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Relationship of body mass, height and weight gain to prostate cancer risk in the Multiethnic Cohort

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Abstract

We investigated the relationship of body size and prostate cancer risk in the Multiethnic Cohort, a longitudinal study of individuals aged 45–75 in Hawaii and California. Self-reported measures of height and weight were obtained at baseline. Of 83,879 men enrolled in 1993–1996, a total of 5,554 were diagnosed with prostate cancer during an average of 9.6 years of follow-up.

The relationship of baseline weight and weight change since age 21 varied by ethnic group. Whites gaining more than 10 lbs had a non-linear, increased risk of advanced and high-grade prostate cancer (RR 2.12, 95% CI 1.19–3.78, for 25–39.9 lb, p trend 0.43; and RR 1.49, 95% CI 1.04–2.14, for ≥40 lb, p trend 0.20, respectively). African American men gaining 40 lb or more (relative to <10 lb) had a non-monotonic, increased risk of localized prostate cancers (RR 1.26, 95% CI 1.02–1.54, p trend 0.09) and those who gained 25 lbs or more were at increased risk of low-grade disease (RR 1.28, 95% CI 1.03–1.58, for ≥40 lb vs. 10 lb, respectively, p trend 0.07). Japanese men had a statistically significant, inverse association of weight gain and localized disease (RR 0.80, 95% CI 0.65–0.99, for ≥40 lb vs. 10 lb, p trend 0.05).

Our findings provide evidence that adiposity and changes in adiposity between younger and older adulthood influence the development of prostate cancer. Ethnic differences in risk may be explained by variation in the distribution of accumulated body fat that could differentially affect prostate carcinogenesis.

Introduction

The relationship between body size and prostate cancer risk is unclear and studies to date have shown inconsistent results (1–3). Among cohort studies published between prior to 2001, 5 of 11 demonstrated a positive association of body mass or weight with prostate cancer risk (1). A meta-analysis of cohort studies published through 2004 found a weak, positive association of body mass index (BMI) with prostate cancer (2). More recent prospective studies have observed inverse associations of BMI and risk of early stage and low-grade prostate cancers (4–6). Studies examining the relationship of body size in early adult life and prostate cancer risk cumulatively provide evidence of a null or weak positive relationship (7). Excessive weight gain was observed to be positively associated with early stage prostate malignancies (8) and prostate cancer mortality (5). In contrast, weight gain was associated with a decreased risk of prostate cancer (9) and weight loss was inversely associated with prostate cancer risk (4). Height has also been inconsistently associated with prostate cancer in cohort studies (1,2). We

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examined the role of anthropometry in the risk for prostate cancer among a multiethnic population characterized by great variation in both body size and prostate cancer risk.

Materials and Methods

Study cohort

The Multiethnic Cohort (MEC) is comprised of more than 215,000 adults aged 45–75 in 1993 living in Hawaii and California. Participants were recruited in 1993–1996 primarily from 5 ethnic populations: African Americans, Japanese, Latinos, Native Hawaiians, and Whites. The study was approved by the institutional review boards overseeing research on human subjects at the University of Hawaii and the University of Southern California. Details of the design and development of the MEC have been previously described (10).

Of the nearly 97,000 men initially enrolled, a total of 83,879 were included in the present analysis based on the following criteria: identifying as one of the 5 ethnic groups targeted by the study, no history of prostate cancer at study enrollment based on questionnaire or registry information, and providing complete height and weight information at baseline. In addition, men with implausible dietary data were excluded as a measure of questionable quality.

Implausible dietary data included log values outside the range of the mean ±3 robust standard deviations for energy and outside the range of the mean ±3.5 robust standard deviations for macronutrients fat, protein and carbohydrate. The robust standard deviation was computed assuming that the middle 80% of the distribution came from a truncated normal distribution to overcome the dietary extremes inflating the general SD (11).

Baseline questionnaire

At study enrollment, all participants completed a mailed questionnaire detailing demographic, medical, and dietary history information. Anthropometric measures were self-reported and included current height, current weight, and weight at age 21.

Case ascertainment

Histologically-confirmed, invasive prostate cancer cases were identified by linkage of the cohort to the Surveillance, Epidemiology, and End Results (SEER) cancer registries covering the state of Hawaii, Los Angeles County, California, and the state of California. The cohort was also linked to death certificate files in Hawaii and California and to the National Death Index. The present analysis includes all prostate cancer cases diagnosed among eligible participants beginning from cohort entry through December 31, 2004. A total of 5,554 invasive prostate cancer cases were diagnosed during the average follow-up period of 9.6 years. Early stage, or localized, cases were defined as tumors confined to the prostate while advanced stage cases were defined as those spread outside the prostate (i.e., regional or metastatic disease). Low- and high-grade prostate tumors were defined as those with Gleason scores of <7 and ≥ 7, respectively.

Statistical analysis

All analyses were performed using SAS statistical software version 9.1 (SAS Institute, Cary, NC). Differences in anthropometric measures between ethnic groups were evaluated using analysis of covariance with adjustment for age and chi-square tests for distribution.

The main analysis focused on the relationship of body size to invasive prostate cancer risk considering all cases, cases classified by stage (advanced versus localized), and cases classified by grade (high-grade versus low-grade). Relative risks (RR) of prostate cancer and 95% confidence intervals (CI) were estimated using Cox proportional hazards models. In general

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for the models of anthropometric variables, age was used as the time metric. However, follow-up from cohort entry was used as the time metric in models examining potential confounders, including age. The entry date for follow-up was the date of questionnaire completion or the 45th birth date (for the <1% of cohort members who were slightly younger than 45 at questionnaire completion). The closure date was the earliest of the following: diagnosis date, date of death, or December 31, 2004.

