Obesity before Age 30 Years and Risk of Advanced Prostate Cancer

Whitney R. Robinson\(^1\), June Stevens\(^{1,2}\), Marilie D. Gammon\(^1\), and Esther M. John\(^3\)

\(^1\) Department of Epidemiology, School of Public Health, University of North Carolina, Chapel Hill, NC.
\(^2\) Department of Nutrition, School of Medicine and School of Public Health, University of North Carolina, Chapel Hill, NC.
\(^3\) Northern California Cancer Center, Fremont, CA.

Received for publication October 8, 2004; accepted for publication February 16, 2005.

Abstract

Adult obesity has shown little association with prostate cancer risk, but obesity at younger ages may be associated with reduced risk. In 1997–2000, the relation between obesity before age 30 years and incident advanced prostate cancer was investigated in a population-based case-control study of African-American and White men (568 cases, 544 controls) in California. Unconditional logistic regression was used to estimate odds ratios and 95% confidence intervals, adjusted for age, race, family history of prostate cancer, and saturated fat intake. Measures of obesity for age 10 years tended to be inversely associated with prostate cancer (odds ratio (OR) = 0.79, 95% confidence interval (CI): 0.46, 1.38 for selecting the “obese” pictogram and OR = 0.76, 95% CI: 0.52, 1.11 for reporting being heavier than peers). The decreased risk was more pronounced at ages 20–29 years (OR = 0.53, 95% CI: 0.28, 1.00 for the “obese” drawing, OR = 0.59, 95% CI: 0.40, 0.88 for being heavier than peers, and OR = 0.40, 95% CI: 0.20, 0.81 for body mass index ≥30 kg/m\(^2\)). In addition, both “obese” and small waist size at ages 20–29 years showed inverse trends. This research implicating early-life body size in prostate cancer development helps to elucidate causal mechanisms, such as altered sex hormone profiles during critical developmental periods, potentially involved in development of the disease.

Keywords: prostate cancer; obesity; body mass index; body size; case-control studies; child; adolescence; risk factors

Abbreviations: BMI, body mass index; CI, confidence interval; OR, odds ratio.

Prostate cancer is the most commonly diagnosed cancer in US men (1). Although the past 20 years have seen many promising advances in prostate cancer research, the number of known risk factors for the disease remains limited (2). One of the most striking attributes of prostate cancer is its great ethnic and international variation; for example, African Americans experience incidence rates of prostate cancer 35 times greater than men in Madras, India (2, 3).

There is some evidence that prostate cancer risk is promoted by androgens, the male sex hormones (4). Androgens, such as testosterone and its metabolite dihydrotestosterone, are essential for male sexual development, including development of the prostate. In addition, testosterone administration has been shown to induce prostatic cancer in laboratory rats, and advanced disease regresses dramatically when androgen levels are completely suppressed (5).

Androgens and body composition are intricately connected. Administration of androgens increases fat-free mass and reduces fat mass (6), while obesity is associated with decreased serum androgen levels, decreased sex hormone-binding globulin, increased estrogen, and increased free insulin-like growth factor-I (7). Because of the connections between body size and androgens, obesity has been extensively studied as a potential risk factor for prostate cancer (7).

Despite repeated study, however, consistent associations between prostate cancer and obesity have not been observed (7). Most studies have examined body size in only the fifth, sixth, and seventh decades of life (5). Yet the years before age 30 could be a critical period for the development of aggressive prostate cancer (5, 8, 9). In response to the limited scope of the research, prostate cancer investigators have called for more studies concerning body size earlier in life (5, 7).
The present study investigated the association between obesity before age 30 years and risk of advanced prostate cancer later in life. One of the novelties of the study is its large number of advanced prostate cancer cases, including more African-American cases than are known to have been investigated in any previous study of this topic.

