



Original Contribution

Anthropometrics and Prostate Cancer Risk

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Studies on obesity and prostate cancer risk are inconsistent, perhaps because of differential effects on aggressive and nonaggressive cancers. Participants included 34,754 men residing in Washington State (aged 50–76 years at baseline) in a prospective cohort study who were recruited between 2000 and 2002; 383 developed aggressive (regional/distant stage or Gleason sum 7–10) and 437 developed nonaggressive disease through December 2004. Compared with normal-weight men (body mass index (kg/m²) <25), obese men (≥30 kg/m²) had a reduced risk of nonaggressive disease (hazard ratio = 0.69, 95% confidence interval: 0.52, 0.93; *p* for trend = 0.01). Overweight men (25–29.9 kg/m²) had an increased risk of aggressive disease (hazard ratio = 1.4, 95% confidence interval: 1.1, 1.8), but there was no increased risk for obese men (*p* for trend = 0.69). Body mass index of >25 at age 18 years was associated with increased risk of aggressive prostate cancer; obesity at ages 30 and 45, but not 18, years was associated with reduced risk of nonaggressive prostate cancer. Height (fourth vs. first quartile) was associated with an increased risk of total prostate cancer (hazard ratio = 1.3, 95% confidence interval: 1.1, 1.6), which did not differ by aggressiveness. There were no associations of prostate cancer with age at which maximum height was reached. Results from this study demonstrate the complexity of prostate cancer epidemiology and the importance of examining risk factors by tumor characteristics.

body height; body mass index; body weight; body weight changes; cohort studies; longitudinal studies; prostatic neoplasms

Abbreviations: BMI, body mass index; CI, confidence interval; HR, hazard ratio; PSA, prostate-specific antigen; SEER, Surveillance, Epidemiology, and End Results; VITAL, VITamins And Lifestyle.

More than 30 percent of adults in the United States are obese, and 17 percent of children and adolescents are overweight (1). Rates have increased dramatically over the past 20 years. Although the role of obesity in diseases such as diabetes, hypertension, and heart disease is well established (2), obesity's role in prostate cancer is less certain (3–6). Well-designed longitudinal studies have observed positive, inverse, and null results. Freedland et al. (7) recently hypothesized that obesity may reduce the risk of nonaggressive disease but simultaneously increase the risk of aggressive disease. It is possible that the inconsistent study results may be at least partly explained by a failure to consistently ex-

amine associations of anthropometric measures separately by prostate cancer tumor characteristics.

The aims of this study were to evaluate associations of weight, body mass index (BMI), and height in late adolescence, early adulthood, and at baseline with total, aggressive, and nonaggressive prostate cancer. Although it is plausible that early or midlife events may influence prostate cancer risk, few studies have investigated associations of BMI in adolescence or early adulthood. Data from this large cohort study provided an opportunity to examine these anthropometric factors throughout the life span and evaluate how associations may differ by demographic, medical, lifestyle, as

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well as tumor characteristics and to help us better understand the etiology and potential mechanisms of this common cancer.

MATERIALS AND METHODS

Recruitment and response rates

Men and women were eligible to join the VITamins And Lifestyle (VITAL) cohort if they were aged 50–76 years and lived in the 13-county area in western Washington State covered by the Surveillance, Epidemiology, and End Results (SEER) cancer registry (8). Because the current study included only men, we discuss here recruitment of men only. Using names purchased from a commercial mailing list, we mailed 195,465 baseline questionnaires between October 2000 and December 2002, followed by a postcard reminder 2 weeks later. Of the 38,143 questionnaires (19.5 percent) that were returned, 37,382 met eligibility criteria and passed questionnaire quality control checks. We excluded men with a history of prostate cancer at baseline ($n = 2,013$), men diagnosed with *in situ* prostate cancer by SEER ($n = 3$), and those who did not answer the question about history of prostate cancer ($n = 125$).

Baseline questionnaire

Participants completed a 24-page, self-administered, optically scanned questionnaire, which included questions on demographic characteristics, physical activity, health history, family history of cancer, and other cancer risk factors.