BMI at cohort entry and BMI at age 21 were calculated as weight in kilograms divided by height in meters squared. BMI was categorized into four clinically defined categories: <18.5 kg/m^2 (underweight), 18.5–24.9 kg/m^2 (normal), 25.0–29.9 kg/m^2 (overweight), and ≥30 kg/m^2 (obese) (12). For BMI at age 21, overweight and obese categories were combined due to limited numbers. Height and weight were categorized into quartiles based on their distributions in the entire cohort. Absolute change in weight since age 21 was calculated by subtracting weight at age 21 from baseline weight. Weight change per year was examined to account for variation in the number of years between age 21 and baseline. In addition, relative weight change was calculated by subtraction weight at age 21 from weight at baseline and dividing this difference by weight at 21.

Anthropometric variables were entered into models as indicator variables representing group membership, with normal BMI groups and the lowest quartile for the other variables as the reference category. Linear trends were evaluated using a variable assigned the median value within the appropriate overall quartiles or categories. The proportional hazards assumption for anthropometric measures was tested using Schoenfeld residuals and the assumption was not violated (13).

Cox proportional hazards models for anthropometric variables were adjusted for the following strata variables: age at cohort entry (<50, 50–59, 60–69, and ≥70 years), ethnicity (African Americans, Japanese, Latino- Mexico/South American-born, Latino- U.S.-born, Native Hawaiians, and Whites), marital status (married, separated/divorced, widowed, and never married), history of prostate cancer in a father or brother (yes and no/do not know), birthplace (USA, Mexico, Central/South American, Japan, Europe, and other), education level (<high school, high school graduate, some college/vocational school, and college graduate), and smoking status (never smokers; former smoker; current smoker of <10 cigarettes/day, 10–19/day, and ≥20/day). These variables were found to be associated with either prostate cancer or prostate cancer screening in this cohort (14). In addition to these covariates, models of baseline weight, baseline BMI, and weight change variables were adjusted for weight at age 21. In separate analyses, weight at age 21, baseline weight, and weight changes since age 21 were additionally adjusted for height. All statistical tests used 2-sided p-values and statistical significance was set at $p<0.05$.

Heterogeneity of effects by disease stage and grade and across ethnic groups was evaluated. The effect of anthropometric measures by disease stage and grade was compared in overall models using competing risk techniques, where localized and advanced cancers are different events and where low- and high-grade tumors are different events (13). In the competing risk models, we allowed ethnic-specific effects by disease severity, as that variable was a strong confounder for height and weight variables. The effect of anthropometry by ethnicity was compared using a Wald test of the cross-product terms of anthropometry measures and ethnic group.

Diabetes was previously found to be protective for prostate cancer and correlated with obesity in this cohort (15). In order to evaluate a possible confounding effect of diabetes on the relationship between BMI and prostate cancer risk, models were run excluding all men with a

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diagnosis of diabetes at baseline. In addition, the joint effects of BMI and diabetes on prostate cancer risk were evaluated.

To evaluate whether PSA screening history influenced the relationship of anthropometry to prostate cancer, the separate main effects models were repeated for the 62,327 men who completed a follow-up questionnaire approximately 5 years after cohort entry that asked about history of PSA screening. The analysis was stratified by PSA screening and adjusted for the covariates listed above. Follow-up for was defined as time from the follow-up questionnaire administration to 2004. Men with a prostate cancer diagnosis between the baseline and follow-up questionnaire were excluded from this analysis.

Results

Of the 5,554 men in the MEC diagnosed with invasive prostate cancer, 632 cases were of advanced stage, 4,434 were localized, and 488 had no stage information. In grouping by grade, there were 1,563 high-grade cases, 3,649 low-grade cases, and 342 cases had no grade information. Cases with no stage and grade information were excluded from all analyses by disease stage and grade, respectively.

Table 1 details the characteristics of the study cohort of 83,879 men and the relationship of these characteristics to prostate cancer risk (adjusted for all factors listed). Risk of prostate cancer increased with age and this trend was significant ($p < 0.001$). Compared to White men, African Americans and U.S.-born Latinos had elevated risks and Japanese men a reduced risk of prostate cancer. Single/never married men were at a lower risk of prostate cancer relative to married men. Prostate cancer risk increased with education level and a positive family history. Cigarette smoking, which was previously found to be related to lack of PSA screening in this cohort (14), was inversely associated with prostate cancer risk.

Body size varied widely by ethnicity and these differences were significant for all anthropometric measures (Table 2). Mean height ranged from 66 inches for Japanese to 70 inches for Whites and African Americans. All other indices of body size were lowest among Japanese and highest in Native Hawaiians. Overall at baseline, approximately 1% of the cohort was underweight, 42% of normal weight, 43% overweight and 14% obese. A total of 11% and 3% of men had a baseline BMI of 30–34.9 kg/m^2 and ≥35.0 kg/m^2, respectively.

Table 3 details the relationship of body size to prostate cancer risk overall and by disease severity. Relative to men weighing <154 lb at baseline, men weighing 172–193.9 lb had an increased risk of localized prostate cancer (RR 1.12, 95% CI 1.01–1.24, p trend 0.74) and an increased risk of high-grade disease, although this relationship was of borderline significance.

Relative to men of normal BMI at age 21, men who were overweight or obese at age 21 were at decreased risk of both localized tumors and low-grade disease, although these relationships were non-monotonic (RR 0.87, 95% CI 0.79–0.97, p trend 0.08 and RR 0.87, 95% CI 0.78–0.98, p trend 0.22, respectively) (Table 3). BMI at age 21 was also inversely associated with total prostate cancer risk.

Absolute and relative weight changes since age 21 were positively associated with risk of high-grade and advanced prostate cancer, although the relationships were non-monotonic (Table 3). Relative to weight gain <10 lb, weight gain of 25–39.0 lb was positively associated with both advanced and high-grade disease: RR 1.34, 95% CI 1.02–01.74, p trend 0.92; and RR 1.19, 95% CI 1.01–1.41, p trend 0.14, respectively. Weight gain of 7–15% since age 21 was positively associated with advanced tumors: RR= 1.34, 95% CI 1.05–1.71, relative to <7% weight gain, p trend 0.82. There was a borderline significant association of relative weight change ≥28% with high-grade disease.

