Dietary Lycopene and Disease Risk
Cancer Risk Reviews

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 Risk Reviews	Peto R	Can dietary beta-carotene materially reduce human cancer rates? Peto R, Doll R, Buckley JD, Sporn MB. Nature. 1981 Mar 19;290(5803):201-8.	1981	Human cancer risks are inversely correlated with (a) blood retinol and (b) dietary beta-carotene. Although retinol in the blood might well be truly protective, this would be of little immediate value without discovery of the important external determinants of blood retinol which (in developed countries) do not include dietary retinol or beta-carotene. If dietary beta-carotene is truly protective--which could be tested by controlled trials--there are a number of theoretical mechanisms whereby it might act, some of which do not directly involve its 'provitamin A' activity.	Review					
Cancer Risk Reviews	Weisburger JH	Mechanisms of action of antioxidants as exemplified in vegetables, tomatoes and tea. Weisburger JH. Food Chem Toxicol. 1999 Sep-Oct;37(9-10):943-8.	1999	Most chronic diseases, including coronary heart disease and many types of cancer depend on the in vivo conversion of cellular macromolecules or of carcinogens to specific reactive, oxidized forms. For that reason, health promoting nutrition involves the daily intake of five to 10 vegetables and fruits, fruit juices, red wine and tea that are rich sources of micronutrients with antioxidant properties, including the antioxidant	Review	(-) ↓ pre and neoplastic cell growth ↓ active oxygen and peroxy compnds				

				vitamins C, E and beta-carotene. Tomatoes contain lycopene, a stable, active antioxidant. Many vegetables contain quercetin and related polyphenolic compounds. Tea is a source of epigallocatechin gallate, in green tea, and theaflavin and the associated thearubigins, in black tea. Red wine contains resveratrol. The diverse antioxidants in foods, red wine and tea provide the necessary antioxidant resources for the body to control oxidation reactions in the body with possible adverse consequences. For example, the oxidation of low density lipoprotein (LDL) cholesterol yields a product that damages the vascular system. Thus, a lower intake of saturated fats to decrease the levels of LDL cholesterol, together with an adequate intake of antioxidants, is the optimal approach to lower heart disease risk. Cancer of the stomach involves the consumption of salted, pickled foods yielding direct-acting carcinogens, and their formation is inhibited by vitamins C and E. Cancer in the colon, breast, prostate and pancreas may be caused by a new class of carcinogens, the heterocyclic amines, formed during the broiling or frying of creatinine-containing foods, including fish and meats. Their formation and action can be inhibited by antioxidants such as those in soy, tea, vitamin C and also by the synthetic						

				antioxidants BHA or BHT. The growth, cell proliferation and development of abnormal preneoplastic and neoplastic cells also involves oxidation reactions, including the formation of active oxygen or peroxy compounds. Such reactions can be inhibited by antioxidants, such as those in tea, tomatoes or vegetables. Even ageing and longevity in good health would be favoured by the availability of adequate amounts of varied antioxidants. Prevention of the formation and of action of reactive products by antioxidants as present in fruits, vegetables, tomatoes, red wine and tea is of great public health importance in decreasing the risk of major diseases. Prevention is the optimal approach to disease control, and also as an effective route to lower costs of medical care.						
Cancer Risk Reviews	Agarwal S	Tomato lycopene and its role in human health and chronic diseases. Agarwal S, Rao AV. CMAJ. 2000 Sep 19;163(6):739-44.	2000	Lycopene is a carotenoid that is present in tomatoes, processed tomato products and other fruits. It is one of the most potent antioxidants among dietary carotenoids. Dietary intake of tomatoes and tomato products containing lycopene has been shown to be associated with a decreased risk of chronic diseases, such as cancer and cardiovascular disease. Serum and tissue lycopene levels have been found to be inversely related to the incidence of several types of cancer, including breast cancer and prostate	Review					

				cancer. Although the antioxidant properties of lycopene are thought to be primarily responsible for its beneficial effects, evidence is accumulating to suggest that other mechanisms may also be involved. In this article we outline the possible mechanisms of action of lycopene and review the current understanding of its role in human health and disease prevention						
Cancer Risk Reviews	Montesano R	Environmental causes of human cancers. Montesano R, Hall J. Eur J Cancer. 2001 Oct;37 Suppl 8:S67-87.	2001	Epidemiological studies have clearly shown a causal association between tobacco exposure and various human cancers, hepatitis B and C infection and hepatocellular carcinoma, human papilloma viruses and cervical cancer, and the occupational origin of certain human cancers is well established. The identification of the environmental causes of human cancers has been a long and difficult process. Much remains to be understood about the role of specific components of the diet and the interaction of different risk factors in the aetiology of human cancers. Withstanding the progress made on the understanding of the cancer process and their potential impact in the therapy of cancer, primary prevention remains, in developed and developing countries, the most effective measure to reduce cancer mortality.	Review					

Cancer Risk Reviews	Cohen LA.	A review of animal model studies of tomato carotenoids, lycopene, and cancer chemoprevention. Cohen LA. Exp Biol Med (Maywood). 2002 Nov;227(10):864-8.	2002	There are relatively few reports on the cancer chemopreventive effects of lycopene or tomato carotenoids in animal models. The majority, but not all, of these studies indicate a protective effect. Inhibitory effects were reported in two studies using aberrant crypt foci, an intermediate lesion leading to colon cancer, as an end point and in two mammary tumor studies, one using the dimethylbenz(a)anthracene model, and the other the spontaneous mouse model. Inhibitory effects were also reported in mouse lung and rat hepatocarcinoma and bladder cancer models. However, a report from the author's laboratory found no effect in the N-nitrosomethylurea-induced mammary tumor model when crystalline lycopene or a lycopene-rich tomato carotenoid oleoresin was administered in the diet. Unfortunately, because of differences in routes of administration (gavage, intraperitoneal injection, intra-rectal instillation, drinking water, and diet supplementation), species and strain differences, form of lycopene (pure crystalline, beadlet, mixed carotenoid suspension), varying diets (grain-based, casein based) and dose ranges (0.5-500 ppm), no two studies are comparable. It is clear that the majority of ingested lycopene is excreted in the feces and that 1000-fold	Review					

				more lycopene is absorbed and stored in the liver than accumulates in other target organs. Nonetheless, physiologically significant (nanogram) levels of lycopene are assimilated by key organs such as breast, prostate, lung, and colon, and there is a rough dose-response relationship between lycopene intake and blood levels. Pure lycopene was absorbed less efficiently than the lycopene-rich tomato carotenoid oleoresin and blood levels of lycopene in rats fed a grain-based diet were consistently lower than those in rats fed lycopene in a casein-based diet. The latter suggests that the matrix in which lycopene is incorporated is an important determinant of lycopene uptake. A number of issues remain to be resolved before any definitive conclusions can be drawn concerning the anticancer effects of lycopene. These include the following: the optimal dose and form of lycopene, interactions among lycopene and other carotenoids and fat soluble vitamins such as vitamin E and D, the role of dietary fat in regulating lycopene uptake and disposition, organ and tissue specificity, and the problem of extrapolation from rodent models to human populations.					
Cancer Risk Reviews	Etminan M	The role of tomato products and lycopene in the prevention of	2004	PURPOSE: To determine whether intake of tomato products reduces the risk of	Meta-Analysis	(-)	(-)	N	N/(-)	

		prostate cancer: a metaanalysis of observational studies. Etminan M, Takkouche B, Caamano-Isorna F. Cancer Epidemiol Biomarkers Prev. 2004;13(3):340–345.		prostate cancer using a meta-analysis. METHODS: We systematically searched MEDLINE and EMBASE and contacted authors to identify potential studies. Log relative risks (RRs) were weighed by the inverse of their variances to obtain a pooled estimate with its 95% confidence interval (CI). Logistic regression and Poisson regression analyses were used to determine the effect produced by a daily intake of one serving of tomato product. RESULTS: Eleven case-control studies and 10 cohort studies or nested case-control studies presented data on the use of tomato, tomato products, or lycopene and met our inclusion criteria. Compared with nonfrequent users of tomato products (1st quartile of intake), the RR of prostate cancer among consumers of high amounts of raw tomato (5th quintile of intake) was 0.89 (95% CI 0.80-1.00). For high intake of cooked tomato products, this RR was 0.81 (95% CI 0.71-0.92). The RR of prostate cancer related to an intake of one serving/day of raw tomato (200 g) was 0.97 (95% CI 0.85-1.10) for the case-control studies and 0.78 (95% CI 0.66-0.92) for cohort studies. CONCLUSIONS: Our results show that tomato products may play a role in the prevention of prostate cancer. However, this effect is modest and restricted to high amounts of tomato intake. Further research is needed to determine the	Specific to prostate cancer	High intake >200g				

				type and quantity of tomato products with respect to their role in preventing prostate cancer.						
Cancer Risk Reviews	Aggarwal BB	Molecular targets of dietary agents for prevention and therapy of cancer. Aggarwal BB, Shishodia S. Biochem Pharmacol. 2006 May 14;71(10):1397-421. Epub 2006 Feb 23.	2006	While fruits and vegetables are recommended for prevention of cancer and other diseases, their active ingredients (at the molecular level) and their mechanisms of action less well understood. Extensive research during the last half century has identified various molecular targets that can potentially be used not only for the prevention of cancer but also for treatment. However, lack of success with targeted monotherapy resulting from bypass mechanisms has forced researchers to employ either combination therapy or agents that interfere with multiple cell-signaling pathways. In this review, we present evidence that numerous agents identified from fruits and vegetables can interfere with several cell-signaling pathways. The agents include curcumin (turmeric), resveratrol (red grapes, peanuts and berries), genistein (soybean), diallyl sulfide (allium), S-allyl cysteine (allium), allicin (garlic), lycopene (tomato), capsaicin (red chilli), diosgenin (fenugreek), 6-gingerol (ginger), ellagic acid (pomegranate), ursolic acid (apple, pears, prunes), silymarin (milk thistle), anethol (anise, camphor, and fennel), catechins (green tea),	Review					