Weight, height, age at which maximum height was reached, and BMI

Participants reported their tallest height to the nearest inch (1 inch = 2.54 cm) and their weight at ages 18, 30, and 45 years and at baseline to the nearest pound (1 pound = 0.45 kg). We calculated BMI at baseline and at ages 18, 30, and 45 years as weight divided by height squared (kg/m^2) and created categories by using the following recommended cut-offs (9, 10): normal weight (18.5–24.9 kg/m^2), overweight (25.0–<30.0 kg/m^2), and obese (≥ 30.0 – ≤ 55.0 kg/m^2). For weight and height, we created quartiles based on the distribution of the cohort. However, because these variables were not completely continuously distributed, some categories included more or less than 25 percent of the cohort. Finally, we examined weight change since age 18 years as a categorical variable: weight loss of ≥ 10 pounds, weight maintenance within 10 pounds, weight gain of 10–29 pounds, and weight gain of ≥ 30 pounds. Men who did not answer or who provided extreme or implausible values for height (<49 or >94 inches, 1.4 percent), weight or BMI (<90 or >500 pounds and >55 kg/m^2 at any age, <15 kg/m^2 at age 18 years (3.9 percent), or <18.5 kg/m^2 at age 30 years (5.1 percent), age 45 years (3.4 percent), and baseline (3.2 percent)), or age at which maximal height was reached (<12 or >25 years, 7.8 percent) were excluded from analyses of those variables.

Follow-up of participants for prostate cancer and censoring

Follow-up of the cohort for cancers and censoring date is described in detail elsewhere (8). We identified 832 men who developed incident prostate cancer from baseline through December 31, 2004, by linking the study cohort to the western Washington SEER cancer registry. To ascertain deaths, we linked to the Washington State death files. To identify moves out of the area, we linked to the National Change of Address system, sent follow-up letters, and telephoned those identified as having possibly moved and who left no forwarding address. The censoring date for each participant was the earliest date of prostate cancer diagnosis (1.7 percent), withdrawal from the study (0.02 percent), death (3.0 percent), a move out of the 13-county catchment area of the SEER registry (3.9 percent), or the last date of linkage (December 31, 2004).

We used SEER records to determine tumor aggressiveness, defined by summary stage (local, regional, distant) and grade. Because there is some controversy regarding the most appropriate way to categorize grade, we used two methods. First, corresponding to the method used since 2004 in SEER, we classified Gleason sum 7–10 as poorly differentiated or high grade (11), which required review of original SEER abstraction forms from 2000–2002 for all cancers classified as “moderately differentiated.” Second, we classified high grade as Gleason sum 8–10, which yields a smaller number of less heterogeneous high-grade tumors. Because we did not have information on Gleason sum for cancers diagnosed in 2003, analyses of aggressive tumors using the more restrictive definition excluded cases diagnosed in that year.

Statistical methods

We fit Cox proportional hazards models to estimate hazard ratios of developing prostate cancer, after adjusting for confounding factors (12). Analysis time was defined as the participant’s age. Thus, all variables were effectively adjusted for age. Participants first became at risk at the age they entered the study, and they were censored at their age-at-censored date, described in the previous section.

For each anthropometric measurement, we created indicator variables for categories of the exposure. To test for trends across the levels of a variable (e.g., categories of BMI), we created a grouped linear variable and assigned the median value for that category (e.g., 23, 27, and 34, respectively, for each category of BMI).

BMI at baseline was used for all models to assess potential confounding. We evaluated whether inclusion of the factors listed in table 1, and certain factors associated with prostate-specific antigen (PSA) screening (sigmoidoscopy, insurance provider (i.e., Group Health Cooperative or not), benign prostatic hyperplasia, and medications for benign prostatic hyperplasia including finasteride, terazosin hydrochloride, doxazosin mesylate, and tamsulosin hydrochloride), changed the beta coefficient of the highest level of BMI by 10 percent or more. Results based on this primary model were then generalized to others. To evaluate the validity of the proportional hazards assumption, we used tabular

TABLE 1. Characteristics of the VITAL* cohort and mean BMI* at age 18 years and at baseline and the prevalence of obesity at baseline, Washington State, 2000–2004

