Body Mass Index, Height, and Prostate Cancer Mortality in Two Large Cohorts of Adult Men in the United States

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Abstract

Body weight and height have both been associated consistently with postmenopausal breast cancer but less consistently with prostate cancer. The present study examined the relationship between body mass index (BMI), height, and death from prostate cancer in two large American Cancer Society cohorts. Men in the study were selected from the male participants in Cancer Prevention Study I (CPS-I; enrolled in 1959 and followed through 1972) and Cancer Prevention Study II (CPS-II; enrolled in 1982 and followed through 1996). After exclusions, 1,590 prostate cancer deaths remained among 381,638 men in CPS-I and 3,622 deaths among 434,630 men in CPS-II. Cox proportional hazards modeling was used to compute rate ratios (RR) and to adjust for confounders. Prostate cancer mortality rates were significantly higher among obese (BMI, ≥30) than nonobese (BMI, <25) men in both cohorts [adjusted RR, 1.27; 95% confidence interval (CI), 1.04–1.56 in CPS-I; RR, 1.21; 95% CI, 1.07–1.37 in CPS-II]. Prostate cancer mortality rates in the CPS-I cohort were lowest for the shortest men (RR, 0.80; 95% CI, 0.63–1.03 for men <65 inches *versus* 65–66 inches) and highest for the tallest men (RR, 1.39; 95% CI, 1.11–1.74 for men ≥73 inches tall *versus* 65–66 inches). Rates remained constant among men 65–72 inches tall. No association between height and prostate cancer mortality was observed in the CPS-II cohort (RR, 1.03; 95% CI, 0.82–1.29 for men ≥75 *versus* 65–66 inches). These results support the hypothesis that obesity increases risk of prostate cancer mortality. Decreased survival among obese men may be a likely explanation for this association.

Introduction

Height and BMI[2], a measure of body weight relative to height, have been proposed to affect risk of several cancers (1–7). The specific mechanisms are unknown but may be mediated through sex hormones, growth hormones, and/or nutrition.

Unlike breast and colon cancer, prostate cancer has not been associated consistently with BMI (Table 1), although continuing exposure to growth hormones (8) and sex hormones (9) have been proposed to increase prostate cancer risk.

A positive association between height and prostate cancer may be expected if shorter stature reflects caloric restriction during childhood and adolescence and if early caloric and nutrient restriction diminishes cell proliferation, inhibits early tumor events (10, 11), and correlates with lower stimulation from growth factors such as IGF-I (12). By the same reasoning, taller stature might be associated with increased prostate cancer risk because of higher concentration of growth factors during adolescence (13).

We examined height and BMI in relation to fatal prostate cancer in two large American Cancer Society cohorts, CPS-I and CPS-II. These cohorts included more than 400,000 men and were similar with respect to study participant selection and follow-up but were conducted during different periods of calendar time.

Materials and Methods

Men in this analysis were selected from 456,490 male participants in the CPS-I cohort (14, 15) and 508,351 male participants in CPS-II cohort (14, 16), two prospective mortality studies of American men and women begun by the American Cancer Society in the fall of 1959 and 1982, respectively. In both cohorts, volunteers identified and enrolled their friends, neighbors, and acquaintances, requesting all of the household members of at least 30 years of age to complete a questionnaire if at least one household member was 45 years of age or older. CPS-I encompassed 25 states; CPS-II encompassed all of the 50 states, the District of Columbia, and Puerto Rico. At enrollment, participants completed a self-administered questionnaire on medical, demographic, and lifestyle characteristics. The median age of male participants at study entry in CPS-I and CPS-II was 52 and 57 years, respectively.

For the first 6 years of CPS-I, volunteers made personal inquiries annually to determine the vital status of the participants they had enrolled. Follow-up through volunteers was done again during 1971 and 1972 and was completed on September 30, 1972. After 13 years of follow-up, 255,532 men (70.8%) were still living, 76,561 (21.2%) had died, and 28,900 (8.0%) were lost to follow-up (included in the latter group are 1,005 participants for whom follow-up was terminated early because some local field units were unable to continue the study; Ref. 15).

The vital status of participants in CPS-II from the month of enrollment through December 31, 1996 was determined using two approaches. Volunteers made personal inquires in September 1984, 1986, and 1988 to determine whether their enrollees were alive and to record the date and place of all of the deaths. Automated linkage using the National Death Index was used to extend follow-up through 1996 (17) and to identify

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[2] The abbreviations used are: BMI, body mass index; IGF, insulin-like growth factor; CI, confidence interval; CPS, Cancer Prevention Study; RR, rate ratio.