				eugenol (cloves), indole-3-carbinol (cruciferous vegetables), limonene (citrus fruits), beta carotene (carrots), and dietary fiber. For instance, the cell-signaling pathways inhibited by curcumin alone include NF-kappaB, AP-1, STAT3, Akt, Bcl-2, Bcl-X(L), caspases, PARP, IKK, EGFR, HER2, JNK, MAPK, COX2, and 5-LOX. The active principle identified in fruit and vegetables and the molecular targets modulated may be the basis for how these dietary agents not only prevent but also treat cancer and other diseases. This work reaffirms what Hippocrates said 25 centuries ago, let food be thy medicine and medicine be thy food.						
Cancer Risk Reviews	Divisi D	Diet and cancer. Divisi D, Di Tommaso S, Salvemini S, Garramone M, Crisci R. Acta Biomed. 2006 Aug;77(2):118-23.	2006	The aim of our study is to evaluate the relationship between diet and cancer development. It has been estimated that 30-40% of all kinds of cancer can be prevented with a healthy lifestyle and dietary measures. A low use of fibres, the intake of red meat and an imbalance of Omega-3 and Omega-6 fats may contribute to increase the risk of cancer. On the other hand, the assumption of lots of fruit and vegetables may lower the risk of cancer. Protective elements in a cancer-preventive diet include selenium, folic acid, vitamin B12, vitamin D, chlorophyll and antioxidants such as carotenoids (alpha-carotene, beta-carotene,	Review					

				lycopene, lutein, cryptoxanthin). Ascorbic acid has limited benefits if taken orally, but it effective through intravenous injection. A supplementary use of oral digestive enzymes and probiotics is also an anticancer dietary measure. A diet drawn up according to the proposed guidelines could decrease the incidence of breast, colon-rectal, prostate and bronchogenic cancer.						
Cancer Risk Reviews	Kavanaugh CJ	The U.S. Food and Drug Administration's evidence-based review for qualified health claims: tomatoes, lycopene, and cancer. Kavanaugh CJ, Trumbo PR, Ellwood KC. J Natl Cancer Inst. 2007 Jul 18;99(14):1059. J Natl Cancer Inst. 2007 Jul 18;99(14):1060-2.	2007	Several studies have reported an inverse association between tomato and/or lycopene intake and the risk of some types of cancer. In 2004, the U.S. Food and Drug Administration (FDA) received two petitions for qualified health claims regarding tomatoes, lycopene, and the risk reduction for some forms of cancer. Health claims that characterize the relationship between a food or food component and a disease or health-related condition require premarket approval by FDA to be included on the labels of conventional foods and dietary supplements. Here we describe FDA's review of the scientific data for tomato and/or lycopene intake with respect to risk reduction for certain forms of cancer. The FDA found no credible evidence to support an association between lycopene intake and a reduced risk of prostate, lung, colorectal, gastric, breast, ovarian, endometrial, or	Review	N/(-) ↓ cancer risk			N ↓ cancer risk	

				pancreatic cancer. The FDA also found no credible evidence for an association between tomato consumption and a reduced risk of lung, colorectal, breast, cervical, or endometrial cancer. The FDA found very limited evidence to support an association between tomato consumption and reduced risks of prostate, ovarian, gastric, and pancreatic cancers.						
Cancer Risk Reviews	Gallicchio L	Carotenoids and the risk of developing lung cancer: a systematic review. Gallicchio L, Boyd K, Matanoski G, Tao XG, Chen L, Lam TK, Shiels M, Hammond E, Robinson KA, Caulfield LE, Herman JG, Guallar E, Alberg AJ. Am J Clin Nutr. 2008 Aug;88(2):372-83.	2008	BACKGROUND: Carotenoids are thought to have anti-cancer properties, but findings from population-based research have been inconsistent. OBJECTIVE: We aimed to conduct a systematic review of the associations between carotenoids and lung cancer. DESIGN: We searched electronic databases for articles published through September 2007. Six randomized clinical trials examining the efficacy of beta-carotene supplements and 25 prospective observational studies assessing the associations between carotenoids and lung cancer were analyzed by using random-effects meta-analysis. RESULTS: The pooled relative risk (RR) for the studies comparing beta-carotene supplements with placebo was 1.10 (95% confidence limits: 0.89, 1.36; P = 0.39). Among the observational studies that adjusted for smoking, the pooled RRs comparing	Review 6 RCT 25 PC				(-)	

				highest and lowest categories of total carotenoid intake and of total carotenoid serum concentrations were 0.79 (0.71, 0.87; P < 0.001) and 0.70 (0.44, 1.11; P = 0.14), respectively. For beta-carotene, highest compared with lowest pooled RRs were 0.92 (0.83, 1.01; P = 0.09) for dietary intake and 0.84 (0.66, 1.07; P = 0.15) for serum concentrations. For other carotenoids, the RRs comparing highest and lowest categories of intake ranged from 0.80 for beta-cryptoxanthin to 0.89 for alpha-carotene and lutein-zeaxanthin; for serum concentrations, the RRs ranged from 0.71 for lycopene to 0.95 for lutein-zeaxanthin. CONCLUSIONS: beta-Carotene supplementation is not associated with a decrease in the risk of developing lung cancer. Findings from prospective cohort studies suggest inverse associations between carotenoids and lung cancer; however, the decreases in risk are generally small and not statistically significant. These inverse associations may be the result of carotenoid measurements' function as a marker of a healthier lifestyle (higher fruit and vegetable consumption) or of residual confounding by smoking.						
Cancer Risk Reviews	Khan N	Cancer chemo-prevention through dietary antioxidants: progress and promise.	2008	It is estimated that nearly one-third of all cancer deaths in the United States could be prevented through	Review					

		Khan N, Afaq F, Mukhtar H. Antioxid Redox Signal. 2008 Mar;10(3):475-510. Review		appropriate dietary modification. Various dietary antioxidants have shown considerable promise as effective agents for cancer prevention by reducing oxidative stress which has been implicated in the development of many diseases, including cancer. Therefore, for reducing the incidence of cancer, modifications in dietary habits, especially by increasing consumption of fruits and vegetables rich in antioxidants, are increasingly advocated. Accumulating research evidence suggests that many dietary factors may be used alone or in combination with traditional chemotherapeutic agents to prevent the occurrence of cancer, their metastatic spread, or even to treat cancer. The reduced cancer risk and lack of toxicity associated with high intake of fruits and vegetables suggest that specific concentrations of antioxidant agents from these dietary sources may produce cancer chemopreventive effects without causing significant levels of toxicity. This review presents an extensive analysis of the key findings from studies on the effects of dietary antioxidants such as tea polyphenols, curcumin, genistein, resveratrol, lycopene, pomegranate, and lupeol against cancers of the skin, prostate, breast, lung, and liver. This research is also leading to the					

				identification of novel cancer drug targets.						
Cancer Risk Reviews	Liu C	Nutrition and gastric cancer risk: an update. Liu C, Russell RM. Nutr Rev. 2008 May;66(5):237-49.	2008	Data from epidemiologic, experimental, and animal studies indicate that diet plays an important role in the etiology of gastric cancer. High intake of fresh fruits and vegetables, lycopene and lycopene-containing food products, and potentially vitamin C and selenium may reduce the risk for gastric cancer. Data also suggest that high intake of nitrosamines, processed meat products, salt and salted foods, and overweight and obesity are associated with increased risk for gastric cancer. However, current data provide little support for an association of beta-carotene, vitamin E, and alcohol consumption with risk for gastric cancer.	Review					N
Cancer Risk Reviews	Mein JR	Biological activity of lycopene metabolites: implications for cancer prevention. Mein JR, Lian F, Wang XD. Nutr Rev. 2008 Dec;66(12):667-83.	2008	While early studies focused on the potential roles in health and disease of provitamin A carotenoids, such as beta-carotene, research over the past decade has provided a framework for our understanding of the functions of non-provitamin A carotenoids such as lycopene, especially in regards to its association with a reduced risk of a number of chronic diseases, including cancer. Recent data suggests that lycopene metabolites may possess specific biological activities on several important cellular	Review				(-) lyco meta-bolites may↓ risk prostate cancer	

				signaling pathways and molecular targets. Carotenoid metabolites may have more important biological roles than their parent compounds in human health and disease. This notion has been reinforced by the observation of both beneficial and detrimental effects of carotenoid metabolites in cancer prevention.						
Cancer Risk Reviews	Seren S	Potential role of lycopene in the treatment of hepatitis C and prevention of hepatocellular carcinoma. Seren S, Mutchnick M, Hutchinson D, Harmanci O, Bayraktar Y, Mutchnick S, Sahin K, Kucuk O. Nutr Cancer. 2008;60(6):729-35.	2008	Hepatitis C virus (HCV) infection and hepatocellular carcinoma (HCC) are growing health problems around the world. Oxidative stress plays a significant role in the initiation and progression of hepatocellular damage and possibly in the development of HCC in HCV infected patients. In vitro, animal and clinical studies suggest that lycopene, a nonprovitamin A carotenoid and a potent antioxidant, may attenuate the liver injury and possibly prevent the development of HCC. In this article, we discuss the relationship between HCV infection and oxidative stress and review the potential role of lycopene in the treatment of HCV and prevention of HCC.					(-) ↓ liver injury	
Cancer Risk Reviews	van Breemen RB	Multitargeted therapy of cancer by lycopene. van Breemen RB, Pajkovic N. Cancer Lett. 2008 Oct	2008	Lycopene (psi,psi-carotene) is the most abundant carotenoid in tomatoes and is the red pigment of not only tomatoes but also rosehips, watermelon, papaya, pink grapefruit, and guava. Unlike beta-carotene, lycopene	Review				N as a chemo-protective agent, needs further study	

