

# Body mass index and the risk of prostate cancer

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**Background:** This article presents cohort studies that use data from the National Health Information Survey from 1986 to 1994 and compares the effectiveness of Cox proportional hazards models that assume a linear relationship between body mass index (BMI) and the risk of prostate cancer with models that assume a J-shaped relationship.

**Methods and results:** Our study found that for black males over 40 years of age, neither a linear nor a J-shaped relationship yielded a statistically significant model. With white males over 40 years, assuming a linear relationship did not yield a statistically significant model ( $P = 0.582$ ). When we assume a J-shaped relationship, the optimal change point where the risk of prostate cancer death is minimized occurs when the BMI is 25.5. Among white males over 40 years with BMI < 25.5, an inverse relationship was found ( $P = 0.009$ ). Among white males over 40 years with BMI > 25.5, a direct relationship was found ( $P = 0.017$ ).

**Conclusion:** With this data set, we found that for white males over 40 years, Cox proportional hazards models that assume a J-shaped relationship between BMI and prostate cancer death provide a much better fit than models assuming a linear relationship.

**Keywords:** body mass index, prostate cancer, J-shaped curve, Cox proportional hazards model, Kaplan-Meier model, National Health Information Survey

## Introduction

Researchers have conducted cohort and case-control studies involving diverse populations to determine the relationship between prostate cancer and obesity, measured in terms of body mass index (BMI). A number of studies that have examined the relationship between BMI and the risk of prostate cancer have shown either no relationship or an inverse relationship between these two factors. Lee et al<sup>1</sup> examined the relationship between physical activity and prostate cancer risk for men enrolled in the Harvard Alumni Study. During the 6-year follow-up, 439 of the 8922 participants developed prostate cancer. The analysis showed no evidence that either physical activity or body weight was associated with prostate cancer. Nilson and Vatten<sup>2</sup> completed a 12-year follow-up of 22,248 Norwegian men and also found no relationship between BMI and prostate cancer. Giovannucci et al<sup>3</sup> studied 2896 cases of prostate cancer from the Health Professionals Follow-up Study and concluded that no relationship exists between BMI and prostate cancer among older males (age  $\geq 60$  years). However, they found that younger males with lower BMI had a higher risk of prostate cancer than did their counterparts with BMI  $\geq 30$ , showing an inverse relationship between BMI and prostate cancer risk for younger males.

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Other studies have found a positive relationship between BMI and prostate cancer. Rodriguez et al<sup>4</sup> examined BMI, height, and prostate cancer mortality in two large cohorts of men selected from the Cancer Prevention Study I (CPS-I), who were enrolled in 1959 and followed through 1972, and then from the Cancer Prevention Study II (CPS-II), who were enrolled in 1982 and followed through 1996. After exclusions, 1590 prostate cancer deaths remained among 381,638 men in CPS-I and 3622 deaths among 434,630 men in CPS-II. The investigators used Cox proportional hazards modeling to compute rate ratios and adjust for confounders. They found prostate cancer mortality rates to be significantly higher among obese men (BMI  $\geq$  30).

The above studies show a representative sample of the research that has been conducted on this subject. There are additional studies<sup>5-9</sup> concluding that the relationship between BMI and prostate cancer is positive and also further studies<sup>10-12</sup> that find no relationship.

In 1997, Durazo-Arvizu et al showed that the relationship between BMI and overall death can be modeled effectively using a J-shaped risk curve.<sup>13</sup> To our knowledge, no study has formally considered the use of a J-shaped curve to model the relationship between BMI and prostate cancer. Goetghebeur and Pocock<sup>14</sup> have suggested an algorithm for determining when the use of a J-shaped curve is appropriate, along with a procedure for modeling when it is appropriate.

Different studies have shown no relationship, a direct relationship, or an inverse relationship between BMI and incidence of prostate cancer. Studies of prostate cancer mortality have shown a direct relationship between BMI and prostate cancer mortality. However, when we modeled the relationship between BMI and prostate cancer mortality using the National Health Information Survey (NHIS) for white males over 40 years and black males over 40 years, no relationship was found for either group ( $P > 0.5$  for both). As the NHIS would indicate, ie, that there is no direct relationship between BMI and prostate cancer death, and because there is controversy between a direct and an inverse relationship between BMI and prostate cancer incidence, our hypothesis is that the relationship between BMI and prostate cancer deaths may be best explained using a J-shaped curve.