Characteristic	No.	%	Mean (SD*) BMI at age 18 years	Mean (SD) BMI at baseline	% Obese at baseline
Overall	34,754	100.0	22.1 (3.0)	27.6 (4.4)	23.8
Age (years) at baseline					
50–54	8,312	24.0	22.4 (3.1)	27.9 (4.6)	25.7
55–59	7,969	23.0	22.2 (3.0)	28.0 (4.5)	26.2
60–64	6,561	18.9	22.2 (3.0)	27.8 (4.4)	25.3
65–69	5,799	16.7	21.9 (2.9)	27.5 (4.3)	23.6
70–77	6,113	17.5	21.5 (2.7)	26.6 (3.9)	16.8
Race					
White	32,272	93.2	22.1 (3.0)	27.6 (4.4)	23.8
Hispanic	289	0.9	22.0 (3.5)	28.5 (4.9)	30.5
Black	430	1.3	21.8 (3.0)	28.8 (4.5)	33.7
American Indian/Alaska Native	518	1.5	22.3 (3.4)	29.1 (5.2)	32.8
Asian or Pacific Islander	841	2.5	20.9 (2.8)	25.6 (3.8)	9.8
Other	263	0.8	21.9 (3.2)	28.2 (4.9)	27.6
Education					
High school graduate/GED* or less	5,481	15.6	22.0 (3.1)	28.1 (4.5)	28.1
Some college/technical school	12,137	35.0	22.1 (3.2)	28.2 (4.7)	28.4
College graduate	9,511	27.6	22.1 (2.9)	27.3 (4.1)	21.2
Advanced degree	7,537	21.9	22.1 (2.7)	26.8 (4.0)	16.9
Income (\$)					
<40,000	6,672	19.0	21.9 (3.2)	27.7 (4.9)	26.2
40,000–59,999	6,994	20.2	22.0 (3.0)	27.7 (4.4)	24.9
60,000–79,999	5,737	16.6	22.2 (3.0)	28.0 (4.4)	25.8
≥80,000	10,214	29.5	22.2 (2.9)	27.5 (4.1)	21.9
Missing	5,137	14.7	21.9 (2.9)	27.2 (4.3)	20.8
Family history of prostate cancer					
None	29,878	87.0	22.1 (3.0)	27.6 (4.4)	23.7
One first-degree relative	4,196	12.2	22.1 (3.0)	27.7 (4.4)	24.5
≥Two first-degree relatives	278	0.8	22.0 (2.9)	27.3 (3.8)	24.6
Smoking status					
Never smoker	13,442	39.0	22.2 (2.9)	27.3 (4.3)	20.9
Current smoker	3,142	9.1	22.2 (3.1)	26.7 (4.5)	19.5
Former smoker (quit <10 years ago)	2,601	7.5	22.2 (3.3)	28.6 (3.3)	30.6
Former smoker (quit ≥10 years ago)	15,300	44.4	22.0 (3.0)	28.0 (4.4)	26.1
Benign prostatic hyperplasia					
No	29,200	84.0	22.1 (3.0)	27.7 (4.4)	24.6
Yes	5,540	16.0	21.8 (2.8)	27.1 (4.1)	20.0
PSA* test in the previous 2 years					
No	9,591	27.9	22.1 (3.0)	27.7 (4.6)	24.9
Yes	24,730	72.1	22.1 (3.0)	27.6 (4.3)	23.4
Recreational physical activity in the 10 years before baseline (average MET*-hours/week)					
None	5,133	14.9	22.2 (3.2)	28.5 (5.2)	32.2
>0–3.9	7,282	21.1	22.1 (3.2)	28.6 (4.8)	32.5
4.0–10.4	7,156	20.9	22.0 (3.0)	27.6 (4.2)	23.7
10.5–21.0	7,416	21.7	22.0 (2.9)	27.1 (3.9)	19.4
>21.0	7,305	21.4	22.1 (2.7)	26.5 (3.6)	14.1

* VITAL, VITamins And Lifestyle; BMI, body mass index (weight (kg)/height (m)²); SD, standard deviation; GED, general equivalency diploma; PSA, prostate-specific antigen; MET, metabolic equivalent task.

and graphic methods. Schoenfeld residuals were plotted against time to determine whether the slope differed from zero, which is equivalent to testing whether the log-hazard ratio function is constant over time (12). Because the proportional hazards assumption did not hold for PSA screening, we accommodated this violation by fitting a stratified Cox model in which a separate baseline hazard was used for participants who did and did not get screened for PSA before baseline. In this model, we assumed that the effect of each of the covariates was the same across strata. Thus, final models were adjusted for age, race (White, Black, other), and number of first-degree relatives with prostate cancer (0, 1, ≥ 2) and were stratified on PSA screening. Additionally, we adjusted analyses of weight change from age 18 years to baseline for BMI at baseline (two indicator variables) to evaluate whether weight gain or loss per se was associated with prostate cancer risk.

