Tomato/Tomato-based foods and Disease Risk
Prostate Cancer Critical Findings

Disease type	First Author	Study Title and Complete Citation	Date	Abstract	Study Type	G.Tom +, N, -	P.Tom +, N, -	F.Tom +, N, -	Lyco +, N, -	Other +, N, -
Cancer: prostate	Mills PK	Cohort study of diet, lifestyle, and prostate cancer in Adventist men. Mills PK, Beeson WL, Phillips RL, Fraser GE. Cancer. 1989 Aug 1;64(3):598-604.	1989	Dietary and lifestyle characteristics were evaluated in relation to subsequent prostatic cancer risk in a cohort of approximately 14,000 Seventh-day Adventist men who completed a detailed lifestyle questionnaire in 1976 and who were monitored for cancer incidence until the end of 1982. During the 6-year follow-up period, 180 histologically confirmed prostatic cancers were detected among some 78,000 man-years of follow-up. Increasing educational attainment was associated with significantly decreased risk of prostate cancer in this study; age at first marriage was also inversely associated with risk, although this was not significant. There was no relationship between body mass index (as measured by Quetelet's Index) and risk. A history of prostate "trouble" was associated with a 60% increase in risk which was highly significant. Although there were suggestive relationships between increasing animal product consumption and increased risk, these results did not persist after accounting for the influence of fruit and vegetable consumption. Nor was exposure to the vegetarian lifestyle during the childhood years associated with alterations in subsequent risk. However, increasing consumption of beans, lentils and peas, tomatoes, raisin, dates, and other dried fruit were all associated with significantly decreased prostate cancer risk.	PC	(-)				
Cancer: prostate	Le Marchand L	Vegetable and fruit consumption in relation to prostate cancer risk in Hawaii: a reevaluation of the effect of	1991	This is a further analysis of a case-control study of 452 prostate cancer cases and 899 population controls that was onducted in 1970-1983 among the multiethnic population of Hawaii. Because a previous analysis had shown a positive association with intake of beta-carotene, a nutrient presently being tested for chemoprevention, the authors	CC	N				

		dietary beta-carotene. Le Marchand L, Hankin JH, Kolonel LN, Wilkens LR. Am J Epidemiol. 1991 Feb 1;133(3):215-9.		reexamined the data for consistency among the main food sources of beta-carotene. Vegetables and fruits containing other phytochemicals suspected to be cancer inhibitors were also examined. With the exception of papaya, which was positively associated with risk among men aged 70 years and older, consumption of other yellow-orange fruits and vegetables, tomatoes, dark green vegetables, and cruciferous vegetables was not associated with prostate cancer risk. These results suggest that: 1) the positive association with beta-carotene intake among older men that the authors previously reported was essentially due to the greater papaya consumption of cases compared with controls; and 2) intake of beta-carotene, lycopene, lutein, indoles, phenols, or other phytochemicals is not associated with prostate cancer risk.						
Cancer: prostate	Giovannucci E	Intake of carotenoids and retinol in relation to risk of prostate cancer. Giovannucci E, Ascherio A, Rimm EB, Stampfer MJ, Colditz GA, Willett WC. J Natl Cancer Inst. 1995 Dec 6;87(23):1767-76.	1995	BACKGROUND: Several human studies have observed a direct association between retinol (vitamin A) intake and risk of prostate cancer; other studies have found either an inverse association or no association of intake of beta-carotene (the major provitamin A) with risk of prostate cancer. Data regarding carotenoids other than beta-carotene in relation to prostate cancer risk are sparse. PURPOSE: We concluded a prospective cohort study to examine the relationship between the intake of various carotenoids, retinol, fruits, and vegetables and the risk of prostate cancer. METHODS: Using responses to a validated, semiquantitative food-frequency questionnaire mailed to participants in the Health Professionals Follow-up Study in 1986, we assessed dietary intake for a 1-year period for a cohort of 47,894 eligible subjects initially free of diagnosed cancer. Follow-up questionnaires were sent to the entire cohort in 1988, 1990, and 1992. We calculated the relative risk (RR) for each of the upper categories of intake of a specific food or	PC	(-)	(-)		(-)	

				nutrient by dividing the incidence rate of prostate cancer among men in each of these categories by the rate among men in the lowest intake level. All P values resulted from two-sided tests. RESULTS: Between 1986 and 1992, 812 new cases of prostate cancer, including 773 non-stage A1 cases, were documented. Intakes of the carotenoids beta-carotene, alpha-carotene, lutein, and beta-cryptoxanthin were not associated with risk of non-stage A1 prostate cancer; only lycopene intake was related to lower risk (age- and energy-adjusted RR = 0.79; 95% confidence interval [CI] = 0.64-0.99 for high versus low quintile of intake; P for trend = .04). Of 46 vegetables and fruits or related products, four were significantly associated with lower prostate cancer risk; of the four--tomato sauce (P for trend = .001), tomatoes (P for trend = .03), and pizza (P for trend = .05), but not strawberries--were primary sources of lycopene. Combined intake of tomatoes, tomato sauce, tomato juice, and pizza (which accounted for 82% of lycopene intake) was inversely associated with risk of prostate cancer (multivariate RR = 0.65; 95% CI = 0.44-0.95, for consumption frequency greater than 10 versus less than 1.5 servings per week; P for trend = .01) and advanced (stages C and D) prostate cancers (multivariate RR = 0.47; 95% CI = 0.22-1.00; P for trend = .03). No consistent association was observed for dietary retinol and risk of prostate cancer. CONCLUSIONS: These findings suggest that intake of lycopene or other compounds in tomatoes may reduce prostate cancer risk, but other measured carotenoids are unrelated to risk. IMPLICATIONS: Our findings support recommendations to increase vegetable and fruit consumption to reduce cancer incidence but suggest that tomato-based foods may be especially beneficial regarding prostate cancer risk.						

