Nutrition and Cancer
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/hnuc20

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Published online: 18 Nov 2009.

To cite this article: Li-Qiang Qin , Jia-Ying Xu , Pei-Yu Wang , Takashi Kaneko , Kazuhiko Hoshi & Akio Sato (2004): Milk Consumption Is a Risk Factor for Prostate Cancer: Meta-Analysis of Case-Control Studies, Nutrition and Cancer, 48:1, 22-27

To link to this article: http://dx.doi.org/10.1207/s15327914nc4801_4

NUTRITION AND CANCER, *48*(1), 22–27

Milk Consumption Is a Risk Factor for Prostate Cancer: Meta-Analysis of Case-Control Studies

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Abstract: *Prostate cancer has become the most common cancer among men in the United States. Although milk consumption is considered to be a risk factor in some epidemiological studies, the results are inconsistent. A meta-analysis method was conducted to estimate the combined odds ratio (OR) between milk consumption and prostate cancer from case-control studies published between 1984 and 2003 using commercial software (comprehensive meta-analysis). The combined OR was 1.68 (95% confidence interval = 1.34–2.12) in the 11 published case-control studies. The combined OR varied little by study stratification. Additionally, we evaluated the possible risk factors in milk for prostate cancer. In conclusion, we found a positive association between milk consumption and prostate cancer. The underlying mechanisms, including fat, calcium, hormones, and other factors, should be investigated further.*

Introduction

Prostate cancer is the third most common cancer worldwide and the most common cancer in Europe, North America, and some parts of Africa. In 2000, the number of new prostate cancer cases was estimated at 513,000 worldwide, and this disease accounts for 9.7% of all male cancers (1). The incidence of prostate cancer is increasing steadily in almost all countries (2), but we know little about what causes this disease.

Results from ecological studies suggest that prostate cancer is associated with a Western lifestyle and, in particular, a diet that includes a high intake of fat, meat, and dairy products. Calculating the relationship between the incidence rate of prostate cancer and dietary practice in 42 countries, milk was the most closely correlated ($r = 0.771$) with incidence (3). In Japan, the mortality rate for prostate cancer, which is still lower than that in Western countries, has shown a rising trend with the westernization of the Japanese diet since World War II. During the same interval, milk consumption increased the most of all observed food items. Its correlation coefficient after age adjustment reached 0.937 (4).

Case-control and cohort studies, two classifications of analytical epidemiological studies, are more credible than ecological studies that evaluate consumption through food disappearances in populations of different countries or different periods. Until now, more than 10 publications of case-control and cohort studies reported the relationship between milk consumption and prostate cancer risk. Some authors descriptively summarized these studies and suggested that milk consumption is a risk factor for prostate cancer (5). Because individual studies have yielded inconsistent results, a statistical method combining these studies is better to draw a conclusion. The purpose of the present study was to collect all relevant published case-control studies and address them by meta-analysis.

Methods

Case-control studies were identified through a Medline search for the period between January 1984 and January 2003. The searches were limited to studies published in English. Titles, abstracts, and subject headings in the database were investigated using the keywords prostate cancer and milk or dairy. Over the period of 20 years, 40 articles were found using the keywords prostate cancer and milk, and 25 articles were found using prostate cancer and dairy. In order not to omit relevant articles, the titles, abstracts, and subject headings identified by the keywords prostate cancer and fat or diet were scanned. The cited references in obtained studies were also reviewed to include all relevant articles.

In all of the case-control studies we found, if the study sample was found to overlap or come from the same study project, only the paper with the largest sample size was retained. When prostate cancer risk was reported separately by different types of milk, whole milk was chosen because it contains all milk substances and thus reflects the true nature of milk. If both hospital and population controls were used for comparison separately, the result of the population control was chosen for the analysis. The cases in the studies were

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confirmed by histological examination. Two researchers performed data collection and extraction independently. Differences in data extraction were resolved by discussion.