Our analysis consists of cohort studies that examined the risk of death from prostate cancer for black and white males over 40 years of age using the NHIS survey data from 1986 to 1994, and explore the appropriateness of using a J-shaped curve to explain the relationship between BMI and death from prostate cancer. We then compare models that assume a J-shaped curve with those that do not. We also discuss the

possibility that several previous studies may have produced negative results only because they did not consider a J-shaped relationship between BMI and the risk of prostate cancer.

## Materials and methods

### Data

The NHIS is a continuing nationwide survey of the US civilian, non-institutionalized population conducted through households. The average annual sample consists of 92,000–125,000 men with a response rate of over 95%. Health and utilization variables include self-reported age, height, weight, level of physical activity, family income, level of education, and self-assessed health status. To ensure accuracy, a 5% sample of all questionnaires is recoded and keyed by other coders. A 100% verification procedure is used if certain error tolerances are exceeded.

Linkage of NHIS respondents with the National Death Index from 1986 through 1997 has provided multiple-cause-of-death data for the NHIS survey years 1986–1994. The National Center for Health Statistics then uses a modification of a probabilistic approach to classify potential matches between the NHIS and National Death Index ([http://www.cdc.gov/nchs/data/datalinkage/matching\\_methodology\\_nhis\\_final.pdf](http://www.cdc.gov/nchs/data/datalinkage/matching_methodology_nhis_final.pdf)). Our analysis uses only cases with the highest probability of a match between NHIS respondents and National Death Index data.<sup>15,16</sup> More complete NHIS implementation procedures and linkage methodology are available on their website (<http://www.cdc.gov/nchs/nhis.htm>). For this study, only white and black males over 40 years with known BMI values were included.

The NHIS data have staggered entry with right truncation. The participants entered the study in an approximately uniform manner over the 8-year period. Because follow-up was truncated, the length of follow-up varies among the participants. Hence, follow-up time is based on time scale and not on calendar time, ie, the first time a participant is contacted is time 0 and follow-up is calculated from that point. Prostate cancer deaths that were cataloged in the National Death Index were the only endpoints used in this research.

### Statistical methods

We began our analysis by tabulating basic statistics of interest. These include the number of people classified by age and race who died from prostate cancer, those who died from other causes, and those who were still living, as well as the average BMI, average family income, and average education for each of these subpopulations.

We also tabulated the rate and age-adjusted rate for prostate cancer deaths and deaths from other causes by race and quartile of BMI. The values for the endpoints for the quartiles of BMI were generated for white males over 40 years and for black males over 40 years from the BMI values which separated the respective populations into four equal parts. The values for these endpoints can be seen in Table 2.

Because our data were right-truncated, the follow-up time for the participants changes depending on which year the participants entered the survey. Each day during the course of follow-up, deaths also reduce the size of the population from which the survival rate can be determined. Kaplan-Meier curves allow us to calculate survival and death rates in an environment where the size of the population is constantly changing. If we let  $S(t)$  be the probability of surviving until time  $t$ , then we can consider the probability of surviving until time  $t$  as the probability of surviving time intervals  $I_1, I_2, I_3, \dots, I_n$  where  $I_1 \cup I_2 \cup I_3 \dots \cup I_n = [0, t]$ . Given an interval  $I$ , we can define  $r_i$  as the number of people at risk of dying of prostate cancer at the beginning of interval  $I$ , and  $d_i$  as the number of prostate cancer deaths that occurred during interval  $I$ . This would make the probability of surviving prostate cancer during an interval  $I$ , assuming one had survived up to the beginning of the interval, equal to  $(1 - d_i/r_i)$  and  $S(t) = \prod_{I_i < t} (1 - d_i/r_i)$ . The death rate is equal to one minus the survival rate.

