Lycopene Supplementation and Disease Risk
Prostate Cancer Critical Findings

Disease type	First Author	Study Title and Complete Citation	Date	Abstract	Study Type	G.Tom +, N, -	P.Tom +, N, -	F.Tom +, N, -	Lyco +, N, -	Other +, N, -
Cancer: prostate	Kucuk O	Phase II randomized clinical trial of lycopene supplementation before radical prostatectomy. Kucuk O, Sarkar FH, Sakr W, Djuric Z, Pollak MN, Khachik F, Li YW, Banerjee M, Grignon D, Bertram JS, Crissman JD, Pontes EJ, Wood DP Jr. Cancer Epidemiol Biomarkers Prev. 2001 Aug;10(8):861-8.	2001	An inverse association has been observed between dietary intake of lycopene and the risk of prostate cancer. We investigated the effects of lycopene supplementation in patients with prostate cancer. Twenty-six men with newly diagnosed, clinically localized (14 T(1) and 12 T(2)) prostate cancer were randomly assigned to receive 15 mg of lycopene (n = 15) twice daily or no supplementation (n = 11) for 3 weeks before radical prostatectomy. Biomarkers of differentiation and apoptosis were assessed by Western blot analysis on benign and malignant parts of the prostate gland. Prostatectomy specimens were entirely embedded, step-sectioned, and evaluated for pathological stage, Gleason score, volume of cancer, and extent of high-grade prostatic intraepithelial neoplasia. Plasma levels of lycopene, insulin-like growth factor-1 (IGF-1), IGF binding protein-3, and prostate-specific antigen were measured at baseline and after 3 weeks of supplementation or observation. Eleven (73%) subjects in the intervention group and two (18%) subjects in the control group had no involvement of surgical margins and/or extra-prostatic tissues with cancer (P = 0.02). Twelve (84%) subjects in the lycopene group and five (45%) subjects in the control group had tumors <4 ml in size (P = 0.22). Diffuse involvement of the prostate by high-grade prostatic intraepithelial neoplasia was present in 10 (67%) subjects in the intervention group and in 11 (100%) subjects in the control group (P = 0.05). Plasma prostate-specific antigen levels decreased by 18% in the intervention group, whereas they increased by 14% in the control group (P = 0.25). Expression of connexin 43 in cancerous prostate tissue was 0.63 +/- 0.19 absorbance in the lycopene group compared with 0.25 +/- 0.08 in the control	RCT				(-) PSA N other markers	

				group (P = 0.13). Expression of bcl-2 and bax did not differ significantly between the two study groups. IGF-1 levels decreased in both groups (P = 0.0002 and P = 0.0003, respectively). The results suggest that lycopene supplementation may decrease the growth of prostate cancer. However, no firm conclusions can be drawn at this time because of the small sample size.						
Cancer: prostate	Kucuk O	Lycopene in the treatment of prostate cancer. Kucuk O, Sarkar FH, Sakr W, Khachik F, Djuric Z, Banerjee M et al. Pure Appl Chem 2002; 74: 1443–1450.	2002	Dietary intake of lycopene is associated with reduced risk of prostate cancer (PCa). We conducted a clinical trial in men with prostate cancer to investigate the biological and clinical effects of lycopene supplementation. Twenty-six men with prostate cancer were randomly assigned to receive a lycopene supplement or no supplement for three weeks before radical prostatectomy. Subjects in the intervention group (n = 15) were instructed to take a tomato oleoresin extract soft gel capsule (Lyc-O-Mato®, LycoRed Company, Beer Sheva, Israel) containing 15 mg lycopene, 1.5 mg phytoene, 1.5 mg phytofluene, and 5 mg tocopherol twice daily with meals. Prostatectomy specimens were evaluated for pathologic stage, Gleason score, volume of cancer, and extent of high-grade prostatic intraepithelial neoplasia (HGPIN). Biomarkers of cell proliferation and apoptosis were assessed by Western blot analysis in benign and cancerous tissue samples obtained from the prostatectomy specimens. Oxidative stress was assessed by measuring the peripheral blood lymphocyte DNA oxidation product 5-hydroxymethyl- deoxyuridine (5-OH-mdU). Plasma levels of lycopene, insulin-like growth factor-1 (IGF-1), insulin-like growth factor binding protein-3 (IGFBP-3), and prostate-specific antigen (PSA) were measured at baseline and after three weeks of study period. After the intervention, more men in the intervention group had smaller (<4 cc) tumors, organ-confined disease without involvement of surgical margins or extra-prostatic tissues, and focal involvement of the prostate with HGPIN compared to the control group. Mean plasma PSA levels were lower in the intervention group compared to the control group.	RCT				(-)	