Table 1 BMI, height, and prostate cancer; results from available studies

Study	Study size/age at entry or birth cohort	BMI	RR (95% CI)	Height (inches)	RR (95% CI)
Cohort studies: incidence					
Severson *et al*., Hawaii (Japanese men) 1988[a] (36)	174 prostate cancer cases (1990–1919)	<22.49	1.00	Leg length	
		22.50–24.99	1.23 (0.85–1.79)	0–29.1	1.00
		≥25.00	1.33 (0.92–1.92)	29.2–30.3	1.41 (0.98–2.04)
				>30.3	1.24 (0.86–1.79)
Thompson *et al*., Rancho Bernardo, United States of America 1989 (29)	54 prostate cancer cases, age 50–84	BMI/2.92 kg/m^2	1.1 (0.9–1.4)		
Mills *et al*., Seventh Day, 1989 (30)	180 prostate cancer cases (born before 1949)	≤23.2	1.00		
		23.3–25.8	0.98 (0.67–1.44)		
		≥25.8	1.17 (0.79–1.72)		
LeMarchand *et al*., Hawaii 1994[a] (31)	198 prostate cancer cases, age 45+	<22	1.00	<63.8	1.00
		22–24	0.8 (0.6–1.2)	63.9–65.7	1.1 (0.6–1.8)
		24–26	0.9 (0.6–1.3)	65.8–68.1	1.8 (1.2–2.9)
		>26	0.7 (0.5–1.2)	>68.1	1.8 (1.0–3.2)
Thune *et al*., Norway, 1994 (54)	Age 19–54	BMI/unit	1.25 (1.05–1.50)	Height/every 3.94 inches	0.99 (0.82–1.19)
Gronberg *et al*., Sweden 1996 (55)	406 prostate cancer cases (1886–1925)	<23	1.00		
		23–25.99	1.14		
		26–28.99	1.44		
		≥29	1.80		
Herbert *et al*., United States of America 1996 (49)	1047 prostate cancer cases (1900–1944), age 40–84			≤67	1.00
				68–69	1.23 (1.00–1.51)
				70–71	1.26 (1.04–1.54)
				72	1.59 (1.27–1.98)
				≥73	1.27 (1.01–1.59)
Andersson *et al*., Swedish 1997[a] (37)	2368 prostate cancer cases, age 20+	<22.1	1.00	<67.7	1.00
		22.1–24.1	1.09 (0.94–1.26)	67.7–69.7	1.05 (0.95–1.16)
		24.2–26.2	1.10 (0.96–1.26)	69.8–70.9	1.07 (0.96–1.21)
		>26.2	1.13 (0.99–1.29)	>70.9	1.14 (1.00–1.29)
Cerhan *et al*., Iowa rural, 1997[a] (38)	69 prostate cancer cases, age 65–101	<23.6	1.00	<68.1	1.00
		23.6–25.8	0.9 (0.5–1.9)	68.1–69.7	0.8 (0.4–1.4)
		25.9–27.8	1.2 (0.6–2.5)	69.8–70.9	0.6 (0.3–1.2)
		>27.8	1.7 (0.8–3.3)	>70.9	1.1 (0.6–2.0)
	17 regional distant prostate cancer cases	<23.6	1.00		
		23.6–25.8	1.6 (0.3–7.4)		
		25.9–27.8	2.8 (0.6–13)		
		>27.8	3.1 (0.7–14)		
Giovannucci *et al*., United States of America 1997 (28)	1369 prostate cancer cases; (1911–1946), age 40–75	<23	1.00	≤68	1.00
		23–23.9	1.25 (1.03–1.51)	69	1.09 (0.91–1.30)
		24–24.9	1.20 (0.98–1.46)	70	1.07 (0.91–1.27)
		25–25.9	1.05 (0.87–1.28)	71	1.08 (0.90–1.30)
		26–26.9	0.94 (0.74–1.18)	72	0.98 (0.80–1.19)
		27–28.9	1.11 (0.90–1.36)	73	1.22 (0.97–1.55)
		≥29	0.90 (0.71–1.15)	≥74	1.37 (1.10–1.70)
	407 advanced cases	<23	1.00	≤68	1.00
		23–23.9	1.23 (0.88–1.72)	69	1.14 (0.81–1.59)
		24–24.9	1.18 (0.83–1.68)	70	1.06 (0.77–1.45)
		25–25.9	1.01 (0.71–1.43)	71	1.29 (0.93–1.79)
		26–26.9	0.89 (0.58–1.36)	72	1.11 (0.78–1.58)
		27–28.9	1.22 (0.85–1.76)	73	1.63 (1.10–2.41)
		≥29	1.19 (0.79–1.82)	≥74	1.68 (1.16–2.43)
Schuurman, A.G. *et al*., Netherlands 1999[a] (41)	681 prostate cancer cases (1917–1931), age 55–69	<22	1.00	<66.9	1.00
		22–24	1.20 (0.84–1.73)	66.9–68.9	0.90 (0.65–1.24)
		24–26	1.35 (0.95–1.90)	69.0–70.9	1.08 (0.79–1.47)
		26–28	1.26 (0.87–1.83)	71.0–72.8	0.98 (0.70–1.37)
		>28	0.89 (0.58–1.37)	72.9–74.8	0.78 (0.51–1.19)
				>74.8	0.96 (0.52–1.75)

