

# Chronic Diseases

Volume 27, Number 4, 2007

*in Canada*



Public Health  
Agency of Canada

Agence de santé  
publique du Canada

Canada

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# Prostate cancer risk and diet, recreational physical activity and cigarette smoking

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## Abstract

Associations between prostate cancer and dietary factors, physical activity and smoking were assessed based on data from a population-based case-control study. The study was conducted among residents of northeastern Ontario. Cases were identified from the Ontario Cancer Registry and diagnosed between 1995 and 1998 at ages 50 to 84 years ( $N = 752$ ). Male controls were identified from telephone listings and were frequency matched to cases on age ( $N = 1,613$ ). Logistic regression analyses investigated history of diet, physical activity and smoking as potential risk factors. Tomato intake had a significant positive association with prostate cancer risk for highest versus lowest quartiles ( $OR = 1.6$ ; 95% CI: 1.2-2.0). Associations were observed for tomato or vegetable juices and ketchup ( $OR = 1.5$ ; 95% CI: 1.2-1.9;  $OR = 1.2$ ; 95% CI: 1.0-1.5, respectively). Neither other dietary variables nor smoking were associated with prostate cancer risk. Strenuous physical activity by men in their early 50s was associated with reduced risk ( $OR = 0.8$ ; 95% CI: 0.6-0.9). While the recreational physical activity association was consistent with results from previous studies, the tomato products association was not.

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**Key words:** case-control study, diet, physical activity, prostate cancer, smoking

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## Introduction

Prostate cancer is the most common cancer in North American males and it is estimated that 20,700 men will be diagnosed with prostate cancer in Canada in 2006.<sup>1,2</sup> Many studies have investigated potential risk factors for prostate cancer, but the only currently established ones are age, family history of prostate cancer and race.<sup>3</sup> There have been inconsistent results in the literature regarding the roles of diet, physical activity and smoking.<sup>4-15</sup> The aim of the current study is to provide further information regarding the potential roles of diet, smoking and physical activity with respect to prostate cancer risk. The results reported here are from a large case-control study of males from northeastern Ontario where the original focus was the investigation of associations among occupational risk

factors and prostate cancer risk. Data about diet, physical activity and smoking were also obtained and results for these variables are reported here.

With respect to diet, fat and meat consumption have been suggested as potential risk factors.<sup>4</sup> Ecological studies show positive correlation between both meat and fat intake and prostate cancer incidence and mortality, but among several case-control and cohort studies the evidence has been equivocal.<sup>4</sup> Suggestion of an association between alcohol consumption and prostate cancer has also not been consistent among studies.<sup>11</sup> Tea consumption is hypothesized to have an inverse association with prostate cancer risk, but few epidemiologic studies in this regard have been performed; some of these indicate an inverse association

between tea consumption and prostate cancer risk while others show no association.<sup>10</sup> Consumption of fish has shown a potential inverse association that is not typically significant.<sup>6</sup> Consumption of fruit and vegetables is hypothesized to have an inverse association. However, in some epidemiologic studies, an inverse association is observed, while there is no association in others.<sup>9</sup> Tomatoes and tomato-based foods are a specific focus since decreased risk has more consistently been observed for high consumption of, primarily, processed tomato products.<sup>9</sup> Given the discrepancies among epidemiological studies of the association between diet and prostate cancer, the results of the large population-based case-control study provided here are important for accumulating evidence both for and against specific nutritional risk factors.

While smoking is an important risk factor for many cancers, associations between smoking and prostate cancer risk have not been consistently demonstrated.<sup>15</sup> In some studies, a lack of differentiation between current and former smokers is suggested to have led to some null results.<sup>15</sup> The data from our study are presented to further investigate the role of cigarette smoking.

A published review of the literature regarding physical activity and prostate cancer risk suggests a potential inverse association, but there are general problems with a lack of control for important confounders.<sup>14</sup> In the results reported here, control for important confounders is considered.

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## Materials and methods

Ethics approval for the study was obtained from the Laurentian Hospital Research Ethics Board in Sudbury, Ontario, Canada.

Cases were men aged 50 to 84 years diagnosed between January 1995 and December 1998 with primary histologically confirmed prostate cancer (ICD9 185)<sup>16</sup> and who were identified in the Ontario Cancer Registry (OCR) as residents of northeastern Ontario. The completeness of the OCR is over 95%.<sup>17</sup> Before cases were approached for participation in the study, consent was obtained from the physician listed on the pathology report. Consenting physicians also provided contact information for patients. Cases received a letter describing the study, with telephone contact occurring approximately ten days after the mailing of the letter. Cases were included if they had a residential telephone and were alive at the time of interviewer contact. We excluded men aged 45 to 49 years (N = 8) included in original data collection<sup>18</sup> to accommodate age-dependent physical activity variables and to remove men whose early onset prostate cancer may have been predominantly genetic.<sup>19</sup> Information on stage and/or grade of prostate tumours was not available nor was information on prostate-specific antigen (PSA) testing.