Meta-analysis is a statistical analysis that combines or integrates the results of several studies to provide increased power for the quantitative identification of trends (6). In the present study, the meta-analysis was performed using commercial software (comprehensive meta-analysis), which was obtained from Biostate, Inc. (Englewood, NJ) (7). This software requires the input of the number of cases and controls into a two-by-two table to calculate the combined odds ratio (OR) and 95% confidence interval (CI). We calculated two combined ORs from the data in the published studies. One compared the highest with the lowest quantile of milk consumption, which took advantage of the range of consumption in a study. The other compared the quantiles together (except for the lowest one) with the lowest one because all numbers of cases and controls can be included in this analysis. Additional subgroup analyses were carried out to examine the effects of the type of control, the kind of milk, and the rate of incidence in observed countries. Because most studies gave the OR adjusted by age and other variables, we also examined the combined OR of these studies using adjusted OR instead of that from the two-by-two table (8).

Because of the diversity in design and analysis of the various studies, we assumed that the true effects being estimated would vary among the studies. Thus, the combined OR, which was estimated using the Mantel-Haenszel method, was described with a fixed-effects model (all study populations were similar) and a random-effects model (the study population differed). Homogeneity among the studies was assessed to test consistency and was tested using χ^2 analysis with a significance of 0.05.

We found 15 studies reporting a relationship between milk consumption and prostate cancer risk in case-control studies (9–23) that were carried out in 8 countries. The outcome of all published studies was regarding the incidence of prostate cancer. The disease was prostate cancer and did not refer to any stage or classification of cancer. In two Japanese studies, the population area partially overlapped. Furthermore, egg consumption was included in the milk category in the study of Ohno et al. (11). Because egg consumption as a risk factor for prostate cancer was discussed separately in some studies (11,13 5,18,21), the study of Ohno et al. was excluded from the meta-analysis. Three Italian studies were conducted in northern Italy (10,13,14). Talamini et al. (14) claimed that the La Vecchia study was the preliminary study and the Talamini study had higher numbers of cases and controls. Therefore, the La Vecchia study was not included in the meta-analysis. Although the study of Talamini et al. (10) had some area overlap with the other two Italian studies, it was included because the cases were diagnosed during a completely different period. Two Uruguayan studies were conducted in Montevideo during completely different periods (15,21). Deneo-Pellegrini et al. also said that this study was a new case-control study and different from the study of De Stefani et al. Two Greek studies apparently came from the same study project with the same numbers of cases and controls using different analysis methods (20,22). Bosetti et al. also mentioned that a detailed description of this study has been published in the study of Tzonou et al. Therefore, the study of Tzonou et al. published earlier was excluded from the meta-analysis. We did not find any relationship among three American studies (12,19,23). Unfortunately, the study of Hayes et al. failed to give the numbers of cases and controls in each group and so did not meet the analysis criteria for this software. Finally, 11 studies were included in the present meta-analysis (9,10,12,14–18,21–23).

Results

Table 1 displays the characteristics of case-control studies, which studied the risk of prostate cancer and milk consumption. OR and CI were compared between the highest and lowest quantile of consumption and reflect the greatest degree of control for confounders. In these 11 studies, included in the final meta-analysis, 6 found a positive relationship between milk consumption and prostate cancer risk when comparing the highest with the lowest quantiles (10,12,14,15,17,18); however, none reported an inverse relationship. Because the 11 studies were found to be heterogeneous in their effect [$\chi^2(10) = 26.6$, $P < 0.05$], the random-effects model was used to estimate the combined OR. The values of combined OR were calculated by the random-effects model in our study, until indicated. Figure 1 shows the OR of each study; the combined OR was 1.68 with a CI of 1.34–2.12. When we compared the other quantiles with the lowest one, the combined OR was 1.44 (CI = 1.12–1.83).