				This pilot study suggests that a tomato extract containing lycopene and other tomato carotenoids and phytochemicals may have a potential role in the treatment of prostate cancer. Larger clinical trials are necessary to definitively address potential uses of lycopene or tomato extract in the prevention or treatment of prostate cancer.						
Cancer: prostate	Kucuk O	Effects of lycopene supplementation in patients with localized prostate cancer. Kucuk O, Sarkar FH, Djuric Z, Sakr W, Pollak MN, Khachik F, Banerjee M, Bertram JS, Wood DP Jr. Exp Biol Med (Maywood). 2002 Nov;227(10):881-5.	2002	Epidemiological studies have shown an inverse association between dietary intake of lycopene and prostate cancer risk. We conducted a clinical trial to investigate the biological and clinical effects of lycopene supplementation in patients with localized prostate cancer. Twenty-six men with newly diagnosed prostate cancer were randomly assigned to receive a tomato oleoresin extract containing 30 mg of lycopene (n = 15) or no supplementation (n = 11) for 3 weeks before radical prostatectomy. Biomarkers of cell proliferation and apoptosis were assessed by Western blot analysis in benign and cancerous prostate tissues. Oxidative stress was assessed by measuring the peripheral blood lymphocyte DNA oxidation product 5-hydroxymethyl-deoxyuridine (5-OH-mdU). Usual dietary intake of nutrients was assessed by a food frequency questionnaire at baseline. Prostatectomy specimens were evaluated for pathologic stage, Gleason score, volume of cancer, and extent of high-grade prostatic intraepithelial neoplasia. Plasma levels of lycopene, insulin-like growth factor-1, insulin-like growth factor binding protein-3, and prostate-specific antigen were measured at baseline and after 3 weeks of supplementation or observation. After intervention, subjects in the intervention group had smaller tumors (80% vs 45%, less than 4 ml), less involvement of surgical margins and/or extra-prostatic tissues with cancer (73% vs 18%, organ-confined disease), and less diffuse involvement of the prostate by high-grade prostatic intraepithelial neoplasia (33% vs 0%, focal involvement) compared with subjects in the control group. Mean plasma prostate-specific antigen levels were lower in the intervention group compared with the control group. This pilot study suggests that lycopene may have beneficial effects in prostate cancer. Larger clinical trials are warranted to investigate the potential	RCT				(-)	

				preventive and/or therapeutic role of lycopene in prostate cancer.						
Cancer: prostate	Ansari MS	A comparison of lycopene and orchidectomy vs orchidectomy alone in the management of advanced prostate cancer. Ansari MS, Gupta NP. BJU Int. 2003;92(4):375–378; discussion 378.	2003	OBJECTIVE: To compare the efficacy of lycopene plus orchidectomy with orchidectomy alone in the management of advanced prostate cancer. PATIENTS AND METHODS: Fifty-four patients with histologically confirmed metastatic prostatic cancer (M1b or D2) and a performance status of 0-2 (World Health Organization) were entered into the trial between March 2000 and June 2002. The trial comprised two treatment arms, i.e. patients were randomized to orchidectomy alone or orchidectomy plus lycopene (OL), each of 27 patients. Lycopene was started on the day of orchidectomy at 2 mg twice daily. Patients were evaluated clinically before and every 3 months after the intervention, with measurements of prostate-specific antigen (PSA), a bone scan and uroflowmetry, with the clinical response assessed as the change in these variables. RESULTS: At 6 months there was a significant reduction in PSA level in both treatments, but more marked in the OL group (mean 9.1 and 26.4 ng/mL, P = 0.9). After 2 years these changes were more consistent in the OL group (mean 3.01 and 9.02 ng/mL; P < 0.001). Eleven (40%) patients in orchidectomy and 21 (78%) in the OL group had a complete PSA response (P < 0.05), with a partial response in nine (33%) and four (15%), and progression in seven (25%) and two (7%), respectively (P < 0.05). Bone scans showed that in the orchidectomy arm only four (15%) patients had a complete response, vs eight (30%) in the OL group (P < 0.02), with a partial response in 19 (70%) and 17 (63%), and progression in four (15%) and two (7%), respectively (P < 0.02). There was a significant improvement in peak flow rate in the OL group, with a mean difference of +1.17 mL/s (P < 0.04). Of the 54 patients who entered the trial, 19 (35%) died, 12 (22%) in orchidectomy and seven (13%) in OL group (P < 0.001).	RCT				(-) Used as adjunct w/orchidectomy	PSA Progression Mortality