Controls were randomly selected from the northeastern Ontario population, based on residential telephone listings, and were 2:1 frequency matched to cases based on five-year age groups. Telephone contact with controls was attempted weekly for five weeks followed by a six-week waiting period, after which contact was again attempted weekly for another five weeks. If contact with a specific control was not successful after this second set of attempts, no further attempt was made.

A mailed questionnaire, sent to consenting cases and controls, was used to collect diet, cigarette smoking and recreational physical activity history. Initially, telephone interviews were used to collect data, but

after eleven months subjects were offered the option of providing questionnaire responses by telephone or by mail. This was due to early high-refusal rates for the telephone questionnaire and a preference expressed by participants to self-complete questionnaires and return them by mail. Prior to this change in the data collection procedure, it was determined by means of a small pilot study that either method of data collection resulted in a similar amount of response information.

Questions about diet and recreational physical activity were derived from the National Enhanced Cancer Surveillance Study in Canada.<sup>19</sup> The questionnaire also included questions regarding socio-demographic variables, physical and health variables, family history of prostate cancer and, as its major focus, occupational history. Telephone follow-up to respondents was conducted if clarification of responses was necessary. Telephone follow-up to non-respondents continued approximately every two weeks for a total of three attempted contacts.

The diet section of the study questionnaire was initially developed for the National Enhanced Cancer Surveillance Study in Canada primarily using two validated instruments: the reduced Block questionnaire and the Nurses Health Study questionnaire.<sup>19</sup> Dietary variables measuring weekly intake of 71 foods two years prior to questionnaire completion were derived based on identified frequency of consumption of specified usual serving sizes. Frequencies of usual serving consumption offered in the questionnaire were as follows: never or less than once per month; 1 to 3 per month; 1 per week; 2 to 4 per week; 5 to 6 per week; 1 per day; 2 to 3 per day; 4 to 5 per day, and; 6 or more per day. Usual serving size specifications were offered in both imperial and metric amounts where appropriate. Caloric intake and fat intake were estimated by adding weekly kilojoules (KJ) and grams of fat, respectively, for each food item in the questionnaire. Quartiles of intake were defined based on the

distribution in the controls. The exception is the variable for tofu: It was defined as "never/ever use" since there was a general lack of intake of this specific food type in the study subjects.

Physical activity indicator variables were based on the frequency and intensity (moderate versus strenuous) of recreational activities for at least twenty minutes based on three times of life (mid-teens, early 30s and early 50s). Specific frequencies of at least twenty minutes of exercise for each of strenuous and moderate activity offered in the questionnaire were as follows: less than once per month; 1 to 3 times per month; 1 to 2 times per week; 3 to 5 times per week; and more than 5 times per week. The questionnaire also offered several examples each of strenuous and moderate activities. For each time of life, a variable was derived that indicated whether or not a subject then participated in relevant activities at least three times per week.

The study questionnaire inquired about cigarette smoking history for individuals who had smoked at least once a day for six months or longer. Details regarding average number of cigarettes per day and number of years of smoking, and information about quitting were requested. From this information, smoking was defined as follows: never; former; or current cigarette smoker. In addition, quartiles of pack-years of cigarette smoking were computed based on the pack-years distribution among controls.

Other variables that were possible confounders were also considered. These "core" potential confounders comprised age (continuous), an indicator of family history of prostate cancer (among first-degree relatives), quartiles of recent (five years ago) body mass index (BMI) and, as surrogates for socio-economic status, level of education (elementary, secondary school, post-secondary school) and type of occupation of longest duration (categorized as blue collar versus white collar, based on standard occupational classification code).

Although race is an established risk factor for prostate cancer, race was not included as one of the core potential confounders since 97% of the study subjects were Caucasian.

Initial descriptive analyses involved examining frequencies and cross-tabulations for variables of interest. Multivariate logistic regression analyses were performed to obtain odds ratio (OR) estimates adjusted for age and other potential confounding variables. These variables included core potential confounders described above as well as variables from each of the diet, physical activity and smoking analyses. If these additional confounders did not change odds ratio estimates for risk factors by more than 15%, they were deleted from the model. All analyses were conducted using version 8.2 of SAS software.<sup>20</sup> Approximate 95% confidence intervals (CI) were computed to provide information on the variability associated with the modeling results. Global *p*-values were used to investigate the significance of categorical variables. Any subjects with missing values for any variables included in a specific model were not included in the estimation of parameters for that particular model.

## Results

Response rates in the original study were 73.6% (760 of 1,033 eligible) for cases and 47.5% (1,632 of 3,433 eligible) for controls.<sup>18</sup> Among the eligible cases and controls who did not respond, 85.4% and 92.4% refused, respectively. The average time between case diagnosis and questionnaire completion was thirteen months; 75% of questionnaires were completed within seventeen months of diagnosis.

