Special Interests

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, -
Bioavail-ability	O'Neill ME	Intestinal absorption of beta-carotene, lycopene and lutein in men and women following a standard meal: response curves in the triacylglycerol-rich lipoprotein fraction. O'Neill ME, Thurnham DI. Br J Nutr. 1998 Feb;79(2):149-59.	1998	A high intake of fruit and vegetables is believed to be protective against heart disease and cancer. beta-Carotene has been closely examined for evidence of these protective properties but evidence is still conflicting and there are many other carotenoids in plant foods which deserve attention. This paper reports studies on the concentrations of lutein and lycopene in the triacylglycerol-rich lipoprotein (TRL) fraction of plasma in comparison with beta-carotene following a large dose of the respective carotenoids fed with a standard meal after an overnight fast. beta-Carotene (40 mg) was given to twelve volunteers (six men and six women) and six of the same volunteers (three men and three women) also received 31.2 mg lutein or 38 mg lycopene. Plasma was collected at hourly intervals for 8 h and the TRL fraction was separated and subsequently analysed for the respective carotenoids and retinyl palmitate in the case of beta-carotene. Intestinal uptake of the three carotenoids was estimated using the 'area under the curve' method and apparent absorption was calculated from these results. The response curves in the TRL fraction for beta-carotene and retinyl palmitate occurred maximally over the fourth to fifth hour postprandially. There was a correlation between the TRL concentrations of beta-carotene and retinyl palmitate (males r 0.62, P < 0.001; females r 0.52, P < 0.001) and there was no significant difference between men and women either in	Interv				(+) [lyco]	TRL fractions

				the total amount of beta-carotene appearing in the TRL fraction or in the amount converted to retinol. On estimation, approximately 1.4 mg of the 40 mg beta-carotene dose was absorbed and this was not significantly different from the amount of lycopene (1.0 mg) but significantly different ($P < 0.05$) from the amount of lutein (0.8 mg) absorbed, after correction for the smaller doses administered. There was approximately a twofold difference between subjects in the uptake of beta-carotene into the TRL fraction, a two- to threefold variation in lycopene and a two- to threefold variation in lutein. Despite these inter-subject differences, in three volunteers between whom there was a threefold difference in beta-carotene in the TRL fraction and a twofold difference in retinol formation, repeat experiments with beta-carotene 4 months later found differences of only 3-6% in the TRL beta-carotene content and 4-9% for the TRL retinol formed. In conclusion, large inter-subject variation in TRL carotene uptake precluded any differences between sexes but surprising intra-subject consistency was observed in TRL beta-carotene uptake of three subjects.						
Bioavail-ability	Boileau TWM	Boileau TW, Boileau AC, Erdman JW Jr. Bioavailability of all-trans and cis-isomers of lycopene. Exp Biol Med (Maywood). 2002 Nov;227(10):914-9.	2002	Lycopene, the predominant carotenoid in tomatoes, is among the major carotenoids in serum and tissues of Americans. Although about 90% of the lycopene in dietary sources is found in the linear, all-trans conformation, human tissues contain mainly cis-isomers. Several research groups have suggested that cis-isomers of lycopene are better absorbed than the all-trans form because of the shorter length of the cis-isomer, the greater solubility of cis-	Review					

				isomers in mixed micelles, and/or as a result of the lower tendency of cis-isomers to aggregate. Work with ferrets, a species that absorbs carotenoids intact, has demonstrated that whereas a lycopene dose, stomach, and intestinal contents contained 6-18% cis-lycopene, the mesenteric lymph secretions contained 77%-cis isomers. The ferret studies support the hypotheses that cis-isomers are substantially more bioavailable then all-trans lycopene. In vitro studies suggest that cis-isomers are more soluble in bile acid micelles and may be preferentially incorporated into chylomicrons. The implications of these findings are not yet clear. Rats appear to accumulate lycopene in tissues within the ranges reported for humans, suggesting that they can be used to study effects of lycopene isomers on disease processes. Investigations are underway to determine whether there are biological differences between all-trans and various cis-isomers of lycopene regarding its antioxidant properties or other biological functions.						
Bioavail-ability	Reboul E	Bioaccessibility of carotenoids and vitamin E from their main dietary sources. Reboul E, Richelle M, Perrot E, Desmoulins-Malezet C, Pirisi V, Borel P. J Agric Food Chem. 2006 Nov 15;54(23):8749-55.	2006	Vitamin E and carotenoids are fat-soluble microconstituents that may exert beneficial effects in humans, including protection against cancer, cardiovascular diseases, and age-related eye diseases. Their bioavailability is influenced by various factors including food matrix, formulation, and food processing. Since human studies are labor-intensive, time-consuming, and expensive, the in vitro model used in this study is increasingly being used to estimate bioaccessibility of these microconstituents. However, the ability of this model to predict	In vitro				N lyco about in the middle of carot-enoids for bioavail-ability in invitro model	

				bioavailability in a healthy human population has not yet been verified. The first aim of this study was to validate this model by comparing model-derived bioaccessibility data with (i) human-derived bioaccessibility data and (ii) published mean bioavailability data reported in studies involving healthy humans. The second aim was to use it to measure alpha- and gamma-tocopherol, beta-carotene, lycopene, and lutein bioaccessibility from their main dietary sources. Bioaccessibility as assessed with the in vitro model was well correlated with human-derived bioaccessibility values ($r = 0.90$, $p < 0.05$), as well as relative mean bioavailability values reported in healthy human groups ($r = 0.98$, $p < 0.001$). The bioaccessibility of carotenoids and vitamin E from the main dietary sources was highly variable, ranging from less than 0.1% (beta-carotene from raw tomato) to almost 100% (alpha-tocopherol from white bread). Bioaccessibility was dependent on (i) microconstituent species (lutein > beta-carotene and alpha-carotene > lycopene and alpha-tocopherol generally > gamma-tocopherol), (ii) food matrix, and (iii) food processing.						
Bone	Keen RW	Can biochemical markers predict bone loss at the hip and spine?: a 4-year prospective study of 141 early postmenopausal women. Keen RW, Nguyen T, Sobnack R, Perry LA, Thompson PW, Spector TD.	1996	A number of recent studies have suggested that non-invasive measures of bone turnover are associated with bone loss at the forearm in postmenopausal women. Whether bone turnover markers are predictive of bone loss from the clinically important sites of lumbar spine and femoral neck remain unclear, and was the aim of this 4-year prospective study. One hundred and forty-one normal, postmenopausal women (mean age 52.0 +/- 3.3 years, mean menopause	PC					N markers of TO ≠ bone loss of hip & bone