		8;269(2):339-51. Epub 2008 Jun 27.		lacks a beta-ionone ring and therefore has no pro-vitamin A activity. However, the 11 conjugated and two non-conjugated double bonds in lycopene make it highly reactive towards oxygen and free radicals, and this anti-oxidant activity probably contributes to its efficacy as a chemoprevention agent. The reactivity of lycopene also explains why it isomerizes rapidly in blood and tissues from the biosynthetic all-trans form to a mixture of cis-isomers. Prospective and retrospective epidemiological studies indicating an inverse relationship between lycopene intake and prostate cancer risk have been supported by in vitro and in vivo experiments showing that oral lycopene is bioavailable, accumulates in prostate tissue and is localized to the nucleus of prostate epithelial cells. In addition to antioxidant activity, in vitro experiments indicate other mechanisms of chemoprevention by lycopene including induction of apoptosis and antiproliferation in cancer cells, anti-metastatic activity, and the upregulation of the antioxidant response element leading to the synthesis of cytoprotective enzymes. Lycopene is a substrate for carotene-9',10'-monooxygenase (CMO2) and can be converted to apo-10'-carotenal. Although Phase I and II studies have been published that establish the safety of lycopene						

				supplementation, carefully designed and adequately powered clinical studies of lycopene are still needed to confirm its efficacy as a chemoprevention agent.						
Cancer Risk Reviews	Coyle YM	Lifestyle, genes, and cancer. Coyle YM. Methods Mol Biol. 2009;472:25-56.	2009	It is estimated that almost 1.5 million people in the USA are diagnosed with cancer every year. However, due to the substantial effect of modifiable lifestyle factors on the most prevalent cancers, it has been estimated that 50% of cancer is preventable. Physical activity, weight loss, and a reduction in alcohol use can strongly be recommended for the reduction of breast cancer risk. Similarly, weight loss, physical activity, and cessation of tobacco use are important behavior changes to reduce colorectal cancer risk, along with the potential benefit for the reduction of red meat consumption and the increase in folic acid intake. Smoking cessation is still the most important prevention intervention for reducing lung cancer risk, but recent evidence indicates that increasing physical activity may also be an important prevention intervention for this disease. The potential benefit of lifestyle change to reduce prostate cancer risk is growing, with recent evidence indicating the importance of a diet rich in tomato-based foods and weight loss. Also, in the cancers for which there are	Review				N However, might ↓ risk by ↓ free radical production= ↓ gene mutatioins= ↓ cancer risk	

				established lifestyle risk factors, such as physical inactivity for breast cancer and obesity for colorectal cancer, there is emerging information on the role that genetics plays in interacting with these factors, as well as the interaction of combinations of lifestyle factors. Integration of genetic information into lifestyle factors can help to clarify the causal relationships between lifestyle and genetic factors and assist in better identifying cancer risk, ultimately leading to better-informed choices about effective methods to enhance health and prevent cancer.						
Cancer Risk Reviews	Musa-Veloso K	Influence of observational study design on the interpretation of cancer risk reduction by carotenoids. Musa-Veloso K, Card JW, Wong AW, Cooper DA. Nutr Rev. 2009 Sep;67(9):527-45.	2009	Recently published literature has been reviewed to determine whether lycopene, beta-carotene, alpha-carotene, and beta-cryptoxanthin are associated with reductions in cancer risk and whether study findings differ by study design. A total of 57 publications meeting pre-defined inclusion and exclusion criteria were identified, with the majority (55) being observational studies. None of the intervention studies supported a significant reduction in cancer risk with carotenoid (beta-carotene) supplementation. The majority of observational studies did not support significant reductions in cancer risk with increased carotenoid dietary intakes/circulating levels. A	Review					

				larger percentage of case-control studies supported significant associations between increased dietary intakes/circulating levels of carotenoids relative to prospective (cohort and nested case-control) studies. Compared to prospective studies, case-control studies cannot be used to establish temporality and may be more susceptible to selection and recall biases. Thus, diet-disease relationships suggested by case-control studies should ideally be confirmed by additional evidence from prospective studies.						
Cancer Risk Reviews	Svennevig K	Re: "Long-term use of beta-carotene, retinol, lycopene, and lutein supplements and lung cancer risk: results from the VITamins and Lifestyle (VITAL) Study". Svennevig K. Am J Epidemiol. 2009 Aug 1;170(3):401-2. Epub 2009 Jul 15.	2009	In their recent article, Satia et al. (1) used data from the VITamins And Lifestyle (VITAL) Study to draw some conclusions about an association between intake of dietary supplements and lung cancer risk. A previous VITAL Study publication concluded that multivitamin use does not increase lung cancer risk (2). The current study focused on long-term use of individual supplements at high doses. The participants using individual lutein supplements were categorized as noncancer cases (n = 1,606) and lung cancer cases (n = 20). Relatively infrequent lutein supplement use by lung cancer cases made it impossible to divide the group with regard to dosage or duration of use. Satia et al. concluded that long-term use	Letter to editor					

				of high doses of individual β-carotene, retinol, and lutein supplements may be harmful in terms of lung cancer risk.						
Cancer Risk Reviews	Giovannucci E	Commentary: Serum lycopene and prostate cancer progression: a re-consideration of findings from the prostate cancer prevention trial. Giovannucci E. Cancer Causes Control. 2011 Jul;22(7):1055-9. Epub 2011 May 15.	2011	A recent analysis in the Prostate Cancer Prevention Trial (PCPT) appeared to show no association between serum lycopene and prostate cancer risk, but the unique study design of the PCPT and the complexity of prostate cancer epidemiology suggest an alternative interpretation of the reported findings.	Commentary					
Cancer Risk Reviews	Key TJ	Fruit and vegetables and cancer risk. Key TJ. Br J Cancer. 2011 Jan 4;104(1):6-11. Epub 2010 Nov 30.	2011	The possibility that fruit and vegetables may help to reduce the risk of cancer has been studied for over 30 years, but no protective effects have been firmly established. For cancers of the upper gastrointestinal tract, epidemiological studies have generally observed that people with a relatively high intake of fruit and vegetables have a moderately reduced risk, but these observations must be interpreted cautiously because of potential confounding by smoking and alcohol. For lung cancer, recent large prospective analyses with detailed adjustment for smoking have not shown a convincing association between fruit and vegetable intake and reduced risk. For other common cancers, including colorectal, breast and prostate cancer, epidemiological studies	Review					

				suggest little or no association between total fruit and vegetable consumption and risk. It is still possible that there are benefits to be identified: there could be benefits in populations with low average intakes of fruit and vegetables, such that those eating moderate amounts have a lower cancer risk than those eating very low amounts, and there could also be effects of particular nutrients in certain fruits and vegetables, as fruit and vegetables have very varied composition. Nutritional principles indicate that healthy diets should include at least moderate amounts of fruit and vegetables, but the available data suggest that general increases in fruit and vegetable intake would not have much effect on cancer rates, at least in well-nourished populations. Current advice in relation to diet and cancer should include the recommendation to consume adequate amounts of fruit and vegetables, but should put most emphasis on the well-established adverse effects of obesity and high alcohol intakes. Portion of above that has "tomato/lycopene" mention. Prostate cancer: The aetiology of prostate cancer is not well understood. Risk is increased in men with relatively high plasma concentrations of insulin-like growth factor-I, and levels of this growth factor can be affected by diet, but more research on this pathway is						

				needed (Roddam et al, 2008). In relation to fruit and vegetables, recent large prospective studies suggest that there is little or no association between total fruit and vegetable intake and prostate cancer risk (Kirsh et al, 2007). There has been much interest in the possibility that fruits and vegetables, such as tomatoes, which are rich in the carotenoid lycopene might reduce the risk for prostate cancer, but overall the data do not support this hypothesis (Kavanaugh et al, 2007). Studies of soyabeans and prostate cancer have suggested that this vegetable may help to reduce risk, but the results are not conclusive (Hwang et al, 2009).						
Cancer Risk Reviews	Niclis C	Dietary Habits and Prostate Cancer Prevention: A Review of Observational Studies by Focusing on South America. Niclis C, Díaz MD, Eynard AR, Román MD, Vecchia CL. Nutr Cancer. 2011 Dec 2. [Epub ahead of print]	2011	There exist several works considering the association between diet and prostate cancer (PC) risk, but the issue is largely unsettled. This article systematically reviews the epidemiological studies on diet and risk of PC focusing on those carried out in countries of South America. There is some suggestion that dairy products, red meat, processed meat, a-linolenic fatty acids, as well as dietary patterns characterized by higher intakes of red and processed meat, eggs, and grains may play some role in the development of PC. There is no clear association with the intake of vegetables and fruits, lycopene, fats, and different types of fatty acids.	Review					

				The evidence on diet and PC is therefore inconclusive in general and specifically in South America. Particular attention must be paid to the study of cancer risk in some countries of South America because of the singularly risky dietary pattern consumed by its population						
Cancer Risk Reviews	Giovannucci E	Tomatoes, tomato-based products, lycopene, and cancer: review of the epidemiologic literature. Giovannucci E. J Natl Cancer Inst. 1999 Feb 17;91(4):317-31.	1999	The epidemiologic literature in the English language regarding intake of tomatoes and tomato-based products and blood lycopene (a compound derived predominantly from tomatoes) level in relation to the risk of various cancers was reviewed. Among 72 studies identified, 57 reported inverse associations between tomato intake or blood lycopene level and the risk of cancer at a defined anatomic site; 35 of these inverse associations were statistically significant. No study indicated that higher tomato consumption or blood lycopene level statistically significantly increased the risk of cancer at any of the investigated sites. About half of the relative risks for comparisons of high with low intakes or levels for tomatoes or lycopene were approximately 0.6 or lower. The evidence for a benefit was strongest for cancers of the prostate, lung, and stomach. Data were also suggestive of a benefit for cancers of the pancreas, colon and rectum,	Review	N/(-) ↓ cancer risk by ↑ fruit/vegetable intake		N/(-) ↓ cancer risk by ↑ fruit-vegetable intake		N/(-) ↓ cancer risk by having ↑ blood [lyco]

				esophagus, oral cavity, breast, and cervix. Because the data are from observational studies, a cause-effect relationship cannot be established definitively. However, the consistency of the results across numerous studies in diverse populations, for case-control and rospective studies, and for dietary-based and blood-based investigations argues against bias or confounding as the explanation for these findings. Lycopene may account for or contribute to these benefits, but this possibility is not yet proven and requires further study. Numerous other potentially beneficial compounds are present in tomatoes, and, conceivably, complex interactions among multiple components may contribute to the anticancer properties of tomatoes. The consistently lower risk of cancer for a variety of anatomic sites that is associated with higher consumption of tomatoes and tomato-based products adds further support for current dietary recommendations to increase fruit and vegetable consumption.						
Cancer Risk Reviews (renal cell)	Lee JE	Intakes of fruit, vegetables, and carotenoids and renal cell cancer risk: a pooled analysis of 13 prospective studies. Lee JE, Männistö S,	2009	Fruit and vegetable consumption has been hypothesized to reduce the risk of renal cell cancer. We conducted a pooled analysis of 13 prospective studies, including 1,478 incident cases of renal cell cancer (709	Review					