Frequencies and age-adjusted odds ratio estimates for study participant characteristics that were included as core potential confounders appear in Table 1. There was a significant positive association between prostate cancer risk and family history of prostate cancer ( $p < 0.0001$ ), a result not surprising, given that family history is an established risk factor. The remaining variables were not significantly

**TABLE 1**  
Frequencies, age-adjusted odds ratio estimates (AOR\*), approximate 95% confidence intervals (CI) and global *p*-values for selected potential confounders for controls (N=1,613) and cases (N=752) from a population sample of northeastern Ontario men aged 50-84 years

| Variable                                  | Controls | Cases | AOR | 95% CI  | <i>p</i> -value |
|---|----------|-------|-----|---------|-----------------|
| <b>Age group</b>                          |          |       |     |         |                 |
| 50-54                                     | 69       | 25    |     |         |                 |
| 55-59                                     | 138      | 50    |     |         |                 |
| 60-64                                     | 271      | 134   |     |         |                 |
| 65-69                                     | 446      | 222   |     |         |                 |
| 70-74                                     | 389      | 181   |     |         |                 |
| 75-79                                     | 204      | 109   |     |         |                 |
| 80-84                                     | 96       | 31    |     |         |                 |
| <b>Family history of prostate cancer</b>  |          |       |     |         |                 |
| No  | 1,522    | 643   | 1.0 |         | < 0.0001        |
| Yes                                       | 91       | 109   | 2.8 | 2.1-3.8 |                 |
| <b>Body mass index (kg/m<sup>2</sup>)</b> |          |       |     |         |                 |
| 5 years ago                               |          |       |     |         |                 |
| Q1 (≤ 24)                                 | 398      | 180   | 1.0 |         | 0.1136          |
| Q2 (24 to 27)                             | 389      | 155   | 0.9 | 0.7-1.1 |                 |
| Q3 (27 to 29)                             | 390      | 211   | 1.2 | 0.9-1.5 |                 |
| Q4 (> 29)                                 | 397      | 184   | 1.0 | 0.8-1.3 |                 |
| Unknown                                   | 39       | 22    |     |         |                 |
| <b>Education</b>                          |          |       |     |         |                 |
| Elementary                                | 538      | 261   | 1.0 |         | 0.0846          |
| Secondary                                 | 737      | 364   | 1.0 | 0.8-1.2 |                 |
| Post-secondary                            | 325      | 122   | 0.8 | 0.6-1.0 |                 |
| Unknown                                   | 13       | 5     |     |         |                 |
| <b>Type of occupation</b>                 |          |       |     |         |                 |
| White collar                              | 704      | 302   | 1.0 |         | 0.1163          |
| Blue collar                               | 909      | 450   | 1.2 | 1.0-1.4 |                 |

\* All AOR estimates presented were adjusted for age and were calculated from valid responses (excluding missing data).

associated with risk of prostate cancer, although education was of borderline significance at the 5% level ( $p = 0.07$ ) and both BMI and type of occupation had *p*-values that were less than 0.15 (0.12 and 0.11, respectively).

Crude frequencies and adjusted odds ratio estimates for self-reported dietary exposures are presented in Table 2. The results presented in this table are based on multivariate models for each diet variable that included total energy along with core potential confounders. None of the physical activity and smoking variables acted as confounders. Overall, the odds

ratio estimate for the highest versus lowest quartile of weekly combined tomato product intake of 1.6 (95% CI: 1.2-2.0) showed a significant positive association. When specific components of this combined variable were explored, similar associations were observed both for tomato or vegetables juices and for ketchup (OR = 1.5; 95% CI: 1.2-1.9 and OR = 1.2; 95% CI: 1.0-1.5, respectively). In contrast, there was no significant association with prostate cancer risk found for the variable representing raw tomato consumption. All remaining specific dietary variables were not associated with risk of prostate cancer. In addition, it was noted that a positive



**TABLE 2**  
**Frequencies, adjusted odds ratio estimates (AOR\*), approximate 95% confidence intervals (CI) and global *p*-values for diet variables based on intake two years prior to questionnaire completion for cases and controls from a population sample of northeastern Ontario men aged 50-84 years, where quartiles are based on the distribution for controls (continued)**