deaths among 8,485 men lost to follow-up between 1982 and 1988. At the completion of CPS-II follow-up, 377,891 men (74.3%) were still living, 129,642 (25.5%) had died, and 818 (0.2%) had follow-up truncated in December 31, 1988 because of insufficient data for linkage with the National Death Index. Death certificates or multiple cause of death codes were ob-

Table 1 Continued

Study	Study size/age at entry or birth cohort	BMI	RR (95% CI)	Height (inches)	RR (95% CI)
Lund Nilsen *et al*., Norway, 1999[a] (32)	642 prostate cancer patients (Born after 1964)	<23.0	1.00	<66.5	1.00
		23.1–24.7	0.8 (0.6–1.1)	66.5–68.1	1.1 (0.9–1.4)
		24.8–26.2	1.0 (0.8–1.3)	68.2–69.3	1.1 (0.8–1.4)
		26.3–28.2	0.9 (0.7–1.2)	69.4–70.9	1.2 (0.9–1.5)
		>28.2	1.0 (0.8–1.3)	>70.9	1.2 (0.9–1.6)
	481 localized cases			<66.5	1.0
				66.5–68.1	0.9 (0.7–1.3)
				68.2–69.3	0.9 (0.7–1.3)
				69.4–70.9	1.0 (0.7–1.5)
				>70.9	1.0 (0.7–1.4)
	161 metastatic cases			<66.5	1.0
				66.5–68.1	1.5 (1.0–2.2)
				68.2–69.3	0.9 (0.8–1.5)
				69.4–70.9	1.3 (0.8–2.1)
				>70.9	1.5 (0.9–2.6)
Cohort studies: mortality					
Snowdon *et al*., Seventh Day Adventist, United States of America 1984 (39)	84 prostate cancer deaths (Born before 1920), age 60+	Percentage of desirable weight			
		70–89	1.6 (0.7–3.4)		
		90–109	1.0		
		110–129	1.2 (0.8–2.0)		
		130–249	2.4 (1.3–4.5)		
Garfinkel CPS-I. United States of America 1986 (40)	(Born before 1929)	Weight only (pounds)	0.9		
		110–119	1.37		
		120–129	1.33		
		130–139	1.29		
		140+			
Andersson, *et al*., Swedish, 1997 (37)	708 prostate cancer deaths (1971–1975), age 20+	<22.2	1.00	<67.7	1.00
		22.2–24.1	1.36 (1.03–1.79)	67.7–69.3	0.99 (0.82–1.18)
		24.2–26.2	1.33 (1.02–1.74)	69.4–70.9	1.08 (0.88–1.34)
		>26.2	1.40 (1.09–1.81)	>70.9	1.28 (1.02–1.60)

[a] Height converted to inches.

tained for all of the known deaths in CPS-I and 98.8% of known deaths in CPS-II.

Prostate cancer deaths were defined as those men who died during the follow-up period with prostate cancer coded as the underlying cause of death using the International Classification of Diseases, seventh revision, code 177 (18) in CPS-I and International Classification of Diseases, ninth revision, code 185 (19) in CPS-II.

In both CPS-I and CPS-II baseline questionnaires, weight in pounds and height in feet and inches were reported by participants at study entry. CPS-I asked additional questions related to change in weight over time, and CPS-II asked about weight 1 year ago. Table 2 shows the number of study participants and prostate cancer deaths excluded from the analyses. Exclusion criteria were prevalent cancer at the time of enrollment (except nonmelanoma skin cancer), missing or extreme (≤0.1 percentile or ≥99.9 percentile) values of height or weight, or recent weight loss (10 or more pounds in the last year). Eligible participants for the current analysis included 381,638 CPS-I men and 434,630 CPS-II men.