Cancer: prostate	Jain MG	Plant foods, antioxidants, and prostate cancer risk: findings from case-control studies in Canada. Jain MG, Hislop GT, Howe GR, Ghadirian P. Nutr Cancer. 1999;34(2):173-84.	1999	Epidemiological data on most cancer sites suggest that consumption of plant foods, which contain high levels of antioxidants, might slow or prevent the appearance of cancer. We used data from three case-control studies to test this hypothesis. The total study population consisted of 617 incident cases of prostate cancer and 636 population controls from Ontario, Quebec, and British Columbia. Dietary information was collected by an in-person interview with a detailed quantitative dietary history. Unconditional logistic regression analyses were performed to estimate odds ratios (ORs) and 95% confidence intervals (CIs). A decreasing, statistically significant association was found with increasing intakes of green vegetables (OR = 0.54, 95% CI = 0.40-0.71 for 4th quartile), tomatoes (OR = 0.64, 95% CI = 0.45-0.91), beans/lentils/nuts (OR = 0.69, 95% CI = 0.53-0.91), and cruciferous vegetables (OR = 0.69, 95% CI = 0.52-0.91 for 3rd quartile). Higher intakes of fruit were associated with higher ORs (OR = 1.51, 95% CI = 1.14-2.01 for 4th quartile), an effect that was seen for total fruit and citrus fruit, as well as for all other noncitrus fruits. Among the grains, refined-grain bread intake was associated with a decrease in risk (OR = 0.65 for 4th quartile), whereas whole-grain breakfast cereals were associated with a higher risk for prostate cancer. Of all the antioxidant nutrients studied, the ORs were higher with higher intakes of cryptoxanthin (OR = 1.44, 95% CI = 1.09-1.89 for 4th quartile). Exposure to certain dietary components of plant origin, which are potentially modifiable, indicates the theoretical scope for reducing the risk from prostate cancer. Future experimental studies or trials are warranted for further understanding.	CC	(-)				
Cancer: prostate	Tzonou A	Diet and cancer of the prostate: a case-control study in Greece. Tzonou A, Signorello LB, Lagiou P, Wuu J, Trichopoulos D, Trichopoulou A	1999	The nutritional aetiology of prostate cancer was evaluated in Athens, Greece, through a case-control study that included 320 patients with histologically confirmed incident prostate cancer and 246 controls without history or symptomatology of benign prostatic hyperplasia or prostate cancer, treated in the same hospital as the cases for minor diseases or conditions. Among major food groups, milk and dairy products as well	CC		(-)	(-)		

		Int J Cancer. 1999 Mar 1;80(5):704-8.		as added lipids were marginally positively associated with risk for prostate cancer. Among added lipids, seed oils were significantly and butter and margarine non-significantly positively associated with prostate cancer risk, whereas olive oil was unrelated to this risk. Cooked tomatoes and to a lesser extent raw tomatoes were inversely associated with the risk for prostate cancer. In analyses focusing on nutrients, rather than foods, polyunsaturated fats were positively and vitamin E inversely associated with prostate cancer. We conclude that several nutrition-related processes jointly contribute to prostate carcinogenesis						
Cancer: prostate	Villeneuve PJ	Risk factors for prostate cancer: results from the Canadian National Enhanced Cancer Surveillance System. The Canadian Cancer Registries Epidemiology Research Group. Villeneuve PJ, Johnson KC, Kreiger N, Mao Y. Cancer Causes Control. 1999 Oct;10(5):355-67.	1999	OBJECTIVES: To evaluate the relationship between prostate cancer and several potential lifestyle risk factors. METHODS: We analyzed data obtained from a population-based case-control study conducted in eight Canadian provinces. Risk estimates were generated by applying multivariate logistic regression methods to 1623 histologically confirmed prostate cancer cases and 1623 male controls aged 50-74. RESULTS: Cases were more likely to have a first-degree relative with a history of cancer, particularly prostate cancer (OR = 3.1, 95% CI = 1.8-5.4). Reduced risks of prostate cancer were observed among those of Indian descent (OR = 0.2, 95% CI = 0.1-0.5) or any Asian descent (OR = 0.3, 95% CI = 0.2-0.6) relative to those of western European descent. Total fat consumption, tomato and energy intake, were not associated with prostate cancer. The risk of prostate cancer was inversely related to the number of cigarettes smoked daily ($p = 0.06$) and cigarette pack-years ($p < 0.01$), while no association was observed between the total number of smoking years or the number of years since smoking cessation. Anthropometric measures and moderate and strenuous levels of leisure time physical activity were not strongly	CC	N				

				related to prostate cancer. In contrast, strenuous occupational activities at younger ages appeared protective. CONCLUSIONS: Our analyses are limited by the absence of data related to tumor severity and screening history. Further studies are needed to investigate the relationship between behavioral risk factors and prostate cancer screening practices.						
Cancer: prostate	Grant WB.	An ecologic study of dietary links to prostate cancer. Grant WB. Altern Med Rev. 1999 Jun;4(3):162-9.	1999	BACKGROUND: The etiology of prostate cancer has not been fully resolved in the scientific and medical literature, although the non-fat portion of milk and calcium are emerging as leading dietary risk factors, with lycopene (found in tomatoes) and vitamin D apparently being risk reduction factors. METHODS: The ecologic (multi-country statistical) approach is used to study dietary links to prostate cancer. Mortality data from 1986 for various age groups in 41 countries are compared with national consumer macronutrient supply values for 1983 and tomato supply values for 1985. RESULTS: For 28 countries with more than five Kcal/day of tomatoes in the consumer supply, a linear combination of non-fat milk (risk factor) and tomatoes (risk reduction factor) was found to have the highest statistical association with prostate cancer mortality rates for men over the age of 35, with the Pearson regression coefficient (R2) for those aged 65-74 years = 0.67 and $p < 0.001$. For the 13 countries with fewer than six Kcal/day of tomatoes, non-fat milk had the highest association ($R2 = 0.92$, $p < 0.001$ for men aged 65-74 years). For 41 countries combined, the non-fat portion of milk had the highest association with prostate cancer mortality rates ($R2 = 0.73$, $p < 0.001$ for men aged 65-74 years). CONCLUSIONS: These results support the results of	ECO	(-)				