| Variable                            | Controls | Cases | AOR | 95% CI  | <i>p</i> -value |
|-------------------------------------|----------|-------|-----|---------|-----------------|
| <b>Total fat (g/week)</b>           |          |       |     |         | <b>0.9248</b>   |
| 0 - 274                             | 395      | 171   | 1.0 |         |                 |
| 274.1 - 364.1                       | 392      | 183   | 1.0 | 0.8-1.3 |                 |
| 364.2 - 475                         | 394      | 184   | 1.0 | 0.7-1.3 |                 |
| > 475                               | 393      | 199   | 0.9 | 0.6-1.3 |                 |
| Unknown                             | 39       | 15    |     |         |                 |
| <b>Total energy (KJ per week)**</b> |          |       |     |         | <b>0.1267</b>   |
| 0 - 44,707.1                        | 392      | 161   | 1.0 |         |                 |
| 44,707.2 - 54,785.2                 | 392      | 176   | 1.1 | 0.9-1.5 |                 |
| 54,785.3 - 66,331.3                 | 396      | 187   | 1.1 | 0.9-1.5 |                 |
| > 66,331.3                          | 390      | 213   | 1.4 | 1.1-1.8 |                 |
| Unknown                             | 43       | 15    |     |         |                 |
| <b>Tomato or vegetable juices</b>   |          |       |     |         | <b>0.0066</b>   |
| 0                                   | 576      | 239   | 1.0 |         |                 |
| 0.1 - 0.5                           | 469      | 197   | 1.0 | 0.8-1.3 |                 |
| 0.6 - 1.0                           | 230      | 107   | 1.1 | 0.8-1.5 |                 |
| > 1.0                               | 302      | 194   | 1.5 | 1.2-1.9 |                 |
| Unknown                             | 36       | 15    |     |         |                 |
| <b>Tomatoes</b>                     |          |       |     |         | <b>0.7476</b>   |
| < 1.0                               | 352      | 150   | 1.0 |         |                 |
| 1.0 - 2.9                           | 382      | 168   | 1.1 | 0.8-1.4 |                 |
| 3.0                                 | 607      | 283   | 1.1 | 0.8-1.4 |                 |
| > 3.0                               | 248      | 142   | 1.2 | 0.9-1.6 |                 |
| Unknown                             | 24       | 9     |     |         |                 |
| <b>Ketchup</b>                      |          |       |     |         | <b>0.0124</b>   |
| 0                                   | 452      | 206   | 1.0 |         |                 |
| 0.1 - 0.5                           | 341      | 135   | 0.9 | 0.7-1.2 |                 |
| 0.6 - 2.9                           | 309      | 113   | 0.8 | 0.6-1.1 |                 |
| ≥ 3.0                               | 458      | 269   | 1.2 | 1.0-1.5 |                 |
| Unknown                             | 53       | 29    |     |         |                 |
| <b>All tomato-based foods</b>       |          |       |     |         | <b>0.0007</b>   |
| 0 - 2.0                             | 374      | 145   | 1.0 |         |                 |
| 2.1 - 4.0                           | 413      | 156   | 1.0 | 0.7-1.3 |                 |
| 4.1 - 7.5                           | 404      | 177   | 1.1 | 0.8-1.4 |                 |
| > 7.5                               | 355      | 240   | 1.6 | 1.2-2.0 |                 |
| Unknown                             | 67       | 34    |     |         |                 |
| <b>Yellow vegetables</b>            |          |       |     |         | <b>0.8823</b>   |
| < 1.0                               | 234      | 108   | 1.0 |         |                 |
| 1.0                                 | 313      | 137   | 0.9 | 0.7-1.3 |                 |
| 1.1 - 3.0                           | 504      | 245   | 1.0 | 0.7-1.3 |                 |
| > 4.0                               | 507      | 243   | 0.9 | 0.7-1.2 |                 |
| Unknown                             | 55       | 19    |     |         |                 |

association of total energy and prostate cancer risk was observed when comparing the highest versus lowest quartiles (OR = 1.4; 95% CI: 1.1-1.8).

Crude frequencies and adjusted odds ratio estimates for self-reported recreational physical activity appear in Table 3. The results presented in this table are based on separate multivariate models for each physical activity indicator that include core potential confounders. Neither diet nor smoking variables confounded these associations. Separate models were used due to concerns of strong associations among the physical activity indicators, although an overall multivariate model was fitted, including all variables, with no change in conclusions (data not shown). Of note is that strenuous activity in life's early 50s shows significantly reduced risk with an odds ratio estimate of 0.8 (95% CI: 0.6-0.9); the reduced risk associated with strenuous activity in early 30s was of borderline significance (OR = 0.9; 95% CI: 0.7-1.0). Only results for dichotomous strenuous physical activity indicator variables are reported since analyses of three-level categorical variables for strenuous activity versus moderate activity versus low activity resulted in the conclusion that moderate activity—relative to low activity—was not associated with prostate cancer risk in our data.

Crude frequencies and adjusted odds ratio estimates for self-reported cigarette-smoking-related exposures are presented in Table 4. None of the diet and physical activity variables confounded the results of these analyses. Although elevated odds ratio estimates were observed, neither of the smoking variables conferred a significant association, nor did additional separate analyses for filter and for non-filter cigarette smoke exposures (data not shown).