				CONCLUSION: Adding lycopene to orchidectomy produced a more reliable and consistent decrease in serum PSA level; it not only shrinks the primary tumour but also diminishes the secondary tumours, providing better relief from bone pain and lower urinary tract symptoms, and improving survival compared with orchidectomy alone. Comment in BJU Int. 2005 Jan;95(1):192.						
Cancer: prostate	Ansari MS	Lycopene: a novel drug therapy in hormone refractory metastatic prostate cancer. Ansari MS, Gupta NP. Urol Oncol. 2004 Sep-Oct;22(5):415-20.	2004	OBJECTIVE: In a prospective study we evaluated the efficacy of lycopene for the treatment of patients with metastatic hormone refractory prostate cancer. MATERIAL AND METHODS: Between January 2001 and December 2002, 20 consecutive patients (median age 72; range 56-90) with metastatic HRPC were enrolled in the study. Lycopene in the dose of 10 mg/day was administered for a period of 3 months.Inclusion criteria were patients previously treated with hormonal therapy now with clinical and biochemical evidence of disease progression. A complete response (CR) was defined as a normalization of PSA (<4 ng/mL) and the disappearance of any sign of disease for at least 8 weeks. A partial response was defined as a >50% decrease in PSA level for at least 8 weeks associated with improvement (or no worsening) in ECOG PS and relief of bone pain if present. Stable disease (SD) was defined as a <50% decrease or <25% increase in the PSA level associated with no worsening of ECOG PS and/or bone pain for at least 8 weeks RESULTS: One patient (5%) had complete response. Partial response was achieved in 6 (30%), disease remained stable in 10 (50%) and progressed in three (15%) patients. ECOG PS was Grade 0 in five, Grade I in 10 and Grade II in five of the 20 patients. It improved from Grade I to 0 in seven and Grade II to I in three patients. It deteriorated in three and remained unchanged in the rest seven patients. Bone pain was present in 16 (Grade 1 in six and Grade 2 in 10) of the 20 patients. Grade 1 changed	Interv				(-)	

				to Grade 0 in five and Grade II changed to Grade 1 in five patients. Bone pain remained unchanged in 5 (31%) and worsened in1 (6%). Ten (62%) patients managed to cut down the dose of analgesics on daily basis. Eighteen patients had associated LUTS, which improved (Q max > or = 12 mL/sec) in 11 (61%) patients. The median duration of response was 25 weeks (range 12-72 weeks). No drug intolerance or toxicity was encountered in any patient. CONCLUSIONS: Lycopene therapy appears to be effective and safe in the treatment of HRPC. It not only takes care of the rising PSA butalso improves the ECOG performance status, bone pain and LUTS. Because of its relative innocuousness it should be tried before the use of more toxic substances.						
Cancer: prostate	Mohanty NK	Lycopene as a chemopreventive agent in the treatment of high-grade prostate intraepithelial neoplasia. Mohanty NK, Saxena S, Singh UP, Goyal NK, Arora RP. Urol Oncol. 2005;23(6):383–385.	2005	OBJECTIVE: Because of its long latency, slow growing nature, and high prevalence, prostate cancer is the best model for chemoprevention. High-grade prostate intraepithelial neoplasia (HGPIN) is a precursor of prostate cancer. Chemoprevention with lycopene has shown definite results in prostate cancer. We undertook a study to use lycopene as a chemopreventive agent in the treatment of HGPIN for preventing prostate cancer from developing in this vulnerable group of patients. MATERIALS AND METHODS: A total of 40 patients with HGPIN were randomized into 2 groups: one received 4 mg lycopene twice a day for one year, and the other was periodically followed up. Total follow-up was one year. RESULTS: Our results show that lycopene can delay or prevent HGPIN from developing into occult prostate cancer, and there exists an inverse relationship between lycopene and prostate-specific antigen. Being a vegetable carotenoid, lycopene is a safe drug to be used for a longer period without any adverse reaction.	RCT 2-arm				(-)	PSA progression from neplastic to occult cancer