				several cohort studies which found the non-fat portion of milk to have the highest association with prostate cancer, likely due to the calcium, and tomatoes to reduce the risk of prostate cancer, most likely due to lycopene						
Cancer: prostate	Bosetti C	Fraction of prostate cancer incidence attributed to diet in Athens, Greece. Bosetti C, Tzonou A, Lagiou P, Negri E, Trichopoulos D, Hsieh CC. Eur J Cancer Prev. 2000 Apr;9(2):119-23.	2000	Diet appears to be a major determinant in the incidence of prostate cancer. In a case-control study conducted in Athens, Greece,we found that dairy products, butter and seed oils were positively associated with risk of prostate cancer, whereas cooked and raw tomatoes were inversely associated. We utilized the data from this study to calculate the population attributable fractions under alternative assumptions of feasible dietary changes. For each subject, a dietary score was calculated and categorized into approximately quintiles, representing increasing levels of prostate cancer risk as a function of the intake of the five discriminatory food groups or items. Population attributable fractions in terms of this dietary score were calculated taking into account multivariate adjustment. We observed that, if all individuals were shifted to the baseline category, the incidence of prostate cancer in this study population would be reduced by 41% (95% confidence interval 23-59%). However, if all individuals were shifted to the adjacent lower risk quintile, the expected incidence reduction would be a more modest 19%. The incidence of prostate cancer in Greece could be reduced by about two-fifths if the population increased the consumption of tomatoes and reduced the intake of dairy products, and substituted olive oil for other added lipids.	CC	(-)				

Cancer: prostate	Kolonel L N	Vegetables, fruits, legumes and prostate cancer: a multiethnic case-control study. Kolonel LN, Hankin JH, Whittemore AS, Wu AH, Gallagher RP, Wilkens LR, John EM, Howe GR, Dreon DM, West DW, Paffenbarger RS Jr. Cancer Epidemiol Biomarkers Prev. 2000 Aug;9(8):795-804.	2000	The evidence for a protective effect of vegetables, fruits, and legumes against prostate cancer is weak and inconsistent. We examined the relationship of these food groups and their constituent foods to prostate cancer risk in a multicenter case-control study of African-American, white, Japanese, and Chinese men. Cases (n = 1619) with histologically confirmed prostate cancer were identified through the population-based tumor registries of Hawaii, San Francisco, and Los Angeles in the United States and British Columbia and Ontario in Canada. Controls (n = 1618) were frequency-matched to cases on ethnicity, age, and region of residence of the case, in a ratio of approximately 1:1. Dietary and other information was collected by in-person home interview; a blood sample was obtained from control subjects for prostate-specific antigen determination. Odds ratios (OR) were estimated using logistic regression, adjusting for age, geographic location, education, calories, and when indicated, ethnicity. Intake of legumes (whether total legumes, soyfoods specifically, or other legumes) was inversely related to prostate cancer (OR for highest relative to lowest quintile for total legumes = 0.62; P for trend = 0.0002); results were similar when restricted to prostate-specific antigen-normal controls or to advanced cases. Intakes of yellow-orange and cruciferous vegetables were also inversely related to prostate cancer, especially for advanced cases, among whom the highest quintile OR for yellow-orange vegetables = 0.67 (P for trend = 0.01) and the highest quintile OR for cruciferous vegetables = 0.61 (P for trend = 0.006). Intake of tomatoes and of fruits was not related to risk. Findings were generally consistent across ethnic groups. These results suggest that legumes (not limited to soy products) and certain categories	CC	N				

				of vegetables may protect against prostate cancer.						
Cancer: prostate	Norrish AE	Prostate cancer and dietary carotenoids. Norrish AE, Jackson RT, Sharpe SJ, Skeaff CM. Am J Epidemiol. 2000 Jan 15;151(2):119-23.	2000	This population-based case-control study investigated associations between prostate cancer risk and dietary intake of the carotenoids beta-carotene and lycopene and their major plant food sources, including carrots, green leafy vegetables, and tomato-based foods. The study was carried out in Auckland, New Zealand, during 1996-1997 and recruited 317 prostate cancer cases and 480 controls. The authors found that dietary intake of beta-carotene and its main vegetable sources was largely unassociated with prostate cancer risk, whereas intake of lycopene and tomato-based foods was weakly associated with a reduced risk. These results suggest that in contrast to the findings regarding many types of cancers, vegetables rich in beta-carotene are not protective against prostate cancer. However, lycopene from tomato-based foods was found to be associated with a small reduction in risk.	CC	(-)			(-)	
Cancer: prostate	Mucci LA	Are dietary influences on the risk of prostate cancer mediated through the insulin-like growth factor system? Mucci LA, Tamimi R, Lagiou P, Trichopoulou A, Benetou V, Spanos E, Trichopoulos D.. BJU Int. 2001 Jun;87(9):814-20.	2001	OBJECTIVES: To investigate whether dietary factors that appear to affect the risk of prostate cancer may be similarly associated with serum levels of insulin-like growth factor 1 (IGF-1). Patients and methods In the context of a case-control study, 112 men were admitted to three teaching hospitals in Athens, Greece, for disorders other than cancer. Sociodemographic data and detailed histories of smoking, alcohol and coffee consumption were recorded. A validated food-frequency questionnaire was administered by an interviewer and serological measurements of IGF-1 and its binding protein-3 conducted. RESULTS: IGF-1 declined significantly by almost 25% among men aged >75 years and there was a small reduction in IGF-1 levels with increased alcohol intake, with a mean	CC		(-)			(-) IGF-1

				(95% confidence interval, CI) change of -1.6 (- 2.2 to -0.9)% for an increment of one drink per day. There was no evidence for an effect of either smoking or coffee consumption on IGF-1 level. Among foods, the consumption of cooked tomatoes was substantially and significantly inversely associated with IGF-1 levels, with a mean (95% CI) change of -31.5 (- 49.1 to -7.9)% for an increment of one serving per day. CONCLUSIONS: The strongest known dietary risk factor for prostate cancer (lycopene deficit, as reflected in a reduced intake of cooked tomatoes) and an important endocrine factor in the aetiology of this disease (IGF-1) seem to be related in a way that suggests that at least one, and perhaps more, exogenous factors in the development of prostate cancer may be mediated through the IGF-1 system.						
Cancer: prostate	Chen L	Oxidative DNA damage in prostate cancer patients consuming tomato sauce-based entrees as a whole-food intervention. Chen L, Stacewicz-Sapuntzakis M, Duncan C, Sharifi R, Ghosh L, van Breemen R, Ashton D, Bowen PE. J Natl Cancer Inst. 2001 Dec 19;93(24):1872-9.	2001	BACKGROUND: Human prostate tissues are vulnerable to oxidative DNA damage. The risk of prostate cancer is lower in men reporting higher consumption of tomato products, which contain high levels of the antioxidant lycopene. We examined the effects of consumption of tomato sauce-based pasta dishes on lycopene uptake, oxidative DNA damage, and prostate-specific antigen (PSA) levels in patients already diagnosed with prostate cancer. METHODS: Thirty-two patients with localized prostate adenocarcinoma consumed tomato sauce-based pasta dishes for the 3 weeks (30 mg of lycopene per day) preceding their scheduled radical prostatectomy. Serum and prostate lycopene concentrations, serum PSA levels, and leukocyte DNA oxidative damage (ratio of 8-hydroxy-2'-deoxyguanosine [8-OHdG] to 2'-deoxyguanosine [dG]) were assessed before and after the dietary intervention. DNA oxidative damage was assessed in resected prostate tissue from study participants and from seven randomly selected	Interv		(-)			Ox damage PSA