**MATERIALS AND METHODS**

**Study population**

Data were derived from a population-based case-control study of advanced prostate cancer among White and African-American men residing in the San Francisco Bay area of California (10). The study received ethical approval from the institutional review board of the Northern California Cancer Center. Participants were required to be aged 40–79 years at the time of diagnosis (cases) or selection into the study (controls) and to be living in the San Francisco Bay area (counties of San Francisco, San Mateo, Santa Clara, Alameda, and Contra Costa) when interviewed. Only English-speaking men who self-identified as African American or non-Hispanic White were eligible. In addition, participating men were required to have no prior history of prostate cancer. Cases were selected from the Greater Bay Area Cancer Registry, which is part of the Surveillance, Epidemiology, and End Results (SEER) Program, and the California Cancer Registry. Cases were potentially eligible if they were diagnosed with a first primary, advanced prostate cancer between July 1, 1997, and December 31, 2000 (African Americans) or between July 1, 1997, and February 29, 2000 (non-Hispanic Whites). Advanced prostate cancer was defined as a tumor invading and extending beyond the prostatic capsule and/or extending into adjacent tissue or involving regional lymph nodes or distant metastatic sites (Surveillance, Epidemiology, and End Results 1995 clinical and pathologic extent of disease codes 41–85).

The cancer registry identified 1,015 advanced prostate cancer cases. After we excluded those already participating in another project (n = 33) and those for whom the physician declined contact (n = 12), 970 were considered for eligibility. Of these, 182 (19 percent) did not meet the eligibility criteria described above, including 106 who died before being contacted. Of the remaining 788 potential participants, 568 (72 percent) took part in the study. Of the 220 cases who did not participate, 156 (20 percent) refused, 21 (3 percent) were too ill, 20 (3 percent) could not be located, 15 (2 percent) could not be contacted, two only partially completed the questionnaire, and six did not finish the study for other reasons. The overall case participation rates (including deceased) were 63 percent and 62 percent for African Americans (participation rate, including deceased = 56 percent). Reasons for nonparticipation included refusal (n = 249), illness (n = 15), inability to be located (n = 32), inability to be contacted (n = 14), and other reasons (n = 13).

**Data collection**

Information on cases and controls was collected by professional interviewers during in-person interviews at participants’ homes (or elsewhere if preferred). Each participant signed a written informed consent. The interviews consisted of two components: 1) a structured questionnaire that inquired about past body size, recent body size, and other suspected risk factors; and 2) measurement of current height and weight. A 74-item food frequency questionnaire adapted from Block’s Health History and Habits Questionnaire (12, 13) assessed usual dietary intake during the reference year, defined as the calendar year preceding diagnosis for cases and, for controls, the calendar year before selection into the study.

**Exposure variables**

Six self-reported measures of body size in youth were examined in this study: weight compared with that of peers at ages 10 and 20 years, body shape at ages 10 and 20 years, usual trouser waist size between ages 20 and 29 years, and usual body mass index (BMI; kg/m²) between ages 20 and 29 years. For each measure, an exposure category (“obese”) consisting of those with the largest body size was defined. For BMI, the cutoff for defining the obese category was that recommended by the World Health Organization: BMI ≥30 (14). For body shape and trouser waist, the cutoffs were based on previous studies showing high sensitivities and specificities for identifying obesity (defined as BMI ≥30.0) with each measure (15–17). (We could not find studies establishing a validated obesity category for peer comparison weight.) For every exposure variable except peer comparison weight and trouser waist, the smallest body size category was the referent.

To assess weight compared with that of peers, participants were asked “‘[W]ere you much lighter in weight, lighter, the same, heavier, or much heavier in weight than your classmates?’” at ages 10 and 20 years. To assess body shape at ages 10 and 20 years, participants were asked to choose one of nine numbered line drawings (18), or pictograms, of male bodies that best “describes [his] body” at ages 10 and 20 years. Responses were grouped into three categories (drawings 1–4, 5, and 6–9), which have been shown to
provide optimal sensitivity and specificity for identifying obesity (drawings 6–9) and thinness (drawings 1–4) (15).