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Height, baseline BMI, weight at age 21, and weight change per year were not associated with prostate cancer risk in this analysis (Table 3). Adjustment of weight variables for height did not alter the results.

When men with diabetes at baseline were excluded from analysis, the relationships of anthropometric measures with prostate cancer risk were unchanged (data not shown). Furthermore, there was no evidence of interaction between body size and diabetes on prostate cancer risk (data not shown).

Ethnic differences in the relationship of body size to prostate cancer risk were evaluated (Table 4). Differential effects of weight at baseline were found across ethnic groups (p for interaction 0.02). Whites and Native Hawaiians had a non-linear, positive association of baseline weight with prostate cancer risk. White men in the 2nd and 3rd quartiles of baseline weight had an increased risk of prostate cancer (RR 1.32, 95% CI 1.06–1.64, for 172–193.9 (3rd quartile) vs. 154 lb, p trend 0.66). Similarly, Native Hawaiian men in the 2nd–4th quartiles of baseline weight had an increased risk of prostate cancer: RR 1.90, 95% CI 1.09–3.34, for ≥194 lb (4th quartile) vs. 154 lb, p trend 0.12. In contrast, among Japanese there was an inverse, dose-response association of baseline weight with prostate cancer: RR 0.69, 95% CI 0.50–0.97, for ≥194 (4th quartile) vs. 154 lb, p trend 0.03. The associations of baseline weight with prostate cancer risk were unchanged after adjustment for height.

The effect of weight change since age 21 on prostate cancer risk differed significantly between groups (p interaction 0.006) but significant associations were seen only for Whites and Japanese. For Whites, there was a non-linear, positive association of weight change with prostate cancer risk: RR 1.23, 95% CI 1.03–1.48, for 10–24.9 vs. 10 lb; and RR 1.25, 95% CI 1.03–1.51, for 25–39.9 vs 10 lb, p trend 0.55. In contrast, Japanese men had an inverse, dose-response association of weight change since age 21 and risk of prostate cancer: RR 0.79, 95% CI 0.65–0.96, p trend 0.01, for ≥40 vs. 10 lb.

The relationship of weight change since age 21 to prostate cancer risk by stage and grade was evaluated across ethnic groups with the exception of Native Hawaiians who were excluded due to small numbers (Table 5). Positive associations of weight change and prostate cancer risk were observed in Whites and African Americans although none of the relationships were monotonic. Relative to weight gain of less than 10 lb since age 21, Whites gaining up to 39.9 lbs were at increased risk of advanced prostate cancer: RR 2.08, 95% CI 1.20–3.60, RR 2.12, 95% CI 1.19–3.78, for 10–24.9 lb and 25–39.9 lb, respectively, p trend 0.43. Among Whites, weight gain was also associated with increased risk of high-grade disease (RR 1.76, 95% CI 1.25–2.48; RR 1.63, 95% CI 1.13–2.35; and RR 1.49, 95% CI 1.04–2.14; for 10–24.9 lb, 25–39.9 lb, and ≥40 lb vs. 10 lb, respectively, p trend 0.20. African American men gaining 40 lb or more (relative to <10 lb) were at increased risk of localized prostate cancers (RR 1.26, 95% CI 1.02–1.54, p trend 0.09) and those who gained 25 lbs or more were at increased risk of low-grade disease (RR 1.30, 95% CI 1.03–1.63 and RR 1.28, 95% CI 1.03–1.58, for weight gain of 25–39.9 lb and ≥40 lb, respectively, p trend 0.07). Japanese men had a statistically significant, inverse association of weight gain and localized disease: RR 0.80, 95% CI 0.65–0.99, for ≥40 lb vs. 10 lb, p trend 0.05. Japanese men also had an inverse association of weight gain with low-grade disease although the association was of borderline significance. The effect of weight change since age 21 on risk of low-grade disease differed significantly between ethnic groups (p interaction 0.04).

Stratification by age at cohort entry (<60, ≥60) and by family history of prostate cancer (yes, no) demonstrated no effect modification by age or family history in the relationship of anthropometric measures and prostate cancer risk (data not shown).

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In order to assess the effects of pre-clinical disease, we performed a lag analysis excluding 980 cases diagnosed within the first two years of follow-up. There were no substantial changes in the association of anthropometric measures with prostate cancer risk with the exception of weight change among Japanese men. Excluding the first two years of follow-up, the inverse association of weight gain since age 21 with localized disease risk observed in Japanese men was no longer significant (RR 0.87, 95% CI 0.69–1.09, for ≥40 vs. 10 lb, p trend 0.15).

In the cohort subset of men who responded to a follow-up questionnaire, 45% of the men reported PSA screening. Screening varied significantly by ethnicity with the highest levels of screening among Whites (51.5%), followed by African Americans (50.7%), Latinos (43.4%), Japanese (43.0%), and Native Hawaiians (28.3%) ($p<0.001$). PSA screening also varied by baseline BMI and was lowest among underweight men and the most overweight men: 39.3%, 46.1%, 45.3%, 42.1%, and 39.4% for <18.5, 18.5–24.9, 25.0–29.9, 30.0–34.9, and ≥35 kg/m^2, respectively, ($p<0.001$). However, within ethnic groups these differences in PSA screening by BMI were significant only among Native Hawaiians and Japanese: Native Hawaiians 25.9% (<18.5 kg/m^2) and 24.3–25.5% (≥30.0 kg/m^2) ($p<0.05$) and Japanese 37.1% (<18.5 kg/m^2) and 32.7–36.0% (≥30 kg/m^2) ($p<0.001$). To evaluate the influence of prostate cancer screening, the main effects models were repeated for the subset of men for whom PSA screening history was available. There was no difference in effects between screened and non-screened men (data not shown).

Discussion

Our findings provide evidence that body mass in both younger and older adulthood, and weight gain between these periods of life, may influence prostate cancer risk. Overall, men who were overweight or obese at age 21 had a non-linear, decreased risk of developing both localized and low-grade prostate cancer.