In Table 5, odds ratio estimates from a final logistic regression model are presented, including only the core potential confounding variables and the significant specific diet and recreational physical activity variables. As observed in previous tables, family history and tomato-

**TABLE 2 (continued)**  
**Frequencies, adjusted odds ratio estimates (AOR\*), approximate 95% confidence intervals (CI) and global *p*-values for diet variables based on intake two years prior to questionnaire completion for cases and controls from a population sample of northeastern Ontario men aged 50-84 years, where quartiles are based on the distribution for controls**

| Variable                       | Controls | Cases | AOR | 95% CI  | <i>p</i> -value |
|--------------------------------|----------|-------|-----|---------|-----------------|
| <b>Cruciferous vegetables</b>  |          |       |     |         | <b>0.2692</b>   |
| < 1.0                          | 340      | 176   | 1.0 |         |                 |
| 1.0                            | 367      | 155   | 0.8 | 0.6-1.1 |                 |
| 1.1 - 3.0                      | 441      | 218   | 1.0 | 0.7-1.2 |                 |
| > 3.0                          | 425      | 191   | 0.8 | 0.6-1.1 |                 |
| Unknown                        | 40       | 12    |     |         |                 |
| <b>Green leafy vegetables</b>  |          |       |     |         | <b>0.7841</b>   |
| 0                              | 517      | 248   | 1.0 |         |                 |
| 0.1 - 0.5                      | 426      | 178   | 0.9 | 0.7-1.1 |                 |
| 0.6 - 1.0                      | 290      | 141   | 1.0 | 0.8-1.3 |                 |
| > 1.0                          | 343      | 168   | 1.0 | 0.8-1.3 |                 |
| Unknown                        | 37       | 17    |     |         |                 |
| <b>Fruit and fruit juice</b>   |          |       |     |         | <b>0.9560</b>   |
| 0 - 11                         | 397      | 185   | 1.0 |         |                 |
| 11.1 - 19.5                    | 396      | 173   | 1.0 | 0.7-1.2 |                 |
| 19.6 - 29.0                    | 366      | 171   | 1.0 | 0.7-1.2 |                 |
| > 29.0                         | 384      | 199   | 1.0 | 0.8-1.3 |                 |
| Unknown                        | 70       | 24    |     |         |                 |
| <b>Rice and noodles</b>        |          |       |     |         | <b>0.7698</b>   |
| 0 - 1.0                        | 533      | 230   | 1.0 |         |                 |
| 1.1 - 1.5                      | 268      | 135   | 1.1 | 0.9-1.5 |                 |
| 1.6 - 3.5                      | 390      | 188   | 1.1 | 0.9-1.4 |                 |
| > 3.5                          | 382      | 187   | 1.1 | 0.8-1.4 |                 |
| Unknown                        | 40       | 12    |     |         |                 |
| <b>Grain and cereals</b>       |          |       |     |         | <b>0.5983</b>   |
| 0 - 13.5                       | 399      | 163   | 1.0 |         |                 |
| 13.6 - 22.5                    | 379      | 185   | 1.1 | 0.8-1.4 |                 |
| 22.6 - 33                      | 386      | 198   | 1.1 | 0.9-1.5 |                 |
| > 33                           | 382      | 179   | 1.0 | 0.7-1.3 |                 |
| Unknown                        | 67       | 27    |     |         |                 |
| <b>Tofu</b>                    |          |       |     |         | <b>0.5475</b>   |
| Never                          | 1,472    | 685   | 1.0 |         |                 |
| Ever                           | 93       | 50    | 1.1 | 0.8-1.6 |                 |
| Unknown                        | 48       | 17    |     |         |                 |
| <b>Baked beans and lentils</b> |          |       |     |         | <b>0.7030</b>   |
| 0                              | 539      | 232   | 1.0 |         |                 |
| 0.1 - 0.5                      | 722      | 342   | 1.1 | 0.9-1.3 |                 |
| 0.6 - 1.0                      | 220      | 104   | 1.1 | 0.8-1.4 |                 |
| > 1.0                          | 96       | 61    | 1.3 | 0.9-1.8 |                 |
| Unknown                        | 36       | 13    |     |         |                 |

based products were associated with increased risk of prostate cancer, while strenuous recreational physical activity was associated with decreased risk.

## Discussion

Recent review articles present summaries of previous research regarding general risk factors for prostate cancer<sup>3,21,22</sup> and for specific exposures of diet,<sup>4-11,23-26</sup> physical activity<sup>13,14</sup> and smoking.<sup>15</sup> Total dietary fat has not been consistently found to be a risk factor for prostate cancer.<sup>4,5</sup> It is suggested that earlier studies identified dietary fat as a significant risk factor since total energy was not typically controlled for in these analyses.<sup>5</sup> In the current study, there was no significant association observed between dietary fat and prostate cancer, after controlling for total energy.

The only significant dietary exposures identified in this study involve consumption of tomato products, specifically tomato or vegetable juices and ketchup, and these positive associations contrast with some studies that have identified a negative association between tomato intake and prostate cancer risk.<sup>9,23,24,26</sup> The tomato associations in this study were examined for the possibility of confounding by—or interactions with—other variables (e.g., pasta), with no change in conclusion. It is important to note that in our study questionnaire, the three questions requesting information about consumption of tomato products involved servings of juices, ketchup and tomatoes. The question about tomatoes did not distinguish between processed and unprocessed tomatoes.