BMI and trouser waist size were used to assess obesity (14, 16, 17) in those aged 20–29 years. BMI between ages 20 and 29 years was calculated as self-reported usual weight (in kilograms) at those ages divided by the square of height (in meters) measured at interview. Self-reported usual height between ages 20 and 40 years was substituted in BMI calculations whenever measured height was not available (7.9 percent (n = 45) of cases and 7.2 percent (n = 39) of controls). BMI was grouped into three categories: normal (18.5 ≤ BMI ≤ 24.9), overweight (25.0 ≤ BMI ≤ 29.9), and obese (BMI ≥30.0) (14). Seven underweight subjects (BMI <18.5) were grouped with the normal-weight subjects. As an alternative to BMI, we also assessed obesity by using trouser waist size. International guidelines suggest a waist circumference of 102 cm or more as a definition of obesity (16, 17). Taking this recommendation into consideration, along with the fact that our measures were recorded in the American trouser size system (which uses 2-inch increments (1 inch = 2.54 cm)) and that observations were sparse in our data at high waist values, we defined obesity as a trouser waist size of 38 inches (96.5 cm) or more.

**Potential covariates**

The following variables were evaluated as possible confounders in the main analyses: education attained (high school degree or less, vocational school or some college, college degree or higher); family history of prostate cancer in first-degree relatives (yes, no); smoking status (never, former, current) in the reference year; intake of saturated fat (continuous) in the reference year; total energy consumed (continuous) in the reference year; and alcohol intake (quartiles based on the distribution among controls) in the reference year. (Reference year is defined above in the description of data collection.)

We also included recent BMI (self-reported weight (kg) in the reference year divided by the square of height (m²) measured at interview) as a covariate in one set of analyses. Recent BMI was used instead of BMI measured at the interview to minimize potential bias for cases, because some treatments for advanced prostate cancer are associated with weight gain (19). Moreover, in older men, BMI calculated from measured height and self-reported weight has been shown to be quite accurate compared with BMI derived from measured height and weight (mean BMI difference = −0.17 (standard error, 0.04)) (20). Self-reported height between ages 20 and 40 years was substituted when measured height was unavailable.

**Statistical analysis**

Odds ratios and 95 percent confidence intervals were estimated by unconditional logistic regression. All models were adjusted for the frequency-matching factors, age and race, by using a 16-level variable with a unique value for each combination of race and 5-year age category (21). For the main analyses, six separate logistic regression models were run to assess the associations between each exposure variable and advanced prostate cancer. Performing backward elimination, we included all potential covariates in each multiple regression model. Then, we removed each covariate individually to examine the resulting change in the estimate for the exposure variable. Only family history of prostate cancer and saturated fat intake resulted in a change of at least 0.05 in the β estimate for any of the six exposure variables. We adjusted all six multivariate models for family history and saturated fat in addition to age and race.

**RESULTS**

Distributions of demographic characteristics and lifestyle factors by case-control status are shown in table 1. The study population was predominantly White; 19 percent were African American. Approximately three quarters had at least some college education. Fewer cases (24 percent) than controls (29 percent) reported a weight considered obese in the reference year.

We examined the concordance among seven measures of obesity (the six measures of body size in youth plus recent BMI) by calculating the percentage classified as “obese” by one measure if they had already been classified as “obese” by a different measure (table 2). Tracking, or increased likelihood of obesity throughout life if one was obese at some earlier time, is evident in table 2. For instance, comparison of the values in the “Recent BMI” column with those in the adjacent column (“Overall % obese by measure”) shows that those who were obese as older adults (“Recent BMI”) were twice as likely than the average study participant to report obesity earlier in life. While only 12 percent of all participants reported an “obese” age 20 years comparison weight, more than twice as many obese older adults (25 percent) reported being “obese” by that measure. One sees this same pattern of tracking between other variables, but the correspondences among the measures are not as great as might be expected. In most instances, only a minority of those classified as “obese” by one measure also report obesity by a different measure.