If a baseline set of characteristics,  $\bar{x}_v$  are observed for a given individual, the hazard at a time  $t$  is defined as the instantaneous probability that a person with characteristics  $\bar{x}_i$  dies after time  $t$  given that the person survived up to the time  $t$ . The Cox proportional hazards model assumes a hazard function of the form  $h(t | \bar{x}_i) = h_0(t) \exp(\bar{\beta}^T \bar{x}_i)$ , where  $\bar{x}$  is the vector of values for characteristics associated with the hazard,  $\bar{\beta}$  is a vector of coefficients associated with these parameters, and  $h_0(t)$  is a baseline hazard function. The proportional hazard between two sets of characteristics,  $\bar{x}_i$  and  $\bar{x}_j$  is:

$$\frac{h(t | \bar{x}_i)}{h(t | \bar{x}_j)} = \frac{h_0(t) \exp(\bar{\beta}^T \bar{x}_i)}{h_0(t) \exp(\bar{\beta}^T \bar{x}_j)} = \exp(\bar{\beta}^T (\bar{x}_i - \bar{x}_j)).$$

This expression is constant if  $\bar{x}$  does not change with respect to  $t$  from which the name “proportional hazards” is derived. The partial likelihood equation for the parameters  $\bar{\beta}$  is defined by:

$$PL(\bar{\beta}) = \prod_{\bar{x}_i \in D} \frac{\exp(\bar{\beta}^T \bar{x}_i)}{\sum_{\bar{x}_j \in R(\bar{x}_i)} \exp(\bar{\beta}^T \bar{x}_j)}$$

where the set of characteristics associated with the  $n$  deaths that occurred in the follow-up period is defined by  $D = \{\bar{x}_1, \bar{x}_2, \bar{x}_3, \dots, \bar{x}_n\}$  and the risk set for a given  $\bar{x}_i, R(\bar{x}_i)$ , is defined as the set of characteristics for all individuals at risk at the time of death of the individual associated with characteristics  $\bar{x}_i$ . The partial likelihood equation is solved numerically to obtain the parameters of the Cox proportional hazards model.

To determine whether a J-shaped risk curve may be appropriate to describe the relationship between BMI and the risk of death from prostate cancer, we graphed cumulative death rates (calculated as  $1 -$  the Kaplan Meier survival rates) for the four quartiles of BMI. These curves were generated for blacks and whites and adjusted for age using a Cox proportional hazards model.<sup>17</sup>

A J-shaped risk curve is characterized by a change point where the relationship between BMI and risk of death from prostate cancer changes from varying inversely to varying directly. To find the value for this change point for white males and for black males, we followed the procedure described by Goetghebeur and Pocock.<sup>14</sup> This procedure basically consists of the following:

- Scan the range of possible values of  $\eta$ , where each  $\eta$  value is a possible change point for the BMI
- Obtain the proportional hazards model  $h(t) = h_0(t) \exp(\beta_0 * age + \beta_1 * (BMI - \eta)^2 * I(BMI \leq \eta) + \beta_1 * (BMI - \eta)^2 * I(BMI > \eta))$  where  $I$  is the indicator function that returns 1 if the event is true and 0 if the event is false
- Obtain the proportional hazards model  $\hat{h}(t) = \hat{h}_0(t) \exp(\beta_0 * age)$
- Perform the log partial likelihood ratio test on the models in parts 2 and 3
- The  $\eta$  value that maximizes the log partial likelihood ratio tests is considered to be the change point.

To compare models assuming linear and J-shaped relationships between BMI and the risk of death from prostate cancer, we fitted Cox proportional hazards models using BMI and age to predict survival time from prostate cancer for six populations, ie, white males over 40 years, white males over 40 years with BMI values above the change point, white males over 40 years with BMI values below the change point, black males over 40 years, black males over 40 years with BMI values above the change point, and black males over 40 years with BMI values below the change point. We then used likelihood ratio tests to determine the nature and the magnitude of the effect of BMI on the risk of death from prostate cancer for these populations. These Cox models and likelihood ratio tests were performed both without adjustment

and adjusting for education, family income, physical activity, and height.