It has been hypothesized that lycopene is the compound in processed tomato products, such as tomato paste and tomato sauce, that may be negatively associated with prostate cancer risk. However, it has been reported that lycopene intake and lycopene blood levels do not strongly correlate.<sup>23</sup> In addition, while several studies have identified significant and non-significant negative associations for tomato products, some recent ones have

**TABLE 2 (continued)**  
**Frequencies, adjusted odds ratio estimates (AOR\*), approximate 95% confidence intervals (CI) and global *p*-values for diet variables based on intake two years prior to questionnaire completion for cases and controls from a population sample of northeastern Ontario men aged 50-84 years, where quartiles are based on the distribution for controls**

| Variable                            | Controls | Cases | AOR | 95% CI  | <i>p</i> -value |
|-------------------------------------|----------|-------|-----|---------|-----------------|
| <b>Fish</b>                         |          |       |     |         |                 |
| 0                                   | 199      | 85    | 1.0 |         | 0.7185          |
| 0.1 - 0.5                           | 497      | 222   | 1.0 | 0.7-1.4 |                 |
| 0.6 - 1.0                           | 516      | 243   | 1.0 | 0.8-1.4 |                 |
| > 1                                 | 356      | 187   | 1.2 | 0.8-1.6 |                 |
| Unknown                             | 45       | 15    |     |         |                 |
| <b>Meat</b>                         |          |       |     |         |                 |
| 0 - 3.0                             | 390      | 184   | 1.0 |         | 0.2374          |
| 3.1 - 5.0                           | 400      | 194   | 1.0 | 0.7-1.3 |                 |
| 5.1 - 7.5                           | 380      | 151   | 0.8 | 0.6-1.0 |                 |
| > 7.5                               | 398      | 204   | 1.0 | 0.7-1.3 |                 |
| Unknown                             | 45       | 19    |     |         |                 |
| <b>Processed meat</b>               |          |       |     |         |                 |
| 0 - 0.5                             | 426      | 207   | 1.0 |         | 0.1198          |
| 0.6 - 1.5                           | 422      | 169   | 0.8 | 0.6-1.0 |                 |
| 1.6 - 3.5                           | 331      | 143   | 0.9 | 0.7-1.1 |                 |
| > 3.5                               | 393      | 218   | 1.1 | 0.8-1.4 |                 |
| Unknown                             | 41       | 15    |     |         |                 |
| <b>Tea</b>                          |          |       |     |         |                 |
| 0                                   | 438      | 198   | 1.0 |         | 0.2677          |
| 0.1 - 7.5                           | 580      | 307   | 1.2 | 0.9-1.5 |                 |
| 7.6 - 18.75                         | 434      | 180   | 0.9 | 0.7-1.2 |                 |
| > 18.75                             | 131      | 59    | 1.0 | 0.7-1.5 |                 |
| Unknown                             | 30       | 8     |     |         |                 |
| <b>Coffee</b>                       |          |       |     |         |                 |
| 0                                   | 105      | 51    | 1.0 |         | 0.9276          |
| 0.1 - 7.5                           | 449      | 218   | 1.0 | 0.7-1.4 |                 |
| 7.6 - 18.75                         | 730      | 336   | 0.9 | 0.6-1.3 |                 |
| > 18.75                             | 316      | 142   | 0.9 | 0.6-1.4 |                 |
| Unknown                             | 13       | 5     |     |         |                 |
| <b>Alcohol (beer, wine, liquor)</b> |          |       |     |         |                 |
| 0                                   | 415      | 198   | 1.0 |         | 0.8821          |
| 0.1 - 3.5                           | 398      | 197   | 1.0 | 0.8-1.3 |                 |
| 3.6 - 11.0                          | 367      | 163   | 0.9 | 0.7-1.2 |                 |
| > 11.0                              | 387      | 177   | 1.0 | 0.7-1.2 |                 |
| Unknown                             | 46       | 17    |     |         |                 |

\* Unless otherwise specified, adjusted for total energy, age, family history of prostate cancer, BMI 5 years ago, education, type of occupation

\*\* Adjusted for age, family history of prostate cancer, BMI 5 years ago, education, type of occupation

not identified this effect for either tomato products or lycopene exposure.<sup>27,28</sup> Our result is indicative of the need to further examine the nature and extent of any potential association between tomato product intake, with a focus on processed versus unprocessed tomatoes, and prostate cancer risk. Thus, the exact role of tomatoes could be elucidated by asking subjects of future studies about specific types of tomato products consumed.

An inverse association has been hypothesized between prostate cancer risk and consumption of plant-based foods.<sup>29</sup> The suggested mechanism is based on the protective effect of antioxidants against exposure to carcinogens. A possible weak inverse association between prostate cancer and vegetables has been found in the literature,<sup>9</sup> but our data indicate no association for all vegetables combined or separately for yellow, cruciferous and green leafy vegetables. Grains and cereals, baked beans and lentils, and tofu also were not associated with prostate cancer risk, nor was intake of rice and noodles. It is also suggested that fruit consumption is not likely related to risk of prostate cancer<sup>9</sup> and the results of this study support this.