				CONCLUSION: Lycopene is an effective chemopreventive agent in the treatment of HGPIN, with no toxicity and good patient tolerance.						
Cancer: prostate	Bemis DL	Lycopene inhibits DNA synthesis in primary prostate epithelial cells in vitro and its administration is associated with a reduced prostate-specific antigen velocity in a phase II clinical study. Barber NJ, Zhang X, Zhu G, Pramanik R, Barber JA, Martin FL, Morris JD, Muir GH. Prostate Cancer Prostatic Dis. 2006;9(4):407-13. Epub 2006 Sep 19.	2006	Interest in lycopene has focused primarily on its use in the chemoprevention of prostate cancer (CaP); there are few clinical trials involving men with established disease. In addition, most data examining its mechanism of action have been obtained from experiments using immortal cell lines. We report the inhibitory effect(s) of lycopene in primary prostate epithelial cell (PEC) cultures, and the results of a pilot phase II clinical study investigating whole-tomato lycopene supplementation on the behavior of established CaP, demonstrating a significant and maintained effect on prostate-specific antigen velocity over 1 year. These data reinforce the justification for a large, randomized, placebo-controlled study.	RCT and cell culture				(-) inhibitory effect on primary prostate epithelial cell cultures	(-) stable PSA
Cancer: prostate	Clark PE	Phase I-II prospective dose-escalating trial of lycopene in patients with biochemical relapse of prostate cancer after definitive local therapy. Clark PE, Hall MC, Borden LS Jr, Miller AA, Hu JJ, Lee WR, Stindt D, D'Agostino R Jr, Lovato J, Harmon M, Torti FM.	2006	OBJECTIVES: To report a prospective trial of lycopene supplementation in biochemically relapsed prostate cancer. METHODS: A total of 36 men with biochemically relapsed prostate cancer were enrolled in a dose-escalating, Phase I-II trial of lycopene supplementation. Six consecutive cohorts of 6 patients each received daily supplementation with 15, 30, 45, 60, 90, and 120 mg/day for 1 year. The serum levels of prostate-specific antigen (PSA) and plasma levels of lycopene were measured at baseline and every 3 months. The primary endpoints were PSA response (defined as a 50% decrease in serum PSA from baseline), pharmacokinetics, and the toxicity/tolerability of this regimen.	RCT				N PSA levels	(+) ↑ plasma [lyco]

		Urology. 2006 Jun;67(6):1257-61.		RESULTS: A total of 36 patients were enrolled. The median age was 74 years (range 56 to 83), with a median serum PSA at entry of 4.4 ng/mL (range 0.8 to 24.9). No serum PSA responses were observed, and 37% of patients had PSA progression. The median time to progression was not reached. Toxicity was mild, with 1 patient discontinuing therapy because of diarrhea. Significant elevations of plasma lycopene were noted at 3 months and then appeared to plateau for all six dose levels. The plasma levels for doses between 15 and 90 mg/day were similar, with additional elevation only at 120 mg/day. CONCLUSIONS: Lycopene supplementation in men with biochemically relapsed prostate cancer is safe and well tolerated. The plasma levels of lycopene were similar for a wide dose range (15 to 90 mg/day) and plateaued by 3 months. Lycopene supplementation at the doses used in this study did not result in any discernible response in serum PSA.						
Cancer: prostate	Bunker CH	A randomized trial of lycopene supplementation in Tobago men with high prostate cancer risk. Bunker CH, McDonald AC, Evans RW, de la Rosa N, Boumosleh JM, Patrick AL. Nutr Cancer. 2007;57(2):130-7.	2007	This unblinded, randomized, Phase I clinical trial was conducted to determine whether lycopene supplementation lowered serum prostate specific antigen (PSA), surrogate endpoint for prostate cancer initiation or progression, in men with elevated prostate cancer risk. Afro-Caribbean men (n=81) with high-grade prostatic intraepithelial neoplasia, atypical foci or repeated non-cancerous biopsies, ascertained in a population-based screening program, were randomized to four months intervention with 30 mg/day lycopene (Lyc-O-Mato) plus a multivitamin, or to multivitamin, only. Serum PSA and lycopene were compared at randomization, 1, and 4 mo using two-sided chi2 and t-tests for independent samples. Treatment groups were similar at baseline. Serum lycopene levels approximately doubled in the lycopene intervention group. Serum PSA declined during the first month of treatment, but returned to randomization level by	RCT				N PSA levels	(+) 2x↑ serum [lyco] with supp