The average age of cases in these published studies was between 66 and 72 years. Three studies matched for age of cases and controls within 1 or 5 years (9,16,17) and seven studies certified that there was no significant difference among age groups between cases and controls (10,12,14,15,18,21,22). However, the cases were slightly older than controls in most of studies. The study of Mishina et al. did not use OR as an index, although age was matched (9). The combined OR of the other10 studies, whose adjusted OR was provided and could be used directly, was 1.56, with a CI of 1.30–1.83 (10,12,14–18,21–23).

There were two studies with fewer than 100 cases (9,23). The combined OR increased slightly to 1.72 (CI = 1.32–2.22) when these two studies were excluded (Table 2). Because the type of control (hospital or population) was a potential source of heterogeneity, the combined OR for milk consumption and prostate cancer risk was 1.81 (CI = 1.31–2.51) for the eight studies selected controls from hospitals (10,12,14–16,21–23). The combined OR of three studies with population controls was 1.46 (CI = 1.18–1.80) (9,17,18). Of these three studies, only two studies met the epidemiological population-based controls. In fact, it was difficult to classify these milk studies because of the ambiguous or different definitions of food items in each questionnaire. In general, the items of milk and dairy products, which were

Table 1. Characteristics of Case-Control Studies Related to Milk Consumption and Prostate Cancer Risk from Published Studies

Reference	Country (area)	Number of Cases/Controls	Type of Control	Quantile	*Items*	OR (95% CI)[a]	*Match or Adjustment*
Mishina et al. (9)[b]	Japan	99/99	Population	2	Milk	1.18 (0.67–2.07)[c]	Age, residence
Talamini e al. (10)[b]	Italy	166/202	Hospital	2	Milk and dairy products	2.46 (1.29–4.69)	Age, marital status, occupation, BMI
Ohno et al. (11)	Japan	100/100	Hospital	2	Eggs and milks	0.80 (0.45–1.40)	Age, date of admission
Mettlin et al. (12)[b]	New York	371/371	Hospital	4	Whole milk, 2% milk, skim milk	2.49 (1.27–4.87)	Age, residence
La Vecchia et al. (13)	Italy	96/292	Hospital	3	Milk, cheese, butter	5.0 (1.5–16.6)	Age, residence, education, BMI
Talamini et al.(14)[b]	Italy	271/685	Hospital	3	Milk, cheese, butter	1.58 (1.06–2.36)	Age, residence, education, BMI
De Stefani et al. (15)[b]	Uruguay	156/302	Hospital	3	Milk	1.7 (1.1–2.9)	Age, residence, education, tobacco, beer
Ewings and Bowie (16)[b]	United Kingdom	159/325	Hospital	4	Milk	0.95 (0.50–1.83)	Age
Chan et al. (17)[b]	Sweden	526/536	Population	4	Dairy	1.49 (1.01–2.19)	Age, family history, energy
Jain ets al. (18)[b]	Canada	617/636	Population	4	Milk, yogurt, cheese	1.47 (1.11–1.94)	Age, energy, vasectomy, marital status, education, BMI
Hayes et al. (19)	United States	932 /1201	Population	4	Dairy	1.2 (0.9–1.5)	Age, study site, race
Tzonou et al. (20)	Greece	320/246	Hospital	5	Milk and dairy products	1.55 (0.92–2.62)	Age, height, Quetelet index, education, energy
Deneo-Pellegrini et al. (21)[b]	Uruguay	175/233	Hospital	4	Dairy food	0.8 (0.4–1.6)	Age, residence, education, family history, BMI
Bosetti et al. (22)[b]	Greece	320/246	Hospital	3	Milk and dairy products, butter	1.34 (0.85–2.09)	Age, height, education, energy
Berndt et al. (23)[b]	United States	69/385	Hospital	3	Milk	1.26 (0.57–2.79)	Age, energy

a: OR and CI compared the highest with the lowest quantile of consumption and reflected the greatest degree of control for confounders. They were the results from the first food item in the **Items** column.
b: Studies included in the calculation of meta-analysis.
c: OR and 95% CI were calculated from the numbers of cases and controls using a standard method.