Table 3 shows the associations between self-reported obesity in youth and advanced prostate cancer risk. Although the magnitudes of the odds ratios varied by age and type of measure, the associations between the youth obesity measures and prostate cancer were consistently inverse. For those who reported being obese at age 10 years, the odds ratios for prostate cancer were inverse but not statistically significant. The variables for age 20 years indicated stronger inverse associations between obesity and advanced prostate cancer than at age 10 years (“obese” line drawings at age 20 years: odds ratio (OR) = 0.53, 95 percent confidence interval (CI): 0.28, 1.00; obese comparison weight at age 20 years: OR = 0.59, 95 percent CI: 0.40, 0.88). The strongest inverse association was seen when we examined usual BMI between ages 20 and 29 years (OR = 0.40, 95 percent CI: 0.20, 0.81).

Obese trouser waist size (≥38 inches vs. 32–37 inches) between ages 20 and 29 years also showed an inverse relation but not as strong as that for BMI. However, small
TABLE 1. Characteristics of advanced prostate cancer cases and controls, San Francisco Bay Area, California, 1997–2000

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Cases</th>
<th>Controls</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 568)</td>
<td>(n = 544)</td>
<td></td>
</tr>
<tr>
<td>Age (years) at diagnosis or selection†</td>
<td>No.</td>
<td>%*</td>
<td>No.</td>
</tr>
<tr>
<td>40–49</td>
<td>22</td>
<td>4</td>
<td>15</td>
</tr>
<tr>
<td>50–59</td>
<td>169</td>
<td>30</td>
<td>144</td>
</tr>
<tr>
<td>60–69</td>
<td>236</td>
<td>42</td>
<td>241</td>
</tr>
<tr>
<td>70–79</td>
<td>141</td>
<td>25</td>
<td>144</td>
</tr>
<tr>
<td>Race†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>450</td>
<td>79</td>
<td>454</td>
</tr>
<tr>
<td>African American</td>
<td>118</td>
<td>21</td>
<td>90</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No high school degree</td>
<td>55</td>
<td>10</td>
<td>42</td>
</tr>
<tr>
<td>High school degree</td>
<td>94</td>
<td>17</td>
<td>81</td>
</tr>
<tr>
<td>Some college</td>
<td>153</td>
<td>27</td>
<td>164</td>
</tr>
<tr>
<td>College degree</td>
<td>109</td>
<td>19</td>
<td>125</td>
</tr>
<tr>
<td>Postgraduate studies</td>
<td>157</td>
<td>28</td>
<td>132</td>
</tr>
<tr>
<td>Smoking status</td>
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<tr>
<td>Never</td>
<td>156</td>
<td>27</td>
<td>156</td>
</tr>
<tr>
<td>Former</td>
<td>293</td>
<td>52</td>
<td>293</td>
</tr>
<tr>
<td>Current</td>
<td>119</td>
<td>21</td>
<td>96</td>
</tr>
<tr>
<td>Daily saturated fat (g/day)</td>
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<td></td>
</tr>
<tr>
<td>≤17.6</td>
<td>110</td>
<td>19</td>
<td>136</td>
</tr>
<tr>
<td>17.7–27.8</td>
<td>152</td>
<td>27</td>
<td>137</td>
</tr>
<tr>
<td>27.9–40.6</td>
<td>143</td>
<td>25</td>
<td>135</td>
</tr>
<tr>
<td>≥40.7</td>
<td>163</td>
<td>29</td>
<td>136</td>
</tr>
<tr>
<td>Daily energy intake (kcal/day)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>≤1,815</td>
<td>127</td>
<td>22</td>
<td>136</td>
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<tr>
<td>1,816–2,432</td>
<td>129</td>
<td>23</td>
<td>136</td>
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<tr>
<td>2,433–3,110</td>
<td>135</td>
<td>24</td>
<td>136</td>
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<tr>
<td>≥3,111</td>
<td>177</td>
<td>31</td>
<td>136</td>
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<tr>
<td>Recent BMI‡.§</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;18.5</td>
<td>3</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>18.5–24.9</td>
<td>145</td>
<td>26</td>
<td>129</td>
</tr>
<tr>
<td>25.0–27.4</td>
<td>153</td>
<td>27</td>
<td>145</td>
</tr>
<tr>
<td>27.5–29.9</td>
<td>130</td>
<td>23</td>
<td>108</td>
</tr>
<tr>
<td>≥30.0</td>
<td>137</td>
<td>24</td>
<td>158</td>
</tr>
<tr>
<td>Missing</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