				prostate cancer patients. All statistical tests were two-sided. RESULTS: After the dietary intervention, serum and prostate lycopene concentrations were statistically significantly increased, from 638 nM (95% confidence interval [CI] = 512 to 764 nM) to 1258 nM (95% CI = 1061 to 1455 nM) (P<.001) and from 0.28 nmol/g (95% CI = 0.18 to 0.37 nmol/g) to 0.82 nmol/g (95% CI = 0.57 to 1.11 nmol/g) (P <.001), respectively. Compared with preintervention levels, leukocyte oxidative DNA damage was statistically significantly reduced after the intervention, from 0.61 8-OHdG/10(5) dG (95% CI = 0.45 to 0.77 8-OHdG/10(5) dG) to 0.48 8-OHdG/ 10(5) dG (95% CI = 0.41 to 0.56 8-OHdG/10(5) dG) (P =.005). Furthermore, prostate tissue oxidative DNA damage was also statistically significantly lower in men who had the intervention (0.76 8-OHdG/10(5) dG [95% CI = 0.55 to 0.96 8-OHdG/10(5) dG]) than in the randomly selected patients (1.06 8-OHdG/10(5) dG [95% CI = 0.62 to 1.51 8-OHdG/10(5) dG]; P =.03). Serum PSA levels decreased after the intervention, from 10.9 ng/mL (95% CI = 8.7 to 13.2 ng/mL) to 8.7 ng/mL (95% CI = 6.8 to 10.6 ng/mL) (P<.001). CONCLUSION: These data indicate a possible role for a tomato sauce constituent, possibly lycopene, in the treatment of prostate cancer and warrant further testing with a larger sample of patients, including a control group.						
Cancer: prostate	Giovannucci E	A prospective study of tomato products, lycopene, and prostate cancer risk. Giovannucci E,	2002	BACKGROUND: Some data, including our findings from the Health Professionals Follow-Up Study (HPFS) from 1986 through January 31, 1992, suggest that frequent intake of tomato products or lycopene, a carotenoid from tomatoes, is associated with reduced risk of prostate cancer. Overall, however, the data are inconclusive. We evaluated	PC		(-)		(-)	

		Rimm EB, Liu Y, Stampfer MJ, Willett WC. J Natl Cancer Inst. 2002 Mar 6;94(5):391-8.		additional data from the HPFS to determine if the association would persist. METHODS: We ascertained prostate cancer cases from 1986 through January 31, 1998, among 47 365 HPFS participants who completed dietary questionnaires in 1986, 1990, and 1994. We used pooled logistic regression to compute multivariate relative risks (RR) and 95% confidence intervals (CIs). All statistical tests were two-sided. RESULTS: From 1986 through January 31, 1998, 2481 men in the study developed prostate cancer. Results for the period from 1992 through 1998 confirmed our previous findings---that frequent tomato or lycopene intake was associated with a reduced risk of prostate cancer. Similarly, for the entire period of 1986 through 1998, using the cumulative average of the three dietary questionnaires, lycopene intake was associated with reduced risk of prostate cancer (RR for high versus low quintiles = 0.84; 95% CI = 0.73 to 0.96; P(trend) =.003); intake of tomato sauce, the primary source of bioavailable lycopene, was associated with an even greater reduction in prostate cancer risk (RR for 2+ servings/week versus <1 serving/month = 0.77; 95% CI = 0.66 to 0.90; P(trend)<.001), especially for extraprostatic cancers (RR = 0.65; 95% CI = 0.42 to 0.99). These associations persisted in analyses controlling for fruit and vegetable consumption and for olive oil use (a marker for Mediterranean diet) and were observed separately in men of Southern European or other Caucasian ancestry. CONCLUSION: Frequent consumption of tomato products is associated with a lower risk of prostate cancer. The magnitude of the association was moderate enough that it could be missed in a small study or one with substantial errors in measurement or based on a single dietary assessment.						

Cancer: prostate	Bowen P	Tomato sauce supplementation and prostate cancer: lycopene accumulation and modulation of biomarkers of carcinogenesis. Bowen P, Chen L, Stacewicz-Sapuntzakis M, Duncan C, Sharifi R, Ghosh L, Kim HS, Christov-Tzelkov K, van Breemen R. Exp Biol Med (Maywood). 2002 Nov;227(10):886-93.	2002	As part of a randomized placebo-controlled study to evaluate the effect of lycopene supplementation on DNA damage in men with prostate cancer, a nonrandomized 5th arm using tomato sauce was included and reported here. Thirty-two patients with localized prostate adenocarcinoma consumed tomato sauce-based pasta dishes for 3 weeks (30 mg of lycopene/day) before their scheduled radical prostatectomy. Prostate tissue was obtained as biopsies at baseline and as resected tissue at the time of the prostatectomy. Serum and prostate lycopene, serum prostate specific antigen (PSA) concentrations, and leukocyte DNA 8-OH-deoxyguanosine/deoxyguanosine (8OHdG) were measured at baseline and at the end of the intervention. Cancer cells in paraffin sections of prostate biopsies and postintervention resected tissue were compared for 8OHdG staining and for apoptosis. Adherence to the daily consumption of tomato-based entrees was 81.6% of the intended dose, and serum and prostate lycopene concentrations increased 1.97- and 2.92-fold ($P < 0.001$), respectively. Mean serum PSA concentrations decreased by 17.5% ($P < 0.002$) and leukocyte 8OHdG decreased by 21.3% ($P < 0.005$) after tomato sauce consumption. Resected tissues from tomato sauce-supplemented patients had 28.3% lower prostate 8OHdG compared with the nonstudy control group ($P < 0.03$). Cancer cell 8OHdG staining of Gleason Score-matched resected prostate sections was reduced by 40.5% in mean nuclear density ($P < 0.005$) and by 36.4% in mean area ($P < 0.018$) compared with the presupplementation biopsy. Apoptotic index was higher in hyperplastic and neoplastic cells in the resected tissue after supplementation. These data taken as a whole indicate significant uptake of lycopene into prostate tissue and a reduction in DNA damage in both leukocyte and prostate tissue. Whether reduction in	RCT/ NRCT 5th arm		(-)			DNA ox PSA