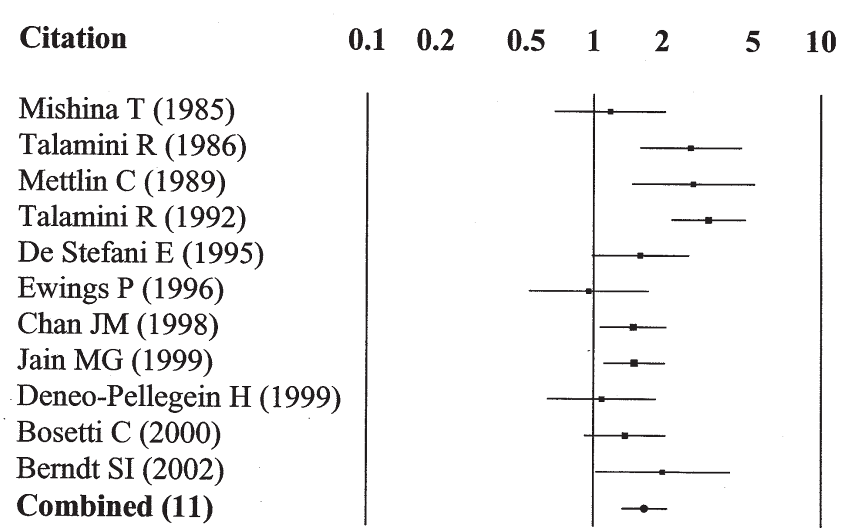

Figure 1. Meta-analysis schematic concerning the OR of prostate cancer associated with milk consumption in 11 case-control studies calculated using Biostat™ software (7). Horizontal bars represent the 95% CI. The combined OR in the random-effects model was 1.68 (CI = 1.34–2.12).

Table 2. Combined OR of Milk Consumption and Prostate Cancer Risk in Different Types of Studies[a]

Types of Studies Combined	*N*	OR[b]	CI
All studies	11	1.68	1.34–2.12
Studies with cases of >100	9	1.72	1.32–2.22
Control type			
Population	3	1.46	1.18–1.80
Hospital	8	1.81	1.31–2.57
Milk type			
Milk	6	1.50	1.25–1.80
Milk and dairy products	5	1.61	1.22–2.12
Rate of incidence in country			
<30/100,000	4	1.96	1.20–3.20
≥30/100,000	7	1.51	1.23–1.86

a: Calculated by a comparison of the highest and lowest categories using Biostat™ software (7).
b: Value was calculated using a random-effects model.

used in the present study, included cheese, butter, and ice cream as well as liquid milk, although small differences existed among studies. According to this classification, the combined ORs were 1.50 (CI = 1.25–1.80) for milk (9,14–16,18,23) and 1.61 (CI = 1.22–2.12) for milk and dairy products (10,17,21–23). The incidence rate of prostate cancer shows a wide international variation, with the lowest rate in China (Qidong County) and the highest in the United States (Detroit, MI; blacks) (24). Dividing the incidence by an arbitrary criterion at the point of 30 per 100,000, we found that 4 studies were carried out in countries with a low rate of incidence (9,10,14,22) and 7 studies in countries with a high rate of incidence (12,15–18,21,23). The combined ORs were 1.96 (CI = 1.20–3.20) and 1.51 (CI = 1.23–1.86), respectively. We found that there was homogeneity in the studies carried out in countries with a high rate of incidence [$\chi^2(6) = 7.95$, $P > 0.05$], where the combined OR of the fixed-effects model was 1.51 (CI = 1.28–1.79), which was similar to the combined OR calculated using the random-effects model. In conclusion, the combined OR changed very little after some studies were excluded according to certain criteria or studies were stratified by some aspects.