We also observed that weight gain between age 21 until study entry—a period of time spanning a minimum of 24 years-- increased risk of both advanced and high-grade disease. The effects of weight gain on advanced and high-grade prostate cancer risk, however, were not monotonic, but remained when we limited our analysis to cases diagnosed after 2 years of follow-up.

The relationship of body size and weight change differed by ethnic group. Baseline weight was positively associated with prostate cancer risk among Whites and Native Hawaiians, although linear increases in risk were not evident across categories. In contrast, there was a inverse, dose-response association of baseline weight with disease risk among Japanese. Weight gain since age 21 increased the risk of prostate cancer among Whites although the relationship was not linear. Among Japanese, weight gain since age 21 decreased disease risk in a dose-response manner. This association was no longer significant after exclusion of cases diagnosed during the early period of follow-up. This is likely a result of lack of power given that Japanese men had the lowest weight gain of any ethnic group rather than an effect of preclinical disease.

When stratified by disease severity, weight gain was positively associated with both advanced and high-grade prostate cancer in Whites and with both localized and low-grade disease among African Americans. These relationships were not monotonic, however. Among Japanese men, weight gain was associated with a significant trend of decreasing risk of early stage prostate cancers. There was evidence of effect modification of weight change and ethnicity with the risk of low-grade disease.

To the best of our knowledge, this is the first report of ethnic differences in the relationship between body size and prostate cancer risk. The Multiethnic Cohort includes groups with wide variation in anthropometric measures and groups with extremely low and high incidences of prostate cancer, i.e., Japanese and African Americans, respectively.

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Consistent with our results, 3 other prospective studies also observed an inverse association of high BMI and risk of non-advanced prostate cancer (4–6). Rodriquez et al (4) found that obesity decreased the risk of localized, low-grade prostate cancer and this was observed for obesity up to 11 years and up to 21 years prior to diagnosis. In another study, both measured BMI and waist circumference were inversely associated with low-grade prostate cancer (6). The mechanism by which high body mass decreases the risk of prostate disease is unclear. Obesity contributes to decreased levels of testosterone, increased levels of estrogen, as well as other hormonal changes (16,17) (18). It has been suggested that testosterone, which functions to promote differentiation in the normal prostate, at lower levels may promote the growth of high-grade prostate cancers while preventing the development or progression of low-grade prostate tumors (18).

Other prospective studies examining weight gain and prostate cancer have included predominantly White populations, and the findings have been mixed. Weight gain of 30 lb or more from age 18 through study baseline was associated with an increased risk of non-advanced prostate cancer in a U.S. cohort (8). Another prospective study in the U.S. found a positive association of weight gain from age 18 to study baseline with risk of prostate cancer mortality, but not incidence (5). Similarly, net weight loss during a ten-year period was inversely associated with prostate cancer risk in another U.S. cohort (4). In contrast to these results, a cohort in Austria observed an inverse association of weight gain and prostate cancer risk (9) although the average period between the two measures was only 7 years—a period of time far shorter than our cohort and therefore only capturing relatively late changes in weight. A Netherlands cohort observed a trend of decreasing prostate cancer risk with increasing BMI from age 20 to study baseline; however, this relationship was not significant after adjustment for initial BMI (19). Another U.S. prospective study observed no association of weight change from age 21 to study entry with prostate cancer risk (20).

Our findings provide evidence that changes in adiposity between younger and older adulthood influence the development of prostate cancer. This suggests that it is the change in amount of adipose tissue that influences disease risk. In general, it is plausible that excessive weight gain may increase the risk of aggressive disease. Excess adipose tissue is associated with a number of conditions that can contribute to cancer development including low-grade chronic inflammation, insulin resistance, metabolic abnormalities, and hormonal imbalances (18). Obese men have higher levels of estradiol, IGF-1, and leptin and relatively lower levels of testosterone, insulin, insulin-like growth factors, and adiponectin, and these alterations may contribute to more aggressive prostate malignancies (18). It is possible that the process of gaining excess adipose tissue from early to older adulthood may impose added metabolic, hormonal, and immunologic stress independent of initial or final body weight. A similar relationship of weight gain between adolescence and adulthood has been shown for post-menopausal breast cancer (21).

Ethnic differences in risk may be explained by differences in the distribution of accumulated body fat that could have a differential effect on prostate carcinogenesis. It is possible that weight gain from younger to older adulthood specifically reflects changes in central obesity and these changes differ across ethnic groups. The accumulation of visceral fat, a form of adipose tissue centralized in and around organs within the abdominal region, has been shown to vary by ethnic group (22–24) Black men have less visceral fat than White men even when adjusting for total body fatness (24). This may explain the association of weight gain with advanced and high-grade prostate cancer in Whites but not in Blacks.

Abdominal obesity relative to lower body obesity is more strongly associated with metabolic abnormalities (25). An Australian cohort study observed a positive association of several indicators of adiposity--body mass index, fat mass, waist circumference, hip circumference—

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with advanced prostate cancers (26). Abdominal adiposity as measured by waist circumference and waist-hip ratio was associated with advanced cancer in a European cohort (27). A limitation of the present study was the absence of other measures of body size such as waist-to-hip ratio that provide a direct measure of central obesity.

Standards for defining normal weight, overweight, and obesity may vary by ethnicity (28) and therefore may be limited for comparing adiposity across diverse ethnic populations such as ours. Notably, the overall prevalence of overweight in this study population (57%) is on the lower end of the range of national estimates of the prevalence of overweight in men ages 45 and older (56.5%–70.5%) for the mid-1990s when this cohort was enrolled (29). This likely reflects the large proportion of Japanese in this cohort relative to national populations.