				month 4. The PSA response was nearly identical in both treatment groups. No adverse effects attributed to lycopene supplementation were documented. We conclude that the PSA lowering response to antioxidant supplementation observed in previous 3-wk studies in men awaiting prostatectomy may have been a transient response, perhaps not specific to lycopene. Lowering of serum PSA may not be an appropriate endpoint for the long-term studies needed to evaluate lycopene supplementation for reducing prostate cancer initiation or progression.						
Cancer: prostate	Jatoi A	A tomato-based, lycopene-containing intervention for androgen-independent prostate cancer: results of a Phase II study from the North Central Cancer Treatment Group. Jatoi A, Burch P, Hillman D, Vanyo JM, Dakhil S, Nikcevich D, Rowland K, Morton R, Flynn PJ, Young C, Tan W; North Central Cancer Treatment Group. Urology. 2007 Feb;69(2):289-94.	2007	OBJECTIVES: Tomatoes are rich in lycopene. This study explored the efficacy of a lycopene-rich tomato product in androgen-independent prostate cancer and the reasons patients participated in an "alternative medicine" study. METHODS: This Phase II study evaluated 46 patients with androgen-independent prostate cancer. All were asymptomatic and had serum prostate-specific antigen elevation despite hormonal manipulation. All patients completed a questionnaire on their motivations for enrolling in an "alternative medicine" study. Patients were prescribed a lycopene-rich tomato supplement at a lycopene dose of 15 mg twice daily. RESULTS: One patient manifested a tumor response with a 50% or greater confirmed decline in serum prostate-specific antigen level, yielding a response rate of 2%. Lycopene was well tolerated, but 1 patient died of a cancer-related hemorrhage, and 1 had grade 4 diarrhea. Grade 1 or 2 events included diarrhea in 18, nausea in 12, abdominal distension in 8, flatulence in 2, vomiting in 2, anorexia in 1, and dyspepsia in 1. The reasons for entering the trial are discussed and were overall positive. CONCLUSIONS: Lycopene, as prescribed in our study, did not appear effective for androgen-independent prostate cancer.	Interv				N	

				The patients' reasons for enrolling in this trial were positive and realistic.						
Cancer: prostate	Vaishampayan U	Lycopene and soy isoflavones in the treatment of prostate cancer. Vaishampayan U, Hussain M, Banerjee M, Seren S, Sarkar FH, Fontana J, Forman JD, Cher ML, Powell I, Pontes JE, Kucuk O. Nutr Cancer. 2007;59(1):1-7.	2007	Dietary intake of lycopene and soy has been associated with a lower risk of prostate cancer. In vitro studies with lycopene and genistein, a soy isoflavone, have shown induction of apoptosis and inhibition of cell growth in androgen-sensitive (LNCaP) and androgen-independent (PC3 and VeCaP) prostate cancer cell lines. In a previous Phase II clinical trial in prostate cancer patients, we observed prostate-specific antigen (PSA) stabilization with soy isoflavone intake. In this Phase II clinical trial, we investigated the efficacy of lycopene alone or in combination with soy isoflavones on serum PSA levels in men with prostate cancer. To be eligible for the study, men with prostate cancer had to have rising serum PSA following local therapy or while on hormone therapy. Study population included 71 eligible patients who had 3 successive rising PSA levels or a minimum PSA of 10 ng/ml at 2 successive evaluations prior to starting therapy. Subjects were randomly assigned to receive a tomato extract capsule containing 15 mg of lycopene alone (n = 38) or together with a capsule containing 40 mg of a soy isoflavone mixture (n = 33) twice daily orally for a maximum of 6 mo. One patient on the lycopene arm did not receive therapy due to his inability to ingest the study pill. There was no decline in serum PSA in either group qualifying for a partial or complete response. However, 35 of 37 (95%) evaluable patients in the lycopene group and 22 of 33 (67%) evaluable patients in the lycopene plus soy isoflavone group achieved stable disease described as stabilization in serum PSA level. The data suggest that lycopene and soy isoflavones have activity in prostate cancer patients with PSA relapse disease and may delay progression of both hormone-refractory and hormone-sensitive prostate cancer. However, there may not be an additive effect between the 2 compounds when taken together. Future studies are warranted to further investigate the efficacy of lycopene and soy isoflavones in prostate cancer as well as the	RCT				N PSA (-) ↓ liklihood of relapse	