Discussion

Our study had several limitations that affected interpretation of the results. In the present study, we only chose case-control studies as the data resource for analysis. As an analytical epidemiological study, a cohort study is more effective than a case-control study. Therefore, we also searched for cohort studies and observed the relationship between milk consumption and prostate cancer risk, finding 11 published studies during the same period of 20 years (25–35). However, several studies originated from the same study project, so ultimately there were only six independent studies. All of those studies were carried out in America (25–31,34,35) and northern Europe (32,33), where milk and dairy products are heavily consumed. This suggested that a group free from milk and dairy products is difficult to find because milk and dairy products are used in a variety of foods, including cakes, candies, ice cream, and chocolates (36). Furthermore, basic data such as the number of cases or populations in exposed and nonexposed groups were not provided by about half of the studies (28,30,31,33–35). It is important to estimate the weight of each study in this meta-analysis. In those cohort studies, the end points were selected as the rate of death (25,28), certain stage of cancer (31,33), or a combination (29,34). Another conflict was that the rates were calculated by person in two studies (27,30) and by person-year in the other studies. For the reasons described previously, it is almost impossible to combine cohort studies for meta-analysis using this commercial software. Some authors also advised against combining results from case-control and cohort studies using the meta-analysis method due to the different designs (37).

When collecting published studies, the most obvious problem is that some studies never get published. Studies with significant results were more likely to have been published than those with nonsignificant results. In the present study, we considered the existence of hypothetical unpublished data. We randomly added 5 null results appearing in the analysis to 11 case-control studies (38). Even if 50 of these null results were added, the combined OR was 1.36 (CI = 1.27–1.45). This suggests that unpublished studies like these published studies with null results do not seem to influence this positive relationship over a large range.

As a statistical method, meta-analysis cannot resolve the confounding and selection bias arising from the design of a case-control study. When the published studies were classified by control type, type of milk, or incidence rate, the combined OR in all classifications was >1.45 and the lower limit was > 1.15. Because population-based control has a great advantage over hospital-based control, the mere two studies that used the population-based controls became the weakness of our study. Although two studies were too few for combination, the results from both studies supported the hypothesis that milk is a risk factor for prostate cancer. In addition to comparing the highest quantitle, whose consumption varied greatly across different studies, with the lowest one, we compared the upper quantitles as a group with the lowest one, where consumption was not used in the most studies. The combined OR (OR = 1.44, CI = 1.12–1.83) still suggested a positive relationship between milk consumption and prostate cancer.

Additional methodological problems came from the software itself because of neglect for adjustments. We examined the results with adjusted OR, which reflected the greatest degree of control for confounders. The combined OR was 1.56 (CI = 1.30–1.83), slightly lower than the combined OR calculated by the software. Therefore, the results from the software of comprehensive meta-analysis are reliable to explain the relationship between milk consumption and prostate cancer. As an independent study, the study of Hayes et al. was excluded from the analysis due to a lack of numbers of cases and controls (19). Because the OR of this study was 1.2, the combined OR would not have been modified much even if it had been included. In conclusion, this meta-analysis suggests that there is positive relationship between milk consumption and prostate cancer risk.

Researchers did not pay attention to milk as a risk factor for prostate cancer until the 1980s. Fat was studied a little earlier, although it is not the only factor in milk linked to prostate cancer according to current thinking. A review, summarizing the studies before 1985, suggested that prostate cancer was positively related in some way to fat intake (39). Because milk is an important source of fat in the Western diet (40), these earlier studies hinted at the possibility that milk intake is positively related to prostate cancer risk.