				DNA damage to prostate cancer cells is beneficial awaits further research, although reduction in serum PSA concentrations is promising.						
Cancer: prostate	Kim HS	Effects of tomato sauce consumption on apoptotic cell death in prostate benign hyperplasia and carcinoma. Kim HS, Bowen P, Chen L, Duncan C, Ghosh L, Sharifi R, Christov K. Nutr Cancer. 2003;47(1):40-7.	2003	Population studies have suggested that lycopene, which is mostly found in tomato and tomato products, may reduce the risk of prostate cancer. We previously found that tomato sauce consumption prior to prostatectomy for prostate cancer decreased serum prostate specific antigen, decreased oxidative DNA damage, and increased lycopene concentrations in prostate tissue (Chen et al., 2001). Here, we extended those investigations to determine whether apoptotic cell death and associated Bcl-2 and Bax proteins were modulated by tomato sauce intervention. Thirty-two patients diagnosed by biopsy with prostate carcinoma were given tomato sauce pasta entrees (30 mg lycopene/day) for 3 wk before prostatectomy. Thirty-four patients with prostate cancer who did not consume tomato sauce and underwent prostatectomy served as controls. When tumor areas with the most apoptotic cells were compared in the biopsy (before) and resected prostate tissue (after), tomato sauce consumption increased apoptotic cells in benign prostate hyperplasia (BPH) from 0.66 +/- 0.10% to 1.38 +/- 0.31% (P = 0.013) and in carcinomas from 0.84 +/- 0.13% to 2.76 +/- 0.58% (P = 0.0003). When comparable morphological areas were counted, apoptotic cell death in carcinomas increased significantly with treatment, from 0.84 +/- 0.13% to 1.17 +/- 0.19% (P = 0.028), and apoptotic cell death in BPH showed a tendency toward an increase from 0.66 +/- 0.10% to 1.20 +/- 0.32% (P = 0.20). When the values of apoptotic cells in BPH and carcinomas of patients who consume tomato sauce were compared with corresponding control lesions of the patients who did not consume tomato sauce in resected prostate tissue, the differences of values	Interv		(-)			

				were not significant [BPH 1.38 +/- 0.31% vs. 1.14 +/- 0.32% (P = 0.97); carcinomas 2.76 +/- 0.58% vs. 1.91 +/- 0.32% (P = 0.24)]. Tomato sauce consumption did not affect Bcl-2 expression but decreased Bax expression in carcinomas. These data provide the first in vivo evidence that tomato sauce consumption may suppress the progression of the disease in a subset of patients with prostate cancer by increasing apoptotic cell death. However, because of the relatively small number of control and tomato sauce-supplemented patients and the variability in the values of apoptotic cells in BPH and carcinomas, a much larger number of patients needs to be examined to support the data generated in this study.						
Cancer: prostate	Hodge AM	Foods, nutrients and prostate cancer. Hodge AM, English DR, McCredie MR, Severi G, Boyle P, Hopper JL, Giles GG. Cancer Causes Control. 2004 Feb;15(1):11-20	2004	OBJECTIVE: To examine the risk of prostate cancer associated with foods and nutrients, including individual fatty acids and carotenoids. METHODS: Population-based case-control study of 858 men aged <70 years at diagnosis with histologically confirmed prostate cancer of Gleason Grade 5 or greater, and 905 age-frequency-matched men, selected at random from the electoral rolls. Dietary intakes were assessed with a 121-item food frequency questionnaire. RESULTS: Inverse associations with prostate cancer were observed for (Odds ratio, OR, 95% confidence intervals, 95% CI for tertile III compared with tertile I) allium vegetables 0.7, 0.5-0.9; p trend 0.01, tomato-based foods 0.8, 0.6-1.0; p trend 0.03 and total vegetables 0.7, 0.5-1.0; p trend 0.04. Margarine intake was positively associated with prostate cancer 1.3, 1.0-1.7; p trend 0.04. The only statistically significant associations observed with nutrients were weak inverse associations for palmitoleic acid (p trend 0.04), fatty acid 17:1 (p	CC	(-)				

				trend 0.04), and 20:5 n-6 (p trend 0.05); and a non-significant trend for oleic acid (p trend 0.09). Neither total, nor beverage-specific, intake of alcohol was associated with risk. CONCLUSIONS: Based on these findings, diets rich in olive oil (a source of oleic acid), tomatoes and allium vegetables might reduce the risk of prostate cancer.						
Cancer: prostate	Sonoda T	A case-control study of diet and prostate cancer in J apan: possible protective effect of traditional Japanese diet. Sonoda T, Nagata Y, Mori M, Miyanaga N, Takashima N, Okumura K, Goto K, Naito S, Fujimoto K, Hirao Y, Takahashi A, Tsukamoto T, Fujioka T, Akaza H. Cancer Sci. 2004 Mar;95(3):238-42.	2004	The age-adjusted incidence of prostate cancer is low in Japan, and it has been suggested that the traditional Japanese diet, which includes many soy products, plays a preventive role against prostate cancer. We performed a case-control study on dietary factors and prostate cancer in order to assess the hypothesis that the traditional Japanese diet reduces the risk of prostate cancer. Four geographical areas (Ibaraki, Fukuoka, Nara, and Hokkaido) of Japan were selected for the survey. Average daily intake of food from 5 years before the diagnosis was measured by means of a semi-quantitative food frequency questionnaire. We studied 140 cases and 140 individually age (+/- 5 years)-matched hospital controls for analysis. Estimates of age-adjusted odds ratios (ORs) and linear trends were calculated by conditional logistic regression models with adjustment for cigarette smoking and total energy intake as confounding factors. Consumption of fish, all soybean products, tofu (bean curds), and natto (fermented soybeans) was associated with decreased risk. ORs of the fourth vs. first quartile and 95% confidence intervals (95%CIs) were 0.45 (0.20-1.02) for fish, 0.53 (0.24-1.14) for all soybean products, 0.47 (0.20-1.08) for tofu, and 0.25 (0.05-1.24) for natto. Consumption of fish and natto showed significantly decreasing linear trends for risk ($P < 0.05$). Consumption of meat was significantly associated with increased risk (the OR of the	CC	N				