		Osteoporos Int. 1996;6(5):399-406.		duration 20.4 +/- 5.7 months) were recruited for the study in 1988. Fasting early morning samples of blood and urine were collected at the baseline visit and stored at -20 degrees C prior to analysis. Serum was assayed for osteocalcin, oestradiol, oestrone, oestrone sulphate, testosterone, sex hormone binding globulin, dehydroepiandrosterone sulphate and total alkaline phosphatase. Urine was assayed for calcium, hydroxyproline, oestrone glucuronide and the collagen cross-links pyridinoline and deoxypyridinoline using high-performance liquid chromatography. Bone density was measured at the lumbar spine and femoral neck using dual photon absorptiometry at time 0, 12, 24 and 48 months. The mean annual percentage change in bone density (SE) was -1.41% (0.18) at the lumbar spine and -0.86% (0.22) at the femoral neck. There was no evidence of bimodality or a fast loser subgroup as the rates of change were normally distributed. Both simple and multiple stepwise regression analyses revealed no significant correlation between the rates of change in bone density with any biochemical marker, either individually or in combination, despite the study having sufficient power (80%) to detect a correlation of 0.5 between any biochemical marker levels and bone loss. We conclude that single measurements of these markers of bone turnover and endogenous sex hormones appear unlikely to be clinically useful in predicting early postmenopausal bone loss from either the spine or the hip.						
Bone	Greenspan SL	Early changes in biochemical	1998	Although the antiresorptive agent alendronate has been shown to	n= 120	CT/RCT				

		markers of bone turnover predict the long-term response to alendronate therapy in representative elderly women: a randomized clinical trial. Greenspan SL, Parker RA, Ferguson L, Rosen HN, Maitland-Ramsey L, Karpf DB. J Bone Miner Res. 1998 Sep;13(9):1431-8.		increase bone mineral density (BMD) at the hip and spine and decrease the incidence of osteoporotic fractures in older women, few data are available regarding early prediction of long-term response to therapy, particularly with regard to increases in hip BMD. Examining short-term changes in biochemical markers incorporates physiologic response with therapeutic compliance and should provide useful prognostic information for patients. The objective of this study was to examine whether early changes in biochemical markers of bone turnover predict long-term changes in hip BMD in elderly women. The study was a double-blind, placebo-controlled, randomized clinical trial which took place in a community-based academic hospital. One hundred and twenty community- dwelling, ambulatory women 65 years of age and older participated in the study. Intervention consisted of alendronate versus placebo for 2.5 years. All patients received appropriate calcium and vitamin D supplementation. The principal outcome measures included BMD of the hip (total hip, femoral neck, trochanter, and intertrochanter), spine (posteroanterior [PA] and lateral), total body, and radius. Biochemical markers of bone resorption included urinary N-telopeptide cross-linked collagen type I and free deoxypyridinoline; markers of bone formation included serum osteocalcin and bone-specific alkaline phosphatase. Long-term alendronate therapy was associated with increased BMD at the total hip (4.0%), femoral neck (3.1%), trochanter (5.5%), intertrochanter (3.8%), PA spine (7.8%), lateral spine	based on alendro-nate					

				(10.6%), total body (2.2%), and one-third distal radius (1.3%) in elderly women (all $p < 0.01$). In the placebo group, bone density increased 1.9-2.1% at the spine ($p < 0.05$) and remained stable at all other sites. At 6 months, there were significant decreases in all markers of bone turnover (-10% to -53%, $p < 0.01$) in women on alendronate. The changes in urinary cross-linked collagen at 6 months correlated with long-term bone density changes at the hip ($r = -0.35$, $p < 0.01$), trochanter ($r = -0.36$, $p < 0.01$), PA spine ($r = -0.41$, $p < 0.01$), and total body ($r = -0.34$, $p < 0.05$). At 6 months, patients with the greatest drop in urinary cross-linked collagen (65% or more) demonstrated the greatest gains in total hip, trochanteric, and vertebral bone density (all $p < 0.05$). A 30% decrease in urinary cross-linked collagen at 6 months predicted a bone density increase of 2.8-4.1% for the hip regions and 5.8-6.9% for the spine views at the 2.5-year time point ($p < 0.05$). There were no substantive associations between changes in biochemical markers and bone density in the placebo group. Alendronate therapy was associated with significant long-term gains in BMD at all clinically relevant sites, including the hip, in elderly women. Moreover, these improvements were associated with early decreases in biochemical markers of bone turnover. Early dynamic decreases in urinary cross-linked collagen can be used to monitor and predict long-term response to bisphosphonate therapy in elderly women. Future studies are needed to determine if early assessment improves long-term patient compliance or uncovers poor compliance, thereby aiding the						

				physician in maximizing the benefits of therapy.						
Bone	Melhus H	Smoking, antioxidant vitamins, and the risk of hip fracture. Melhus H, MichaÃ«lsson K, Holmberg L, Wolk A, Ljunghall S. J Bone Miner Res. 1999 Jan;14(1):129-35.	1999	Smoking increases the concentrations of free radicals, which have been suggested to be involved in bone resorption. We examined whether the dietary intake of antioxidant vitamins may modify the increased hip fracture risk associated with smoking. We prospectively studied 66,651 women who were 40-76 years of age. Forty-four of the cohort members who sustained a first hip fracture within 2-64 months of follow-up (n = 247) and 93 out of 873 age-matched controls were current smokers. Information on diet was obtained by a validated food-frequency questionnaire. The relative risk of hip fracture for current versus never smokers was analyzed in relation to the dietary intake of antioxidant vitamins stratified into two categories (low/high), where median intakes among the controls were used as cut-off points. After adjustment for major osteoporosis risk factors, the odds ratio (OR) for hip fracture among current smokers with a low intake of vitamin E was 3.0 (95% confidence interval 1.6-5.4) and of vitamin C 3.0 (1.6-5.6). In contrast, the OR decreased to 1.1 (0.5-2.4) and 1.4 (0.7-3.0) with high intakes of vitamin E and C, respectively. This effect was not seen for beta-carotene, selenium, calcium, or vitamin B6. In current smokers with a low intake of both vitamins E and C, the OR increased to 4.9 (2.2-11.0). The influence of the intake of these two antioxidant vitamins on hip fracture risk was less pronounced in former smokers. Our results suggest a role for oxidant stress in the adverse effects on the skeleton of smoking, and that an insufficient dietary intake of	PC					(-) ↓ Vit C ↑ risk of hip fracture in smokers