* Some percentages do not total 100 because of rounding.
† Controls were frequency matched to cases on this variable.
‡ BMI, body mass index (weight [kg]/height [m]²).
§ Based on self-reported weight during the reference year and height measured at interview. When measured height was missing, self-reported height between ages 20 and 40 years was substituted.

trouser waist size (<32 inches) between ages 20 and 29 years was associated with a marked reduction in the odds ratio (OR = 0.65, 95 percent CI: 0.50, 0.85). For those reporting an even smaller trouser waist size, less than 30 inches, the inverse association was even more extreme (OR = 0.5, 95 percent CI: 0.35, 0.72). In contrast, there was no indication that an increasingly thin body size was associated with decreased odds ratios for prostate cancer when size was assessed by using the line drawings at ages 10 or 20 years or self-reported BMI during a participant’s twenties (data not shown).

We also investigated potential interactions with early-onset disease (<60 years of age at diagnosis), family history of prostate cancer, and race. We found no evidence of effect modification by any of these factors. When we stratified by race, all of the multivariate-adjusted odds ratios for African Americans were found to be inverse, except for the “obese” line drawing at age 10 years (OR = 1.22, 95 percent CI: 0.25, 6.00). This odds ratio was based on very small cell counts and was the most unstable of all of the race-stratified estimates. The other odds ratios for African Americans ranged from 0.09 (95 percent CI: 0.01, 0.75) for BMI during the twenties to 0.73 (95 percent CI: 0.30, 1.79) for comparison weight at age 10 years.

Finally, we investigated whether the inverse associations between youth obesity and prostate cancer were confounded by the effects of obesity later in life. Including recent obesity (BMI ≥30) in the models somewhat attenuated each of the odds ratios, but most did not change substantially. Obese BMI and obese waist size between ages 20 and 29 years were the exceptions: the change in the β estimates was greater than 0.10 for both of these measures. When recent BMI was included in the models, the odds ratio for obese BMI between ages 20 and 29 years was 0.49 (95 percent CI: 0.24, 1.02) and that for obese waist size was 0.83 (95 percent CI: 0.45, 1.56) compared with 0.40 (95 percent CI: 0.20, 0.81) and 0.73 (95 percent CI: 0.40, 1.35), respectively, when not adjusted for recent BMI.

DISCUSSION

In this population-based study of African-American and White men, we observed consistently inverse associations of preadolescent and early-adult obesity with a diagnosis of advanced prostate cancer later in life. The inverse associations were stronger and statistically significant (α = 0.05, two sided) for measures of obesity in the third decade (age 20 years and between ages 20 and 29 years) compared with measures of obesity at age 10 years. In addition, for the third decade of life, the associations for measures of overall obesity were more strongly inverse than that for trouser waist size, a more specific measure of abdominal obesity. These trends remained after including recent BMI in the models (refer to the previous paragraph). However, only heavier comparison weight at age 20 years remained statistically significant after adjusting for recent BMI.

We know of only one other study of prostate cancer and preadolescent obesity: the Health Professionals Follow-up Study found rate ratios of 0.72 (95 percent CI: 0.47, 1.10) and 0.38 (95 percent CI: 0.19, 0.77) for advanced and metastatic prostate cancers, respectively, for those choosing the largest line drawings to describe their bodies at age 10 years (9). Results were similar for large body size at age 5 years.
Most prostate cancer studies examining large body size in the first three decades of life have focused on BMI during the college years and subjects’ twenties (22–30). The results from these cohort and case-control studies have been fairly consistent. Of the eight studies reporting results for large body size, seven have shown null or slightly elevated effect estimates (risk/odds ratios ranging from 1.0 to 1.4), none of which was statistically significant (22–28). An investigation of large body size in the Health Professionals Follow-up Study was the one exception (9). Inverse associations were observed between BMI ≥26 at age 21 years and advanced and metastatic prostate cancer (multivariate-adjusted rate ratio = 0.53, 95 percent CI: 0.33, 0.86 for advanced disease and rate ratio = 0.57, 95 percent CI: 0.29, 1.10 for metastatic disease). Inverse associations were also observed for the largest line drawings at age 20 years (rate ratio = 0.62, 95 percent CI: 0.38, 1.02 for advanced prostate cancer and rate ratio = 0.31, 95 percent CI: 0.12, 0.76 for metastatic cancer).