The biological interpretation of the adverse effect of milk remains controversial because milk is an important source of several nutrients, such as animal fat, calcium, some vitamins, and total energy. For a long time, special attention has been given to the fat and calcium in milk. As for the fat in milk and dairy products, we found only one study where whole milk, skim milk was observed (12) and three studies where cheese and butter were analyzed twice, respectively (14,18,22). It is impossible to do a meta-analysis using these as subgroups. In six studies with a positive association between milk consumption and prostate cancer, three studies attributed it to fat intake (10,14,15) and two studies did not (12,17). In two studies on milk as a risk factor, cheese and butter, whose fat content is high, did not show any relationship with prostate cancer risk (14,18). In a prospective study, red meat showed a significant positive association with prostate cancer. However, fat from milk and dairy products was unrelated to risk (29). This inconsistent evidence might be due to other unknown dietary compound(s) contained in milk and dairy products at different levels. Chan et al. considered the calcium in milk (17). The authors proposed that high calcium intake suppressed the conversion of 25(OH) vitamin D to $1,25(OH)_2$ vitamin D, which has an antitumor effect against prostate cancer (17,31,33,34). Nevertheless, milk, which was a risk factor in two other studies, did not influence carcinogenesis via a high calcium concentration (32,41). Overall, fat and calcium in milk are likely to be risk factors. However, they cannot completely explain why milk consumption increases prostate cancer risk.

Recently, we hypothesized that estrogen in commercial milk may be responsible for prostate cancer (36). Because commercial milk is mainly produced by pregnant cows in developed countries, it contains considerable amounts of estrogen (36,42). Some studies in humans also demonstrated that milk consumption increased the estrogen level in the circulation (43,44). Because 17β-estradiol, an estrogen, is a carcinogen for prostate cancer, estrogen in milk should not be ignored when considering milk as a risk factor for prostate cancer (45). Moreover, cow's milk contains high levels of insulin-like growth factor-I (IGF- I) (46). IGF-I has attracted increasing attention as a risk factor for prostate cancer (47). In our previous study, commercial low-fat milk promoted the development of DMBA-induced mammary tumors, another hormone-dependent cancer, in rats. The high levels of estrogen and IGF-I in milk were considered to be responsible for this promotional effect (in preparation).

In conclusion, we found a positive association between milk consumption and prostate cancer risk using meta-analysis to analyze published case-control studies. The underlying mechanism, including fat, calcium, hormones, and other factors, requires further study.

Acknowledgments and Notes

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Submitted 9 September 2003; accepted in final form 15 December 2003.

References

1. Gröerg H: Prostate cancer epidemiology. *Lancet* **361,** 859–864, 2003.
2. Parkin DM, Bray FI, and Devesa SS: Cancer burden in the year 2000: the global picture. *Eur J Cancer* **37,** S4–S66, 2001.
3. Ganmaa D, Li XM, Wang J, Qin LQ, Wang PYm and Sato A: Incidence and mortality of testicular and prostate cancer in relation to world dietary practices. *Int J Cancer* **98,** 262–267, 2002.
4. Tominaga S and Kuroishi T: An ecological study on diet/nutrition and cancer in Japan. *Int J Cancer* **10(suppl),** 2–6, 1997.
5. Giovannucci E: Dietary influences of 1,25 $(OH)_2$ vitamin D in relation to prostate cancer: a hypothesis. *Cancer Causes Control* **9,** 567–582, 1998.
6. Egger M and Davey Smith G: Meta-analysis: potential and promise. *Br Med J* **315,** 1371–1374, 1997.
7. Borenstein M and Rorhstein H: Comprehensive meta-analysis: a computer program for research synthesis. Biostat™. Englewood, NJ.
8. Dersimonian R and Laird N: Meta-analysis in clinical trial. *Control Clin Trials* **7,** 177–188, 1986.
9. Mishina T, Watanabe H, Araki H, and Nakao M: Epidemiological study of prostatic cancer by matched-pair analysis. *Prostate* **6,** 423–436, 1985.
10. Talamini R, La Vecchia C, Decarli A, Negri E, and Franceschi S: Nutrition, social factors and prostatic cancer in a northern Italian population. *Br J Cancer* **53,** 817–821, 1986.
11. Ohno Y, Yoshida O, Oishi K, Okada K, Yamabe H, and Schroeder FH: Dietary β-carotene and cancer of the prostate: a case-control study in Kyoto, Japan. *Cancer Res* **48,** 1331–1336, 1988.
12. Mettlin C, Selenskas S, Natarajan N, and Huben R: Beta-carotene and animal fats and their relationship to prostate cancer risk—a case-control study. *Cancer* **64,** 605–612, 1989.
13. La Vecchia C, Negri E, D vanzo B, Franceschi S, and Boyle P: Dairy products and the risk of prostatic cancer. Oncology 48, 406–410, 1991.
14. Talamini R, Franceschi S, La Vecchia C, Serraino D, Barra S, and Negri E: Diet and prostatic cancer: a case-control study in northern Italy. *Nutr Cancer* **18,** 277–286, 1992.
15. De Stefani E, Fierro L, Barrios E, and Ronco A: Tobacco, alcohol, diet and risk of prostate cancer. *Tumori* **81,** 315–320, 1995.
16. Ewings P and Bowie C: A case-control study of cancer of the prostate in Somerset and east Devon. *Br J Cancer* **74,** 661–666, 1996.
17. Chan JM, Giovannucci E, Andersson S-O, Yuen J, Adami H-O, and Wolk A: Dairy products, calcium, phosphorus, vitamin D, and risk of prostate cancer (Sweden). *Cancer Causes Control* **9,** 559–566, 1998.