				mechanism of potential negative interaction between them.						
Cancer: prostate	Kristal AR	Dietary patterns, supplement use, and the risk of symptomatic benign prostatic hyperplasia: results from the prostate cancer prevention trial. Kristal AR, Arnold KB, Schenk JM, Neuhouser ML, Goodman P, Penson DF, Thompson IM. Am J Epidemiol. 2008 Apr 15;167(8):925-34. Epub 2008 Feb 7.	2008	This study examined dietary risk factors for incident benign prostatic hyperplasia (BPH) in 4,770 Prostate Cancer Prevention Trial (1994-2003) placebo-arm participants who were free of BPH at baseline. BPH was assessed over 7 years and was defined as medical or surgical treatment or repeated elevation (>14) on the International Prostate Symptom Score questionnaire. Diet, alcohol, and supplement use were assessed by use of a food frequency questionnaire. There were 876 incident BPH cases (33.6/1,000 person-years). The hazard ratios for the contrasts of the highest to lowest quintiles increased 31% for total fat and 27% for polyunsaturated fat and decreased 15% for protein (all p(trend) < 0.05). The risk was significantly lower in high consumers of alcoholic beverages (0 vs. > or =2/day: hazard ratio (HR) = 0.67) and vegetables (<1 vs. > or =4/day: HR = 0.68) and higher in daily (vs. <1/week) consumers of red meat (HR = 1.38). There were no associations of supplemental antioxidants with risk, and there was weak evidence for associations of lycopene, zinc, and supplemental vitamin D with reduced risk. A diet low in fat and red meat and high in protein and vegetables, as well as regular alcohol consumption, may reduce the risk of symptomatic BPH.	PC				N PBH	use of supple-ments
Cancer: prostate	Kumar NB	Results of a Randomized Clinical Trial of the Action of Several Doses of Lycopene in Localized Prostate Cancer: Administration Prior to Radical Prostatectomy. Kumar NB, Besterman-Dahan K, Kang L, Pow-Sang J, Xu P, Allen	2008	PURPOSE: The purpose of this Phase II randomized-controlled trial was to evaluate the safety and effect of administering several doses of lycopene to men with clinically localized prostate cancer, on intermediate endpoint biomarkers implicated in prostate carcinogenesis. METHODS: Forty-five eligible men with clinically localized prostate cancer were supplemented with 15, 30 or 45 mg of lycopene or no supplement from biopsy to prostatectomy. Compliance to study agent, toxicity, changes in plasma lycopene, serum steroid hormones, PSA and tissue Ki-67 were analyzed from baseline to completion of intervention. RESULTS: Forty-two of forty-five five subjects completed the intervention for approximately 30	RCT				N PSA	

		K, Riccardi D, Krischer JP. Clin Med Urol. 2008 Apr 16;1:1-14.		days from the time of biopsy until prostatectomy. Plasma lycopene increased from baseline to post treatment in all treatment groups with greatest increase observed in the 45 mg lycopene-supplemented arm compared to the control arm without producing any toxicity. Overall, subjects with prostate cancer had lower baseline levels of plasma lycopene similar to those observed in previous studies in men with prostate cancer. Serum free testosterone decreased with 30 mg lycopene supplementation and total estradiol increased significantly with 30 mg and 45 mg supplementation from baseline to end of treatment, with no significant increases in serum PSA or tissue Ki-67. These changes were not significant compared to the control arm for this sample size and duration of intervention. CONCLUSIONS: Although antioxidant properties of lycopene have been hypothesized to be primarily responsible for its beneficial effects, our study suggests that other mechanisms mediated by steroid hormones may also be involved.						
Cancer: prostate	Schwarz S	Lycopene inhibits disease progression in patients with benign prostate hyperplasia. Schwarz S, ObermÃ¼ller-Jevic UC, Hellmis E, Koch W, Jacobi G, Biesalski HK. J Nutr. 2008 Jan;138(1):49-53.	2008	Lycopene is a promising nutritional component for chemoprevention of prostate cancer (PCa). A possibly beneficial role of lycopene in patients diagnosed with benign prostate hyperplasia (BPH), who are at increased risk of developing PCa, has been suggested, although clinical data are lacking. Therefore, this pilot study aimed to investigate the effects of lycopene supplementation in elderly men diagnosed with BPH. A total of 40 patients with histologically proven BPH free of PCa were randomized to receive either lycopene at a dose of 15 mg/d or placebo for 6 mo. The effects of the intervention on carotenoid status, clinical diagnostic markers of prostate proliferation, and symptoms of the disease were assessed. The primary endpoint of the study was the inhibition or reduction of increased serum prostate-specific antigen (PSA) levels. The 6-mo lycopene supplementation decreased PSA levels	RCT				(-) ↓ PSA	(+) ↑ plasma [lyco] ↓ BPH progression

				in men (P < 0.05), whereas there was no change in the placebo group. The plasma lycopene concentration increased in the group taking lycopene (P < 0.0001) but other plasma carotenoids were not affected. Whereas progression of prostate enlargement occurred in the placebo group as assessed by trans-rectal ultrasonography (P < 0.05) and digital rectal examination (P < 0.01), the prostate did not enlarge in the lycopene group. Symptoms of the disease, as assessed via the International Prostate Symptom Score questionnaire, were improved in both groups with a significantly greater effect in men taking lycopene supplements. In conclusion, lycopene inhibited progression of BPH.						
Cancer: prostate	Schwenke C	Lycopene for advanced hormone refractory prostate cancer: a prospective, open phase II pilot study. Schwenke C, Ubrig B, Tharmann P, Eggersmann C, Roth S. J Urol. 2009 Mar;181(3):1098-103. Epub 2009 Jan 15.	2009	PURPOSE: We investigated the influence of lycopene on the clinical and laboratory course in men with hormone refractory prostate cancer. To our knowledge this study represents the first time that subjective assessments of the course of therapy have been recorded. MATERIAL AND METHODS: We performed a prospective, open phase II pilot study, in which patients with progressive hormone refractory prostate cancer were included. Lycopene supplementation (15 mg) was given daily for 6 months. Followup laboratory tests and clinical examinations were done monthly. Changes to analgesic use and quality of life (European Organisation for Research and Treatment of Cancer QLQ-C30) were measured. The study end point was a significant change in serum prostate specific antigen, clinical progression or the end of the 6-month observation period. RESULTS: A total of 18 patients 64 to 85 years old (median age 73) were enrolled in the study during a 20-month period, of whom 17 could be analyzed. Five of the 17 patients (29%) withdrew from the study prematurely, including 4 of 5 because of prostate	Interv				N no benefits for those with advanced disease state	