High prostate cancer mortality rates among those with low BMI values may be a result of systemic weight loss in response to illness. To determine the effect of imminent death on the relationship between BMI values and death from prostate cancer, we removed deaths that occurred within 3 years of the interview and repeated our analyses with this reduced population.

## Results

Tables 1 and 2 show a description of the number of cases, the average BMI for prostate cancer deaths, other deaths, and the living by age and race. Tables 3 and 4 show the rate and age-adjusted rate of deaths from prostate cancer and deaths from all other causes by race and quartiles of BMI. For white males, when adjusted for age, the second quartile of BMI values has the lowest risk of death from prostate cancer and the third quartile of BMI values has the lowest risk of death from other causes. For black males, the third quartile of BMI values has the lowest risk of both prostate cancer death and deaths from other causes.

Figure 1 shows the death rate (calculated as  $1 - \text{Kaplan-Meier survival rate}$ ) adjusted for age for the four quartiles of BMI among black males. During the first 7 years of follow-up, the highest death rates occur in the first and fourth quartiles. This decrease and subsequent increase in the death rate as BMI increases indicates that a J-shaped curve may be appropriate to model the relationship between BMI and the risk of death from prostate cancer. After the seventh year of follow-up, there is no justification for a J-shaped relationship. As can be seen in Table 1, there are not many cases of prostate cancer among black males. Hence, there is the possibility that excessive censoring may affect the later years of follow-up. When considering the entire follow-up period, we found no statistically significant model, neither linear nor J-shaped, to associate BMI with the risk of death from prostate cancer. Restricting our follow-up to the first

seven years, we also found no statistically significant model, neither linear nor J-shaped, to associate BMI with the risk of death from prostate cancer. Hence, for black males over 40 years in this data set we were unable to find any relationship between BMI and the risk of prostate cancer.

Figure 2 presents the same information for white males. This time, the first and fourth quartiles have the highest death rates due to prostate cancer for the entire follow-up period. Hence, a J-shaped curve may be appropriate to describe the relationship between BMI and the risk of death from prostate cancer.<sup>14</sup> When the estimated cumulative incidence with competing risks was graphed, the rates were slightly lower. However, there was no significant change in the nature of the curves (data not shown). Our analysis of the quartiles indicates that the relationship between BMI and the risk of prostate cancer in white males may follow a J-shaped curve which, in turn, implies a BMI value that minimizes risk. We used the procedure outlined by Goetghebeur and Pocock<sup>14</sup> and found that a BMI value of 25.5 should minimize the risk of prostate cancer death.

We then fitted Cox proportional hazards models with three populations, ie, all white males over 40 years, white males over 40 years with  $\text{BMI} \leq 25.5$ , and white males over 40 years with  $\text{BMI} > 25.5$ . Table 5 shows the results of these three Cox proportional hazards models using age and BMI to predict survival time for prostate cancer. When all white males over 40 years are included, the model shows that as BMI increases, the risk of prostate cancer death declines. However, both the confidence interval and the *P* value indicate that the overall inverse relationship determined by this model is not statistically significant. When only white males over 40 years with  $\text{BMI} > 25.5$  are included, the model shows that the risk of prostate cancer grows as BMI increases. Both the likelihood ratio test and the confidence interval indicate that this result is statistically significant. When only white males over 40 years with BMI values less than 25.5 are included, the model shows that the risk of prostate cancer diminishes as BMI increases. Once again, both the likelihood ratio test and the confidence

**Table 1** Participant numbers and average BMI for black males by age group for prostate deaths, other deaths, and the living

| Age (years) | Living |          | Prostate deaths |          | Other deaths |          |
|-------------|--------|----------|-----------------|----------|--------------|----------|
|             | n      | Mean BMI | n               | Mean BMI | n            | Mean BMI |
| 40–49       | 6157   | 27.3     | 1               | 33.1     | 399          | 27.5     |
| 50–59       | 4194   | 27.7     | 19              | 29.1     | 620          | 27.0     |
| 60–69       | 3113   | 27.3     | 63              | 27.2     | 1030         | 26.5     |
| 70–79       | 1408   | 26.6     | 79              | 26.8     | 852          | 25.5     |
| >89         | 328    | 25.2     | 35              | 24.6     | 457          | 24.6     |
| Total       | 15,200 | 27.3     | 197             | 26.8     | 3,358        | 26.2     |