A possible explanation for the results of the seven studies that reported little or no effect is the cutoffs used to define large body size. The previous studies used tertile, quartile, or quintile groupings to categorize their study populations of lean young men rather than the definition of obesity recommended by the World Health Organization (31). For example, in the study by Cerhan et al. (23), using quartiles of BMI to classify their participants at age 25 years resulted in a “large” body size group consisting of all those of BMI ≥24.4, even though values of less than 25 are within the “normal” BMI range for adults and only those of BMI ≥30 are considered obese (31). Because that study and the others used such low thresholds for defining the “large” body size category, previous studies’ conclusions about large body size and prostate cancer risk were relevant for slightly overweight men or even men at the high end of the normal range, but not for those who were obese in youth. (In our analysis, increased body size within the nonobese range (e.g., 25 < BMI < 30) was associated with no increase or slightly increased odds of advanced prostate cancer (refer to table 3).) Further supporting this argument, of all eight studies mentioned above, the one that found an inverse association with “large” body size was also the one that used the highest threshold (BMI >26) for defining its large body size group (9).

The present study has several of its own limitations. An obvious weakness is the use of recalled and/or subjective body size measures, potentially leading to misclassification of obesity in youth. In a validation study of self-reported BMI and line drawings among elderly men, Must et al. (32) found that recalled obesity was specific but not sensitive. That is, only 25–37 percent of the heaviest boys reported being fat (as classified by Must et al.), whereas virtually none of the slimmer boys reported being heavy. This pattern of misclassification would lead our data to only overstate the inverse effects of obesity on prostate cancer if cases were less likely than controls to report obesity. However, researchers are usually more concerned with controls underreporting less socially desirable traits such as obesity than with cases underreporting (33). Therefore, it is unlikely that greater recall bias among cases accounts for the inverse associations observed.

The second important limitation of the present study is that 11 percent (n = 106) of potentially eligible cases died before they could be interviewed. Evidence exists that, compared with nonobese men, obese men have a higher prostate-cancer-specific mortality rate (34, 35). The absence of a disproportionate number of obese cases from the data set could have resulted in an undercount of cases who were obese in youth, which could lead to an overstatement of the inverse association between youth obesity and advanced prostate cancer. The extent of the undercount would depend on two factors: the mortality rate ratio from prostate cancer for obese men (1.3 in the Cancer Prevention Study II (34))

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TABLE 2. Percent agreement between recalled measures of obesity and recent BMI* for all study subjects, San Francisco Bay Area, California, 1997–2000

<table>
<thead>
<tr>
<th>% also classified obese by this measure</th>
<th>Of participants classified as obese by this measure</th>
<th>Overall % obese by measure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Line drawing, age 10 years</td>
<td>Comparison weight, age 10 years</td>
</tr>
<tr>
<td>Line drawing, age 10 years</td>
<td>86</td>
<td>56</td>
</tr>
<tr>
<td>Comparison weight, age 10 years</td>
<td>17</td>
<td>16</td>
</tr>
<tr>
<td>Line drawing, age 20 years</td>
<td>26</td>
<td>38</td>
</tr>
<tr>
<td>Comparison weight, age 20 years</td>
<td>12</td>
<td>13</td>
</tr>
<tr>
<td>BMI, ages 20–29 years</td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>Trouser waist size, ages 20–29 years</td>
<td>33</td>
<td>52</td>
</tr>
</tbody>
</table>

* BMI, body mass index (weight (kg)/height (m)^2).
and the percentage of the missing obese men who would have reported obesity in youth (the corresponding percentages in the present study were fairly low (refer to table 2)). Assuming that obese cases were twice as likely to die as nonobese cases and that 40 percent of deceased obese cases would have reported youth obesity by any given measure, none of the inverse associations were reversed in unadjusted sensitivity analyses (data not shown). Only by assuming that