				vitamin E and C may substantially increase the risk of hip fracture in current smokers, whereas a more adequate intake seems to be protective.						
Bone	Sellmeyer DE	Potassium citrate prevents increased urine calcium excretion and bone resorption induced by a high sodium chloride diet. Sellmeyer DE, Schloetter M, Sebastian A. J Clin Endocrinol Metab. 2002 May;87(5):2008-12.	2002	The amount of sodium chloride in the diet of industrialized nations far exceeds physiological requirements. The impact of abundant dietary salt on skeletal health has yet to be established, but is potentially detrimental through increased urinary calcium losses. We examined the effect of increased dietary sodium chloride on urine calcium excretion and bone turnover markers in postmenopausal women and, further, whether potassium citrate attenuates the effects of increased dietary salt. Postmenopausal women (n = 60) were adapted to a low-salt (87 mmol/d sodium) diet for 3 wk, then randomized to a high-salt (225 mmol/d sodium) diet plus potassium citrate (90 mmol/d) or a high-salt diet plus placebo for 4 wk. Urine calcium, urine N-telopeptide, urine cAMP, serum osteocalcin, and fasting serum PTH were measured at the end of the low- and high-salt diets. On the high salt plus placebo diet, urine calcium increased 42 +/- 12 mg/d (mean +/- SEM), but decreased 8 +/- 14 mg/d in the high salt plus potassium citrate group (P = 0.008, potassium citrate vs. placebo, unpaired t test). N-telopeptide increased 6.4 +/- 1.4 nanomoles bone collagen equivalents per millimole creatinine in the high salt plus placebo group and 2.0 +/- 1.7 nanomoles bone collagen equivalents per millimole creatinine in the high salt plus potassium citrate group (P < 0.05, potassium citrate vs. placebo, unpaired t test). Osteocalcin, PTH, and cAMP were not significantly altered. The addition	CT/RCT	(-)				No Lyco Na, K

				of oral potassium citrate to a high-salt diet prevented the increased excretion of urine calcium and the bone resorption marker caused by a high salt intake. Increased intake of dietary sources of potassium alkaline salts, namely fruit and vegetables, may be beneficial for postmenopausal women at risk for osteoporosis, particularly those consuming a diet generous in sodium chloride.						
Bone	Kim L	Lycopene II--effect on osteoblasts: the carotenoid lycopene stimulates cell proliferation and alkaline phosphatase activity of SaOS-2 cells. Kim L, Rao AV, Rao LG. J Med Food. 2003 Summer;6(2):79-86.	2003	We explored the possibility that lycopene, a carotenoid that is abundant in tomatoes, has effects on proliferation and differentiation of osteoblasts, the cells responsible for bone formation. Human osteoblast-like osteosarcoma SaOS-2 cells were cultured for 24 hours, after which varying doses of a water-dispersible microemulsion preparation of lycopene or vehicle of the same dilution were added. The cells were further cultured for 24 to 144 hours, and then the cell numbers were counted. Lycopene at 10(-6) and 10(-5) M had significant stimulatory effects on cell numbers, compared with the corresponding vehicle treatment, at all time points from 24 to 144 hours. The effects of lycopene on activity of the differentiation marker alkaline phosphatase activity in the absence or presence of dexamethasone were shown to be dependent on the stage of cell differentiation. This is the first report on the effects of lycopene on osteoblasts of human origin; the results may have important applications in the prevention of osteoporosis.	Cell culture				(-) affected alkaline phosphatase activity, indep of cell stage	
Bone	Maggio D	Marked decrease in plasma antioxidants in	2003	Although recent epidemiological studies found a positive correlation between dietary vitamin C intake	CC					(-) ↓ anti-ox

		aged osteoporotic women: results of a cross-sectional study. Maggio D, Barabani M, Pierandrei M, Polidori MC, Catani M, Mecocci P, Senin U, Pacifici R, Cherubini A. J Clin Endocrinol Metab. 2003 Apr;88(4):1523-7.		and bone mineral density, data on plasma levels of vitamin C or other antioxidants in osteoporotic subjects are scanty. The aim of this study was to evaluate whether antioxidant defenses are decreased in elderly osteoporotic women and, if this is the case, to understand whether osteoporosis is a condition characterized by increased oxidative stress. To answer these questions, plasma vitamins C, E, and A; uric acid; and the enzymatic activities of superoxide dismutase in plasma and erythrocytes and of glutathione peroxidase in plasma were measured in 75 subjects with osteoporosis and 75 controls. Dietary and endogenous antioxidants were consistently lower in osteoporotic than in control subjects. On the other hand, plasma levels of malondialdehyde, a byproduct of lipid peroxidation, did not differ between groups. Our results reveal that antioxidant defenses are markedly decreased in osteoporotic women. The mechanisms underlying antioxidant depletion and its relevance to the pathogenesis of osteoporosis deserve further investigation.						defense in osteo women vs non-osteo No Lyco
Bone	Zhang J	Antioxidant intake and risk of osteoporotic hip fracture in Utah: an effect modified by smoking status. Zhang J, Munger RG, West NA, Cutler DR, Wengreen HJ, Corcoran CD. Am J Epidemiol. 2006 Jan	2006	The role of antioxidant intake in osteoporotic hip fracture risk is uncertain and may be modified by smoking. In the Utah Study of Nutrition and Bone Health, a statewide, population-based case-control study, the authors investigated whether antioxidant intake was associated with risk of osteoporotic hip fracture and whether this association was modified by smoking status. The analyses included data on 1,215 male and female cases aged > or = 50 years who incurred a hip fracture during 1997-2001 and 1,349 age- and	CC					(-) anti-ox status on hip fracture risk

		1;163(1):9-17. Epub 2005 Nov 23.		sex-matched controls. Diet was assessed by food frequency questionnaire. Among ever smokers, participants in the highest quintile of vitamin E intake (vs. the lowest) had a lower risk of hip fracture after adjustment for confounders (odds ratio = 0.29, 95% confidence interval (CI): 0.16, 0.52; p-trend < 0.0001). The corresponding odds ratio for beta-carotene intake was 0.39 (95% CI: 0.23, 0.68; p-trend = 0.0004), and for selenium intake it was 0.27 (95% CI: 0.12, 0.58; p-trend = 0.0003). Vitamin C intake did not have a significant graded association with hip fracture risk among ever smokers. Similar findings were obtained when an overall antioxidant intake score was used (odds ratio = 0.19, 95% CI: 0.10, 0.37; p-trend < 0.0001). No similar associations were found in never smokers. Antioxidant intake was associated with reduced risk of osteoporotic hip fracture in these elderly subjects, and the effect was strongly modified by smoking status.						
Bone	Rao LG	Lycopene consumption decreases oxidative stress and bone resorption markers in postmenopausal women. Rao LG, Mackinnon EF, Josse RG, Murray TM, Strauss A, Rao AV. Osteoporoos Int. 2007 Jan;18(1):109-15.	2007	INTRODUCTION: Oxidative stress induced by reactive oxygen species (ROS) is associated with the risk of osteoporosis, and can be reduced by certain dietary antioxidants. Lycopene is an antioxidant known to decrease the risk of age-related chronic diseases, such as cancer. However, the role of lycopene in osteoporosis has not yet been investigated. MATERIALS AND METHODS: In a cross-sectional study, 33 postmenopausal women aged 50-60 years provided seven-day dietary records and blood samples. Serum samples were used to measure serum lycopene, lipid peroxidation, protein thiols, bone	CS				(-)	