				specific antigen progression and/or tumor associated complications, and 1 due to an allergic reaction to lycopene. Median prostate specific antigen doubled in 6 months from 42.7 ng/ml (range 13.8 to 521.6) in 17 patients to 96.4 ng/ml (range 13.5 to 1,240) in 12. Stable prostate specific antigen was observed in 5 of 17 patients (29%). None of the patients had a greater than 50% decrease in prostate specific antigen. Patients experienced a slight deterioration in mean health status at the end of the study compared to the outset. However, two-thirds of the patients experienced an improved or unchanged situation regardless of the clinical and biochemical course. CONCLUSIONS: No clinically relevant benefits were shown for patients with advanced stages of the disease.						
Cancer: prostate	Kristal AR	Diet, supplement use, and prostate cancer risk: results from the prostate cancer prevention trial. Kristal AR, Arnold KB, Neuhouser ML, Goodman P, Platz EA, Albanes D, Thompson IM. Am J Epidemiol. 2010 Sep 1;172(5):566-77. Epub 2010 Aug 6.	2010	The authors examined nutritional risk factors for prostate cancer among 9,559 participants in the Prostate Cancer Prevention Trial (United States and Canada, 1994-2003). The presence or absence of cancer was determined by prostate biopsy, which was recommended during the trial because of an elevated prostate-specific antigen level or an abnormal digital rectal examination and was offered to all men at the trial's end. Nutrient intake was assessed using a food frequency questionnaire and a structured supplement-use questionnaire. Cancer was detected in 1,703 men; 127 cancers were high-grade (Gleason score 8-10). There were no associations of any nutrient or supplement with prostate cancer risk overall. Risk of high-grade cancer was associated with high intake of polyunsaturated fats (quartile 4 vs. quartile 1: odds ratio = 2.41, 95% confidence interval (CI): 1.33, 4.38). Dietary calcium was positively associated with low-grade cancer but inversely associated with high-grade cancer (for quartile 4 vs. quartile 1, odds ratios were 1.27 (95% CI: 1.02, 1.57) and 0.43 (95% CI: 0.21, 0.89), respectively). Neither dietary nor supplemental intakes of nutrients often suggested for prostate	PC				N Diet N Suppl	

				cancer prevention, including lycopene, long-chain n-3 fatty acids, vitamin D, vitamin E, and selenium, were significantly associated with cancer risk. High intake of n-6 fatty acids, through their effects on inflammation and oxidative stress, may increase prostate cancer risk.						
Cancer: prostate	Chan JM	Nutritional supplements, COX-2 and IGF-1 expression in men on active surveillance for prostate cancer. Chan JM, Weinberg V, Magbanua MJ, Sosa E, Simko J, Shinohara K, Federman S, Mattie M, Hughes-Fulford M, Haqq C, Carroll PR. Cancer Causes Control. 2011 Jan;22(1):141-50. Epub 2010 Nov 20	2011	BACKGROUND: Nutritional factors are associated with reduced risk of prostate cancer progression, yet mechanisms remain unclear. We examined the effects of lycopene and fish oil supplements versus placebo on the normal prostate microenvironment, among men pursuing active surveillance for low-burden prostate cancer. We hypothesized that lycopene or fish oil supplements would down-regulate insulin-like growth factor-1 (IGF-1) and cyclooxygenase 2 (COX-2) gene expression, respectively, reflecting putative proliferation (IGF-1) and inflammatory (COX-2) pathways relevant to carcinogenesis. METHODS: We conducted a 3-month randomized, double-blinded, clinical trial comparing prostate tissue gene expression profiles (assessed by qRT-PCR) among men with favorable-risk prostate cancer receiving either 30 mg/day lycopene, 3 g/day fish oil (including 1,098 mg eicosapentaenoic and 549 mg docosahexaenoic fatty acids) or placebo. RESULTS: Among 69 men (22 assigned to lycopene, 21 to fish, and 26 to placebo), there was no difference in the change from baseline to the 3 months in IGF-1 expression level between the placebo and lycopene arms (p = 0.93) nor in COX-2 expression between the placebo and fish arms (p = 0.99). CONCLUSION: Compared to placebo, 3-month intervention with lycopene or fish oil did not significantly change IGF-1 and COX-2 gene expression in the normal prostate microenvironment in men with low-burden prostate cancer. Further analysis of global gene expression profiles may shed	RCT				N Gene expression of COX-2 or IGF-1 in prostate tissue	