<table>
<thead>
<tr>
<th>Measure and category*</th>
<th>No. of cases (n = 568)</th>
<th>No. of controls (n = 544)</th>
<th>Adjusted for age and race</th>
<th>Multivariate adjusted†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Odds ratio</td>
<td>95% confidence interval</td>
</tr>
<tr>
<td>Line drawing, age 10 years</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1–4</td>
<td>508</td>
<td>484</td>
<td>Referent</td>
<td>Referent</td>
</tr>
<tr>
<td>5</td>
<td>34</td>
<td>25</td>
<td>1.31 0.76, 2.24</td>
<td>1.32 0.77, 2.29</td>
</tr>
<tr>
<td>6–9</td>
<td>24</td>
<td>34</td>
<td>0.70 0.41, 1.21</td>
<td>0.79 0.46, 1.38</td>
</tr>
<tr>
<td>Missing</td>
<td>2</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Comparison weight, age 10 years</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Much lighter or lighter</td>
<td>255</td>
<td>242</td>
<td>0.98 0.76, 1.27</td>
<td>0.96 0.74, 1.25</td>
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<td>Same</td>
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<td>216</td>
<td>Referent</td>
<td>Referent</td>
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<td>Much heavier or heavier</td>
<td>70</td>
<td>84</td>
<td>0.73 0.50, 1.06</td>
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</tr>
<tr>
<td>Line drawing, age 20 years</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>1–4</td>
<td>460</td>
<td>438</td>
<td>Referent</td>
<td>Referent</td>
</tr>
<tr>
<td>5</td>
<td>90</td>
<td>77</td>
<td>1.09 0.78, 1.53</td>
<td>1.08 0.77, 1.52</td>
</tr>
<tr>
<td>6–9</td>
<td>16</td>
<td>29</td>
<td>0.49 0.36, 0.92</td>
<td>0.53 0.28, 1.00</td>
</tr>
<tr>
<td>Missing</td>
<td>2</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Comparison weight, age 20 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Much lighter or lighter</td>
<td>184</td>
<td>195</td>
<td>0.78 0.60, 1.01</td>
<td>0.76 0.58, 0.99</td>
</tr>
<tr>
<td>Same</td>
<td>322</td>
<td>269</td>
<td>Referent</td>
<td>Referent</td>
</tr>
<tr>
<td>Much heavier or heavier</td>
<td>59</td>
<td>77</td>
<td>0.59 0.40, 0.86</td>
<td>0.59 0.40, 0.88</td>
</tr>
<tr>
<td>Don’t know</td>
<td>3</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>4</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI,† ages 20–29 years§</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;25.0</td>
<td>361</td>
<td>347</td>
<td>Referent</td>
<td>Referent</td>
</tr>
<tr>
<td>25.0–29.9</td>
<td>191</td>
<td>162</td>
<td>1.12 0.86, 1.45</td>
<td>1.13 0.87, 1.47</td>
</tr>
<tr>
<td>≥30.0</td>
<td>12</td>
<td>31</td>
<td>0.36 0.18, 0.71</td>
<td>0.40 0.20, 0.81</td>
</tr>
<tr>
<td>Missing</td>
<td>4</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trouser waist size (inches¶), ages 20–29 years</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>&lt;32</td>
<td>164</td>
<td>201</td>
<td>0.66 0.51, 0.85</td>
<td>0.65 0.50, 0.85</td>
</tr>
<tr>
<td>32–37</td>
<td>376</td>
<td>312</td>
<td>Referent</td>
<td>Referent</td>
</tr>
<tr>
<td>≥38</td>
<td>20</td>
<td>25</td>
<td>0.66 0.36, 1.22</td>
<td>0.73 0.40, 1.35</td>
</tr>
<tr>
<td>Missing</td>
<td>8</td>
<td>6</td>
<td></td>
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</tr>
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</table>