Meat intake has been positively associated with prostate cancer risk in several studies,<sup>4</sup> with two studies of processed meat reporting no association.<sup>30,31</sup> It is suggested that these significant associations may be due to fat consumption associated with meat consumption or due to chemicals associated with meat preparation. In this study, there was no association observed between meat and prostate cancer risk and between processed meat and prostate cancer risk. As indicated previously, fat consumption was not identified either as a significant risk factor. A possible inverse association is suggested for fish intake due to the possible reduction of testosterone levels resulting from polyunsaturated n-3 fatty acids found in fish. However, reported study results<sup>6</sup> are inconsistent. In this study, no such association was observed.

**TABLE 3**  
**Frequencies, adjusted odds ratio estimates (AOR\*), approximate 95% confidence intervals (CI) and global p-values for strenuous physical activity variables for cases and controls from a population sample of northeastern Ontario men aged 50-84 years**

| Variable                        | Controls | Cases | AOR | 95% CI  | p-value |
|---------------------------------|----------|-------|-----|---------|---------|
| Strenuous activity in mid-teens |          |       |     |         | 0.9455  |
| No                              | 461      | 217   | 1.0 |         |         |
| Yes                             | 1,111    | 523   | 1.0 | 0.8-1.2 |         |
| Unknown                         | 41       | 12    |     |         |         |
| Strenuous activity in early 30s |          |       |     |         | 0.1022  |
| No                              | 695      | 348   | 1.0 |         |         |
| Yes                             | 875      | 393   | 0.9 | 0.7-1.0 |         |
| Unknown                         | 43       | 11    |     |         |         |
| Strenuous activity in early 50s |          |       |     |         | 0.0045  |
| No                              | 862      | 447   | 1.0 |         |         |
| Yes                             | 709      | 294   | 0.8 | 0.6-0.9 |         |
| Unknown                         | 42       | 11    |     |         |         |

\* Adjusted for age, family history of prostate cancer, BMI 5 years ago, education, type of occupation.

**TABLE 4**  
**Frequencies, adjusted odds ratio estimates (AOR\*), approximate 95% confidence intervals (CI) and global p-values for smoking variables for cases and controls from a population sample of northeastern Ontario men aged 50-84 years**

| Variable                  | Controls | Cases | AOR | 95% CI  | p-value |
|---------------------------|----------|-------|-----|---------|---------|
| Cigarette smoking         |          |       |     |         | 0.3192  |
| Never                     | 373      | 158   | 1.0 |         |         |
| Former smoker             | 952      | 454   | 1.1 | 0.9-1.4 |         |
| Current smoker            | 270      | 133   | 1.2 | 0.9-1.7 |         |
| Unknown                   | 18       | 7     |     |         |         |
| Pack-years for cigarettes |          |       |     |         | 0.5265  |
| 0                         | 373      | 158   | 1.0 |         |         |
| > 0 and ≤ 20              | 385      | 189   | 1.2 | 0.9-1.5 |         |
| > 20 and ≤ 43             | 391      | 191   | 1.2 | 0.9-1.5 |         |
| > 43                      | 387      | 174   | 1.1 | 0.8-1.4 |         |
| Unknown                   | 77       | 40    |     |         |         |

\* Adjusted for age, family history of prostate cancer, BMI 5 years ago, education, type of occupation.

While a possible negative association between tea and prostate cancer risk has been identified previously,<sup>10</sup> no such result was observed here. A potential weak positive association between high levels of alcohol consumption and prostate cancer is noted in a review of the literature,<sup>11</sup> but no association was observed in the current study.

With respect to physical activity, this study identified significantly reduced risk

associated with strenuous recreational physical activity later in life (i.e., early 50s) and an effect of borderline significance for strenuous physical activity for those in their early 30s. Moderate physical activity was not associated with prostate cancer risk in this study (data not shown) and there is therefore no dose-response relationship identified between level of physical activity and risk of prostate cancer. A general negative association between physical activity and prostate cancer risk has been

identified in previous studies,<sup>13,14</sup> where one review of the literature identified a median relative risk of 0.8.<sup>13</sup> This median coincides with the odds ratio estimate observed here. The specific identification of strenuous physical activity as negatively associated with prostate cancer risk also was found in a prospective study of middle-aged men as well as in a recent case-control study.<sup>32,33</sup> It is suggested that prostate cancer is a hormone-related disease<sup>14</sup> and, as such, changes in hormone levels, specifically reduction of testosterone levels as a result of strenuous physical activity, may lead to reduced risk of prostate cancer.

The identification of an inverse association between recent physical activity and renal cell carcinoma has been found where past physical activity was not associated.<sup>34</sup> It is suggested that more accurate recall of recent activity could explain why only recent physical activity is a significant risk factor. This also may be the case for this study of prostate cancer where earlier strenuous physical activity may be important but is not identified as significant, possibly because of recall issues.