				alkaline phosphatase (BAP), and cross-linked N-telopeptides of type I collagen (NTx). The serum lycopene per kilogram body weight of the participants was grouped into quartiles and associated with the above serum parameters using one-way ANOVA and the Newman-Keuls post-test. RESULTS: The results showed that groups with higher lycopene intake, as determined from the dietary records, had higher serum lycopene ($p<0.02$). A higher serum lycopene was found to be associated with a low NTx ($p<0.005$). Similarly, groups with higher serum lycopene had lower protein oxidation ($p<0.05$). DISCUSSION: In conclusion, these results suggest that the dietary antioxidant lycopene reduces oxidative stress and the levels of bone turnover markers in postmenopausal women, and may be beneficial in reducing the risk of osteoporosis.						
Bone MOA	Kim L	Lycopene effect on osteoblasts: the carotenoid lycopene stimulates cell proliferation and alkaline phosphatase activity of SaOS-2 cells. Kim L, Rao AV, Rao LG. J Med Food 2003;6:79–86.	2003	We explored the possibility that lycopene, a carotenoid that is abundant in tomatoes, has effects on proliferation and differentiation of osteoblasts, the cells responsible for bone formation. Human osteoblast-like osteosarcoma SaOS-2 cells were cultured for 24 hours, after which varying doses of a water-dispersible microemulsion preparation of lycopene or vehicle of the same dilution were added. The cells were further cultured for 24 to 144 hours, and then the cell numbers were counted. Lycopene at 10-6 and 10-5 M had significant stimulatory effects on cell numbers, compared with the corresponding vehicle	Cell culture: human				(-) ↑ ALP in more differnetiated osteoblasts (bone builders)	

				treatment, at all time points from 24 to 144 hours. The effects of lycopene on activity of the differentiation marker alkaline phosphatase activity in the absence or presence of dexamethasone were shown to be dependent on the stage of cell differentiation. This is the first report on the effects of lycopene on osteoblasts of human origin; the results may have important applications in the prevention of osteoporosis.						
Bone MOA	Rao LG	Lycopene I—Effect on Osteoclasts: Lycopene Inhibits Basal and Parathyroid Hormone-Stimulated Osteoclast Formation and Mineral Resorption Mediated by Reactive Oxygen Species in Rat Bone Marrow Cultures Rao LG, Krishnadev N, Banasikowska K, Rao AV Journal of Medicinal Food. July 2003, Vol. 6, No. 2: 69-78	2003	Osteoclasts have been shown to produce reactive oxygen species (ROS) that can stimulate bone resorption. We explored the hypothesis that lycopene, the antioxidant carotenoid from tomatoes, can inhibit mineral resorption by inhibiting osteoclast formation and the production of ROS. Cells from bone marrow prepared from rat femur were plated into 16-well calciumphosphate–coated Osteologic Multi-test Slides and cultured in a-minimal essential medium supplemented with dexamethasone, b-glycerophosphate, and ascorbic acid. The cells were treated with varying doses of lycopene in the absence or presence of parathyroid hormone (PTH) at the start of culture and at each medium change (i.e., every 48 hours). On day 8, mineral resorption pits were quantitated. Similar, parallel experiments were carried out in 12–well plastic dishes to assess tartrate-resistant acid phosphatase (TRAP) activity. Results showed that lycopene inhibited TRAP1 formation of multinucleated cells in both vehicleand PTH-treated cultures. Osteoclasts reduced nitroblue tetrazolium (NBT) to purple-colored formazan, indicating the	Cell culture: rat				(-) ↓ osteoclast formation	

				presence of ROS in these cells. The formazan-staining cells were decreased by treatment with 10-5 M lycopene, indicating that lycopene inhibited the formation of ROS-secreting osteoclasts. In conclusion, we have shown that lycopene inhibits basal and PTH-stimulated osteoclastic mineral resorption and formation of TRAP1 multinucleated osteoclasts, as well as the ROS produced by osteoclasts. These findings are novel and may be important in the pathogenesis, treatment, and prevention of osteoporosis						
Brain	Craft NE	Carotenoid, tocopherol, and retinol concentrations in elderly human brain. Craft NE, Haitema TB, Garnett KM, Fitch KA, Dorey CK. J Nutr Health Aging. 2004;8(3):156-62.	2004	BACKGROUND: Antioxidants, such as tocopherols and carotenoids, have been implicated in the prevention of degenerative diseases. Although correlations have been made between diseases and tissue levels of antioxidants, to date there are no reports of individual carotenoid concentrations in human brain. OBJECTIVE: To measure the major carotenoids, tocopherols, and retinol in frontal and occipital regions of human brain. DESIGN: Ten samples of brain tissue from frontal lobe cortex and occipital cortex of five cadavers were examined. Sections were dissected into gray and white matter, extracted with organic solvents, and analyzed by HPLC. RESULTS: At least 16 carotenoids, 3 tocopherols, and retinol were present in human brain. Major carotenoids were identified as lutein, zeaxanthin, anhydrolutein, alpha- cryptoxanthin, beta- cryptoxanthin, alpha-carotene, cis- and trans-betacarotene, and cis- and trans-lycopene. Xanthophylls (oxygenated carotenoids)						↓ total carotenoids found in frontal cortex of cadavers