				second vs. first quartile was 2.19, 95%CI 1.00-4.81). Consumption of milk, fruits, all vegetables, green-yellow vegetables, and tomatoes showed no association. Our results provide support to the hypothesis that the traditional Japanese diet, which is rich in soybean products and fish, might be protective against prostate cancer.						
Cancer: prostate	Jian L	Do dietary lycopene and other carotenoids protect against prostate cancer? Jian L, Du CJ, Lee AH, Binns CW. Int J Cancer. 2005 Mar 1;113(6):1010-4.	2005	To determine whether dietary intake of lycopene and other carotenoids has an etiological association with prostate cancer, a case-control study was conducted in Hangzhou, southeast China during 2001-2002. The cases were 130 incident patients with histologically confirmed adenocarcinoma of the prostate. The controls were 274 hospital inpatients without prostate cancer or any other malignant diseases. Information on usual food consumption, including vegetables and fruits, was collected by face-to-face interviews using a structured food frequency questionnaire. The risks of prostate cancer for the intake of carotenoids and selected vegetables and fruits rich in carotenoids were assessed using multivariate logistic regression, adjusting for age, locality, education, income, body mass index, marital status, number of children, family history of prostate cancer, tea drinking, total fat and caloric intake. The prostate cancer risk declined with increasing consumption of lycopene, alpha-carotene, beta-carotene, beta-cryptoxanthin, lutein and zeaxanthin. Intake of tomatoes, pumpkin, spinach, watermelon and citrus fruits were also inversely associated with the prostate cancer risk. The adjusted odds ratios for the highest versus the lowest quartiles of intake were 0.18 (95% CI: 0.08-0.41) for lycopene, 0.43 (95% CI: 0.21-0.85) for alpha-carotene, 0.34 (95% CI: 0.17-0.69) for beta-carotene, 0.15 (95% CI: 0.06-0.34) for beta-cryptoxanthin and 0.02 (95% CI: 0.01-0.10)	CC	(-) ↓ risk prostate cancer			(-) ↓ risk prostate cancer	

				for lutein and zeaxanthin. The corresponding dose-response relationships were also significant, suggesting that vegetables and fruits rich in lycopene and other carotenoids may be protective against prostate cancer.						
Cancer: prostate	Gallus S	Pizza consumption and the risk of breast, ovarian and prostate cancer. Gallus S, Talamini R, Bosetti C, Negri E, Montella M, Franceschi S, Giacosa A, La Vecchia C. Eur J Cancer Prev. 2006 Feb;15(1):74-6.	2006	Pizza has been favourably related to the risk of prostate cancer in North America. Scanty information, however, is available on sex hormone-related cancer sites. We therefore studied the role of pizza consumption on the risk of breast, ovarian and prostate cancers using data from three hospital-based case-control studies conducted in Italy between 1991 and 2002. These included 2569 women with breast cancer, 1031 with ovarian cancer, 1294 men with prostate cancer, and a total of 4864 controls. Compared with non-pizza eaters, the multivariate odds ratios for eaters were 0.97 (95% confidence interval (CI) 0.86-1.10) for breast, 1.06 (95% CI 0.89-1.26) for ovarian and 1.04 (95% CI 0.88-1.23) for prostate cancer. Corresponding estimates for regular eaters (i.e. > or =1 portion per week) were 0.92 (95% CI 0.78-1.08), 1.00 (95% CI 0.80-1.25) and 1.12 (95% CI 0.88-1.43), respectively. Our results do not show a relevant role of pizza on the risk of sex hormone-related cancers. The difference with selected studies from North America suggests that dietary and lifestyle correlates of pizza eating vary between different populations and social groups.	CC		N			
Cancer: prostate	Edinger MS	Effect of the consumption of tomato paste on plasma prostate-specific antigen levels in patients with benign prostate hyperplasia. Edinger MS, Koff WJ. Braz J Med Biol	2006	The consumption of tomatoes and tomato products has been associated with a reduced risk of prostate cancer. We observed a decrease of 10.77% in prostate-specific antigen (PSA) levels in patients with benign prostate hyperplasia who were submitted to daily ingestion of tomato paste. This was an experimental rather than a controlled study with a sample of 43 men ranging in age from 45 to 75 years, all with histological diagnoses of benign prostate hyperplasia and plasma PSA levels of 4-10 ng/mL. All patients received 50 g of tomato paste once a day for 10 consecutive weeks and PSA levels were	Interv		(-) ↓ PSA levels			

		Res. 2006 Aug;39(8):1115-9.		analyzed before, during and after the consumption of tomato paste. ANOVA for repeated measures was used to compare PSA levels before, during and after the consumption of tomato paste. The mean +/- SD PSA level was 6.51 +/- 1.48 ng/mL at baseline and 5.81 +/- 1.58 ng/mL (P = 0.005) after 10 weeks. Acceptance was good in 88.3, regular in 9.3, and poor in 2.3% of the patients. Dietary ingestion of 50 g of tomato paste per day for 10 weeks significantly reduced mean plasma PSA levels in patients with benign prostate hyperplasia, probably as a result of the high amount of lycopene in tomato paste. This was not a prostate cancer prevention study, but showed some action of tomato paste in prostate biology. The development of prostate cancer is typically accompanied by an increase in plasma PSA levels, thus any intervention that affects plasma PSA levels can suggest an impact in the progression of disease.						
Cancer: prostate	Chan JM	Diet after diagnosis and the risk of prostate cancer progression, recurrence, and death (United States). Chan JM, Holick CN, Leitzmann MF, Rimm EB, Willett WC, Stampfer MJ, Giovannucci EL. Cancer Causes Control. 2006 Mar;17(2):199-208.	2006	OBJECTIVES: We examined post-diagnostic diet and risk of cancer progression in a cohort of men with prostate cancer from the Health Professionals Follow-up Study. METHODS: We observed 392 progression outcomes among 1,202 men diagnosed with incident localized/regional prostate cancer between 1986 and 1996. Men completed prospective dietary surveys before and after diagnosis and were followed through 2000. We examined post-diagnostic consumption of red meat, grains, vegetables, fruits, milk, tomatoes, tomato sauce, and fish as predictors of progression using Cox proportional hazard regression models adjusted for total energy, age, clinical factors, and pre-diagnostic diet. RESULTS: Men in the highest versus lowest quartile of post-diagnostic fish consumption had a multivariate hazard ratio (HR) of progression of 0.73 (95% CI 0.52-1.02);	PC		(-)	(+)		Disease prog.