While cigarette smoking is an established risk factor for many cancers, cigarette smoking in this study was not associated with prostate cancer risk. Similarly, a review of previous studies of incident prostate cancer generally found no association.<sup>15</sup> A suggestion that the effect of smoking (pack-years) on prostate cancer may exist for obese men<sup>35</sup> was investigated in this study by exploring an interaction between an indicator of obesity (highest quartile of BMI versus remaining levels of BMI) and quartiles of pack-years of smoking with a null finding ( $p$ -value = 0.12; data not shown).

There are several statistical comparisons made in this study and the confidence intervals and  $p$ -values presented are therefore anti-conservative. Any significant results must be taken as hypothesis confirming or hypothesis generating. The specific results for consumption of tomato-based foods may be spurious due to the issue of multiple testing and this may explain the direction of the observed association. As for strenuous physical activity, the fact that such an association



**TABLE 5**  
**Adjusted odds ratio estimates (AOR\*), approximate 95% confidence intervals (CI) and global *p*-values for diet and recreational physical activity variables in final model along with core potential confounders for cases and controls from a population sample of northeastern Ontario men aged 50-84 years**

| Variable   | AOR | 95% CI  | <i>p</i> -value |
|--|-----|---------|-----------------|
| Family history of prostate cancer                |     |         | < 0.0001        |
| No   | 1.0 |         |                 |
| Yes  | 2.9 | 2.2-4.0 |                 |
| Body mass index (kg/m <sup>2</sup> ) 5 years ago |     |         | 0.2397          |
| ≤ 24   | 1.0 |         |                 |
| 24-27  | 0.9 | 0.7-1.2 |                 |
| 27-29  | 1.2 | 0.9-1.6 |                 |
| > 29   | 1.0 | 0.8-1.3 |                 |
| Unknown  |     |         |                 |
| Education  |     |         | 0.0673          |
| Elementary                                       | 1.0 |         |                 |
| Secondary  | 1.0 | 0.8-1.2 |                 |
| Post-secondary                                   | 0.7 | 0.6-1.0 |                 |
| Unknown  |     |         |                 |
| Type of occupation                               |     |         | 0.0299          |
| White collar                                     | 1.0 |         |                 |
| Blue collar                                      | 1.2 | 1.0-1.5 |                 |
| Tomato or vegetable juices                       |     |         | 0.0043          |
| 0  | 1.0 |         |                 |
| 0.1 - 0.5  | 1.0 | 0.8-1.3 |                 |
| 0.6 - 1.0  | 1.1 | 0.9-1.5 |                 |
| > 1.0  | 1.5 | 1.2-2.0 |                 |
| Ketchup  |     |         | 0.0071          |
| 0  | 1.0 |         |                 |
| 0.1 - 0.5  | 0.9 | 0.7-1.1 |                 |
| 0.6 - 2.9  | 0.8 | 0.6-1.0 |                 |
| ≥ 3.0  | 1.2 | 1.0-1.5 |                 |
| Strenuous activity in early 50s                  |     |         | 0.0047          |
| No   | 1.0 |         |                 |
| Yes  | 0.8 | 0.6-0.9 |                 |

\* Adjusted for age and other variables in table

has been observed in other studies adds credence to this result.

It is recognized that the current study may suffer from potential recall bias, as is true for all case-control studies that involve self-reported exposures. It is not likely that there is any systematic difference between cases and controls with respect to recall since the study was described as a men's

health study and telephone interviews and data coding were performed blind to the disease status of the subject. The low response rate among controls, again a common issue with case-control studies, may contribute to study bias, depending on the representativeness of participating controls. A brief refusal questionnaire of smoking status was conducted as part of this study and it was found that,

while participating cases were similar to non-participating cases with respect to proportion of current smokers, significantly fewer participating controls were current smokers compared to non-participating controls. Thus, any potential bias in our results for the smoking analysis will be bias away from the null.

Information on stage and grade of prostate tumours of cases was not known and information on PSA testing was also not available. If screen-detected prostate cancers were common in our data, this could bias our effect estimates toward the null. However, it must be noted that, in the population from which cases and controls were sampled (northeastern Ontario and Ontario in general), PSA testing in asymptomatic men is not insured, which reduces this potential source of bias.

The results presented here were derived from a large population-based study that had adequate power to investigate the exposures considered. These findings suggest that, while smoking is not associated with prostate cancer risk, there is evidence to suggest a negative association between prostate cancer risk and strenuous physical activity. Further research is necessary to investigate the role of tomato product intake.

## Acknowledgements

This investigation was supported by research grants from the National Health Research and Development Program (Project No. 6606-5574-502), The Northern Cancer Research Foundation, The Natural Sciences and Engineering Research Council and The Canadian Union of the Mine, Mill & Smelter Workers, Local 598. The Ontario Cancer Registry confidentially supplied pathology reports to identify cases in this study. Analysis assistance of Ms. Tara Gomes is greatly appreciated. Also, Mr. Zahid Naseer is thanked for assistance with data quality evaluation and data analysis. The authors are grateful for the cooperation of urologists in northeastern Ontario.

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