				accounted for 66-77% of total carotenoids in all brain regions examined. Similar to neural retina, the ratio of zeaxanthin to lutein was high and these two xanthophylls were significantly correlated (p <0.0001). The tocopherol isomers occurred in the brain over a wider range of mean concentrations (0.11-17.9 nmol/g) than either retinol (87.8 - 163.3 pmol/g) or the identified carotenoids (1.8-23.0 pmol/g). CONCLUSIONS: The frontal cortex, generally vulnerable in Alzheimer's disease, had higher concentrations of all analytes than the occipital cortex which is generally unaffected. Moreover, frontal lobes, but not occipital lobes, exhibited an age-related decline in retinol, total tocopherols, total xanthophylls and total carotenoids. The importance of these differences and the role(s) of these antioxidants in the brain remain to be determined. Article not avail online						
Brain	Youm JW	Transgenic tomatoes expressing human beta-amyloid for use as a vaccine against Alzheimer's disease. Youm JW, Jeon JH, Kim H, Kim YH, Ko K, Joung H, Kim H. Biotechnol Lett. 2008 Oct;30(10):1839-45. Epub 2008 Jul 5.	2008	Human beta-amyloid (Abeta) is believed to be one of the main components of Alzheimer's disease, so reduction of Abeta is considered a key therapeutic target. Using Agrobacterium-mediated nuclear transformation, we generated transgenic tomatoes for Abeta with tandem repeats. Integration of the human Abeta gene into the tomato genome and its transcription were detected by PCR and Northern blot, respectively. Expression of the Abeta protein was confirmed by western blot and ELISA, and then the transgenic tomato line expressing the highest protein level was selected for vaccination. Mice immunized orally with total soluble extracts from the						

				transgenic tomato plants elicited an immune response after receiving a booster. The results indicate that tomato plants may provide a useful system for the production of human Abeta antigen.						
Brain	Kumar P	Lycopene modulates nitric oxide pathways against 3-nitropropionic acid-induced neurotoxicity. Kumar P, Kalonia H, Kumar A. Life Sci. 2009 Nov 4;85(19-20):711-8. Epub 2009 Oct 12.	2009	AIM: The present study has been designed to investigate the involvement of the nitric oxide mechanism in the protective effect of lycopene against 3-nitropropionic acid-induced Huntington's disease-like symptoms in rats. MAIN METHODS: The present experimental protocol design includes systemic 3-nitropropionic acid (10mg/kg i.p) treatment for 14 days. Lycopene (2.5, 5 and 10mg/kg) was given orally, once a day, 1h before 3-nitropropionic acid treatment for 14 days. Body weight and behavioral parameters (locomotor and rotarod activity) were assessed on 1st, 5th, 10th and 15th day post-3-nitropropionic acid administration. Malondialdehyde, nitrite concentration, superoxide dismutase and catalase levels were measured on the 15th day in the striatum, cortex and hippocampus. Mitochondrial enzyme complexes were also assessed in these brain areas. Systemic 3-nitropropionic acid treatment significantly reduced body weight, locomotor activity and oxidative defense. The mitochondrial enzyme activities were also significantly impaired in he examined brain regions in 3-nitropropionic acid-treated animals. KEY FINDINGS: Lycopene (2.5, 5 and 10mg/kg) treatment significantly attenuated the impairment in behavioral, biochemical and mitochondrial enzyme activities as compared to	Rat				(-) attenuated behavioral, biochem, and cellular response to 3-nitropropionic acid	

				the 3-nitropropionic acid-treated group. l-arginine (50mg/kg) pretreatment with a sub-effective dose of lycopene (5mg/kg) significantly attenuated the protective effect of lycopene. Furthermore, L-NAME (10mg/kg) pretreatment with a sub-effective dose of lycopene (5mg/kg) for 14 days significantly potentiated the protective effect. SIGNIFICANCE: The results of the present study suggest that the nitric oxide modulation is involved in the protective effect of lycopene against 3-NP-induced behavioral, biochemical and cellular alterations in rats.						
Brain	Kumar P	Effect of lycopene and epigallocatechin-3-gallate against 3-nitropropionic acid induced cognitive dysfunction and glutathione depletion in rat: a novel nitric oxide mechanism. Kumar P, Kumar A. Food Chem Toxicol. 2009 Oct;47(10):2522-30. Epub 2009 Jul 17	2009	Huntington's disease is a neurodegenerative disorder characterized by symptoms like chorea and dementia. There is no exact therapeutic agent available to manage and cure this disease. 3-Nitropropionic acid, a neurotoxin causes gait and memory impairment which leads to oxidative damage and upsets glutathione defense in animals. 3-NP model is a useful tool to develop suitable therapeutic agent in the treatment of Huntington's disease. Present study compares the effects of lycopene and epigallocatechin-3-gallate (EGCG) on memory impairment and disturbs glutathione system against 3-NP treatment. 3-NP treatment significantly impaired memory as assessed in Morris water maze and elevated plus maze tasks. On the 15 day, the levels of reduced glutathione, total glutathione and glutathione-S-transferase were also significantly decreased in the striatum, hippocampus and cortex	Rat				(-) improved memory and glutothione system function in response to 3-nitropropionic acid	

				areas of the brain. The treatment with lycopene (2.5, 5 and 10mg/kg) and EGCG (10, 20 and 40 mg/kg) significantly improved memory and restored glutathione system functioning. Further, L-arginine and L-NAME pretreatment with the sub effective dose of lycopene (5mg/kg) and EGCG (20mg/kg) reversed and potentiate their protective effects respectively. In conclusion, lycopene and EGCG could be used to mange 3-NP induced behavioral and biochemical alterations by involving nitric oxide pathways.						
Brain	Wang W	Nutritional biomarkers in Alzheimer's disease: the association between carotenoids, n-3 fatty acids, and dementia severity. Wang W, Shinto L, Connor WE, Quinn JF. J Alzheimers Dis. 2008 Feb;13(1):31-8.	2008	Carotenoids are fat-soluble antioxidants that may protect polyunsaturated fatty acids, such as n-3 fatty acids from oxidation, and are potentially important for Alzheimer's disease (AD) prevention and treatment. Fasting plasma carotenoids were measured in 36 AD subjects and 10 control subjects by HPLC. Correlations between plasma carotenoid levels, red blood cell (RBC) n-3 fatty acids, and dementia severity were examined in AD patients. Moderately severe AD patients (MMSE=16-19) had much lower plasma levels of two major carotenoids: lutein and beta-carotene, compared to mild AD patients (MMSE=24-27) or controls. Among AD patients, variables (lutein, beta-carotene, RBC docosahexaenoic acid (DHA) and LDL-cholesterol) were significantly correlated with MMSE. A lower MMSE score was associated with lower lutein, beta-carotene and RBC DHA levels, and a higher LDL-cholesterol level. These variables explained the majority of variation in dementia severity (55% of variance in MMSE). Lutein, beta-carotene and beta-cryptoxanthin were positively	CC					Lutein, b-carotene