BMI (weight in kg/height in m^2) was calculated from reported height and weight and was categorized as follows: <18.50, 18.50–22.49, 22.50–24.99, 25.0–27.49, 27.50–29.99, 30.0–32.49, and ≥32.50. We used a BMI of 18.50–22.49 as the referent group for analyses. These categories were chosen to be consistent with cut points that have been proposed by the WHO (20) for underweight (BMI, <18.50), normal range (BMI, 18.50–24.99), overweight (BMI, 25.00–29.99), and obesity (BMI, 30.00–39.99). When WHO-recommended categories were used, we used a referent category of BMI <25.00 because of insufficient numbers in the underweight category. Height in inches was categorized in increments of 2 inches. The minimum category was <65 inches in both cohorts, whereas the maximum category was ≥73 inches in CPS-I and ≥75 inches in CPS-II. We used a height of 65–66 inches as the referent group for all of the analyses.

Age-standardized death rates and RRs were calculated at each level of BMI and height. These were directly standardized to the age distribution of the male population for both cohorts combined. We also used Cox proportional hazards modeling (21) to compute RRs and to adjust for potential confounders. For all of the Cox models, we stratified on the exact year of age at enrollment and controlled for race (white, black, and other), education (less than high school, high school graduate, some college, and college graduate), smoking status (never, former, current, ever pipe/cigar, and ever-smoker but status at entry unknown), family history of prostate cancer in a father or a brother (yes/no), physical activity at work or play (none, slight, moderate, and heavy). BMI was a covariate in models assessing prostate cancer mortality risk associated with height, and height was a covariate in models assessing mortality and BMI. The test of linear trend was used to assess the statistical significance of the association between the risk of prostate cancer death and levels of increased BMI and/or height.

To test whether other factors modified the association between BMI and fatal prostate cancer, we entered multiplica-

Table 2 Cohort eligible for analysis, CPS-I and CPS-II

	CPS-I		CPS-II	
	No. of men[a]	No. of deaths, prostate cancer[a]	No. of men[a]	No. of deaths, prostate cancer[a]
Full cohort	456,490	2,277	508,351	5,414
Exclusions				
Prevalent prostate cancer	508 (0.1)	192 (8.4)	3,314 (0.7)	1,003 (18.5)
Other prevalent cancers[b]	19,117 (4.2)	198 (8.7)	21,928 (4.3)	396 (7.3)
Missing race	3,616 (0.8)	21 (0.9)	2,309 (0.5)	20 (0.4)
Missing or extreme height, weight, or BMI	26,243 (5.7)	165 (7.2)	15,963 (3.1)	161 (3.0)
Weight loss >10 pounds in past year	25,368 (5.6)	111 (4.9)	30,207 (5.9)	212 (3.9)
Total number of exclusions	74,852 (16.4)	687 (30.2)	73,721 (14.5)	1,792 (33.1)
Total number available for analysis	381,638	1,590	434,630	3,622

[a] Numbers in parentheses, percentages.
[b] Cancer reported at enrollment other than nonmelanoma skin cancer.

tive interaction terms between BMI (<25, 25–29.99, ≥30) and each of the above risk factors in separate multivariate models. To assess whether height modified the association between BMI and prostate cancer mortality, we entered multiplicative interaction terms between height (≤70 inches and >70 inches) and each of the other risk factors in separate models. Statistical significance of the interaction terms was assessed at the $P = 0.05$ level using the likelihood ratio test (22).

Results

Age-adjusted prostate cancer death rates were similar in the two cohorts, 39.32/100,000 man-years in CPS-I and 38.99/100,000 man-years in CPS-II, and were higher among black men than among white men (83.18 *versus* 38.52/100,000 man-years in CPS-I and 85.25 *versus* 38.06/100,000 man-years in CPS-II). Prostate cancer death rates increased with age in a virtually identical pattern in both cohorts, with more than 500 prostate cancer deaths/100,000 man-years among men 85 years of age or over.

Men in the CPS-II cohort were taller and slightly heavier than men in the CPS-I cohort (Fig. 1). Mean BMI was an average of 2% higher at any given age in the CPS-II cohort and in both cohorts decreased with age among men 50 years of age or older. Mean attained height increased continuously by birth cohort in CPS-I. A similar increase was observed in CPS-II until the 1935–1939 birth cohort, at which point (70.55 inches) height reached a plateau.

Table 3 shows the age-standardized distribution of demographic characteristics across broad BMI categories. Men in the CPS-I cohort were less educated and were more likely to be current smokers of cigarettes or pipes/cigars than were men included in the CPS-II cohort. In both cohorts, men in the highest BMI categories were more likely to be black, have less education, and exercise less. Men in the BMI lowest category were more likely to be current smokers.