**Abbreviation:** BMI, body mass index.

**Table 2** Number and average BMI for white males by age group for prostate deaths, other deaths, and the living

| Age (years) | Living  |          | Prostate deaths |          | Other deaths |          |
|-------------|---------|----------|-----------------|----------|--------------|----------|
|             | n       | Mean BMI | n               | Mean BMI | n            | Mean BMI |
| 40–49       | 47,584  | 27.2     | 12              | 27.2     | 1452         | 27.4     |
| 50–59       | 32,271  | 27.3     | 25              | 27.1     | 2761         | 27.2     |
| 60–69       | 25,165  | 27.0     | 173             | 27.2     | 5673         | 26.6     |
| 70–79       | 12,740  | 26.2     | 294             | 25.7     | 6904         | 25.6     |
| >89         | 2776    | 25.2     | 173             | 24.3     | 4005         | 24.2     |
| Total       | 120,536 | 27.1     | 677             | 25.8     | 20,795       | 25.9     |

**Abbreviation:** BMI, body mass index.

interval indicate that this result is statistically significant. Hence, these models support a J-shaped curve to describe the relationship between BMI values and the risk of prostate cancer in white males.

We performed the same analyses outlined in the previous paragraph on black males over 40 years. However, no statistically significant models ( $P < 0.05$ ) were found and the data did not suggest that a J-shaped curve was more appropriate than a linear curve for modeling the relationship between BMI and the risk of death from prostate cancer (data not shown).

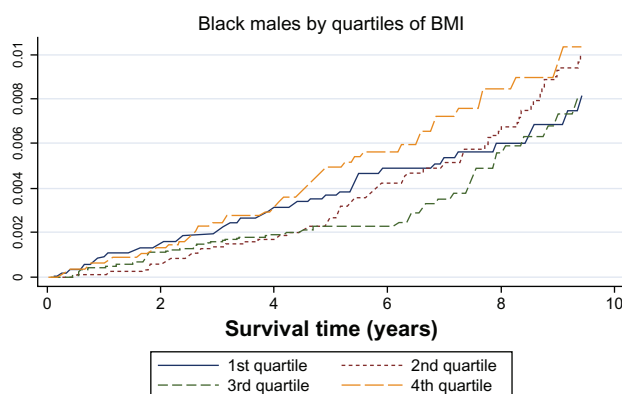
In Table 6, we present the results when the procedures used to generate Table 5 are adjusted for education, family income, physical activity, and height. The minimum risk of prostate cancer is found at a BMI value of 24.9 instead of 25.5. A linear model that does not assume a minimum risk is not statistically significant. If we assume a minimum risk and separately model each side of this minimum, we obtain two statistically significant models. Hence, while the adjusted models are slightly less significant than the unadjusted models, the general nature of the relationship between BMI and the risk of death from prostate cancer does not change when we adjust for these variables.

High mortality rates among those with low BMI values could be due to systemic weight loss in response to disease. Table 7 presents the same data as Table 3 when all deaths within 3 years are removed from the population. Because 40% of prostate deaths were removed from the population, the statistical significance of all models was reduced. However, the inverse relationship between BMI values and the risk of prostate cancer death for white males with BMI  $< 25.5$  remained statistically significant ( $P = 0.04$ ), which would suggest that the J-shaped relationship is not solely the result of systemic weight loss in response to illness.

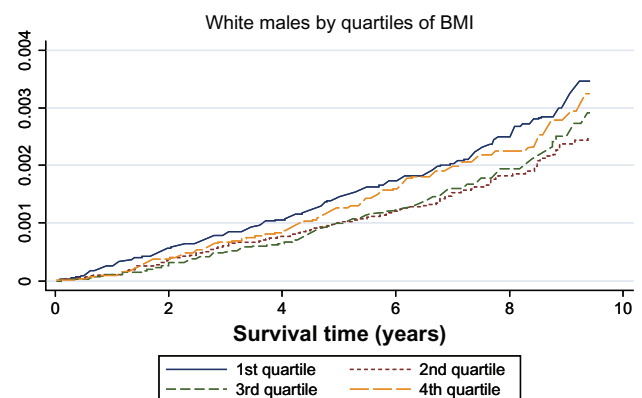
It should be noted that numerous hazard ratio models were performed with various covariates and controlled for different variables. They all consistently maintained the J-shaped relationship between prostate cancer mortality and BMI. Tables 5–7 are presented as the most representative models for the data.