				correlated with RBC DHA in AD patients. The association between higher carotenoids levels and DHA and higher MMSE scores, supports a protective role of both types of nutrients in AD. These findings suggest targeting multiple specific nutrients, lutein, beta-carotene, and DHA in strategies to slow the rate of cognitive decline.						
BW	Kaufmann NA	Eating habits and opinions of teen-agers on nutrition and obesity. Kaufmann NA, Poznanski R, Guggenheim K. J Am Diet Assoc. 1975 Mar;66(3):264-8.	1975	Opinions about good nutrition, causes of obesity and its prevention, as well as certain eating habits, were studied in 482 Israeli children (251 boys and 231 girls), thirteen to fourteen years old. Height, weight, and triceps skinfolds were measured. Mean relative weight and relative logarithmic skinfold thickness were close to standard, although 8 per cent of the boys and 9 per cent of the girls weighed more than 120 per cent of standard weight for their age and sex.Weight was closely associated with skinfold thickness. Over two-thirds of both boys and girls believed that daily consumption of milk, bread, fruits, eggs, cheese, meat, and tomatoes is desirable, and about two-thirds stated that overeating is a cause of obesity. More overweight than thin and normal-weight children indicated that, to prevent obesity, all kinds of food are permissible, but only in limited amounts. Most children believed in the fattening value of cakes, sweets, fried and fatty food, potatoes, bread, and nuts. The belief in the fattening value of potatoes, bread, and nuts was shared by a higher percentage of overweight than of under- and normal-weight children. Overweight children, particularly girls, reported eating less bread, cake, and cream, adding less sugar to beverages, and eating	CS					(+) Children believe ↑ tomato intake = good eating habits

				sweets and ice cream less frequently than thin and normal-weight children. A higher percentage of the obese group reported skipping one meal and eating no snack at school. Overweight teen-agers appear to be more conscious of their food intake than under- and normal-weight children.						
BW	Guggenheim K	Attitudes of adolescents to their body build and the problem of juvenile obesity. Guggenheim K, Poznanski R, Kaufmann NA. Int J Obes. 1977;1(2):135-49.	1977	Prevalence of obesity, attitude to body weight and dimensions, eating habits, opinions on good nutrition and on the causes and prevention of obesity were studied in two groups of Israeli children, each comprising about 500 boys and girls, 13--14 years old. Mean relative weight was close to median weight for height, although 9 per cent of both boys and girls weighed more than 120 per cent of median weight. Weight was closely related to triceps skinfold thickness. Twenty-six per cent of the boys and 15 per cent of the girls rated themselves as thin, 61 per cent of children of both sexes as medium, and 13 per cent of the boys and 25 per cent of the girls as obese. Self-perception of body build was more closely related to weight than to skinfold thickness. Two-thirds of the boys and over one-half of the girls were satisfied with their weight, but dissatisfaction with size and shape was often expressed. Boys wished to have larger muscles and chest circumference and many girls, even when not obese, wanted to be smaller in size and shape. Most of the obese children wanted to lose weight. Of 499 children examined, 16 boys (7 per cent of the sample) and 58 (21 per cent) girls reported for dietary therapy. While most of these children were obese, by either subjective or objective criteria, an appreciable number of nonobese	CS					(+) Children believe ↑ tomato intake = good eating habits

				children were also dieting. The children's own perception of their body build seemed to be a strong motivation to diet for weight control. Most of the dieters did not receive any dietary advice from professional people. Over two-thirds of both boys and girls believed that daily consumption of milk, bread, fruits, eggs, cheese, meat, and tomatoes is desirable. More overweight than thin and normal-weight children indicated that, to prevent obesity, all kinds of food are permissible, but only in limited amounts. Most children believed in the fattening value of cakes, sweets, fried and fatty foods, potatoes, bread and nuts. Overweight children, particularly girls, reported eating less bread, cake and cream, adding less sugar to beverages, and eating sweets and ice cream less frequently than thin and normal-weight children. Overweight teen-agers appear to be more conscious of their food intake than under- and normal-weight children.						
BW	Nolan LJ	Elevated plasma cholecystokinin and appetitive ratings after consumption of a liquid meal in humans. Nolan LJ, Guss JL, Liddle RA, Pi-Sunyer FX, Kissileff HR. Nutrition. 2003 Jun;19(6):553-7.	2003	OBJECTIVE: This study had two objectives. The first was to evaluate the possibility that, in a previous study, a soup preload augmented the reduction of food intake in a test meal induced by an exogenous infusion of cholecystokinin (CCK) because the soup also endogenously released CCK. The second was to compare CCK release by soup between men and women to determine whether the increased satiating effectiveness of soup in women as opposed to men could have been partly attributable to differences in CCK release.	RCT		(+) ↑CCK= ↑satiety			

				METHODS: By using a bioassay that measures all of its known isoforms, we determined plasma CCK levels at baseline and at several times postprandially in eight healthy, non-obese men and women (four of each sex). Each subject ingested 800 g of tomato soup, which was followed 30 min later by 300 g of a yogurt shake. Appetitive ratings were also collected and related to CCK levels. RESULTS: Ingestion of tomato soup significantly increased plasma CCK levels by 3.81 pmol/L (+/- 1.21 standard error, P = 0.016) over baseline within 30 min in all subjects combined. When CCK concentrations at 5 min after soup and 5 min after yogurt were averaged, the women's mean averaged concentration was 5.58 pmol/L (+/- 1.994, t = 2.80, P = 0.0073) higher than the men's. The elevated levels persisted but did not rise further upon consumption of the yogurt shake. Hunger ratings declined and fullness ratings increased after eating, although patterns of ratings did not match exactly patterns of CCK release. CONCLUSIONS: A large quantity of tomato soup stimulates significant CCK release; therefore, some of the satiating effects of soup preloads could have been mediated by an elevation in endogenous CCK.						
BW	Cullen KW	Validity and reliability of a behavior-based food coding system for measuring fruit, 100% fruit juice,	2004	BACKGROUND: This paper presents the rationale, reliability, and validity of a behavior-based food coding system for measuring fruit (F), juice (J), vegetable (V), sweetened	Interv				N	Methods validation test-retest