18. Jain MG, Hislop GT, Howe GR, and Ghadirian P: Plant foods, antioxidants, and prostate cancer risk: findings from case-control studies in Canada. *Nutr Cancer* **34,** 173–184, 1999.
19. Hayes RB, Ziegler RG, Gridley G, Swanson C, Greenberg RS, et al.: Dietary factors and risks for prostate cancer among blacks and whites in the United States. *Cancer Epidemiol Biomarkers Prev* **8,** 25–34, 1999.
20. Tzonou A, Signorello LB, Lagiou P, Wuu J, Trichopoulos D, and Trichopoulou A: Diet and cancer of the prostate: a case-control study in Greece. *Int J Cancer* **80,** 704–708, 1999.
21. Deneo-Pellegrini H, De Stehfani E, Ronco A, and Mendilaharsu M: Foods, nutrients and prostate cancer: a case-control study in Uruguay. *Br J Cancer* **80,** 591–597, 1999.
22. Bosetti C, Tzonou A, Lagiou P, Negri E, Trichopoulos D, and Hsieh C-C: Fraction of prostate cancer incidence attributed to diet in Athens, Greece. *Eur J Cancer Prev* **9,** 119–123, 2000.
23. Berndt SI, Carter HB, Landis PK, Tucker KL, Hsieh LJ, Metter EJ, and Platz EA: Calcium intake and prostate cancer risk in a long-term aging study: the Baltimore Longitudinal Study of Aging. *Urology* **60,** 1118–1123, 2002.
24. Parkin DM, Whelan SL, Ferlay J, Teppo L, and Thomas DB (eds). *Cancer Incidence in Five Continents*, Lyon, France: International Agency for Research on Cancer, 2002, vol III, pp 633–635.
25. Snowdon DA, Phillips RL, and Choi W: Diet, obesity, and risk of fatal prostate cancer. *Am J Epidemiol* **120,** 244–250, 1984.
26. Mills PK, Beeson WL, Phillips RL, and Fraser GE: Cohort study of diet, lifestyle, and prostate cancer in Adventist men. *Cancer* **64,** 598–604, 1989.
27. Severson RK, Nomura AMY, Grove JS, and Stemmermann GN: A prospective study of demographics, diet, and prostate cancer among men of Japanese ancestry in Hawaii. *Cancer Res* **49,** 1857–1860, 1989.
28. Hsing AW, McLaughlin JK, Schuman LM, Bjelke E, Gridley G, et al.: Diet, tobacco use, and fatal prostate cancer: results from the Lutheran Brotherhood cohort study. *Cancer Res* **50,** 6836–6840, 1990.
29. Giovannucci E, Rimm EB, Colditz GA, Stampfer MJ, Ascherio A, Chute CC, and Willett WC: A prospective study of dietary fat and risk of prostate cancer. *JNCI* **85,** 1571–1579, 1993.
30. Le Marchand L, Kolonel LN, Wilkens LR, Myers BC, and Hirohata T: Animal fat consumption and prostate cancer: a prospective study in Hawaii. *Epidemiology* **5,** 276–282, 1994.
31. Giovannucci E, Rimm EB, Wolk A, Ascherio A, Stampfer MJ, Colditz GA, and Willett WC: Calcium and fructose intake in relation to risk of prostate cancer. *Cancer Res* **58,** 442–447, 1998.