				the comparable HR for tomato sauce was 0.56 (95% CI 0.38-0.82). We observed inverse linear relationships for fish and tomato sauce and risk of progression (HR = 0.83, p-value = 0.006 and HR = 0.80, p-value = 0.04 for a two serving/week increase of fish and tomato sauce, respectively). Milk and fresh tomato consumption were associated with small elevations in risk. CONCLUSIONS: These data suggest that diet after diagnosis may influence the clinical course of prostate cancer, and fish and tomato sauce may offer some protection against disease progression.						
Cancer: prostate	Kirsh VA	A prospective study of lycopene and tomato product intake and risk of prostate cancer. Kirsh VA, Mayne ST, Peters U, Chatterjee N, Leitzmann MF, Dixon LB, Urban DA, Crawford ED, Hayes RB. Cancer Epidemiol Biomarkers Prev. 2006 Jan;15(1):92-8.	2006	BACKGROUND: Dietary lycopene and tomato products may reduce risk of prostate cancer; however, uncertainty remains about this possible association. METHODS: We evaluated the association between intake of lycopene and specific tomato products and prostate cancer risk in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, a multicenter study designed to investigate cancer early detection methods and etiologic determinants. Participants completed both a general risk factor and a 137-item food frequency questionnaire at baseline. A total of 1,338 cases of prostate cancer were identified among 29,361 men during an average of 4.2 years of follow-up. RESULTS: Lycopene intake was not associated with prostate cancer risk. Reduced risks were also not found for total tomato servings or for most tomato-based foods. Statistically nonsignificant inverse associations were noted for pizza [all prostate cancer: relative risk (RR), 0.83; 95% confidence interval (95% CI), 0.67-1.03 for >or=1 serving/wk versus < 0.5 serving/mo; P(trend)=0.06 and advanced prostate cancer: RR, 0.79; 95% CI, 0.56-1.10; P(trend)=0.12] and spaghetti/tomato sauce consumption (advanced prostate cancer: RR=0.81,	PC	N			N	

				95% CI, 0.57-1.16 for >or=2 servings/wk versus<1 serving/mo; P(trend)=0.31). Among men with a family history of prostate cancer, risks were decreased in relation to increased consumption of lycopene (P(trend)=0.04) and specific tomato-based foods commonly eaten with fat (spaghetti, P(trend)=0.12; pizza, P(trend)=0.15; lasagna, P(trend)=0.02). CONCLUSIONS: This large study does not support the hypothesis that greater lycopene/tomato product consumption protects from prostate cancer. Evidence for protective associations in subjects with a family history of prostate cancer requires further corroboration. (Cancer Epidemiol Biomarkers Prev 2006;15(1):92-8).						
Cancer: prostate	Darlington GA	Prostate cancer risk and diet, recreational physical activity and cigarette smoking. Darlington GA, Kreiger N, Lightfoot N, Purdham J, Sass-Kortsak A. Chronic Dis Can. 2007;27(4):145-53.	2007	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 percent CI: 1.2-2.0). Associations were observed for tomato or vegetable juices and ketchup (OR=1.5; 95 percent CI: 1.2-1.9; OR=1.2; 95 percent 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 percent CI: 0.6-0.9). While the	CC	(+)				

				recreational physical activity association was consistent with results from previous studies, the tomato products association was not.						
Cancer: prostate	Giovannucci E	Risk factors for prostate cancer incidence and progression in the health professionals follow-up study. Giovannucci E, Liu Y, Platz EA, Stampfer MJ, Willett WC. Int J Cancer. 2007 Oct 1;121(7):1571-8.	2007	Risk factors for prostate cancer could differ for various sub-groups, such as for "aggressive" and "non-aggressive" cancers or by grade or stage. Determinants of mortality could differ from those for incidence. Using data from the Health Professionals Follow-Up Study, we re-examined 10 factors (cigarette smoking history, physical activity, BMI, family history of prostate cancer, race, height, total energy consumption, and intakes of calcium, tomato sauce and alpha-linolenic acid) using multivariable Cox regression in relation to multiple subcategories for prostate cancer risk. These were factors that we previously found to be predictors of prostate cancer incidence or advanced prostate cancer in this cohort, and that have some support in the literature. In this analysis, only 4 factors had a clear statistically significant association with overall incident prostate cancer: African-American race, positive family history, higher tomato sauce intake (inversely) and alpha-linolenic acid intake. In contrast, for fatal prostate cancer, recent smoking history, taller height, higher BMI, family history, and high intakes of total energy, calcium and alpha-linolenic acid were associated with a statistically significant increased risk. Higher vigorous physical activity level was associated with lower risk. In relation to these risk factors, advanced stage at diagnosis was a good surrogate for fatal prostate cancer, but high-grade (Gleason >/= 7 or Gleason >/= 8) was not. Only for high calcium intake was there a close correspondence for associations among high-grade cancer, advanced and fatal prostate cancer. Tomato sauce (inversely) and alpha-linolenic acid (positively) intakes were strong	PC		(-) ↓ risk prostate cancer			