We evaluated whether the association between BMI and prostate cancer risk differed by age, family history, PSA screening, and physical activity by including a grouped linear (trend) variable in our models and comparing the likelihood ratio test between a model with terms for the main effects and an interaction term (plus covariates) with a model with the terms for the main effects only (plus covariates). Because studies indicate that obesity may be differentially associated with high-grade or aggressive prostate cancer, we assessed associations for anthropometric measures separately by tumor grade and stage. In analyses of aggressive disease, men who developed nonaggressive disease were excluded. Finally, we used logistic regression to evaluate the statistical significance of differences in associations of anthropometric measures and aggressive compared with nonaggressive tumors.

RESULTS

Table 1 gives the distributions of various demographic, medical, and lifestyle characteristics of men in the VITAL study. The mean age of participants was 61.9 years, and more than 93 percent were White. Nearly 50 percent had a college education or more, and 46 percent had incomes of \$60,000 or more. Thirteen percent had one or more first-degree relatives with a history of prostate cancer. Seventy-two percent of men had had a PSA test in the 2 years before baseline.

At age 18 years and at baseline, the mean BMIs of participants were 22.1 kg/m² and 27.6 kg/m², respectively. The prevalence of overweight and obesity was much higher at age at baseline (49 percent and 24 percent, respectively) than at age 18 years (15.3 percent and 1.6 percent, respectively). Age at baseline was the only characteristic associated with BMI at age 18 years; men who were older at baseline had lower mean BMIs at age 18 years (table 1). BMI and the percentage of men who were obese at baseline decreased with increasing age, education, and physical activity. About 33 percent of Blacks and American Indians/Alaska Natives were obese at baseline age compared with fewer than 10 percent of Asians or Pacific Islanders and 24 percent of Whites. Current smokers had lower BMIs than never smokers; mean BMI was greatest among former smokers who quit in the 10 years before baseline. BMI at baseline age did not

vary by family history, benign prostatic hyperplasia, or PSA screening.

A total of 832 participants were diagnosed with prostate cancer during follow-up; 347 men were diagnosed with Gleason sum 7–10 tumors, 73 with Gleason sum 8–10 tumors, 126 with regional/distant stage tumors, and 383 and 176, respectively, with aggressive disease after including or excluding Gleason sum 7 tumors (refer to the Materials and Methods section). There were no associations of weight at age 18 or 30 years with aggressive disease (table 2). Higher weights at age 45 years and baseline age were inversely associated with nonaggressive prostate cancer. Men in the fourth quartile of weight at baseline age had a 29 percent reduced risk (95 percent confidence interval (CI): 0.54, 0.93) of nonaggressive disease (p for trend = 0.02). Conversely, weights at ages 18, 30, and 45 years were associated with increased risks of aggressive prostate cancer (all p for trend < 0.05), with a similar but nonsignificant association for BMI at baseline age. The strongest association was for weight at age 30 years; compared with the reference weight category, men in the fourth quartile of weight had a 50 percent increased risk of aggressive prostate cancer (p for trend = 0.01).

In contrast to the findings for weight, BMIs at ages 30 years, 45 years, and baseline were inversely associated with nonaggressive disease, but only for BMI at age 18 years and at baseline was there a suggestion that higher BMIs were associated with increased risks of aggressive disease. Specifically, obesity at baseline age was associated with a reduced risk of nonaggressive disease (hazard ratio (HR) = 0.69, 95 percent CI: 0.52, 0.93; p for trend = 0.01). Overweight at baseline age was associated with an increased risk of aggressive disease (HR = 1.4, 95 percent CI: 1.1, 1.8), but obesity was not (HR = 1.1, 95 percent CI: 0.83, 1.6; p for trend = 0.69). Associations of BMI at baseline with prostate cancer risk did not differ by age, family history, or PSA (data not presented). Furthermore, associations of BMI with aggressive cancer were similar when the definition of aggressive disease excluded Gleason sum 7 tumors. For example, men who were overweight at baseline age had an increased risk of more restrictively defined aggressive disease (HR = 1.3, 95 percent CI: 0.89, 1.9), but obese men still did not (HR = 1.1, 95 percent CI: 0.71, 1.8; p for trend = 0.77).