Detection of prostate cancers in obese men may be delayed as a result of lower PSA levels due to hemodilution of prostate-specific antigen (30) (18). Furthermore, the prostate glands of obese men are larger than those of men of normal weight so that tumors are more likely to be missed in biopsies (18). In a subset of the cohort, we observed that both underweight men and the most obese men had the lowest levels of screening. It is likely that these differences were largely driven by Japanese and Native Hawaiians who had the lowest and highest proportion of overweight/obese men, respectively, and who also had the lowest levels of screening. Although our evaluation of this subset of the cohort showed no differences in the association of anthropometric measures with prostate cancer risk between PSA screened and unscreened men, we were unable to control for prostate cancer screening in the overall analyses. Nonetheless, it is not likely that detection bias influenced our findings. Delayed detection would have been consistent with an increased risk of aggressive prostate cancers among obese men and not the decreased risk of early stage, low grade tumors that we observed.

It is likely that there was some degree of misclassification of body size due to inaccuracy of self-reported anthropometric measures. Nevertheless, although weight tends to be underreported and height overreported in U.S. surveys, in general there is a high correlation between self-reported and measured weight across ethnic groups (31). Systematic underreporting of weight and overreporting of height could bias risk estimates toward the null. Therefore, the significant associations observed in the present study may actually be underestimated. Furthermore, as anthropometric measures were collected prospectively and prior to cancer diagnosis, any bias should be non-differential. The power in our cohort to investigate more extreme obesity was limited.

Our findings provide some evidence that adiposity, as well as increases in adiposity between younger and older adulthood, may influence the development of prostate cancer. Ethnic differences in risk associated with weight gain may be explained by group differences in the distribution of accumulated body fat that could have a differential effect on prostate carcinogenesis.

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Table 1

Baseline characteristics of males in the Multiethnic Cohort Study and prostate cancer risk, 1993–2004

Characteristics	Total cohort (n=83879)		Prostate cancer cases (n=5554)	
	No.	%	No.	RR (95% CI)[1]
Age at cohort entry (years)				
<50	13853	16.5	201	1.00
50–59	25804	30.8	1109	3.00 (2.58–3.50)
60–69	29707	35.4	2741	6.98 (6.04–8.08)
≥70	14515	17.3	1503	8.63 (7.42–10.04)
Ethnicity				
White	21311	25.4	1179	1.00
African American	10934	13.0	1413	2.28 (2.10–2.48)
Native Hawaiian	5921	7.1	250	0.91 (0.79–1.05)
Japanese	25275	30.1	1382	0.89 (0.82–0.97)
Latino-US born	10452	12.5	774	1.19 (1.08–1.31)
Latino-Mexico/South America born	9986	11.9	555	1.16 (0.83–1.63)
Marital status[2]				
Married	63967	76.8	4314	1.00
Separated	1908	2.3	140	0.99 (0.83–1.18)
Divorced	8451	10.2	534	0.98 (0.89–1.07)
Widowed	3121	3.8	268	0.92 (0.81–1.04)
Never married	5844	7.0	264	0.84 (0.75–0.96)
Birthplace[2]				
USA	69677	83.3	4753	1.00
Mexico	7745	9.3	404	0.87 (0.62–1.24)
Central/South America	2750	3.3	197	1.06 (0.78–1.43)
Japan	1219	1.5	37	0.76 (0.55–1.05)
Europe	1023	1.2	64	1.05 (0.81–1.36)
Other	1272	1.5	85	1.00 (0.80–1.24)
Education[2]				
Less than high school	9271	11.2	614	1.00
Any high school	25073	30.2	1851	1.17 (1.06–1.30)
Some college/vocational school	24268	29.2	1560	1.15 (1.04–1.28)
College graduate	24462	29.5	1468	1.19 (1.07–1.33)
Family history (father/brother) of prostate cancer				
No	78202	93.2	4993	1.00
Yes	5677	6.8	561	1.47 (1.34–1.60)

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Characteristics	Total cohort (n=83879)		Prostate cancer cases (n=5554)	
	No.	%	No.	RR (95% CI)[1]
Cigarette smoking[2,3]				
Never	24839	29.9	1704	1.00
Former	43091	51.9	2938	0.91 (0.86–0.97)
Current	15097	18.2	835	0.86 (0.79–0.94)

[1] Relative risk and 95% confidence interval estimated using Cox proportional hazards models with follow-up as the time metric and adjusted for all other variables in the table.

[2] Missing data: marital status n=587; birthplace n=193; education n=805; cigarette smoking n=852;

[3] Smoked 20 or more packs of cigarettes in lifetime

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Table 2

Anthropometric measures of men by ethnicity, the Multiethnic Cohort Study, 1993–2004

Measure (mean ± SD)[1]	All (n=83879)	White (n=21311)	African American (n=10934)	Native Hawaiian (n=5921)	Japanese (n=25275)	Latino (n=20438)	p[2]
Height at baseline (in.)	68.2 ± 3.2	70.0 ± 2.8	70.1 ± 2.8	68.9 ± 2.8	66.2 ± 2.8	67.6 ± 2.7	<0.001
Weight at baseline (lb)	176.4 ± 33.6	184.1 ± 30.2	190.9 ± 30.2	196.6 ± 30.3	157.5 ± 30.2	178.2 ± 30.1	<0.001
BMI at baseline (kg/m^2)	26.1 ± 4.2	25.9 ± 4.0	26.8 ± 4.0	28.4 ± 4.0	24.8 ± 4.0	26.9 ± 4.0	<0.001
% underweight (<18.5)	1.1	1.0	1.3	0.7	1.7	0.7	<0.001
% normal (18.5–24.9)	41.9	44.0	35.0	23.9	56.1	31.0	
% overweight (25.0–29.9)	42.8	41.3	45.1	43.0	36.2	51.0	
% obese (≥30.0)	14.2	13.7	18.6	32.4	6.0	17.3	
% obese (30.0–34.9)	11.0	10.6	14.4	21.2	5.1	13.7	
% obese (≥35.0)	3.3	3.1	4.2	11.2	0.9	3.6	
Weight at age 21 (lb)	150.0 ± 26.1	158.7 ± 24.3	160.1 ± 24.7	161.6 ± 24.4	138.1 ± 24.3	147.0 ± 24.6	<0.001
BMI at age 21 (kg/m^2)	22.2 ± 3.2	22.3 ± 3.2	22.5 ± 3.3	23.4 ± 3.2	21.7 ± 3.2	22.2 ± 3.2	<0.001
% underweight (<18.5)	7.2	6.9	7.2	5.7	6.8	8.4	<0.001
% normal (18.5–24.9)	78.3	77.8	76.7	65.3	83.3	77.1	
% overweight (25.0–29.9)	12.6	13.7	14.3	23.4	8.7	12.5	
% obese (≥30.0)	1.9	1.6	1.9	5.7	1.2	2.0	
Weight change since age 21 (lb)	26.6 ± 26.8	25.6 ± 26.7	31.3 ± 27.2	35.3 ± 26.8	19.5 ± 26.7	31.7 ± 27.1	<0.001

[1] Means and SDs by ethnicity are adjusted for age using analysis of covariance.