## Discussion

The overall rate of death due to prostate cancer for males over 40 years was greater than 1% among blacks and slightly less than 0.5% among whites. We checked the appropriateness of a J-shaped curve associating BMI with the risk of prostate



**Figure 1** Age adjusted death rate due to prostate cancer.



**Figure 2** Age adjusted death rate due to prostate cancer.

**Table 3** Death rates and age-adjusted death rates for white males by quartiles of BMI within the ten-year follow-up period

| Quartile of BMI | Prostate deaths (n) | Prostate death rate/1000 | Age-adjusted prostate death rate/1000 | Other deaths (n) | Other death rate/1000 | Age-adjusted other death rate/1000 |
|-----------------|---------------------|--------------------------|---------------------------------------|------------------|-----------------------|------------------------------------|
| <24.2           | 246                 | 7                        | 9.6                                   | 7516             | 213                   | 0.180                              |
| 24.2–26.4       | 152                 | 4.3                      | 6.7                                   | 4738             | 133                   | 0.135                              |
| 26.5–29.0       | 149                 | 4.2                      | 7.0                                   | 4288             | 121                   | 0.131                              |
| >29.0           | 130                 | 3.7                      | 7.3                                   | 4753             | 120                   | 0.145                              |

Abbreviation: BMI, body mass index.

**Table 4** Death rates and age-adjusted death rates for black males by quartiles of BMI within the ten-year follow-up period

| Quartile of BMI | Prostate deaths (n) | Prostate death rate/1000 | Age-adjusted prostate death rate/1000 | Other deaths (n) | Other death rate/1000 | Age-adjusted other death rate/1000 |
|-----------------|---------------------|--------------------------|---------------------------------------|------------------|-----------------------|------------------------------------|
| <24.1           | 57                  | 12.4                     | 1.90                                  | 1177             | 256                   | 0.241                              |
| 24.1–26.4       | 51                  | 10.8                     | 1.80                                  | 783              | 166                   | 0.177                              |
| 26.5–29.5       | 42                  | 8.9                      | 1.60                                  | 689              | 146                   | 0.164                              |
| >29.5           | 47                  | 9.9                      | 1.80                                  | 709              | 150                   | 0.177                              |

Abbreviation: BMI, body mass index.

**Table 5** BMI hazard ratios for Cox regression models using age as a covariate

|                   | Linear model                  | J-shaped curve                            |   |
|-------------------|-------------------------------|---|---|
|                   | All white males over 40 years | White males over 40 years with BMI ≤ 25.5 | White males over 40 years with BMI > 25.5 |
| BMI hazards ratio | 0.994                         | 0.933                                     | 1.041                                     |
| Standard error    | 0.011                         | 0.025                                     | 0.018                                     |
| P value           | 0.582                         | 0.009                                     | 0.017                                     |
| 95% CI            | [0.974–1.015]                 | [0.885–0.983]                             | [1.007–1.077]                             |

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

**Table 6** BMI hazard ratios for Cox regression models using age as a covariate (adjusted for education, family income, physical activity, and height)

|                   | Linear model                  | J-shaped curve                            |   |
|-------------------|-------------------------------|---|---|
|                   | All white males over 40 years | White males over 40 years with BMI ≤ 24.9 | White males over 40 years with BMI > 24.9 |
| BMI hazards ratio | 0.997                         | 0.923                                     | 1.037                                     |
| Standard error    | 0.011                         | 0.032                                     | 0.019                                     |
| P value           | 0.793                         | 0.020                                     | 0.046                                     |
| 95% CI            | [0.975–1.020]                 | [0.863–0.988]                             | [1.001–1.075]                             |