Because it is unclear whether weight gain, obesity, or both are associated with prostate cancer risk, we evaluated whether weight change per se, independent of BMI at baseline age, was associated with risk of aggressive or nonaggressive prostate cancer. After we adjusted for baseline BMI, weight gain of 30 or more pounds from age 18 years was associated with a 33 percent reduced risk (95 percent CI: 0.47, 0.95) of nonaggressive disease (p for trend excluding weight loss category = 0.04) but was not associated with aggressive disease. Weight loss of 10 or more pounds was also associated with a reduced risk of nonaggressive disease (HR = 0.25, 95 percent CI: 0.09, 0.68), although few cases lost weight.

Height was associated with a modestly elevated total prostate cancer risk. Those who were in the top quartile of height (≥ 73 inches) had a 30 percent (95 percent CI: 1.1, 1.6) increased risk of total prostate cancer and a similarly elevated

risk of nonaggressive (HR = 1.3, 95 percent CI: 0.97, 1.8) and aggressive (HR = 1.4, 95 percent CI: 0.98, 1.9) prostate cancer. A trend of increasing risk across quartile of height was significant for total ($p = 0.02$) and aggressive ($p = 0.04$), but not for nonaggressive, prostate cancer ($p = 0.20$). Age at which maximum height was reached was not associated with prostate cancer risk.

DISCUSSION

Findings from the current study support the hypothesis that obesity may increase the risk of aggressive disease and decrease the risk of nonaggressive cancer. Results were generally suggestive that obesity from age 30 years and weight gain from age 18 years, independent of baseline BMI, were associated with decreased risks of nonaggressive disease. However, increased risks of aggressive prostate cancer from age 18 years were generally more consistent for the highest category of weight than for BMI. The positive associations observed for weight and aggressive disease may be due in part to height, because weight and height are correlated (r for weight at different ages and height ranged between 0.42 and 0.50 in this cohort). Finally, although previous studies have found that reaching one's maximum height at an earlier age is associated with an increased risk of breast (13, 14) and prostate (15) cancers, associations were null in the current study.

Similar to the findings in the current study, most previous studies have observed a weak, positive association between height and prostate cancer risk, with 20–40 percent increased risks observed for the tallest compared with the shortest men (6, 16, 17). Height has been proposed as a marker of other exposures that may be related to prostate cancer risk, including the prenatal environment, diet in childhood, timing of puberty, and insulin-like growth factors (17–20).

In the literature, there is relatively consistent evidence that obesity increases the risk of prostate cancer mortality, aggressive or high-grade disease, and biochemical progression following surgery (21–28). The hypothesis that obesity may be associated with a decreased risk of nonaggressive disease is comparatively new, however (7). While relatively few studies have looked at nonaggressive disease exclusively, a number (29–34) have observed inverse associations of obesity and prostate cancer risk either overall or in subgroups defined by age at baseline (<60 years (31), <65 years (33), or ≥ 70 years (34)), family history (31), and obesity before age 30 years with advanced disease risk (29, 32). In the current study, associations of obesity with prostate cancer did not differ by age or family history, but we had limited ability to investigate these interactions after stratifying on tumor characteristics.

Investigators have hypothesized that obesity during puberty or early adulthood may be more strongly associated with prostate cancer risk than body size later in life. Studies have observed both positive (35, 36) and null (37) associations for total prostate cancer and increased (36) and decreased (29, 32) risks of high-grade or advanced tumors. When we classified participants by their weight at age 18 or 30 years, we observed consistently increased risks of aggressive prostate cancer. Associations were weaker based on category of BMI

at each age. Conversely, there were no associations of either weight or BMI at age 18 or 30 years with nonaggressive disease.

The few studies that have investigated weight change from early adulthood have not observed statistically significant associations (35, 37–39). The current study suggested that both weight loss and weight gain, after adjusting for BMI at baseline, were associated with decreased risks of nonaggressive disease, although weight change was not associated with an increased risk of aggressive disease. These results were similar to what we observed for BMI at baseline age but suggest that, independent of BMI at baseline, weight gain itself may reduce the risk of nonaggressive prostate cancer. These findings are intriguing and warrant replication.