		Spiegelman D, Hunter DJ, Bernstein L, van den Brandt PA, Buring JE, Cho E, English DR, Flood A, Freudenheim JL, Giles GG, Giovannucci E, Håkansson N, Horn-Ross PL, Jacobs EJ, Leitzmann MF, Marshall JR, McCullough ML, Miller AB, Rohan TE, Ross JA, Schatzkin A, Schouten LJ, Virtamo J, Wolk A, Zhang SM, Smith-Warner SA. Cancer Epidemiol Biomarkers Prev. 2009 Jun;18(6):1730-9.		women and 769 men) among 530,469 women and 244,483 men followed for up to 7 to 20 years. Participants completed a validated food-frequency questionnaire at baseline. Using the primary data from each study, the study-specific relative risks (RR) were calculated using the Cox proportional hazards model and then pooled using a random effects model. We found that fruit and vegetable consumption was associated with a reduced risk of renal cell cancer. Compared with <200 g/d of fruit and vegetable intake, the pooled multivariate RR for >or=600 g/d was 0.68 [95% confidence interval (95% CI) = 0.54-0.87; P for between-studies heterogeneity = 0.86; P for trend = 0.001]. Compared with <100 g/d, the pooled multivariate RRs (95% CI) for >or=400 g/d were 0.79 (0.63-0.99; P for trend = 0.03) for total fruit and 0.72 (0.48-1.08; P for trend = 0.07) for total vegetables. For specific carotenoids, the pooled multivariate RRs (95% CIs) comparing the highest and lowest quintiles were 0.87 (0.73-1.03) for alpha-carotene, 0.82 (0.69-0.98) for beta-carotene, 0.86 (0.73-1.01) for beta-cryptoxanthin, 0.82 (0.64-1.06) for lutein/zeaxanthin, and 1.13 (0.95-1.34) for lycopene. In conclusion, increasing fruit and vegetable consumption is associated with decreasing risk of renal cell cancer; carotenoids present in fruit						

				and vegetables may partly contribute to this protection.						
Cancer Risk Reviews (prostate)	Rackley JD	Complementary and alternative medicine for advanced prostate cancer. Rackley JD, Clark PE, Hall MC. Urol Clin North Am. 2006 May;33(2):237-46, viii.	2006	Complimentary and alternative medicines (CAM) have increased drastically in popularity in the past decade. These are largely in the form of nutritional supplements. Despite a wealth of information sources on the subject, the fundamental problem with CAM herapies is a dearth of evidence-based medicine. Advanced prostate cancer has significant long-term morbidity, and there is a growing interest in alternative and complimentary forms of therapy that will improve the outcomes of patients who have recurrent or advanced prostate cancer while obviating the need for more toxic forms of therapy. In this article we summarize the use of some of the more common CAM nutritional supplements and review the scientific data that are available to support their use.	Review					
Cancer Risk Reviews (prostate)	Giovannucci E	Does prostate-specific antigen screening influence the results of studies of tomatoes, lycopene, and prostate cancer risk? Giovannucci E. J Natl Cancer Inst. 2007 Jul 18;99(14):1060-2. Epub 2007 Jul 10.	2007	In this issue of the Journal, Kavanaugh et al. (1) describe how the U. S. Food and Drug Administration (FDA) evaluated the scientific evidence for proposed qualified health claims for tomatoes and lycopene with respect to the risks of prostate cancer and other types of cancers. After the authors qualitatively reviewed the studies, they concluded that there was "a very low level of comfort that a relationship	Editorial				N	

				exists between the consumption of tomatoes and/or tomato sauce and prostate cancer risk." This conclusion is disappointing given that some initial studies of tomato product intake or circulating lycopene levels suggested an association with a reduced risk of prostate cancer, providing some hope for prostate cancer prevention (2–6). However, a number of recent studies, including some (7–9) too recent to be included in the review by Kavanaugh et al. (1), have not supported this association or have been equivocal. Should we now conclude that tomatoes or lycopene are unlikely to have any role in prostate carcinogenesis? Before we do, we should consider a potentially complicating factor, which is that most of the recent studies have been conducted in populations in which most prostate cancers are identified through prostate-specific antigen (PSA) screening. In interpreting the evidence for a risk factor in relation to prostate cancer risk, two major considerations are how PSA screening influences the diagnosis and epidemiology of prostate cancer and when during prostate carcinogenesis that risk factor is operative.					
Cancer Risk Reviews (skin)	Dinkova-Kostova AT	Phytochemicals as protectors against ultraviolet radiation: versatility of effects and	2008	Ultraviolet (UV) radiation is one of the most abundant carcinogens in our environment, and the	Review					

		mechanisms. Dinkova-Kostova AT. Planta Med. 2008 Oct;74(13):1548-59. Epub 2008 Aug 11.		development of non-melanoma skin cancers, the most common type of human malignancy worldwide, represents one of the major consequences of excessive exposure. Because of growing concerns that the level of UV radiation is increasing as a result of depletion of the stratospheric ozone and climate change, the development of strategies for protection of the skin is an urgent need. Many phytochemicals that belong to various families of secondary metabolites, such as alkaloids (caffeine, sanguinarine), flavonoids [(-)-epigallocatechin 3-gallate, genistein, silibinin], carotenoids (beta-carotene, lycopene), and isothiocyanates (sulforaphane), offer exciting platforms for the development of such protective strategies. These phytochemicals have been consumed by humans for many centuries as part of plant-rich diets and are presumed to be of low toxicity, an essential requirement for a chemoprotective agent. Mechanistically, they affect multiple signalling pathways and protect against UV radiation-inflicted damage by their ability to act as direct and indirect antioxidants, as well as anti-inflammatory and immunomodulatory agents. Such "pluripotent character" is a critical prerequisite for an agent that is designed to counteract the multiple					

				damaging effects of UV radiation. Especially attractive are inducers of the Keap1/Nrf2/ARE pathway, which controls the gene expression of proteins whose activation leads to enhanced protection against oxidants and electrophiles. Such protection is comprehensive, long-lasting, and unlikely to cause pro-oxidant effects or interfere with the synthesis of vitamin D.						
Cancer Risk Reviews (liver)	Glauert HP	Dietary antioxidants in the prevention of hepatocarcinogenesis: a review. Glauert HP, Calfee-Mason K, Stemm DN, Tharappel JC, Spear BT. Mol Nutr Food Res. 2010 Jul;54(7):875-96. Review.	2010	In this review, the role of dietary antioxidants in the prevention of hepatocarcinogenesis is examined. Both human and animal models are discussed. Vitamin C, vitamin E, and selenium are antioxidants that are essential in the human diet. A number of non-essential chemicals also contain antioxidant activity and are consumed in the human diet, mainly as plants or as supplements, including beta-carotene, ellagic acid, curcumin, lycopene, coenzyme Q(10), epigallocatechin gallate, N-acetyl cysteine, and resveratrol. Although some human and animal studies show protection against carcinogenesis with the consumption of higher amounts of antioxidants, many studies show no effect or an enhancement of carcinogenesis. Because of the conflicting results from these studies, it is difficult to make dietary recommendations as to	Review				N	

				whether consuming higher amounts of specific antioxidants will decrease the risk of developing hepatocellular carcinoma.						
Cancer Risk Reviews (lung)	Gallicchio L	Carotenoids and the risk of developing lung cancer: a systematic review. Gallicchio L, Boyd K, Matanoski G, Tao XG, Chen L, Lam TK, Shiels M, Hammond E, Robinson KA, Caulfield LE, Herman JG, Guallar E, Alberg AJ. Am J Clin Nutr. 2008 Aug;88(2):372-83. Review.	2008	BACKGROUND: Carotenoids are thought to have anti-cancer properties, but findings from population-based research have been inconsistent. OBJECTIVE: We aimed to conduct a systematic review of the associations between carotenoids and lung cancer. DESIGN: We searched electronic databases for articles published through September 2007. Six randomized clinical trials examining the efficacy of beta-carotene supplements and 25 prospective observational studies assessing the associations between carotenoids and lung cancer were analyzed by using random-effects meta-analysis. RESULTS: The pooled relative risk (RR) for the studies comparing beta-carotene supplements with placebo was 1.10 (95% confidence limits: 0.89, 1.36; P = 0.39). Among the observational studies that adjusted for smoking, the pooled RRs comparing highest and lowest categories of total carotenoid intake and of total carotenoid serum concentrations were 0.79 (0.71, 0.87; P < 0.001) and 0.70 (0.44, 1.11; P = 0.14), respectively. For beta-carotene, highest compared	Meta-Analysis				N	

				with lowest pooled RRs were 0.92 (0.83, 1.01; P = 0.09) for dietary intake and 0.84 (0.66, 1.07; P = 0.15) for serum concentrations. For other carotenoids, the RRs comparing highest and lowest categories of intake ranged from 0.80 for beta-cryptoxanthin to 0.89 for alpha-carotene and lutein-zeaxanthin; for serum concentrations, the RRs ranged from 0.71 for lycopene to 0.95 for lutein-zeaxanthin. CONCLUSIONS: beta-Carotene supplementation is not associated with a decrease in the risk of developing lung cancer. Findings from prospective cohort studies suggest inverse associations between carotenoids and lung cancer; however, the decreases in risk are generally small and not statistically significant. These inverse associations may be the result of carotenoid measurements' function as a marker of a healthier lifestyle (higher fruit and vegetable consumption) or of residual confounding by smoking.					
Cancer Risk Reviews (panc)	Nitsche C	Environmental risk factors for chronic pancreatitis and pancreatic cancer. Nitsche C, Simon P, Weiss FU, Fluhr G, Weber E, Gärtner S, Behn CO, Kraft M, Ringel J, Aghdassi A, Mayerle J, Lerch MM.	2011	Chronic pancreatitis has long been thought to be mainly associated with immoderate alcohol consumption. The observation that only ~10% of heavy drinkers develop chronic pancreatitis not only suggests that other environmental factors, such as tobacco smoke, are potent additional risk factors, but also that the genetic	Review					

		Dig Dis. 2011;29(2):235-42. Epub 2011 Jul 5.		component of pancreatitis is more common than previously presumed. Either disease-causing or protective traits have been indentified for mutations in different trypsinogen genes, the gene for the trypsin inhibitor SPINK1, chymotrypsinogen C, and the cystic fibrosis transmembane conductance regulator (CFTR). Other factors that have been proposed to contribute to pancreatitis are obesity, diets high in animal protein and fat, as well as antioxidant deficiencies. For the development of pancreatic cancer, preexisting chronic pancreatitis, more prominently hereditary pancreatitis, is a risk factor. The data on environmental risk factors for pancreatic cancer are, with the notable exception of tobacco smoke, either sparse, unconfirmed or controversial. Obesity appears to increase the risk of pancreatic cancer in the West but not in Japan. Diets high in processed or red meat, diets low in fruits and vegetables, phytochemicals such as lycopene and flavonols, have been proposed and refuted as risk or protective factors in different trials. The best established and single most important risk factor for cancer as well as pancreatitis and the one to clearly avoid is tobacco smoke.						