The exposure-response relationship between BMI and prostate cancer death rates was similar in both cohorts (Table 4). Prostate cancer death rates were the lowest among very lean men (BMI, <18.50), remained constant among men of normal BMI and grade 1 overweight (BMI, 18.50-< 30.00), and were the highest among men with grade 2 overweight (BMI, ≥30). Compared with men in the reference group (BMI, 18.50–22.99), prostate cancer mortality rates were 34 and 36% higher among the heaviest men in CPS-I and CPS-II, respectively. Test for linear trend was statistically significant for both cohorts. When WHO categories were used (Table 5), statistically significant increased risk was observed at BMI ≥30 (RR, 1.27 for CPS-I; and RR, 1.21 for CPS-II).

Height was associated with prostate cancer mortality only in the earlier CPS-I cohort. Prostate cancer death rates were lowest among the shortest men (<65 inches tall; RR, 0.80; 95% CI, 0.63–1.03), remained constant among men 65–72 inches tall, and were highest among the tallest men (≥73 inches; RR, 1.39; 95% CI, 1.11–1.74; Table 6). No association was observed between prostate cancer mortality and height in the CPS-II cohort.

The joint association between BMI and height on prostate cancer mortality in both cohorts is illustrated in Table 7. The referent group consisted of men less than 70 inches tall and with a BMI less than 25. The strongest increase in risk was observed among men who were both tall (≥70 inches) and obese (BMI, ≥30). However, neither the interaction between height and BMI in relation to prostate cancer nor the modification of these associations by other variables was statistically significant in either cohort.

The association between BMI and height and risk of prostate cancer mortality was not modified significantly by race. However, analysis of height and BMI by race suggested that anthropometry measurements may not be associated with risk of prostate cancer among black men, although the estimates were based on very small numbers. Black obese men (BMI, ≥30) were not at increased risk of prostate cancer mortality, as compared with black men with a BMI <25 (RR, 1.20; 95% CI, 0.52–2.76, based on 7 deaths in CPS-I; RR, 0.85; 95% CI, 0.53–1.34 based on 23 deaths in CPS-II). The RR for prostate cancer mortality for black men ≥70 inches tall *versus* ≤66 inches was 0.63 (95% CI, 0.32–1.25; based on 12 deaths) in the CPS-I cohort and 0.89 (95% CI, 0.66–1.21; based on 111 deaths) in the CPS-II cohort.

Discussion

These two large prospective cohorts provide support for the hypothesis that obesity is associated with higher prostate cancer death rates. In addition, height was positively associated with increased prostate cancer mortality in the CPS-I cohort, but no association was observed between height and prostate cancer mortality in CPS-II.

Previous studies of the relationship between incident prostate cancer and BMI have been inconsistent (Table 1), predominantly finding no association (23–32) or a small increased risk among heavy men (33–38). However, the increased risk associated with obesity is observed consis-