Numerous biologic mechanisms explain how obesity could increase and decrease prostate cancer risk. Obese men have higher levels of estrogen and lower sex hormone-binding globulin levels, resulting in lower free testosterone levels than are found in normal-weight men (5). Although the dogma for several decades has been that androgens increase prostate cancer risk (40), the epidemiologic evidence has failed to consistently support that contention (41). In several recently published large and well-designed cohort studies, a high-androgenic environment (high testosterone and/or low estradiol/testosterone ratio) was associated with a reduced risk of high-grade prostate cancer, whereas a high-estrogenic environment was associated with a reduced risk of low-grade disease (42–44). Testosterone may be necessary for tumor development, but testosterone also helps maintain the differentiated state of normal prostatic epithelium and may play a similar role to help maintain tumor differentiation (45). In other words, only aggressive and partially androgen-insensitive cancers may be able to grow in a low-androgen “hostile environment.” This hypothesis was supported by findings from the Prostate Cancer Prevention Trial, a randomized trial that found that finasteride, a drug that blocks the enzyme which converts testosterone to dihydrotestosterone, reduced prostate cancer risk overall but increased the risk of high-grade cancer (46). Although estrogens are effective antiandrogens in prostate cancer treatment, there is also evidence that they can increase cellular proliferation and decrease cellular differentiation and apoptosis (47).

Obesity is also associated with factors such as caloric excess, high-fat diet, and alterations in multiple mitogenic hormones including insulin, leptin, and insulin-like growth factor-1 that may all promote the development and progression of aggressive prostate cancer (19, 26, 48, 49). In some studies, high-fat diets have been linked to an increased risk of aggressive disease and death following prostate cancer diagnosis (50), but not nonaggressive disease (51), suggesting that high-fat diets may promote the development of high-grade disease (52).

Confounding or detection bias could also possibly explain the lower risk of nonaggressive disease among obese men. Obese men may have lower PSA screening rates, falsely low PSA values (53, 54), lower sensitivity of digital rectal examinations (55), and larger prostates, making it more difficult to detect tumors (56). In our study, the prevalence of PSA screening in the 2 years before baseline was similar among normal and obese men (71.1 percent and 70.8

TABLE 2. Adjusted* hazard ratios and 95% confidence intervals for total, nonaggressive, and aggressive† prostate cancer associated with anthropometric measures at age 18 years, age 30 years, age 45 years, and baseline, Washington State, 2000–2004