Cancer Risk Reviews (prostate)	Gerster H	The potential role of lycopene for human health. Gerster H. J Am Coll Nutr. 1997 Apr;16(2):109-26.	1997	Lycopene is one of the major carotenoids in Western diets and is found almost exclusively in tomatoes and tomato products. It accounts for about 50% of carotenoids in human serum. Among the common dietary carotenoids lycopene has the highest singlet oxygen quenching capacity in vitro. Other outstanding features are its high concentration in testes, adrenal gland and prostate. In contrast to other carotenoids its serum values are not regularly reduced by smoking or alcohol consumption but by increasing age. Remarkable inverse relationships between lycopene intake or serum values and risk have been observed in particular for cancers of the prostate, pancreas and to a certain extent of the stomach. In some of the studies lycopene was the only carotenoid associated with risk reduction. Its role in cancer risk reduction still needs to be clarified. Patients with HIV infection, inflammatory diseases and hyperlipidemia with and without lipid lowering treatment may have depleted lycopene serum concentrations. Before embarking on large-scale human trials the distribution of lycopene and its biological functions need to be further evaluated.	Review				(-) ↓ cancer risk by having ↑ blood [lyco]	
Cancer Risk Reviews (prostate)	Hadley CW	Tomatoes, lycopene, and prostate cancer: progress and promise.	2002	Prostate cancer has emerged as a major public health problem in nations that have	Review					

		Hadley CW, Miller EC, Schwartz SJ, Clinton SK. Exp Biol Med (Maywood). 2002 Nov;227(10):869-80.		an affluent culture with an aging population. The search for etiologic risk factors and an emphasis on the development of chemopreventive agents has gained momentum over the last decade. Among the landmark epidemiologic findings during this period has been the association between the consumption of tomato products and a lower risk of prostate cancer. The traditional reductionist scientific approach has led many investigators to propose that lycopene, a carotenoid consumed largely from tomato products, may be the component responsible for lowering the risk of prostate cancer. Thus, many laboratory and clinical studies are now underway with the goal of assessing the ability of pure lycopene to serve as a chemopreventive agent for prostate and other malignancies. The focus on lycopene should continue, and an improved understanding of lycopene absorption, distribution, role in antioxidant reactions, and metabolism is critical in the quest to elucidate mechanisms whereby this compound could possibly reduce prostate cancer risk. In contrast to the pharmacologic approach with pure lycopene, many nutritional scientists direct their attention upon the diverse array of tomato products as a complex mixture of biologically active phytochemicals that together						

				may have anti-prostate cancer benefits beyond those of any single constituent. These contrasting approaches will continue to be explored in clinical, laboratory and epidemiologic studies in the near future, providing hope that the next generation will benefit from this knowledge and experience a lower risk of prostate cancer.						
Cancer Risk Reviews (prostate)	Oh WK	Complementary and alternative therapies in prostate cancer. Oh WK, Small EJ. Semin Oncol 2002; 29: 575–584.	2002	Complementary and alternative therapies are used with increasing frequency in men with prostate cancer. However, little is known about the efficacy of such therapies for this cancer. While epidemiological data support the association between intake of certain micronutrients with development of prostate cancer, there exist limited prospective data that support the chemopreventative or therapeutic value of such nutritional agents in prostate cancer. To date, one of the most studied treatments has been PC-SPES, a combination of eight herbal therapies with activity against prostate cancer. Studies in cell lines of human prostate cancer demonstrate significant dose-dependent decreases in cellular viability after exposure to extracts of this agent. Clinical studies suggested that PC-SPES could reduce prostate specific antigen levels in patients with either androgen-dependent	Review					

				or androgen-independent prostate cancer. Toxicity was mild, although there was a low risk of thromboembolic events with such treatment. Manufacture of PC-SPES was recently halted, after revelations that the herbal combination was contaminated with warfarin, which led to a recall by the manufacturer. Subsequent analyses also revealed the presence of diethylstilbestrol (DES) and indomethicin in some lots of PC-SPES. Available data regarding other alternative therapies are reviewed as well. Semin Oncol 29:575-584.						
Cancer Risk Reviews (prostate)	Campbell JK	Tomato phytochemicals and prostate cancer risk. Campbell JK, Canene-Adams K, Lindshield BL, Boileau TW, Clinton SK, Erdman JW Jr. J Nutr. 2004 Dec;134(12 Suppl):3486S-3492S.	2004	Mounting evidence over the past decade suggests that the consumption of fresh and processed tomato products is associated with reduced risk of prostate cancer. The emerging hypothesis is that lycopene, the primary red carotenoid in tomatoes, may be the principle phytochemical responsible for this reduction in risk. A number of potential mechanisms by which lycopene may act have emerged, including serving as an important in vivo antioxidant, enhancing cell-to-cell communication via increasing gap junctions between cells, and modulating cell-cycle progression. Although the effect of lycopene is biologically relevant, the tomato is also an excellent source of nutrients, including	Review					

				folate, vitamin C, and various other carotenoids and phytochemicals, such as polyphenols, which also may be associated with lower cancer risk. Tomatoes also contain significant quantities of potassium, as well as some vitamin A and vitamin E. Our laboratory has been interested in identifying specific components or combination of components in tomatoes that are responsible for reducing prostate cancer risk. We carried out cell culture trials to evaluate the effects of tomato carotenoids and tomato polyphenols on growth of prostate cancer cells. We also evaluated the ability of freeze-dried whole-tomato powder or lycopene alone to reduce growth of prostate tumors in rats. This paper reviews the epidemiological evidence, evaluating the relationship between prostate cancer risk and tomato consumption, and presents experimental data from this and other laboratories that support the hypothesis that whole tomato and its phytochemical components reduce the risk of prostate cancer.						
Cancer Risk Reviews (prostate)	Bemis DL	Clinical trials of natural products as chemopreventive agents for prostate cancer. Bemis DL, Katz AE, Buttyan R.	2006	Epidemiological research on prostate cancer risk in men throughout the world has identified significant correlations between dietary habits and prostate cancer occurrence. These studies served as a catalyst for exploration into the potential	Review					

		Expert Opin Investig Drugs. 2006 Oct;15(10):1191-200.		of dietary substances to act as chemopreventive agents against this disease, and include green tea catechins, lycopene, soy isoflavones, pomegranate phenolics, selenium, vitamins E and D, curcumin and resveratrol. Before these agents (in the dietary or purified forms) can be recommended as useful chemopreventive strategies for patients, their activity must be confirmed in rigorously designed clinical trials. This review discusses the preclinical and clinical data available for these dietary agents and describes relevant clinical trials currently being conducted.						
Cancer Risk Reviews (prostate)	Bemis DL	The use of herbal and over-the-counter dietary supplements for the prevention of prostate cancer. Bemis DL, Capodice JL, Costello JE, Vorys GC, Katz AE, Buttyan R. Curr Urol Rep. 2006 May;7(3):166-74.	2006	Having a high probability of experiencing prostate cancer during their lifetime, men are increasingly seeking protection against this disease with the use of over-the-counter dietary supplements containing herbs, vitamins, or plant-derived biochemical agents. The use of these agents for prostate cancer prevention is driven by epidemiology supporting the idea that regional diets and consumption of specific dietary components (certain herbs, vitamins, isoflavones, and polyphenols) are associated with a lower risk for prostate cancer, in conjunction with basic research that is defining molecules within food substances that kill or suppress growth of cultured	Review				N	

				human prostate cancer cells. Moreover, there is a sense that these dietary agents lack side effects, although this assumption often is faulty. Unfortunately, at this time, there is insufficient clinical evidence to support the widespread use of these dietary supplements for chemoprevention of prostate cancer, although ongoing clinical trials of the most promising vitamins and minerals are approaching conclusion.						
Cancer Risk Reviews (prostate)	Ellinger S	Tomatoes, tomato products and lycopene in the prevention and treatment of prostate cancer: do we have the evidence from intervention studies? Ellinger S, Ellinger J, Stehle P. Curr Opin Clin Nutr Metab Care. 2006 Nov;9(6):722-7.	2006	PURPOSE OF REVIEW: Lycopene-rich foods such as fresh tomatoes and tomato products are discussed as potential effectors in the prevention and therapy of prostate cancer. This review provides an overview on the efficacy of supplementation with tomatoes, tomato products and lycopene on appropriate surrogate endpoint biomarkers such as DNA damage and metabolites of the insulin-like growth factor pathway in healthy individuals and prostate cancer patients. RECENT FINDINGS: Intervention studies show that the daily consumption of one serving of tomatoes or tomato products, but not supplementation with lycopene alone, increases the resistance of mononuclear leukocytes against DNA strand breaks induced by reactive oxygen species in healthy volunteers. Data from clinical trials with	Review	(-) ↓ DNA strand breaks in mononuclear leukocyte			N	