		vegetable, and sweetened beverage consumption: results from the Girls Health Enrichment Multisite Studies. Cullen KW, Himes JH, Baranowski T, Pettit J, Stevens M, Slawson DL, Obarzanek E, Murtaugh M, Matheson D, Sun W, Rochon J. Prev Med. 2004 May;38 Suppl:S24-33.		beverage, and water consumption in children. METHODS: Coding algorithms for FJV, sweetened beverages, and water were developed for use with the Nutrition Data System for Research (NDS-R). Two hundred and ten 8- to 10-year-old African American girls at four field centers completed two 24-h dietary recalls at baseline and at 12 weeks follow-up after a weight gain prevention intervention. Differences in mean baseline consumption of selected food variables and other selected nutrients across the four field centers were analyzed. Intraclass correlation coefficients (ICCs) for reliability across 2 days of food recalls and 12-week test-retest reliability correlations were calculated. For the purposes of this paper, nutrient intake estimates were considered construct validators of food intake, and validity was assessed by correlating the coded food variable servings with nutrient intake. RESULTS: ICCs varied from zero (0.001 for beta carotene equivalents) to moderate (0.44 for sucrose), indicating substantial instability in consumption or reporting. Twelve-week test-retest correlations were slight to moderate (0.09 for lycopene to 0.49 for folate). FJV consumption was negatively related to percent energy from fat (r = -0.28; P = 0.001) and positively related to other nutrients. Sweetened beverage consumption was positively related to energy, sucrose, fructose, and vitamin C consumption. CONCLUSIONS: This behavior-based food coding system demonstrated construct validity among 8- to 10-						

				year-old African American girls and can measure the desired food groups.						
Cancer	Bossola M	Taste intensity and hedonic responses to simple beverages in gastrointestinal cancer patients. Bossola M, Cadoni G, Bellantone R, Carriero C, Carriero E, Ottaviani F, Borzomati D, Tortorelli A, Doglietto GB. J Pain Symptom Manage. 2007 Nov;34(5):505-12. Epub 2007 Jul 5.	2007	Changes in the taste of food have been implicated as a potential cause of reduced dietary intake among cancer patients. However, data on intensity and hedonic responses to the four basic tastes in cancer are scanty and contradictory. The present study aimed at evaluating taste intensity and hedonic responses to simple beverages in 47 anorectic patients affected by gastrointestinal cancer and in 55 healthy subjects. Five suprathreshold concentrations of each of the four test substances (sucrose in black current drinks, citric acid in lemonade, NaCl in unsalted tomato juice, and urea in tonic water) were used. Patients were invited to express a judgment of intensity and pleasantness ranging from 0 to 10. Mean intensity scores directly correlated with concentrations of sour, salty, bitter, and sweet stimuli, in both normals and those with cancer. Intensity judgments were higher in cancer patients with respect to sweet (for median and high concentrations, $P<0.05$), salty (for all concentrations, $P<0.05$), and bitter tastes (for median concentration, $P<0.01$). Hedonic function increased with the increase of the stimuli only for the sweet taste. A negative linear correlation was found between sour, bitter, and salty concentrations and hedonic score. Both in cancer patients and in healthy subjects, hedonic judgments increased with the increase of the stimulus for the sweet taste ($r=0.978$ and $r=0.985$, $P=0.004$ and $P=0.002$, respectively), and decreased for the salty ($r=-0.827$ and $r=-0.884$, $P=0.084$	CS					cancer patients had higher like of salty flavor

				and P=0.047, respectively) and bitter tastes (r=-0.990 and r=-0.962, P=0.009 and P=0.001, respectively). For the sour taste, the hedonic scores remained stable with the increase of the stimulus in noncancer controls (r=-0.785, P=0.115) and decreased in cancer patients (r=-0.996, P=0.0001). The hedonic scores for the sweet taste and the bitter taste were similar in cancer patients and healthy subjects, and these scores were significantly higher in cancer patients than in healthy subjects for most of the concentrations of the salty taste and all the concentrations of the sour taste. The present study suggests that cancer patients, compared to healthy individuals, have a normal sensitivity, a normal liking for pleasant stimuli, and a decreased dislike for unpleasant stimuli. Moreover, when compared to controls, they show higher hedonic scores for middle and high concentrations of the salty taste and for all concentrations of the sour taste. Further studies are needed to evaluate whether these changes observed in cancer patients translate into any alteration in dietary behavior and/or food preferences.						
Cancer MOA	Huang CS	Lycopene inhibits matrix metalloproteinase-9 expression and down-regulates the binding activity of nuclear factor-kappa B and stimulatory protein-1. Huang CS, Fan YE, Lin CY, Hu ML. J Nutr Biochem. 2007 Jul;18(7):449-	2007	The carotenoid lycopene has been associated with decreased risks of several types of cancer, such as hepatoma. Although lycopene has been shown to inhibit metastasis, its mechanism of action is poorly understood. Here, we used SK-Hep-1 cells (from a human hepatoma) to test whether lycopene exerts its anti-invasion activity via down-regulation of the expression of matrix metalloproteinase (MMP)-9, an important enzyme in the degradation of basement membrane in cancer invasion. The activity and expressions of MMP-9	Cell culture				(-) ↓ MMP-9 expression ↓ NFkB , activator protein-1 and Sp1 binding to MMP-9 promoter ↓ IGF-1R	

		56. Epub 2006 Oct 17.		protein and mRNA were detected by gelatin zymography, Western blotting and RT-PCR, respectively. The binding abilities of nuclear factor-kappa B (NF-kappaB), activator protein-1 and stimulatory protein-1 (Sp1) to the binding sites in the MMP-9 promoter were measured by the electrophoretic mobility shift assay. We showed that lycopene (1-10 microM) significantly inhibited SK-Hep-1 invasion (P<.05) and that this effect correlated with the inhibition of MMP-9 at the levels of enzyme activity (r(2)=.94, P<.001), protein expression (r(2)=.80, P=.007) and mRNA expression (r(2)=.94, P<.001). Lycopene also significantly inhibited the binding abilities of NF-kappaB and Sp1 and decreased, to some extent, the expression of insulin-like growth factor-1 receptor (IGF-1R) and the intracellular level of reactive oxygen species (P<.05). The antioxidant effect of lycopene appeared to play a minor role in its inhibition of MMP-9 and invasion activity of SK-Hep-1 cells because coincubation of cells with lycopene plus hydrogen peroxide abolished the antioxidant effect but did not significantly affect the anti-invasion ability of lycopene. Thus, lycopene decreases the invasive ability of SK-Hep-1 cells by inhibiting MMP-9 expression and suppressing the binding activity of NF-kappaB and Sp1. These effects of lycopene may be related to the down-regulation of IGF-1R, while the antioxidant activity of lycopene appears to play a minor role.						
Cancer: breast	Ewertz M	Dietary factors and breast-cancer risk in Denmark. Ewertz M, Gill C.	1990	The influence of dietary factors, in particular the intake of fat and beta-carotene, on breast-cancer risk was evaluated in a case-control study including 1,486 breast cancer cases	CC					N Veg