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

**Table 7** BMI hazard ratios for Cox regression models using age as a covariate when all deaths within 3 years are removed

|                   | Linear model                  | J-shaped curve                            |   |
|-------------------|-------------------------------|---|---|
|                   | All white males over 40 years | White males over 40 years with BMI ≤ 25.5 | White males over 40 years with BMI > 25.5 |
| BMI hazards ratio | 1.004                         | 0.927                                     | 1.03                                      |
| Standard error    | 0.014                         | 0.034                                     | 0.023                                     |
| P value           | 0.774                         | 0.040                                     | 0.157                                     |
| 95% CI            | [0.977–1.031]                 | [0.862–0.997]                             | [0.988–1.077]                             |

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

cancer death for black males and found no evidence for a J-shaped curve in this population. We also applied a likelihood ratio test with a Cox proportional hazards model using BMI to predict survival time among black males with age as a covariate and found insufficient evidence to assume a relationship between BMI and risk of death from prostate cancer among this population. Although the rate of death from prostate cancer is far higher for black males than for white males, there are far fewer black males who died of prostate cancer in our data set. Hence, our inconclusive results for black males are not necessarily indicative that a relationship between BMI and prostate cancer does not exist.

As stated above, we are not aware of prior discussions of the use of a J-shape curve to describe prostate cancer mortality or incidence due to BMI. However, while we only studied prostate cancer mortality, data from several studies suggest that the risk of prostate cancer due to BMI first lowers as BMI increases and then rises as BMI increases further. Nilson et al<sup>2</sup> in their study of 22,248 Norwegian men found that the lowest risk of prostate cancer was associated with BMI values between 23.1 and 24.7. Nomura et al<sup>11</sup> in a study of 8006 Japanese men from 1965 to 1968 found that the minimum risk of prostate cancer was for males whose BMI values were in the second quintile. Hsing et al<sup>18</sup> in their study of 238 cases of newly diagnosed prostate cancer included BMI and history of BMI in their analysis. For current BMI values, the minimum risk of prostate cancer occurred in the third quartile of BMI. Historical evidence indicated that for 20–29-year-olds, the lowest long-term risk of prostate cancer occurred for those with BMI values in the first quartile. However, for all other historical age ranges presented, men with BMI values in the second or third quartile had the lowest long-term risk of developing prostate cancer.

In studies where the minimum risk of prostate cancer as related to BMI occurred in the second or third quartile, the investigators concluded that there was no relationship between BMI and risk of prostate cancer. Our analysis of prostate cancer mortality using the NHIS data also produced this negative result before we modeled using a J-shaped curve. Given our finding, some of the negative results of these earlier studies that considered prostate cancer incidence may reflect their not having considered the possibility of a J-shaped relationship.

Other studies<sup>19,20</sup> that found no relationship between BMI and the risk of prostate cancer reached this conclusion because there was no statistically significant difference between the mean BMI value of males who developed

prostate cancer and the mean BMI value of males who did not develop prostate cancer. Our experience with prostate cancer mortality using the NHIS data also indicated that there was no statistically significant difference between the mean BMI values of males who developed prostate cancer and males who did not develop prostate cancer. Correspondingly, these datasets may also warrant further analysis. When we fitted the Cox proportional hazards model without assuming a J-shaped curve, the hazards ratio was almost equal to one. Therefore, if a J-shaped curve is not assumed, the data do not support a relationship between BMI and the risk of prostate cancer death. However, when we determined a change point value, two statistically significant models ( $P < 0.02$ ) were produced for the populations on each side of the change point. This relationship does not significantly change when controlled for education, income, height, and physical activity. Because the inverse relationship between lower BMI values and risk of prostate cancer death remains statistically significant when deaths occurring within 3 years of the interview are removed from the population, response to an illness alone does not appear to explain the relationship.

In conclusion, we found that among white males over 40 years, only by assuming a J-shaped risk curve could we produce statistically significant models. Because the inverse relationship between the risk of prostate cancer and low BMI persisted when deaths within three years of the interview were removed, imminent death alone does not explain the J-shaped relationship between BMI and the risk of death from prostate cancer.

## Disclosure

The authors report no conflicts of interest in this work.

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