[2] p-value for statistical significance of differences between ethnic groups based on analysis of variance (F statistic) for means and chi-square test for distribution.

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Table 3

Relationship of body size to prostate cancer risk by disease severity in the Multiethnic Cohort Study, 1993–2004

	Total		Advanced [1]		Localized [1]		High grade [2]		Low grade [2]	
	No.	RR (95% CI) [3]	No.	RR (95% CI) [3,4]	No.	RR (95% CI) [3,4]	No.	RR (95% CI) [3,4]	No.	RR (95% CI) [3,4]
Height at baseline (in.)										
<66	1061	1.00	114	1.00	864	1.00	324	1.00	684	1.00
66–67.9	1296	0.99 (0.91–1.08)	141	0.96 (0.74–1.26)	1043	1.00 (0.91–1.10)	388	1.08 (0.92–1.26)	832	0.94 (0.85–1.05)
68–69.9	1227	0.98 (0.89–1.08)	146	1.08 (0.81–1.43)	954	0.96 (0.87–1.07)	330	1.04 (0.87–1.24)	817	0.95 (0.84–1.07)
≥70	1970	1.01 (0.92–1.11)	231	1.03 (0.78–1.37)	1573	1.03 (0.93–1.14)	521	1.09 (0.91–1.30)	1316	0.98 (0.87–1.10)
p for trend		0.71		0.79		0.50		0.37		0.89
Weight at baseline (lbs) [5]										
<154	1333	1.00	150	1.00	1078	1.00	411	1.00	852	1.00
154–171.9	1405	1.04 (0.95–1.13)	150	0.89 (0.69–1.15)	1121	1.05 (0.96–1.16)	404	1.13 (0.96–1.31)	918	0.99 (0.89–1.10)
172–193.9	1488	1.09 (0.99–1.19)	175	1.01 (0.77–1.32)	1182	1.12 (1.01–1.24)	405	1.19 (1.00–1.41)	974	1.02 (0.91–1.14)
≥194	1328	1.00 (0.90–1.12)	157	0.89 (0.65–1.21)	1053	1.03 (0.91–1.15)	343	1.10 (0.90–1.35)	905	0.95 (0.84–1.08)
p for trend		0.98		0.57		0.74		0.39		0.45
BMI at baseline (kg/m^2) [5]										
<18.5	60	0.87 (0.66–1.17)	7	0.93 (0.38–2.29)	47	0.89 (0.65–1.22)	16	0.69 (0.38–1.26)	39	0.92 (0.65–1.30)
18.5–24.9	2366	1.00	267	1.00	1896	1.00	686	1.00	1541	1.00
25.0–29.9	2462	1.04 (0.97–1.11)	281	1.07 (0.88–1.29)	1970	1.04 (0.97–1.12)	690	1.12 (0.99–1.26)	1614	0.99 (0.92–1.07)
≥30.0	666	0.94 (0.85–1.04)	77	0.93 (0.69–1.25)	521	0.92 (0.83–1.03)	171	1.00 (0.82–1.21)	455	0.91 (0.80–1.02)
p for trend		0.62		0.83		0.52		0.37		0.21

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	Total		Advanced [1]		Localized [1]		High grade [2]		Low grade [2]	
	No.	RR (95% CI) [3]	No.	RR (95% CI) [3,4]	No.	RR (95% CI) [3,4]	No.	RR (95% CI) [3,4]	No.	RR (95% CI) [3,4]
Weight at age 21 (lbs) [6]										
<130	1093	1.00	117	1.00	897	1.00	338	1.00	698	1.00
130–144.9	1362	1.00 (0.92–1.09)	144	0.93 (0.72–1.21)	1100	1.01 (0.92–1.11)	400	1.06 (0.91–1.24)	875	0.97 (0.87–1.08)
145–164.9	1468	0.97 (0.89–1.06)	174	1.03 (0.79–1.33)	1155	0.96 (0.87–1.05)	379	0.97 (0.83–1.15)	980	0.95 (0.86–1.06)
≥165	1362	0.97 (0.89–1.07)	167	1.02 (0.77–1.34)	1079	0.96 (0.86–1.07)	383	1.10 (0.93–1.32)	905	0.94 (0.83–1.05)
p for trend		0.47		0.71		0.31		0.36		0.28
BMI at age 21 (kg/m^2) [6]										
<18.5	398	0.96 (0.86–1.07)	41	0.96 (0.69–1.35)	320	0.95 (0.84–1.07)	115	1.00 (0.82–1.23)	251	0.90 (0.79–1.04)
18.5–24.9	4276	1.00	475	1.00	3442	1.00	1213	1.00	2805	1.00
≥25.0	611	0.91 (0.83–0.99)	86	1.09 (0.85–1.40)	469	0.87 (0.79–0.97)	172	0.97 (0.82–1.15)	402	0.87 (0.78–0.98)
p for trend		0.17		0.46		0.08		0.76		0.22
Weight change since age 21 (lbs) [5,6]										
<10	1034	1.00	114	1.00	835	1.00	293	1.00	690	1.00
10–24.9	1562	1.06 (0.98–1.15)	188	1.29 (1.00–1.66)	1234	1.03 (0.94–1.13)	450	1.14 (0.97–1.33)	1000	1.00 (0.90–1.11)
25–39.9	1232	1.06 (0.97–1.15)	151	1.34 (1.02–1.74)	986	1.02 (0.92–1.13)	364	1.19 (1.01–1.41)	797	0.98 (0.87–1.09)
≥40	1457	1.03 (0.94–1.12)	149	1.06 (0.81–1.40)	1176	1.02 (0.93–1.13)	393	1.15 (0.97–1.36)	971	0.95 (0.85–1.06)
p for trend		0.87		0.92		0.77		0.14		0.30
Weight change per year (lbs) [5,6]										
<0.28	1426	1.00	161	1.00	1139	1.00	404	1.00	936	1.00
0.28–0.61	1431	1.01 (0.93–1.09)	173	1.18 (0.93–1.48)	1140	0.99 (0.91–1.08)	424	1.11 (0.96–1.29)	909	0.95 (0.86–1.05)
0.62–1.07	1354	1.00 (0.92–1.08)	158	1.15 (0.90–1.46)	1089	0.98 (0.90–1.07)	396	1.13 (0.97–1.31)	882	0.94 (0.85–1.04)
≥1.08	1074	1.02 (0.93–1.11)	110	0.89 (0.67–1.17)	863	1.03 (0.93–1.13)	276	1.14 (0.95–1.35)	731	0.95 (0.85–1.06)
p for trend		0.79		0.33		0.66		0.16		0.40