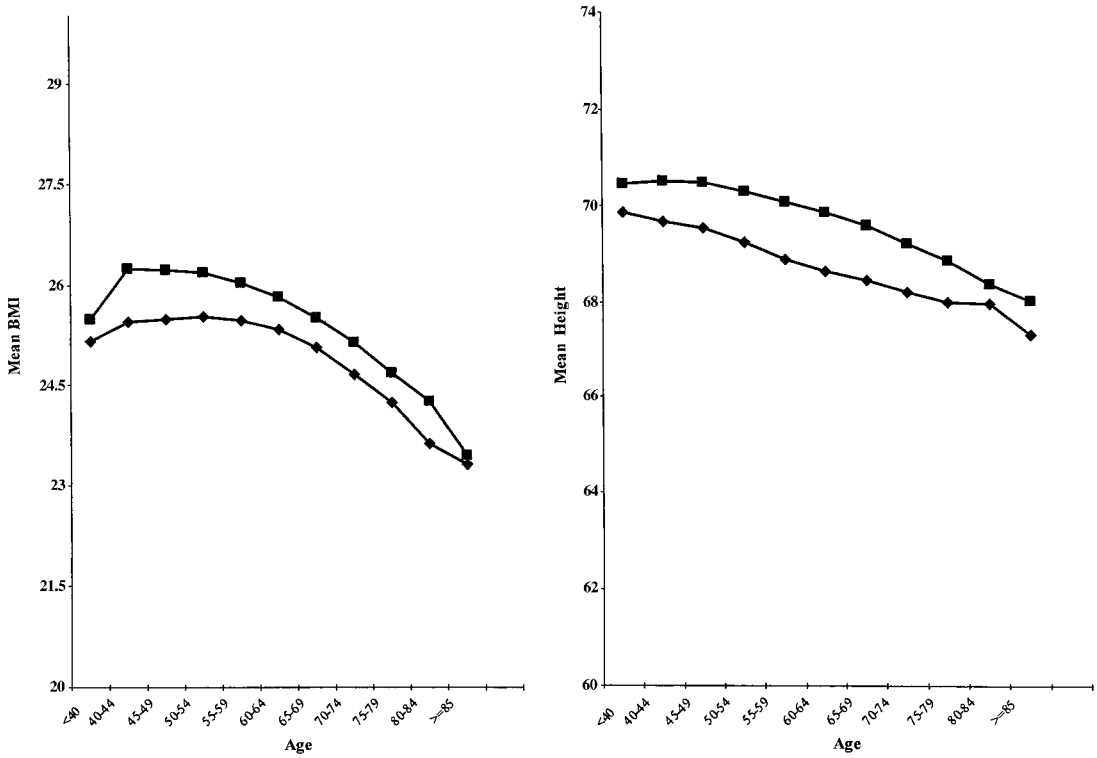

Fig. 1. Mean BMI and height by age, CPS-I, 1959–1972, and CPS-II, 1982–1996. CPS-I, ◆; CPS-II, ■.

Table 3 Demographic characteristics of men by BMI at study entry, CPS-I and CPS-II

Covariate	CPS-I BMI Age-adjusted percentage[a]			CPS-II BMI Age-adjusted percentage[a]		
	BMI (<25.0) 172,497	BMI (25.0–<30.0) 182,981	BMI (>30.0) 26,160	BMI (<25.0) 175,794	BMI (25.0–<30.0) 215,977	BMI (>30.0) 42,859
Race/ethnicity						
White	98.0	98.0	96.3	94.8	95.0	92.9
Black	1.9	1.9	3.5	3.1	3.5	5.6
Other	0.1	0.1	0.1	2.1	1.5	1.5
Family history of prostate cancer	1.4	1.3	1.2	3.0	3.0	2.8
Smoking status						
Never	18.3	23.0	26.5	26.0	25.3	25.3
Current	39.7	29.7	25.7	24.6	18.5	16.7
Former	9.3	11.7	10.5	26.4	31.1	31.4
Ever, unknown status				1.4	1.5	1.8
Ever, pipe/cigar	31.0	33.4	34.8	18.9	20.6	21.0
Education						
<High school graduate	42.4	41.9	51.7	13.4	15.4	21.2
High school graduate	18.8	18.4	16.9	18.1	20.4	22.0
Some college	18.1	18.3	16.0	26.0	27.1	27.3
≥College graduate	19.9	20.5	14.0	41.2	35.7	27.9
Exercise						
None	2.4	2.6	4.2	1.7	1.9	4.1
Slight	18.5	20.7	21.7	18.9	22.3	30.5
Moderate	62.1	61.7	56.9	64.8	63.8	55.3
Heavy	15.9	13.9	15.8	13.6	11.0	9.0

[a] Percentages are directly adjusted to the age distribution of CPS-I and CPS-II combined. Percentages may not add to 100% because of missing data.

tently among heavy men in mortality studies (37, 39, 40), one being a shorter follow-up of the CPS-I cohort (40). The study by Andersson *et al.* (37), a large retrospective cohort study of prostate cancer incidence and mortality in Sweden, reported a stronger association between BMI and prostate cancer mortality (RR, 1.40) than was seen with incidence (RR, 1.13). That analysis was based on 277 prostate cancer deaths among men with a BMI greater than 26.2. Three other

Table 4 RRs (95% CI) for prostate cancer mortality and BMI, adjusted for various risk factors, CPS-I 1959–1972, and CPS-II 1982–1996

	<18.50	18.50–22.49	22.50–24.99	25.00–27.49	27.50–29.99	30.00–32.49	≥32.50
CPS-I							
No. of deaths	21	301	460	509	189	78	32
Person-years	37,408	668,151	1,175,271	1,435,709	599,080	200,682	84,062
Age-standardized rate[a]	32.5	38.5	38.9	39.1	39.1	46.7	50.1
RR[b]	0.81	1.00	1.04	1.06	1.01	1.28	1.34
95% CI	0.52–1.27		0.90–1.20	0.91–1.22	0.84–1.22	0.99–1.64	0.93–1.94
							$P = 0.06$
CPS-II							
No. of deaths	23	510	1,036	1,177	553	201	122
Person-years	34,988	647,639	1,532,894	1,917,821	886,142	350,763	200,510
Age-standardized rate[a]	29.9	38.4	37.8	38.0	43.3	44.1	55.0
RR[b]	0.66	1.00	0.98	0.99	1.11	1.11	1.36
95% CI	0.44–1.01		0.88–1.09	0.89–1.10	0.99–1.26	0.94–1.31	1.11–1.66
							$P = 0.0002$

[a] Rate/100,000.
[b] Adjusted for age at interview, race, height, education, exercise, smoking status, and family history of prostate cancer.