				prostate cancer patients are scarce and contradictory. There is a paucity of reliable data on DNA damage in prostate tissue. SUMMARY: Increasing evidence suggests that a single serving of tomatoes or tomato products ingested daily may contribute to protect from DNA damage. As DNA damage seems to be involved in the pathogenesis of prostate cancer, the regular ingestion of tomatoes or tomato products might prevent the disease. Further well-designed studies are necessary to establish the role of tomatoes and tomato products in the prevention and therapy of prostate cancer.						
Cancer Risk Reviews (prostate)	Theobald S	[Nutrition and prostate cancer--what is the scientific evidence?] Theobald S. Med Monatsschr Pharm. 2006 Oct;29(10):371-7.	2006	Prostate cancer is the most frequently occurring form of cancer in German men with an incidence of 49.000 in the year 2002. Epidemiological studies indicate diet and physical activity may play major roles in both incidence and progression of the disease. Obesity may increase both primary risk and biochemical (increase in prostate specific antigen) or clinical recurrence. Among individual food groups/nutrients a high consumption of total fat, saturated fats, meat, dairy, and calcium are related to an increased risk. Tomato products, soy, lycopene, selenium, marine omega-3-fatty acids and vitamin E in smokers may inversely be	Review	(-) ↓ risk			(-) ↓ risk	

				associated with prostate cancer. Interventional studies with supplemental tomato products and selenium also showed a delay in disease progression. Evidence from experimental studies and clinical experience suggest that application of selenium during chemotherapy and/or radiotherapy may decrease therapy related toxicities and increases the effect of the standard therapy on cancer cells. For expert patients it is essential to participate in decisions concerning their standard as well as complementary therapy by developing individual self-help concepts. These often include both changing dietary habits and taking dietary supplements. Physicians should consider these needs when they counsel cancer patients.						
Cancer Risk Reviews (prostate)	Coates PM	Evidence-based reviews in support of health policy decisions. Coates PM. J Natl Cancer Inst. 2007 Jul 18;99(14):1059. Epub 2007 Jul 10.	2007	In this issue of the Journal, Kavanaugh et al. (2) describe the approach that the U. S. Food and Drug Administration (FDA) has used to incorporate evidence-based review principles into the challenging area of evaluating qualified claims for health benefits of foods and food components that are marketed as dietary supplements (2). The particular topic of this paper was qualified health claims for tomatoes and for lycopene, a constituent of tomatoes that is marketed as a dietary supplement, in reducing the risk of some forms of cancer, including	Editorial				N	

				prostate cancer. FDA's systematic review of the relevant literature followed the rules that are crucial to evidence-based review and, as such, exemplifies the transparency and neutrality of an evidence-based review approach in evaluating the strength of the available evidence in an area where the expectation of risk reduction sometimes results in a biased interpretation of the evidence. However, there are several issues that must be taken into account when considering the processes that FDA was obliged to use to meet its needs.						
Cancer Risk Reviews (prostate)	Fleshner N	Prostate cancer prevention: past, present, and future. Fleshner N, Zlotta AR. Cancer. 2007 Nov 1;110(9):1889-99.	2007	Prostate cancer is the most common male malignancy and the second or third leading cause of cancer death among men in the West. The descriptive epidemiology of prostate cancer suggests that it is a preventable disease. Prevention has the theoretical advantage of not only saving lives, but also reduce the morbidity of radical prostate cancer therapy. This article reviews the past, present, and future of prostate cancer prevention. In particular, the evidence and scientific data of a variety of prevention strategies are reviewed. Strategies reviewed include dietary fat reduction and supplementation with vitamins D and E, and selenium. Dietary intake of soy, green tea, and tomato-rich products (lycopene) are	Review					

				also reviewed. Data regarding pharmacological intervention with cyclo-oxygenease inhibitors, antiestrogens, and in particular 5-alpha reductase inhibitors are reviewed. The results of the Prostate Cancer Prevention Trial including the controversy surrounding higher-grade cancers among men randomized to finasteride are also summarized. Finally, a variety of trial designs as well as a roster of current phase 2 trials are presented. Probably no cancer is being investigated more thoroughly in the context of prevention as prostate cancer in 2007. Definitive answers to pivotal phase 3 trials will be available in the coming 2 to 7 years.						
Cancer Risk Reviews (prostate)	Lindshield BL	Lycopenoids: are lycopene metabolites bioactive? Lindshield BL, Canene-Adams K, Erdman JW Jr. Arch Biochem Biophys. 2007 Feb 15;458(2):136-40. Epub 2006 Oct 4.	2007	In vitro lycopene is the most potent antioxidant among carotenoids. While antioxidant function may be relevant to health, we hypothesize that metabolites of lycopene may be bioactive and responsible for the beneficial effects of tomato product consumption. We term these metabolites "lycopenoids," which we believe may be produced from carotenoid monooxygenase (CMO) II, paralleling the production of retinoids from beta-carotene by CMO I. We present evidence suggesting that tomato carotenoid metabolites may be responsible for the reduced risk of prostate cancer seen in	Review	(-) ↓ risk			(-) ↓ risk	

				men consuming high levels of tomato products. Finally, we identify gaps in knowledge in this evolving area of carotenoid research.						
Cancer Risk Reviews (prostate)	Syed DN	Chemoprevention of prostate cancer through dietary agents: progress and promise. Syed DN, Khan N, Afaq F, Mukhtar H. Cancer Epidemiol Biomarkers Prev. 2007 Nov;16(11):2193-203.	2007	Prostate cancer (CaP) is second only to lung cancer as the cause of cancer-related deaths in American men and is responsible for over 29,000 deaths per year. One promising approach to reduce the incidence of CaP is through chemoprevention, which has been recognized as a plausible and cost-effective approach to reduce cancer morbidity and mortality by inhibiting precancerous events before the occurrence of clinical disease. Indeed, CaP is an ideal candidate disease for chemoprevention because it is typically diagnosed in the elderly population with a relatively slower rate of growth and progression, and therefore, even a modest delay in the development of cancer, achieved through pharmacologic or nutritional intervention, could result in substantial reduction in the incidence of clinically detectable disease. In this review, we have summarized the recent investigations and mechanistic studies on CaP chemoprevention using dietary agents, such as selenium, vitamins D and E, lycopene, phytoestrogens, flavonoids, and green tea polyphenols. Well-designed trials are required to delineate the potential	Review					

				clinical usefulness of these agents through issues, such as determining the optimal period and route of administration, systemic bioavailability, optimal dosing and toxicity of the agent, and single or combinatorial approach. It is hoped that, combining the knowledge based on agents with targets, effective approaches for CaP chemoprevention can be established.						
Cancer Risk Reviews (prostate)	Von Low EC	Review. Facts and fiction of phytotherapy for prostate cancer: a critical assessment of preclinical and clinical data. Von Low EC, Perabo FG, Siener R, Muller SC. In Vivo. 2007 Mar-Apr;21(2):189-204.	2007	The objective of this work was to substantially review all preclinical and clinical data on phytochemicals, such as genistein, lycopene, curcumin, epigallocatechin-gallate, and resveratrol, in terms of their effects as a potential treatment of prostate cancer. It is known, that prostate cancer patients increasingly use complementary and alternative medicines in the hope of preventing or curing cancer. The preclinical data for the phytochemicals presented in this review show a remarkable efficacy against prostate cancer cells in vitro, with molecular targets ranging from cell cycle regulation to induction of apoptosis. In addition, well-conducted animal experiments support the belief that these substances might have a clinical activity on human cancer. However, it is impossible to make definite statements or conclusions on the clinical efficacy in cancer patients	Review				N	

				because of the great variability and differences of the study designs, small patient numbers, short treatment duration and lack of a standardised drug formulation. Although some results from these clinical studies seem encouraging, reliable or long-term data on tumor recurrence, disease progression and survival are unknown. At present, there is no convincing clinical proof or evidence that the cited phythochemicals might be used in an attempt to cure cancer of the prostate.						
Cancer Risk Reviews (prostate)	Dahan K	Lycopene in the prevention of prostate cancer. Dahan K, Fennal M, Kumar NB. J Soc Integr Oncol. 2008 Winter;6(1):29-36.	2008	Based on the evidence from epidemiologic, animal, and in vitro data and human clinical trials, it is evident that lycopene, a non-provitamin A carotenoid, is a promising agent for prostate cancer chemoprevention. It is also clear that the form of lycopene used (purified versus food sources), dose of lycopene and concomitant use with other carotenoids and antioxidants, duration of exposure, specific target populations, and stage of disease appear to play a major role in determining agonistic or antagonistic effects. Based on our review, there is enough evidence to warrant use of lycopene in phase I and II clinical trials to examine its safety and efficacy as a potential chemopreventive agent for prostate cancer. The objective of this article is to review this evidence from	Review				(-) ↓ risk prostate cancer	

				epidemiologic, animal, in vitro, and clinical trials and provide the need and rationale to examine further the role of lycopene for prostate cancer prevention.						
Cancer Risk Reviews (prostate)	Magri V	Activity of Serenoa repens, lycopene and selenium on prostatic disease: evidences and hypotheses. Magri V, Trinchieri A, Perletti G, Marras E. Arch Ital Urol Androl. 2008 Jun;80(2):65-78.	2008	An increasing number of preclinical data, epidemiological evidences and clinical trials point to a potential role of natural compounds like herbal extracts, carotenoids and specific metals in the prevention and/or treatment of different prostate conditions, like hyperplasia, inflammation, cancer. The present article reviews some of the major and most recent findings on the therapeutic properties of three of the most widely used compounds, i.e. Serenoa repens, lycopene and selenium. Although the mechanism of action of these compounds ought to be further characterized by focused investigation, it appears that a common feature of these agents may be a dual activity on proliferative disorders as well as on inflammatory conditions at the level of the prostate gland.	Review					(-) ↓ infla-mmation	
Cancer Risk Reviews (prostate)	Van Patten CL	Diet and dietary supplement intervention trials for the prevention of prostate cancer recurrence: a review of the randomized controlled trial evidence.	2008	PURPOSE: We review the effect of diet and dietary supplement interventions on prostate cancer progression, recurrence and survival. MATERIALS AND METHODS: A literature search was conducted in MEDLINE, EMBASE and CINAHL to	Review					N	