Measure	No. of cases	No. in the cohort	HR‡	95% CI‡	No. of cases	No. in the cohort	HR	95% CI	No. of cases	No. in the cohort	HR	95% CI	No. of cases	No. in the cohort	HR	95% CI	p for trend
Weight at age 18 years (pounds §)																	
	1st quartile (<139, reference)				2nd quartile (139–154)				3rd quartile (155–170)				4th quartile (≥171)				
Total	166	7,790	1.0		203	8,024	1.2	0.96, 1.5	198	8,471	1.1	0.93, 1.4	231	9,770	1.2	1.0, 1.5	0.08
Nonaggressive	94	7,718	1.0		107	7,928	1.0	0.89, 1.5	104	8,377	1.1	0.81, 1.4	112	9,651	1.1	0.81, 1.4	0.73
Aggressive	71	7,695	1.0		94	7,915	1.3	0.92, 1.7	89	8,362	1.2	0.86, 1.6	117	9,656	1.4	1.0, 1.9	0.04
p for difference¶																	0.20
Weight at age 30 years (pounds)																	
	1st quartile (<154, reference)				2nd quartile (154–169)				3rd quartile (170–184)				4th quartile (≥185)				
Total	174	8,076	1.0		192	7,801	1.2	0.95, 1.4	188	8,069	1.1	0.93, 1.4	241	10,075	1.3	1.0, 1.6	0.03
Nonaggressive	100	8,002	1.0		104	7,713	1.1	0.83, 1.5	93	7,974	0.99	0.74, 1.3	119	9,953	1.1	0.85, 1.5	0.55
Aggressive	72	7,974	1.0		84	7,693	1.2	0.90, 1.7	93	7,974	1.4	0.99, 1.9	119	9,953	1.5	1.1, 2.0	0.01
p for difference¶																	0.10
Weight at age 45 years (pounds)																	
	1st quartile (<165, reference)				2nd quartile (165–179)				3rd quartile (180–199)				4th quartile (≥200)				
Total	194	8,079	1.0		182	7,676	1.0	0.82, 1.2	224	9,155	1.1	0.91, 1.3	200	9,347	1.1	0.87, 1.3	0.46
Nonaggressive	120	8,005	1.0		93	7,587	0.84	0.63, 1.1	109	9,040	0.87	0.67, 1.1	96	9,243	0.84	0.64, 1.1	0.30
Aggressive	72	7,957	1.0		86	7,580	1.3	0.93, 1.8	111	9,042	1.5	1.1, 2.0	102	9,249	1.4	1.1, 2.0	0.032
p for difference¶																	0.02
Weight at baseline age (pounds)																	
	1st quartile (<173, reference)				2nd quartile (174–189)				3rd quartile (190–214)				4th quartile (≥215)				
Total	211	8,563	1.0		181	7,153	1.0	0.83, 1.2	233	9,527	0.99	0.82, 1.2	192	9,110	0.92	0.75, 1.1	0.35
Nonaggressive	130	8,482	1.0		90	7,062	0.82	0.62, 1.1	116	9,410	0.81	0.63, 1.1	92	9,010	0.71	0.54, 0.93	0.02
Aggressive	78	8,430	1.0		87	7,059	1.3	0.96, 1.8	115	9,409	1.3	0.97, 1.7	98	9,016	1.3	0.93, 1.7	0.23
p for difference¶																	<0.01
BMI‡ at age 18 years (kg/m ²)																	
	<21.5 (reference)				21.5–24.9				≥25								
Total	353	15,009	1.0		320	13,627	1.0	0.89, 1.2	118	5,160	1.1	0.89, 1.4					
Nonaggressive	191	14,847	1.0		168	13,475	1.0	0.81, 1.2	55	5,097	0.95	0.70, 1.3					
Aggressive	158	14,814	1.0		148	13,455	1.1	0.86, 1.4	61	5,103	1.3	0.94, 1.7					
p for difference¶																	0.22
BMI at age 30 years (kg/m ²)																	
	<25 (reference)				25–29.9				≥30								
Total	504	20,849	1.0		248	10,940	1.0	0.86, 1.2	26	1,559	0.86	0.58, 1.3					
Nonaggressive	271	20,616	1.0		126	10,818	0.95	0.77, 1.2	10	1,543	0.62	0.33, 1.2					
Aggressive	226	20,571	1.0		118	10,810	1.1	0.85, 1.3	16	1,549	1.2	0.71, 2.0					
p for difference¶																	0.16

BMI at age 45 years (kg/m ²)		<25 (reference)			25-29.9				≥30								
Total	365	14,627	1.0		360	15,288	1.0	0.88, 1.2	66	4,050	0.84	0.64, 1.1		0.34			
Nonaggressive	199	14,461	1.0		187	15,115	0.98	0.80, 1.2	29	4,013	0.69	0.46, 1.0		0.11			
Aggressive	160	14,422	1.0		168	15,096	1.1	0.86, 1.3	37	4,021	1.1	0.73, 1.5		0.65			
<i>p</i> for difference¶														0.08			
BMI at baseline age (kg/m ²)		<25 (reference)			25-29.9				≥30								
Total	218	9,271	1.0		435	16,640	1.1	0.97, 1.4	155	8,149	0.87	0.71, 1.1		0.13			
Nonaggressive	129	9,182	1.0		222	16,427	0.99	0.79, 1.2	73	8,067	0.69	0.52, 0.93		0.01			
Aggressive	85	9,138	1.0		209	16,414	1.4	1.1, 1.8	79	8,073	1.1	0.83, 1.6		0.69			
<i>p</i> for difference¶														0.03			
Weight change from age 18 years to baseline#,**		Lost ≥10 pounds			Maintained weight within 10 pounds (reference)				Gained 10-29 pounds			Gained ≥30 pounds					
Total	17	1,012	0.59	0.34, 1.0	78	2,677	1.0		264	10,790	0.83	0.64, 1.1	432	19,229	0.77	0.59, 1.0	0.11
Nonaggressive	5	1,000	0.25	0.09, 0.68	48	2,647	1.0		147	10,673	0.78	0.56, 1.1	212	19,009	0.67	0.47, 0.95	0.04
Aggressive	12	1,007	1.2	0.59, 2.3	29	2,628	1.0		112	10,638	0.91	0.60, 1.4	216	19,013	0.94	0.61, 1.5	0.92
<i>p</i> for difference¶																	0.36
Height (inches††)		≤68 (reference)			69-70				71-72			≥73					
Total	148	7,375	1.0		229	9,139	1.2	0.98, 1.5	231	10,086	1.1	0.91, 1.4	214	8,154	1.3	1.1, 1.6	0.02
Nonaggressive	80	7,307	1.0		137	9,047	1.4	1.0, 1.8	106	9,961	0.99	0.73, 1.3	109	8,049	1.3	0.97, 1.8	0.20
Aggressive	66	7,293	1.0		88	8,998	1.0	0.75, 1.4	121	9,976	1.3	0.98, 1.7	103	8,043	1.4	0.98, 1.9	0.04
<i>p</i> for difference¶																	0.48
Age at which maximal height was reached (years)		≤16 (reference)			17				18			≥19					
Total	144	6,647	1.0		129	5,498	1.0	0.82, 1.3	234	9,866	1.0	0.84, 1.3	244	10,524	1.0	0.82, 1.2	0.98
Nonaggressive	79	6,582	1.0		59	5,428	0.84	0.59, 1.2	128	9,760	1.0	0.78, 1.4	127	10,407	0.94	0.71, 1.3	0.99
Aggressive	62	6,565	1.0		68	5,437	1.3	0.93, 1.9	104	9,736	1.1	0.78, 1.5	113	10,393	1.1	0.80, 1.5	0.95
<i>p</i> for difference¶																	0.99

