohort studies (45, 57) found that BMI was positively related to prostate cancer risk, (although one (57) only to mortality and not incidence), but that was not confirmed by three other cohort studies (55, 59, 60) which found that BMI was not independently related to the risk of prostate cancer. One case-control study (61) found that BMI was positively related to risk of prostate cancer but another (58) did not.

Among men in this NHEFS cohort, neither weight nor skinfold thickness emerged as a prostate cancer risk factor. One prospective study (46) and two case-control studies (62, 63) have shown that weight was not related to the risk of prostate

cancer while four prospective cohort studies (60, 64–66) and one case-control study (67) have found a relationship. The majority of adipose tissue is deposited s.c., and skinfold measurements provide a more direct measure of adiposity than weight. Skinfold determination of very obese men is subject to error, and it is possible that adiposity was underestimated in these men. However, it is unlikely that these men were misclassified into lower quartiles of skinfold thicknesses.

Overall, the data do not indicate that adiposity correlates with a higher risk of prostate cancer. If adiposity is a risk factor for prostate cancer, possible explanations include a failure to identify the appropriate index and/or the relevant exposure period. Furthermore, the variation in findings for BMI could be a result, in part, of population differences (age range, race, and so forth) that determine whether BMI correlates more strongly with lean body mass or with adiposity.

In order to study the effects of fat and lean body mass independently, we looked separately at area of fat in the arm and area of muscle in the arm. These two measurements are considered to be the most accurate indicators of adipose and lean body tissue (32, 33). We found no relationship between the area of fat in the arm and prostate cancer risk. These findings are consistent with a previous prospective cohort study by Severson *et al.* (23). However, for arm muscle area, whereas Severson *et al.* found a significant increase in risk with increasing area, we did not find such a trend. One main difference is that Severson *et al.* studied Japanese men with typically much lower values of arm muscle and fat area than the NHEFS cohort of predominantly Caucasian United States men.

Lean body mass is another estimate of body components that are not adipose. A previous study by Andersson *et al.* (57) found a significant increase in the risk of prostate cancer with increasing lean body mass. Our results do not confirm these findings. In order to calculate the lean body mass index, a prediction is made of the total body water for men. The validity of the equation predicting the total body water is not perfect ( $r = 0.84$ ) as a result of variation between populations. Furthermore, to calculate the lean body mass index, it is assumed that the proportion of water in the lean body mass is constant. In reality, this proportion varies depending on the state of hydration and the relative subcomponents of the mass. These two issues may account for the variation between our results and those of Andersson *et al.* (57), who studied Swedish construction workers.

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# BLOOD CANCER DISCOVERY

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Geraldine Clarke and Alice S. Whittemore

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