				light on the bioactivity and relevance of these nutrients in prostate cancer.						
Cancer: prostate	Magbanua MJ	Gene expression and biological pathways in tissue of men with prostate cancer in a randomized clinical trial of lycopene and fish oil supplementation. Magbanua MJ, Roy R, EV, Weinberg V, Federman S, Mattie MD, Hughes-Fulford M, Simko J, Shinohara K, Haqq CM, Carroll PR, Chan JM. PLoS One. 2011;6(9):e24004. Epub 2011 Sep 1	2011	BACKGROUND: Studies suggest that micronutrients may modify the risk or delay progression of prostate cancer; however, the molecular mechanisms involved are poorly understood. We examined the effects of lycopene and fish oil on prostate gene expression in a double-blind placebo-controlled randomized clinical trial. METHODS: Eighty-four men with low risk prostate cancer were stratified based on self-reported dietary consumption of fish and tomatoes and then randomly assigned to a 3-month intervention of lycopene (n=29) or fish oil (n=27) supplementation or placebo (n=28). Gene expression in morphologically normal prostate tissue was studied at baseline and at 3 months via cDNA microarray analysis. Differential gene expression and pathway analyses were performed toidentify genes and pathways modulated by these micronutrients. RESULTS: Global gene expression analysis revealed no significant individual genes that were associated with high intake of fish or tomato at baseline or after 3 months of supplementation with lycopene or fish oil. However, exploratory pathway analyses of rank-ordered genes (based on p-values not corrected for multiple comparisons) revealed the modulation of androgen and estrogen metabolism in men who routinely consumed more fish (p=0.029) and tomato (p=0.008) compared to men who ate less. In addition, modulation of arachidonic acid metabolism (p=0.01) was observed after 3 months of fish oil supplementation compared with the placebo group; and modulation of nuclear factor (erythroid derived-2) factor 2 or Nrf2-mediated oxidative stress response for either supplement versus placebo (fish oil: p=0.01, lycopene: p=0.001). CONCLUSIONS: We did not detect significant individual genes associated with dietary intake and supplementation of lycopene and fish oil. However, exploratory	RCT				N	Gene expression

				analyses revealed candidate in vivo pathways that may be modulated by these micronutrients. TRIAL REGISTRATION: ClinicalTrials.gov NCT00402285.						
Cancer: prostate	van Breemen RB	Antioxidant effects of lycopene in African American men with prostate cancer or benign prostate hyperplasia: a randomized, controlled trial. van Breemen RB, Sharifi R, Viana M, Pajkovic N, Zhu D, Yuan L, Yang Y, Bowen PE, Stacewicz-Sapuntzakis M. Cancer Prev Res (Phila). 2011 May;4(5):711-8. Epub 2011 Mar 23.	2011	Consumption of tomato products is associated with a decreased risk of developing prostate cancer, and lycopene, the red carotenoid in the tomato, is a potent antioxidant that might contribute to this chemoprevention activity. A double-blind, randomized, placebo-controlled trial of 105 African American men veterans, recommended for prostate biopsy to detect cancer, was carried out to investigate whether oral administration of lycopene increases lycopene levels in blood and prostate tissue and lowers markers of oxidative stress. Urology patients were randomly assigned to receive 30 mg/d of lycopene as a tomato oleoresin or placebo for 21 days prior to prostate biopsy for possible diagnosis of prostate cancer. A total of 47 men had a diagnosis of prostate cancer, and 58 men had a diagnosis of benign prostate hyperplasia. Diet, smoking, and drinking habits were assessed. For the men receiving lycopene, the mean lycopene concentration increased from 0.74 ± 0.39 to 1.43 ± 0.61 μmol/L in plasma ($P < 0.0001$) and from 0.45 ± 0.53 to 0.59 ± 0.47 pmol/mg in prostate tissue ($P = 0.005$). No significant changes in the DNA oxidation product 8-oxo-deoxyguanosine and the lipid peroxidation product alondialdehyde were observed in prostate tissue and plasma, respectively, as a result of lycopene administration.	RCT				N DNA ox (8-oxo-deoxyguanosine) Lipid peroxidation (MDA= malondialdehyde)	