Table 5 RRs (95% CI) for prostate cancer mortality and BMI (WHO cut-points), adjusted for various risk factors, CPS-I 1959–1972, and CPS-II, 1982–1996

	<25.00	25.00–29.99	>=30.00
CPS-I			
# deaths	782	698	110
Person-years	1,800,830	2,034,789	284,744
Age-standardized rate[a]	38.7	39.0	47.5
RR[b]	1.00	1.02	1.27
95% CI	—	0.92–1.14	1.04–1.56
			P-trend = 0.06
CPS-II			
# deaths	1,569	1,730	323
Person-years	2,215,521	2,803,963	551,273
Age-standardized rate[a]	37.8	39.5	47.4
RR[b]	1.00	1.05	1.21
95% CI	—	0.98–1.12	1.07–1.37
			P-trend = 0.004

[a] Rate per 100,000.
[b] Adjusted for age at interview, race, height, education, exercise, smoking status, and family history of prostate cancer.

studies (28, 38, 41) assessed whether BMI predicted more advanced incidence prostate cancer with inconsistent results; all of these analyses were limited by few prostate cancer cases with advanced disease.

Decreased survival rather than increased incidence among obese men may be an explanation for the association between BMI and prostate cancer mortality. Obesity, particularly abdominal adiposity, may be related to progression of existing disease. Abdominal obesity is associated with insulin resistance and hyperinsulinemia (42), and the exposure to elevated blood levels of insulin and IGFs may increase prostate cancer progression (43). Slowing of tumor progression and increased apoptosis have been achieved in mice by lowering IGF-I levels through dietary restriction (44). In addition, higher levels of leptin among obese men could adversely affect survival in prostate cancer patients. Leptin is a circulating hormone secreted by adipocytes and positively correlated with body mass (45, 46). Recent *in vitro* and *in vivo* experiments have revealed that leptin can promote angiogenesis (47). Because the degree of angiogenesis within prostate cancer tumors can predict the probability of metastasis (48), higher BMI may be associated with increased mortality with this pathway.

Height has been associated previously with prostate cancer incidence in six (28, 31, 32, 36, 37, 49) of nine prospective studies (28, 31, 32, 36–38, 41, 49, 50), and the association was stronger for more advanced or metastatic cases at diagnosis (28) and for prostate cancer mortality (37). We found an association between height and prostate cancer mortality in CPS-I. Risk was lowest among very short men and highest among the tallest men. No association with height was observed in the CPS-II cohort. Adult height is determined by both genetic and nutritional factors. The development of the prostate occurs during puberty at the same time as rapid growth in height. It is possible that tall men may have been exposed during puberty to higher levels of testosterone and growth-promoting factors such as IGF-I than shorter men (12, 13), stimulating prostatic epithelial division (28) and influencing subsequent disease risk.

The difference in the two studies regarding height could be attributable to chance or to temporal changes in nutritional factors between the two cohorts, which were started 23 years apart. In CPS-I, height may reflect energy restriction during childhood and adolescent growth, whereas in CPS-II, most men may have achieved their genetically maximum adult height. This explanation is supported by the fact that mean height increased continuously with temporal birth cohorts in CPS-I, suggesting some degree of energy restriction in earlier birth cohorts. In contrast, in CPS-II there was less difference in height across birth cohorts, with little or no increase for men born after 1935. Adults who have experienced energy restriction during childhood or adolescence tend to be shorter and experience lower stimulation from growth hormones such as IGF-I (12). Lack of an association with height in CPS-II supports the hypothesis that in populations where nutritional inadequacy is not widespread, height is predominantly determined by genetic factors and is, therefore, less likely to be associated with prostate cancer. However, it should be noted that height was positively associated with prostate cancer in two (28, 49) of the three prospective studies of predominantly white men in the United States of similar birth cohorts as those represented in CPS-II (28, 38, 49).