* Adjusted for age, family history of prostate cancer, and race and stratified on prostate-specific antigen (PSA) screening in the 2 years before baseline.

† Aggressive tumors are Gleason sum 7-10 or regional/distant stage.

‡ HR, hazard ratio; CI, confidence interval; BMI, body mass index.

§ One pound = 0.45 kg.

¶ *p* for difference in trend comparing risk of aggressive disease with risk of nonaggressive disease.

Adjusted for age, family history of prostate cancer, race, and BMI at baseline and stratified on PSA screening in the 2 years before baseline.

** *p* for trend of weight gain only.

†† One inch = 2.54 cm.

percent, respectively) and was higher in overweight men (73.3 percent). Thus, it is unlikely that underdiagnosis due to less screening could explain our results. Furthermore, in the Prostate Cancer Prevention Trial, a study whose design eliminated the potential for detection bias because all participants received an end-of-study biopsy, results for obesity were similar to those observed in the current study (30).

Limitations of our study include errors of recall and reporting. We used self-reported height and weight at baseline and recalled weight at ages 18, 30, and 45 years. Self-report of weight has been found to be valid, but people tend to underreport their current and previous weight, and those who are obese may underreport their weight more than those who are lean (57–60). Although we were unable to verify reported weights or heights, in a sample of 101 men, weight and height at previous ages had excellent 3-month test-retest reliability (Spearman's rank order correlation coefficients ranged between 0.91 and 0.99). Correlations were somewhat lower for age at which maximum height was reached (Spearman's $r = 0.74$). In addition, because data on weight and other anthropometric factors were collected before cancer diagnosis, any misclassification should not differ between men who developed prostate cancer and men who did not. Other limitations include the fact that we did not update information on PSA testing after baseline. Although history of PSA testing is a good indicator for future PSA testing, it is imperfect. Men in the VITAL cohort were self-selected and therefore possibly more health conscious than other men. However, compared with men in Washington State, a higher percentage of those in the VITAL cohort were overweight (48 percent vs. 43 percent), whereas obesity rates were similar (24 percent) (61). Finally, we acknowledge that BMI, weight, height, and weight change are all interrelated. By examining each, we are able to better understand the associations between the various anthropometric factors and prostate cancer risk.

In summary, we found that obesity was differentially associated with aggressive and nonaggressive prostate cancer risk, and this difference by cancer type could help explain inconsistent results from previous studies (5–7, 16). When the proportion of aggressive disease is high, as in the pre-PSA era, obesity may be associated with an increased risk of total prostate cancer. When the prevalence of aggressive disease is low, it may appear that obesity is unrelated to prostate cancer or is associated with a reduced risk. Lower androgenic and higher estrogenic activity among obese men may result in a lower risk of nonaggressive prostate cancer but an increased risk of aggressive prostate cancer. These results demonstrate the complexity of prostate cancer epidemiology and the importance of examining risk factors by tumor characteristics.

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