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	Total		Advanced [1]		Localized[1]		High grade[2]		Low grade[2]	
	No.	RR (95% CI) [3]	No.	RR (95% CI) [3, 4]	No.	RR (95% CI) [3, 4]	No.	RR (95% CI) [3, 4]	No.	RR (95% CI) [3, 4]
Relative weight change (lbs) [5,6]										
<0.07	1228	1.00	139	1.00	985	1.00	346	1.00	815	1.00
0.07–0.15	1312	1.03 (0.95–1.12)	167	1.34 (1.05–1.71)	1032	1.00 (0.91–1.10)	385	1.10 (0.95–1.29)	837	0.98 (0.88–1.09)
0.16–27.9	1367	1.02 (0.94–1.11)	154	1.18 (0.91–1.51)	1104	0.99 (0.91–1.09)	379	1.07 (0.91–1.25)	906	0.98 (0.88–1.09)
≥0.28	1378	1.02 (0.93–1.11)	142	1.06 (0.81–1.39)	1110	1.02 (0.92–1.12)	390	1.18 (1.00–1.39)	900	0.94 (0.84–1.05)
p for trend		0.80		0.82		0.74		0.08		0.25

[1] Excluded 342 cases missing stage information

[2] Excluded 488 cases missing grade information

[3] Relative risk and 95% confidence interval estimated using Cox proportional hazards models with age as the time metric and adjusted for age at cohort entry, ethnicity, family history of prostate cancer, marital status, education level, birthplace, and smoking history.

[4] Interaction across stage and grade groups was insignificant based on type III Wald test

[5] Additional adjustment for weight at age 21

[6] 269 prostate cancer cases were missing data on weight at age 21

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Table 4

Relationship of body size to prostate cancer risk by ethnicity in the Multiethnic Cohort Study, 1993–2004

	White (n=21311) RR (95% CI) [1]	African American (n=10934) RR (95% CI) [1]	Native Hawaiian (n=5921) RR (95% CI) [1]	Japanese (n=25275) RR (95% CI) [1]	Latino (n=20438) RR (95% CI) [1]	p for interaction [2]
No. of cases	1179	1413	250	1383	1329	
Height at baseline (in.)						
<66	1.00	1.00	1.00	1.00	1.00	0.44
66–67.9	0.92 (0.67–1.27)	0.91 (0.68–1.21)	1.14 (0.67–1.94)	0.96 (0.84–1.08)	1.11 (0.94–1.31)	
68–69.9	0.98 (0.73–1.33)	0.92 (0.70–1.22)	1.05 (0.62–1.76)	0.89 (0.75–1.05)	1.08 (0.91–1.29)	
≥70	0.96 (0.72–1.29)	0.94 (0.72–1.23)	1.09 (0.66–1.81)	1.04 (0.83–1.30)	1.12 (0.94–1.34)	
p trend	0.97	0.92	0.86	0.53	0.25	
Weight at baseline (lb) [3]						
<154	1.00	1.00	1.00	1.00	1.00	0.02
154–171.9	1.32 (1.06–1.65)	1.11 (0.88–1.40)	1.89 (1.07–3.33)	0.88 (0.77–1.01)	1.12 (0.93–1.35)	
172–193.9	1.32 (1.06–1.64)	1.24 (0.99–1.55)	1.85 (1.07–3.20)	0.92 (0.77–1.11)	1.12 (0.93–1.35)	
≥194	1.19 (0.94–1.52)	1.14 (0.90–1.44)	1.90 (1.09–3.34)	0.69 (0.50–0.97)	1.04 (0.85–1.29)	
p trend	0.66	0.54	0.12	0.03	0.93	
BMI at baseline (kg/m^2) [3]						
<18.5	0.59 (0.26–1.34)	0.62 (0.30–1.28)	0.61 (0.08–4.64)	1.04 (0.69–1.55)	1.17 (0.59–2.34)	0.18
18.5–24.9	1.00	1.00	1.00	1.00	1.00	
25.0–29.9	1.06 (0.93–1.21)	1.15 (1.01–1.32)	1.27 (0.89–1.81)	0.92 (0.82–1.04)	1.04 (0.91–1.19)	
≥30.0	0.94 (0.76–1.17)	0.99 (0.83–1.19)	1.20 (0.79–1.83)	0.78 (0.57–1.08)	0.96 (0.79–1.16)	
p trend	0.90	0.62	0.41	0.07	0.69	
Weight at age 21 (lb)[4]						
<130	1.00	1.00	1.00	1.00	1.00	0.13
130–144.9	1.02 (0.80–1.30)	1.16 (0.89–1.52)	1.03 (0.63–1.68)	0.98 (0.86–1.11)	1.00 (0.85–1.18)	
145–164.9	0.95 (0.76–1.19)	1.21 (0.94–1.55)	1.06 (0.68–1.65)	0.89 (0.77–1.05)	0.97 (0.81–1.15)	
≥165	0.94 (0.75–1.17)	1.18 (0.92–1.51)	0.98 (0.63–1.54)	0.91 (0.71–1.16)	1.01 (0.84–1.22)	
p trend	0.36	0.50	0.83	0.19	0.98	
BMI at age 21 (kg/m^2)[4]						
<18.5	0.94 (0.74–1.19)	0.83 (0.65–1.06)	1.48 (0.94–2.32)	1.00 (0.81–1.23)	0.96 (0.77–1.19)	0.69
18.5–24.9	1.00	1.00	1.00	1.00	1.00	