* Refer to the Materials and Methods section of the text for more information.
† Multivariate adjustment for age, race, family history of prostate cancer, and recent saturated fat intake.
‡ BMI, body mass index (weight (kg)/height (m)²).
§ Based on recalled usual weight from ages 20 to 29 years and height measured at interview. When measured height was unavailable, self-reported height was substituted.
¶ One inch = 2.54 cm.
Obese men were twice as likely to die before being reached for interview and that 45 percent of them would have chosen an “obese” body picture (more than five times the rate in the study population) would one see an unadjusted odds ratio of 1.0. Therefore, we think it unlikely that, by itself, the missing data for deceased men accounts for the inverse associations seen here.

This study has several important strengths. First, study eligibility was limited to men with advanced prostate cancer. Admixture of “latent,” or clinically unimportant, cancers with more serious disease reduces investigators’ ability to detect associations with prostate cancer (36). Furthermore, notably, our study was the first known to include more than a nominal number of African-American cases, a group with a heavy burden of prostate cancer. Finally, the data were derived from population-based samples of cases and controls, and the study used multiple, cognitively distinct assessments of obesity at different ages.

As described earlier, obesity is associated with a number of physiologic conditions that could influence prostate cancer development, including decreased androgen levels, decreased sex hormone-binding globulin, increased estrogen, increased free insulin-like growth factor-I, and hyperinsulinemia (8, 37, 38). In addition, several authors have suggested that the years before age 30 could be a critical window in which physiologic traits act to promote development of aggressive prostate cancer (5, 8). An analysis of US surveillance data found that obesity in boys was associated with delayed pubertal development (39). This phenomenon presents a mechanism by which obese prepubertal males could experience a lower risk of developing prostate cancer because of less cumulative exposure to androgens over their lifetimes. Additionally, because puberty triggers a steep rise in insulin-like growth factor-I (40), a delay in this increase due to delayed puberty could mean less cumulative exposure to insulin-like growth factor-I and/or less exposure at critical ages.

Promoting obesity in youth is not a viable means of reducing prostate cancer morbidity. Although this paper has demonstrated a possible inverse relation with later risk of prostate cancer, other research has definitively demonstrated that overweight in children and adolescents is associated with cardiovascular risk factors and type 2 diabetes, as well as tracking of obesity into adulthood (41, 42). In addition, obese middle-aged and elderly men are more likely than their nonobese peers to die of prostate cancer (34, 35).

Research to identify prostate cancer risk factors operating in youth is still in its early stages. Examining early-life exposures is challenging because of the difficulty in obtaining markers of metabolic activity from decades before diagnosis, the complexities of endocrine pathways likely involved in prostate cancer etiology, and the methodological challenge of separating effects exerted at different times in life. Studying intermediate markers of cancer in pediatric populations, exploiting existing data from cohorts with long-term follow-up of young men, and conducting more research by using recalled early-life exposures offers the promise of building upon our research. The value of such work lies in better understanding which metabolic pathways are likely to influence prostate cancer development and at which stages in life certain risk factors are most important. Such knowledge will advance the development of a conceptual framework for prostate cancer’s natural history and hopefully its prevention and treatment.

ACKNOWLEDGMENTS

This work was supported by grant 99-00527V-10182 (to E. M. J.) from the California Cancer Research Program, as well as grant P30ES10126 (to M. D. G.) from the National Institute of Environmental Health Sciences (National Institutes of Health (NIH)) and grant T32-CA09330 from the National Cancer Institute (NIH). W. R. R. was partially supported by the Thomas S. and Caroline H. Royster, Jr. Fellowship (University of North Carolina, Chapel Hill), the Minority Training Program in Cancer Control Research (University of California, San Francisco), and the Julie Gatewood Latane´ Residential Fellowship (Latane´ Center for Human Science). Cancer incidence data used in this paper were collected by the Greater Bay Area Cancer Registry, of the Northern California Cancer Center, under contract N01-PC-35136 with the National Cancer Institute (NIH) and with the support of the California Cancer Registry, California Department of Health Services.

REFERENCES