				predictors of advanced cancer among those with low-grade cancers at diagnosis. Although the proportion of advanced stage cancers was much lower after PSA screening began, risk factors for advanced stage prostate cancers were similar in the pre-PSA and PSA era. The complexity of the clinical and pathologic manifestations of prostate cancer must be considered in the design and interpretation of studies.						
Cancer: prostate	Grainger EM	A combination of tomato and soy products for men with recurring prostate cancer and rising prostate specific antigen. Grainger EM, Schwartz SJ, Wang S, Unlu NZ, Boileau TW, Ferketich AK, Monk JP, Gong MC, Bahnson RR, DeGroff VL, Clinton SK. Nutr Cancer. 2008;60(2):145-54.	2008	Tomato and soy products are hypothesized to reduce the risk of prostate cancer or enhance efficacy of therapy. A study was completed to determine if men with active prostate cancer will adhere to a dietary intervention rich in tomato products and a soy protein supplement men (n = 41) with recurrent, asymptomatic prostate cancer were randomized among 2 groups: Group A (n = 20) consumed tomato products (no soy) for Weeks 0 through 4, targeting a minimum of 25 mg of lycopene/day. Group B (n = 21) consumed soy (no tomatoes) for Weeks 0 through 4, providing 40 g of soy protein/day. For Weeks 4 through 8, all men consumed a combined tomato-rich diet and soy supplements. No grade II through IV toxicities were observed. During Weeks 0 through 4, mean daily lycopene intake for Group A was 43 mg (+/- 15 mg) and mean soy intake for Group B was 39 g (+/- 1 g), remaining similar during Weeks 4 through 8. Serum lycopene increased from 0.72 +/- 0.09 micromol/l to 1.21 +/- 0.10 micromol/l (P < 0.0001) and urinary isoflavone excretion increased from not detectable to 54.1 +/- 5.7 micromol/l (P < 0.05) with 8 wk of diet intervention. Serum prostate-specific antigen decreased between Weeks 0 and 8 for 14 / 41 men (34%). Mean serum vascular endothelial growth factor for the entire group was reduced from 87 to 51 ng/ml (P < 0.05) over 8 wk. In conclusion,	RCT	(-) ↓ PSA levels ↓ vascular endothelial growth factor				(+) ↑ serum [lyco]

				prostate cancer patients will consume diets rich in tomato products and soy with excellent compliance and bioavailability of phytochemicals. Further studies combining tomato and soy foods to determine efficacy for prostate cancer prevention or management are encouraged.						
Cancer: prostate	Talvas J	Differential effects of lycopene consumed in tomato paste and lycopene in the form of a purified extract on target genes of cancer prostatic cells. Talvas J, Caris-Veyrat C, Guy L, Rambeau M, Lyan B, Minet-Quinard R, Lobaccaro JM, Vasson MP, Georgé S, Mazur A, Rock E. Am J Clin Nutr. 2010 Jun;91(6):1716-24. Epub 2010 Apr 14	2010	BACKGROUND: Prospective studies indicate that tomato consumers are protected against prostate cancer. Lycopene has been hypothesized to be responsible for tomato health benefits. OBJECTIVE: Our aim was to differentiate the effects of tomato matrix from those of lycopene by using lycopene-rich red tomatoes, lycopene-free yellow tomatoes, and purified lycopene. DESIGN: Thirty healthy men (aged 50-70 y old) were randomly assigned to 2 groups after a 2-wk washout period. In a crossover design, each group consumed yellow and red tomato paste (200 g/d, which provided 0 and 16 mg lycopene, respectively) as part of their regular diet for 1 wk separated by 2 wk of washout. Then, in a parallel design, the first group underwent supplementation with purified lycopene (16 mg/d) for 1 wk, whereas the second group received a placebo. Sera collected before and after the interventions were incubated with lymph node cancer prostate cells to measure the expression of 45 target genes. RESULTS: Circulating lycopene concentration increased only after consumption of red tomato paste and purified lycopene. Lipid profile, antioxidant status, prostate-specific antigen, and insulin-like growth factor I were not modified by consumption of tomato pastes and lycopene. We observed significant up-regulation of IGFBP-3 and Bax:Bcl-2 ratio and down-regulation of cyclin-D1, p53, and Nrf-2 after cell incubation with sera from men who consumed red tomato paste when compared with	RCT		N Lipids Ox status PSA IGF-1		N Lipids Ox status PSA IGF-1	

				sera collected after the first washout period, with intermediate values for yellow tomato paste consumption. Cell incubation with sera from men who consumed purified lycopene led to significant up-regulation of IGFBP-3, c-fos, and uPAR compared with sera collected after placebo consumption. CONCLUSION: Dietary lycopene can affect gene expression whether or not it is included in its food matrix. This trial was registered by the French Health Ministry at http://www.sante-sports.gouv.fr as 2006-A00396-45.						
Cancer: prostate	Richman EL	Vegetable and fruit intake after diagnosis and risk of prostate cancer progression. Richman EL, Carroll PR, Chan JM. Int J Cancer. 2011 Aug 5. doi: 10.1002/ijc.26348. [Epub ahead of print]	2011	Cruciferous vegetables, tomato sauce, and legumes have been associated with reduced risk of incident advanced prostate cancer. In vitro and animal studies suggest these foods may inhibit progression of prostate cancer, but there are limited data in men. Therefore, we prospectively examined whether intake of total vegetables, and specifically cruciferous vegetables, tomato sauce, and legumes, after diagnosis reduce risk of prostate cancer progression among 1,560 men diagnosed with non-metastatic prostate cancer and participating in the Cancer of the Prostate Strategic Urologic Research Endeavor, a United States prostate cancer registry. As a secondary analysis, we also examined other vegetable sub-groups, total fruit, and sub-groups of fruits. The participants were diagnosed primarily at community-based clinics and followed from 2004-2009. We assessed vegetable and fruit intake via a semi-quantitative food frequency questionnaire, and ascertained prostate cancer outcomes via urologist report and medical records. We observed 134 events of progression (53 biochemical recurrences, 71 secondary treatments likely due to recurrence, six bone metastases, four prostate cancer	PC		N			Prostate cancer progression

				deaths) during 3,171 person-yrs. Men in the fourth quartile of post-diagnostic cruciferous vegetable intake had a statistically significant 59% decreased risk of prostate cancer progression compared to men in the lowest quartile (hazard ratio (HR): 0.41; 95% confidence interval (CI): 0.22, 0.76; p-trend: 0.003). No other vegetable or fruit group was statistically significantly associated with risk of prostate cancer progression. In conclusion, cruciferous vegetable intake after diagnosis may reduce risk of prostate cancer progression.						