		Van Patten CL, de Boer JG, Tomlinson Guns ES. J Urol. 2008 Dec;180(6):2314-21; discussion 2721-2. Epub 2008 Oct 18. Review		identify diet and dietary supplement intervention studies in men with prostate cancer using prostate specific antigen or prostate specific antigen doubling time as a surrogate serum biomarker of prostate cancer recurrence and/or survival. RESULTS: Of the 32 studies identified 9 (28%) were randomized controlled trials and the focus of this review. In these studies men had confirmed prostate cancer and elevated or increasing prostate specific antigen. Only 1 trial included men with metastatic disease. When body mass index was reported, men were overweight or obese. A significant decrease in prostate specific antigen was observed in some studies using a low fat vegan diet, soy beverage or lycopene supplement. While not often reported as an end point, a significant increase in prostate specific antigen doubling time was observed in a study on lycopene supplementation. In only 1 randomized controlled trial in men undergoing orchiectomy was a survival end point of fewer deaths with lycopene supplementation reported. CONCLUSIONS: A limited number of randomized controlled trials were identified in which diet and dietary supplement interventions appeared to slow disease progression in men with prostate cancer, although results vary. Studies						

				were limited by reliance on the surrogate biomarker prostate specific antigen, sample size and study duration. Well designed trials are warranted to expand knowledge, replicate findings and further assess the impact of diet and dietary supplement interventions on recurrence and treatment associated morbidities.						
Cancer Risk Reviews (prostate)	Wigle DT	Role of hormonal and other factors in human prostate cancer. Wigle DT, Turner MC, Gomes J, Parent ME. J Toxicol Environ Health B Crit Rev. 2008 Mar;11(3-4):242-59.	2008	American men have a lifetime risk of about 18% for prostate cancer diagnosis. Large international variations in prostate cancer risks and increased risks among migrants from low- to high-risk countries indicate important roles for environmental factors. Major known risk factors include age, family history, and country/ethnicity. Type 2 diabetes appears to reduce risk, while high birth weight and adult height are linked to increased risk of aggressive prostate cancer. Limited evidence supports an association with a history of sexually transmitted infections. A previous meta-analysis of eight cohort studies indicated no associations with plasma androgen, estrogen, or sex hormone binding globulin (SHBG) levels. However, there were dose-response relationships with baseline plasma testosterone levels in two studies that adjusted for other serum hormones and obesity. Finasteride (a drug that blocks testosterone	Review	(-) protective role			(-) protective role	

				activation) reduced prostate cancer risk by 25%. Low-frequency genes linked to familial prostate cancer only explain a small fraction of all cases. Sporadic cases were linked to relatively common polymorphisms of genes involved in (1) androgen synthesis, activation, inactivation and excretion, (2) hormone and vitamin D receptors, (3) carcinogen metabolism, and (4) DNA repair. Epidemiologic evidence supports protective roles for dietary selenium, vitamin E, pulses, tomatoes/lycopene, and soy foods, and high plasma 1,25-dihydroxyvitamin D levels. There is inadequate evidence that vegetables, fruit, carotenoids, and vitamins A and C reduce risk and that animal fat, alpha-linoleic acid, meat, coffee, and tea increase risk. Two major cohort studies found dose-response relationships with dietary calcium intake. Total dietary energy intake may enhance risk. Limited evidence supports a protective role for physical activity and elevated risk for farmers and other men with occupational pesticide exposure, particularly to organochlorine compounds and phenoxy herbicides. There is inadequate evidence for a relationship with alcohol or smoking. Most known or suspected external risk factors may act through hormonal mechanisms, but our review found little supporting					

				evidence, and substantial further research is needed.						
Cancer Risk Reviews (prostate)	Chan R	Prostate cancer and vegetable consumption. Chan R, Lok K, Woo J. Mol Nutr Food Res. 2009 Feb;53(2):201-16.	2009	Epidemiological studies have shown marked variations in prostate cancer incidence and mortality across different geographic regions, leading to the rising interest in the role of nutrition in prostate cancer risk. There is also a large body of evidence that a diverse diet, rich in vegetables, can reduce the risk of prostate cancer. In this review, the role of various kinds of vegetables and their bioactive compounds associated with prostate cancer risk, and the underlying mechanisms of these associations are summarized. There is accumulating evidence to support the consumption of lycopene, in particular tomato and tomato-based products, as protective factors against prostate cancer. Evidence on the protective role of beta-carotene was inconsistent from cohort and case-control studies. Evidence on the effect of pulses or soy consumption on prostate cancer risk was limited but suggestive of decreased risk with increased pulses or soy consumption. However, the role of vitamin C, vitamin E, allium vegetables, and cruciferous vegetables on prostate cancer risk remains to be determined due to limited evidence. Although the impact on prostate cancer risk differs among various vegetables and their	Review	(-) ↓ risk			(-) ↓ risk	

				constituent nutrients, the overall benefits of plant based diet on cancer prevention and other diet-related diseases should be promoted.						
Cancer Risk Reviews (prostate)	Colli JL	Chemoprevention of prostate cancer: what can be recommended to patients? Colli JL, Amling CL. Curr Urol Rep. 2009 May;10(3):165-71.	2009	Prostate cancer is third to lung and colon cancer as the cause of cancer-related deaths in American men. It is estimated that there will have been more than 28,000 deaths and 186,000 new cases in 2008 that will impose a significant burden on national health care costs. Chemoprevention aims to reduce both incidence and mortality through the use of agents to prevent, reverse, or delay the carcinogenic process. This study provides clinicians with information on some chemoprevention agents that have been considered to reduce prostate cancer risks, including 5-alpha-reductase inhibitors; statins (a class of compounds used to reduce cholesterol); NSAIDs; selenium; vitamins E and D; lycopene; allium vegetables (garlic, scallions, onions, chives, and leeks); soy/isoflavones; and green tea polyphenols. The evidence to support prostate cancer risk reduction benefits for each chemoprevention agent based on a review of the literature is provided.	Review				(-) ↓ risk	
Cancer Risk Reviews (prostate)	Ellinger S	[Tomatoes and lycopene in prevention and therapy--is there an evidence for prostate	2009	Tomatoes are discussed to have an important role in the prevention of and therapy for prostate cancer (PCA).	Review	N/(-) may be protective			N/(-) may be pro-tective	

		diseases?] Ellinger S, Ellinger J, MÃller SC, Stehle P. Aktuelle Urol. 2009 Jan;40(1):37-43. Epub 2009 Jan 28.		Whether or not they are also useful in the primary and secondary prevention of benign prostate hyperplasia (BPH) is not clear. This review summarises the results of original contributions with a focus on interventional studies. Whereas epidemiological studies on BPH prevention provide no evidence for a preventive potential of tomatoes and tomato products, the majority of interventional trials points to an increased DNA resistance against oxidative-induced damage. Even though their effect on a surrogate marker of the IGF pathway cannot be evaluated so far due to insufficient data, the consumption of tomatoes and tomato products may probably protect from PCA--at least when considering low-grade PCA. Thus, regular consumption of these foods can be recommended for the prevention of PCA. Tomato products might also be useful in the therapy for BPH and PCA. The intake of isolated lycopene does not protect from the development of PCA. However, in the doses achieved by consumption of tomato products, lycopene ingestion might also be effective in PCA therapy.						
Cancer Risk Reviews (prostate)	Haseen F	Is there a benefit from lycopene supplementation in men with prostate cancer? A systematic review.	2009	Lycopene has a chemopreventive effect against prostate cancer but its role in prostate cancer progression is unknown; many	Review				(-)	PSA (6/8) studies

		Haseen F, Cantwell MM, O'Sullivan JM, Murray LJ. Prostate Cancer Prostatic Dis. 2009;12(4):325-32. Epub 2009 Sep 1. Review		patients increase their intake of lycopene, although there are no evidence-based guidelines to suggest an effect. Our objective was to conduct a systematic review of literature to evaluate the association between lycopene intake and prostate cancer progression. MEDLINE, EMBASE CINAHL Plus, Web of Science, AMED and CENTRAL databases were systematically searched using terms for lycopene and prostate cancer progression to identify studies published before January 2009. Eight intervention studies were identified (five with no control group; one with an unmatched control group; and two randomized controlled trials (RCTs)). An inverse association was observed between lycopene intake and PSA levels in six studies. The rates of progression measured by bone scan in one RCT were lower in the intervention group. Lycopene resulted in lowering cancer-related symptoms (pain, urinary tract symptoms), and severe toxicity or intolerance was not evident. However, the evidence available to date is insufficient to draw a firm conclusion with respect to lycopene supplementation in prostate cancer patients and larger RCTs are required in broader patient groups.						
Cancer Risk Reviews (prostate)	Itsiopoulos C	Can the Mediterranean diet prevent prostate cancer?	2009	Prostate cancer is the second most common cancer in men worldwide. Despite the global	Review				(-) ↓ risk	

		Itsiopoulos C, Hodge A, Kaimakamis M. Mol Nutr Food Res. 2009 Feb;53(2):227-39.		importance of this cancer, until recently little was known about risk factors apart from the well-established factors: age, family history and country of birth. The large worldwide variation in prostate cancer risk and increased risk in migrants moving from low to high risk countries provides strong support for modifiable environmental factors. We have based our review on the findings of a systematic review undertaken by an expert panel on behalf of the World Cancer Research Fund and the American Institute for Cancer Research, and new data since then, linking identified foods and nutrients with prostate cancer. Evidence indicates that foods containing lycopene, as well as selenium and foods containing it, probably protect against prostate cancer, and excess consumption of foods or supplements containing calcium are a probable cause of this cancer. The expert panel also concluded that it is unlikely that beta-carotene (whether from foods or supplements) has a substantial effect on the risk of this cancer. A recent review on environmental factors in human prostate cancer also found that there were protective effects of vitamin E, pulses, soy foods and high plasma 1,25-dihydroxyvitamin D levels. The Mediterranean diet is abundant in foods that may protect against prostate						

				cancer and is associated with longevity and reduced cardiovascular and cancer mortality. Compared with many Western countries Greece has lower prostate cancer mortality and Greek migrant men in Australia have retained their low risk for prostate cancer. Consumption of a traditional Mediterranean diet, rich in bioactive nutrients, may confer protection to Greek migrant men, and this dietary pattern offers a palatable alternative for prevention of this disease.						
Cancer Risk Reviews (prostate)	Ma RW	A systematic review of the effect of diet in prostate cancer prevention and treatment. Ma RW, Chapman K. Hum Nutr Diet. 2009 Jun;22(3):187-99; quiz 200-2. Epub 2009 Apr 1.	2009	Dietary therapy has been proposed as a cost effective and noninvasive means of reducing the risk of prostate cancer (PC) and its progression. There is a large volume of published studies describing the role of diet in the prevention and treatment of PC. This article systematically reviews the data for dietary-based therapy in the prevention of PC, as well as in the management of patients with PC, aiming to provide clarity surrounding the role of diet in preventing and treating PC. Although conclusive evidence is limited, the current data are indicative that a diet low in fat, high in vegetables and fruits, and avoiding high energy intake, excessive meat, excessive dairy products and calcium intake, is possibly effective in preventing PC. However, caution must be taken to	Review					