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	White (n=21311) RR (95% CI) [1]	African American (n=10934) RR (95% CI) [1]	Native Hawaiian (n=5921) RR (95% CI) [1]	Japanese (n=25275) RR (95% CI) [1]	Latino (n=20438) RR (95% CI) [1]	p for interaction [2]
≥25.0	0.96 (0.80–1.15)	0.86 (0.73–1.02)	0.96 (0.69–1.35)	0.85 (0.68–1.07)	0.94 (0.78–1.13)	
p trend	0.94	0.47	0.26	0.27	0.70	
Weight change since age 21 (lb)[3,4]						
<10	1.00	1.00	1.00	1.00	1.00	0.006
10–24.9	1.23 (1.03–1.48)	1.19 (0.99–1.44)	1.07 (0.65–1.77)	0.97 (0.85–1.12)	0.92 (0.76–1.12)	
25–39.9	1.25 (1.03–1.51)	1.20 (0.99–1.46)	1.03 (0.62–1.70)	0.91 (0.78–1.07)	0.97 (0.80–1.19)	
≥40	1.12 (0.93–1.35)	1.17 (0.98–1.41)	1.36 (0.87–2.12)	0.79 (0.65–0.96)	0.97 (0.80–1.18)	
p trend	0.55	0.25	0.08	0.01	0.87	

[1] Relative risk and 95% confidence interval estimated using Cox proportional hazards models with age as the time metric and adjusted for age at cohort entry, family history of prostate cancer, marital status, education level, birthplace, and smoking history.

[2] Significance of type III Wald test based on Cox proportional hazards models including ethnicity and anthropometric measures as interaction terms.

[3] Additional adjustment for weight at age 21

[4] 269 prostate cancer cases were missing data on weight at age 21

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Table 5

Relationship of weight change to prostate cancer risk in ethnic groups[1], Multiethnic Cohort

Weight change since age 21 (lb)	White (n=21311) RR (95% CI) [2]	African American (n=10934) RR (95% CI) [2]	Japanese (n=25275) RR (95% CI) [2]	Latino (n=20438) RR (95% CI) [2]	p interaction[3]
Advanced					
<10	1.00	1.00	1.00	1.00	0.55
10–24.9	2.08 (1.20–3.60)	1.07 (0.60–1.91)	1.13 (0.75–1.71)	1.18 (0.65–2.14)	
25–39.9	2.12 (1.19–3.78)	1.52 (0.85–2.70)	0.93 (0.57–1.52)	1.22 (0.67–2.24)	
≥40	1.57 (0.87–2.80)	0.87 (0.49–1.56)	0.75 (0.41–1.38)	1.07 (0.58–1.97)	
p trend	0.43	0.54	0.29	0.96	
Localized					
<10	1.00	1.00	1.00	1.00	0.09
10–24.9	1.11 (0.91–1.35)	1.23 (1.00–1.53)	0.95 (0.82–1.11)	0.89 (0.71–1.11)	
25–39.9	1.17 (0.94–1.44)	1.18 (0.95–1.47)	0.93 (0.79–1.11)	0.89 (0.71–1.12)	
≥40	1.05 (0.85–1.30)	1.26 (1.02–1.54)	0.80 (0.65–0.99)	0.93 (0.74–1.16)	
p trend	0.77	0.09	0.05	0.86	
High-grade					
<10	1.00	1.00	1.00	1.00	0.18
10–24.9	1.76 (1.25–2.48)	1.12 (0.76–1.66)	0.97 (0.78–1.22)	1.06 (0.67–1.68)	
25–39.9	1.63 (1.13–2.35)	0.90 (0.60–1.36)	1.06 (0.83–1.36)	1.51 (0.96–2.37)	
≥40	1.49 (1.04–2.14)	0.97 (0.66–1.43)	0.80 (0.58–1.11)	1.52 (0.97–2.36)	
p trend	0.20	0.60	0.36	0.02	

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Weight change since age 21 (lb)	White (n=21311) RR (95% CI) [2]	African American (n=10934) RR (95% CI) [2]	Japanese (n=25275) RR (95% CI) [2]	Latino (n=20438) RR (95% CI) [2]	p interaction[3]
Low-grade					
<10	1.00	1.00	1.00	1.00	0.04
10–24.9	1.01 (0.81–1.26)	1.23 (0.98–1.54)	0.93 (0.77–1.11)	0.86 (0.68–1.07)	
25–39.9	1.06 (0.83–1.34)	1.30 (1.03–1.63)	0.81 (0.66–1.00)	0.85 (0.68–1.07)	
≥40	0.88 (0.69–1.11)	1.28 (1.03–1.58)	0.80 (0.62–1.02)	0.83 (0.67–1.04)	
p trend	0.24	0.07	0.03	0.21	

[1] Native Hawaiians excluded from analysis due to small numbers.

[2] Relative risk and 95% confidence interval estimated using Cox proportional hazards models with age as the time metric and adjusted for age at cohort entry, family history of prostate cancer, marital status, education level, birthplace, smoking history, and weight at age 21.

[3] Significance of type III Wald test based on Cox proportional hazards models including ethnicity and anthropometric measures as interaction terms.