The association between BMI, height, and prostate cancer mortality should be interpreted within the limitations of the study. First, we have no direct measure of central adiposity or of lean body mass. Although BMI is an adequate measure of adiposity in young adults and middle-aged populations (51), it may perform less well in older adults, such as the men included in these two cohorts. As people age, individuals may lose substantial amounts of lean body mass while maintaining the same weight, thus re-

Table 6 RRs (95% CI) for prostate cancer mortality and height, adjusted for various risk factors, CPS-I 1959–1972, and CPS-II 1982–1996

	<65	65–66	67–68	69–70	71–72	73–74[a]	≥75
CPS-I							
No. of deaths	88	248	439	425	277	113	
Person-years	172,610	504,603	1,022,776	1,198,709	936,000	365,665	
Age-standardized rate[a]	32.5	37.7	39.0	40.7	40.4	51.4	
RR[b]	0.80	1.00	1.07	1.07	1.07	1.39	
95% CI	0.63–1.03		0.91–1.25	0.90–1.25	0.90–1.27	1.11–1.74	
						$P = 0.002$	
CPS-II							
No. of deaths	133	347	707	1,037	976	324	98
Person-years	125,292	405,058	1,029,405	403,121	1,664,268	628,615	222,629
Age-standardized rate[a]	35.2	37.9	35.6	41.4	40.0	42.9	38.4
RR[b]	1.02	1.00	0.96	1.12	1.06	1.11	1.03
95% CI	0.83–1.25		0.84–1.09	0.99–1.26	0.93–1.20	0.96–1.30	0.82–1.29
							$P = 0.076$

[a] For CPS-I this category is ≥73 inches.
[b] Rate/100,000.
[c] Adjusted for age at interview, race, BMI, smoking status, education, exercise, and family history of prostate cancer.

Table 7 RRs and 95% CI for BMI and height interactions, CPS-I, 1959–1972, and CPS-II, 1982–1996

	BMI <25.00	BMI 25.00–<30.00	BMI ≥30.00
CPS-I			
Height <70 inches			
No. of deaths	443	442	66
Person-years	942,068	1,089,212	164,017
Age-standardized rate[a]	36.2	38.7	40.7
RR[b] (95% CI)	1.00	1.08 (0.95–1.23)	1.16 (0.89–1.50)
Height ≥70 inches			
No. of deaths	339	256	44
Person-years	938,762	945,577	120,726
Age-standardized rate[a]	42.6	40.0	72.6
RR[b] (95% CI)	1.17 (1.01–1.34)	1.08 (0.92–1.27)	1.68 (1.23–2.29)
			P-for interaction = 0.13
CPS-II			
Height <70 inches			
No. of deaths	654	802	143
Person-years	838,082	1,143,665	225,579
Age-standardized rate[a]	33.6	37.1	42.1
RR[b] (95% CI)	1.00	1.08 (0.97–1.19)	1.13 (0.94–1.36)
Height <70 inches			
No. of deaths	915	928	180
Person-years	1,377,439	1,660,298	325,694
Age-standardized rate[a]	40.7	41.6	52.2
RR[b] (95% CI)	1.15 (1.04–1.27)	1.18 (1.07–1.31)	1.48 (1.25–1.75)
			P-for interaction = 0.35

[a] Death rates standardized to the combined CPS-I and CPS-II male population.
[b] Adjusted for age at interview, race, education, exercise, smoking status, and family history of prostate cancer.

ducing the validity of BMI as a measure of adiposity. Second, we used self-reported weight and height at study entry, both of which are subject to error (52). In addition, both studies relied on reported weight at a single point in time, and information was not available on weight in young adulthood or long-term weight change.

No information on screening practices was available for men included in these two cohorts. The possibility that the reported association could be attributable to more frequent screening for prostate cancer or earlier diagnosis among leaner men, however, seems unlikely. Risk was similarly increased among heavier men in both cohorts, despite the fact that prostate-specific antigen (PSA) for prostate cancer screening was not available before 1972 when follow-up for CPS-I ended.

Strengths of this study include the opportunity to explore the association between height, BMI, and prostate cancer mortality in two prospective cohorts from different time periods but with similar study populations and study design. Each of these cohorts was large, allowing us to examine risk over a wide range of BMI and height with unusual precision.

In conclusion, the results of this study suggest that obesity is associated with increased risk of prostate cancer mortality. Previous reports that have not found an association between BMI and incident prostate cancer may be attributable to an

inability to investigate a wide range of BMI or to a greater effect of BMI on prostate cancer survival than on incidence. The increased risk associated with obesity observed in these two cohorts is modest. However, because the proportion of obese men in United States has increased 51.5% between 1991 and 1998 (53), any effect of obesity on prostate cancer mortality may add substantially to its strong detrimental effects on health.

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