				ensure that members of the public do not take excessive amounts of dietary supplements because there may be adverse affects associated with their over consumption. The dietary recommendations for patients diagnosed with PC are similar to those aiming to reduce their risk of PC						
Cancer Risk Reviews (prostate)	Ilic D	Lycopene for the prevention of prostate cancer. Ilic D, Forbes KM, Hassed C. Cochrane Database Syst Rev. 2011 Nov 9;11:CD008007.	2011	BACKGROUND: Prostate cancer is a common cause of death in developed countries, yet the benefits of screening for prostate cancer still remain controversial. A prostate-specific antigen (PSA) test result greater than 4 ng/mL (nanograms/millilitre) has commonly been used as the cut-off level for seeking further tests to diagnose the presence (or absence) of prostate cancer. An increase in PSA levels may not necessarily be associated with an increased risk of prostate cancer, as PSA levels may also be increased in men with benign prostatic hyperplasia and prostatitis. Despite the uncertainty of the net benefit of early detection and treatment, safe and effective methods to prevent prostate cancer are of value. Consumers, seeking greater involvement in their healthcare, are increasingly turning to lifestyle modification and complementary and alternative medicines (CAMs) to maintain their health and prevent disease. Lycopene is a member of the carotenoid	Review					

				family, which is found abundantly in tomatoes, tomato-based products, strawberries, and watermelon. It has been hypothesised that lycopene is a strong antioxidant, which may lower the risk of cancer (including prostate cancer) in people who have diets rich in lycopene. OBJECTIVES: To determine whether lycopene reduces the incidence of prostate cancer and prostate cancer-specific mortality. Secondary objectives include changes in PSA levels, prostate symptoms and the nature of adverse events associated with lycopene use. SEARCH STRATEGY: Electronic searches were conducted across MEDLINE, EMBASE and the Cochrane Central Register of Controlled Trials (CENTRAL) databases. No language or other limitations were imposed. SELECTION CRITERIA: Randomised controlled trials (RCTs) that investigated the use of lycopene for the prevention of prostate cancer were eligible for inclusion in this review. DATA COLLECTION AND ANALYSIS: A search of electronic databases, performed in August 2011, identified 64 citations. All articles were selected for full-text review. From these citations, three studies were identified as meeting the inclusion criteria. Handsearching did not provide any additional studies.						

Cancer Risk Reviews (prostate)	Lippi G	Tomatoes, lycopene-containing foods and cancer risk. Lippi G, Targher G. Br J Cancer. 2011 Mar 29;104(7):1234-5. Epub 2011 Feb 22.	2011	EXCERPT: We read with interest the recent review article by Key (2011), who concluded that the published results from the epidemiological studies suggest little or no association between the total intake of fruit and vegetables and the risk of common cancers, including colorectal, breast and prostate cancer. Although the association between food intake and cancer is still under intense debate, we believe that there is a growing body of clinical evidence suggesting that certain types of food, for example, those rich in lycopene such as tomatoes, might have beneficial effects on the development of certain cancers, especially prostate cancer. First and foremost, the most recent expert report issued by the World Cancer Research Fund, together with the American Institute for Cancer Research, has reviewed the strength of the evidence that causally correlates food intake to the risk of several forms of cancer. Basically, it has been concluded that a higher consumption of several plant foods might protect against cancers of various sites. In particular, foods rich in folate may protect against pancreatic cancer, those rich in carotenoids against cancers of the mouth, pharynx, larynx and lung cancer, those rich in β-carotene or vitamin C against oesophageal cancer, and	RCT				(-)	

				those rich in lycopene against prostate cancer (World Cancer Research Fund/American Institute for Cancer Research, 2007).						
Cancer Risk Reviews (prostate)	Van Patten CL	Diet and dietary supplement intervention trials for the prevention of prostate cancer recurrence: a review of the randomized controlled trial evidence. Van Patten CL, de Boer JG, Tomlinson Guns ES. J Urol. 2008 Dec;180(6):2314-21; discussion 2721-2. Epub 2008 Oct 18.	2008	PURPOSE: We review the effect of diet and dietary supplement interventions on prostate cancer progression, recurrence and survival. MATERIALS AND METHODS: A literature search was conducted in MEDLINE, EMBASE and CINAHL to identify diet and dietary supplement intervention studies in men with prostate cancer using prostate specific antigen or prostate specific antigen doubling time as a surrogate serum biomarker of prostate cancer recurrence and/or survival. RESULTS: Of the 32 studies identified 9 (28%) were randomized controlled trials and the focus of this review. In these studies men had confirmed prostate cancer and elevated or increasing prostate specific antigen. Only 1 trial included men with metastatic disease. When body mass index was reported, men were overweight or obese. A significant decrease in prostate specific antigen was observed in some studies using a low fat vegan diet, soy beverage or lycopene supplement. While not often reported as an endpoint, a significant increase in prostate specific antigen doubling time was observed in a study on lycopene	Review	(-) ↓ PSA ↑ PSA doubling time			(-) ↓ PSA ↑ PSA doubling time	

				supplementation. In only 1 randomized controlled trial in men undergoing orchiectomy was a survival end point of fewer deaths with lycopene supplementation reported. CONCLUSIONS: A limited number of randomized controlled trials were identified in which diet and dietary supplement interventions appeared to slow disease progression in men with prostate cancer, although results vary.Studies were limited by reliance on the surrogate biomarker prostate specific antigen, sample size and study duration. Well designed trials are warranted to expand knowledge, replicate findings and further assess the impact of diet and dietary supplement interventions on recurrence and treatment associated morbidities.						
Cancer Risk Reviews (skin)	Wright TI	Chemoprevention of nonmelanoma skin cancer. Wright TI, Spencer JM, Flowers FP. J Am Acad Dermatol. 2006 Jun;54(6):933-46; quiz 947-50.	2006	Skin cancer is the most common cancer in human beings. The increased incidence of skin cancer has brought much attention to the process by which these tumors develop and how they can be revented. Efforts have been made to educate the public about the importance of protecting skin from excessive ultraviolet light. Despite this work, the incidence of skin cancer continues to increase. Available compounds may be useful in the chemoprevention of skin cancer. Chemoprevention is	Review					

				defined as oral or topical use of dietary or pharmacologic agents to inhibit or reverse the development of cancer. Potential agents included are the retinoids; difluoromethylornithine; T4 endonuclease V; polyphenolic antioxidants, such as (-)-epigallocatechin gallate, found in green tea and grape seed extract; silymarin; isoflavone genestein; nonsteroidal anti-inflammatory drugs; curcumin; lycopene; vitamin E; beta-carotene; and selenium. Many of these agents are available over the counter as topical or oral preparations. LEARNING OBJECTIVE: At the conclusion of this activity, participants should be familiar with the chemopreventive agents and their efficacy, as well as any significant side effects associated with them.						
Cancer: breast	Hu F	Carotenoids and breast cancer risk: a meta-analysis and meta-regression. Hu F, Wang Yi B, Zhang W, Liang J, Lin C, Li D, Wang F, Pang D, Zhao Y. Breast Cancer Res Treat. 2011 Sep 7. [Epub ahead of print]	2011	The purpose of this article is to comprehensively summarize the associations between carotenoids and breast cancer and quantitatively estimate their dose-response relationships. We searched PubMed, Embase, and Cochrane databases (from January 1982 to 1 May 2011) and the references of the relevant articles in English with sufficient information to estimate relative risk or odds ratio and the 95% confidence intervals, and comparable categories of carotenoids. Two reviewers independently	Meta-Analysis				N	

				extracted data using a standardized form; with any discrepancy adjudicated by the third reviewer. 33 studies met the inclusion criteria. Comparing the highest with the lowest intake: dietary a-carotene intake significantly reduced the breast cancer risk by 9.0% (pooled RR = 0.91; 95% CI: 0.85-0.98; P = 0.01), dietary β-carotene intake reduced the risk by 6.0% (pooled RR = 0.94; 95% CI: 0.88-1.00; P = 0.05); total β-carotene intake reduced the risk by 5.0% (pooled RR = 0.95; 95% CI: 0.90-1.01; P = 0.08) when data from cohort studies were pooled. Significant dose-response relationships were observed in both the higher intake of dietary and total β-carotene with reduced breast cancer risk when data from cohort studies (P (trend) < 0.01, P (trend) = 0.03) and case-control studies (P (trend) < 0.01, P (trend) < 0.01) were pooled, respectively. Dietary a-carotene intake could reduce the breast cancer risk. The relationships between dietary and total β-carotene intake and breast cancer need to be confirmed. No significant association between dietary intake of β-cryptoxanthin, lutein/+zeaxanthin, and lycopene and breast cancer was observed.						
	Ilic D	Continuation of: Lycopene for the	2011	MAIN RESULTS: Three RCTs, with a total of 154 participants were included in						

		prevention of prostate cancer.		this review. None of the studies reported data on prostate cancer mortality. All of the included studies differed with respect to design, participants included and allocation of lycopene. This clinical heterogeneity limits the value on the pooled estimated of the meta-analyses. The methodological quality of two of the three included studies was assessed as posing a 'high' risk of bias. Meta-analysis indicated no statistical difference in PSA levels between men randomised to receive lycopene and the comparison group (MD (mean difference) -0.34, 95% CI (confidence interval) -2.01, 1.32). Only one study reported incidence of prostate cancer (10% in the lycopene group versus 30% in control group). The level of lycopene was also not statistically different in men randomised to receive lycopene and the comparison group (MD 0.39 µg/mL (micrograms/millilitre), 95% CI -0.19, 0.98). No other meta-analyses were possible since other outcomes assessed only had one study contributing data. AUTHORS' CONCLUSIONS: Given that only three RCTs were included in this systematic review, and the high risk of bias in two of the three studies, there is insufficient evidence to either support, or refute, the use of lycopene for the prevention of prostate cancer. Similarly, there is no robust evidence	

				from RCTs to identify the impact of lycopene consumption upon the incidence of prostate cancer, prostate symptoms, PSA levels or adverse events.	