32. Schuurman AG, van den Brandt PA, Dorant E, and Goldbohm RA: Animal products, calcium and protein and prostate cancer risk in The Netherlands Cohort Study. *Br J Cancer* **80,** 1107–1113, 1999.
33. Chan JM, Pietinen P, Virtanen M, Malila N, Tangrea J, Albanes D, and Virtamo J: Diet and prostate cancer risk in a cohort of smokers, with a specific focus on calcium and phosphorus (Finland). *Cancer Causes Control* **11,** 859–867, 2000.
34. Michaud DS, Augustsson K, Rimm EB, Stampfer MJ, Willett WC, and Giovannucci E: A prospective study on intake of animal products and risk of prostate cancer. *Cancer Causes Control* **12,** 557–567, 2001.
35. Chan JM, Stampfer MJ, Ma J, Gann PH, Gaziano JM, and Giovannucci EL: Dairy products, calcium, and prostate cancer risk in the Physicians Health Study. *Am J Clin Nutr* **74,** 549–554, 2001.
36. Ganmaa D, Wang PY, Qin LQ, Hoshi K, and Sato A: Is milk responsible for male reproductive disorders? *Med Hypotheses* **57,** 510–514, 2001.
37. Coughlin SS, Giustozzi A, Smith SJ, and Lee NC: A meta-analysis of estrogen replacement therapy and risk of epithelial ovarian cancer. *J Clin Epidemiol* **53,** 367–375, 2000.
38. Boyd NF, Martin LJ, Noffel M, Lockwood GA, and Tritchler DL: A meta-analysis of studies of dietary fat and breast cancer risk. *Br J Cancer* **68,** 627–636, 1993.
39. Joossens JV and Geboers J: Nutrition and cancer. *Biomed Pharmacother* **40,** 127–138, 1986.
40. Subar AF, Krebes-Smith SM, Cook AC, and Kahle LA: Dietary sources of nutrients among US adults, 1989 to 1991. *J Am Diet Assoc* **98,** 537–547, 1998.
41. Tavani A, Gallus S, Franceschi S, and La Vecchia C: Calcium, dairy products, and the risk of prostate cancer. *Prostate* **48,** 118–121, 2001.
42. Heap RB and Hamon M: Oestrone sulphate in milk as an indicator of a viable conceptus in cows. *Br Vet J* **135,** 355–363, 1979.
43. Hill P, Wynder EL, Garnes H, and Walker ARP. Environmental factors, hormones, and prostatic cancer. *Prev Med* **9,** 657–666, 1980.
44. Bernstein L and Ross RK: Endogenous hormones and breast cancer risk. *Epidemiol Rev* **15,** 48–65, 1993.
45. Bosland MC: The role of steroid hormones in prostate carcinogenesis. *JNCI Monogr* **27,** 39–66, 2000.
46. Outwater JL, Nicholson A, and Barnard N: Dairy products and breast cancer: the IGF-I, estrogen, and bGH hypothesis. *Med Hypotheses* **48,** 453–461, 1997.
47. Chan JM, Stampfer MJ, Giovannucci E, Gann PH, Ma J, et al.: Plasma insulin-like growth factor-I and prostate cancer risk: a prospective study. *Science* **279,** 563–566, 1998.