		Int J Cancer. 1990 Nov 15;46(5):779-84.		diagnosed over a 1 year period in Denmark. The control group was an age-stratified random sample of 1,336 women from the general population. Data on usual diet prior to the breast cancer diagnosis were collected by self-administered questionnaires of the semi-quantitative food frequency type. A highly significant trend (p less than 0.001) of increasing risk was observed with increasing fat intake, the RR for the highest quartile being 1.45 (95% CI 1.17-1.80) compared with the lowest. However, information was not available to allow adjustment for the possible confounding effect of energy intake. The risk of breast cancer was not associated with consumption of vegetables rich in beta-carotene, multi-vitamin tablets or other dietary supplements, coffee, tea, sugar or artificial sweeteners.						
Cancer: breast	Graham S	Nutritional epidemiology of postmenopausal breast cancer in western New York. Graham S, Hellmann R, Marshall J, Freudenheim J, Vena J, Swanson M, Zielezny M, Nemoto T, Stubbe N, Raimondo T. Am J Epidemiol. 1991 Sep 15;134(6):552-66.	1991	The authors studied 439 postmenopausal breast cancer cases, identified in hospitals throughout western New York, with an interview schedule that considered frequency and amount ingested of 172 foods and provided data for an estimate of total calories ingested. These were compared with age-matched controls comprising a random sample of the same communities as the cases. The extensive interviews, requiring 2.0 hours on average to administer, also covered alcohol ingestion, Quetelet index, and a wide variety of reproductive factors. The authors found, as have most investigators over the past 25 years, that risk increased with increases in age at first pregnancy, decreased with increases in numbers of children and pregnancies, and increased in those with history of benign breast disease	CC					N retinol (-) carotene

				and in those with female relatives previously affected with breast cancer. Risk adjusted for potential confounders was highest among women with the lowest ingestion of carotene or a substance correlated with its ingestion. Risk was not associated with retinol ingestion. It increased with increases in Quetelet index. Fat intake, whether studied in terms of quantity or the proportion of total calories derived from fat, was not associated with risk of breast cancer. Our analyses of these factors were adjusted for age, education, and the reproductive history traits described above.						
Cancer: breast	Potischman N	Effects of breast cancer treatments on plasma nutrient levels: implications for epidemiological studies. Potischman N, Byers T, Houghton L, Root M, Nemoto T, Campbell TC. Cancer Epidemiol Biomarkers Prev. 1992 Nov-Dec;1(7):555-9.	1992	The interpretation of case-control studies in which blood nutrient levels are examined as etiological factors in cancer is complicated by the possibility that either the disease or its treatment may alter these levels. Circulating levels of selected nutrients were examined prior to diagnostic biopsy and compared with levels 3 to 4 months after diagnosis among 71 women with breast cancer and 95 women with benign breast disease. Among women with benign breast disease or women with breast cancer who were not given postsurgical adjuvant drug therapy, levels of alpha-carotene, lycopene, alpha-tocopherol, cholesterol, and triglycerides did not change over time. In contrast, women who received chemotherapy had increased levels of cholesterol, retinol, and alpha- and gamma-tocopherol, and women on antiestrogen therapy showed increased levels of triglycerides and alpha-tocopherol. Overall, the concentrations of carotenoids (lycopene, alpha-carotene, and	CC					

				beta-carotene) did not change in breast cancer cases, although subgroup analyses showed increased levels of beta-carotene among cases not receiving drug treatment and decreased levels among those receiving antiestrogens. In summary, blood levels of some nutrients did not appear to be affected by breast cancer or its treatments, but changes were noted for levels of plasma lipids, tocopherols, retinol, and beta-carotene. Those investigating the etiological relationship between breast cancer and circulating nutrients need to consider these effects in designing and interpreting epidemiological studies.						
Cancer: breast	Levi F	Dietary factors and breast cancer risk in Vaud, Switzerland. Levi F, La Vecchia C, Gulie C, Negri E. Nutr Cancer. 1993; 19(3):327-35.	1993	The relationship between dietary factors and the risk of breast cancer was investigated in a case-control study conducted in the Canton of Vaud, Switzerland as a pilot phase for a larger cooperative study within the SEARCH Programme of the International Agency for Research on Cancer (Lyon, France). A total of 107 incident, histologically confirmed cases of breast cancer and 318 controls admitted to hospital for acute, nonhormone-related, gynecological, metabolic, or neoplastic disorders were interviewed. Significant direct trends in risk were observed with total energy intake [relative risk (RR) for highest vs. lowest intake tertile = 1.9] and, after allowance for energy intake, with frequency of consumption of various types of meat (RR = 2.1 for the highest tertile), cheese (RR = 2.7), and alcohol (RR = 2.1). Significant protections, on the order of 40-60% reductions for the highest vs. lowest consumption tertile, were conferred by total green vegetable consumption, selected	CC					(-) F/V

				types of vegetables and fruits (cucumbers, onions, pears), and a summary index of beta-carotene intake (RR = 0.4 for highest consumption tertile). Thus the present study confirmed the existence of an unfavorable dietary pattern for breast cancer risk (characterized by high-calorie, selected sources of animal fat and alcohol intake). Moreover, a significant protection could be gained by consuming a diet rich in vegetables and perhaps fruits.						
Cancer: breast	Pierce JP	Increases in plasma carotenoid concentrations in response to a major dietary change in the women's healthy eating and living study. Pierce JP, Natarajan L, Sun S, Al-Delaimy W, Flatt SW, Kealey S, Rock CL, Thomson CA, Newman VA, Ritenbaugh C, Gold EB, Caan BJ; Women's Healthy Eating and Living Study Group. Cancer Epidemiol Biomarkers Prev. 2006 Oct;15(10):1886-92	2006	BACKGROUND: Cohort studies suggest that higher circulating carotenoid concentrations through food sources may reduce breast cancer events. Other intervention studies have not achieved the level of change in circulating carotenoids required to properly test this hypothesis. METHODS: In a randomized trial of 2,922 breast cancer survivors, we examined blood and self-reported diet at baseline and 1 year. Intensive telephone counseling encouraged a plant-based diet in the intervention group. Diet was measured via 24-hour recalls, and a panel of plasma carotenoid concentrations was assessed at both time points. RESULTS: The study intervention was associated with a 51% increase in total carotenoid concentration, from 2.272 +/- 1.294 to 3.440 +/- 2.320 micromol/L, achieved mainly by marked increases in targeted carotenoids: alpha-carotene, beta-carotene, and lutein. For each of these targeted carotenoids, the proportion of the intervention sample remaining below the cutpoint for the						

				lowest baseline quartile decreased by one third to one half. After 1 year of study, half of the intervention group was in the highest baseline quartile. No change in distribution was observed in comparison group. Intervention participants achieved this change by both dietary pattern and vegetable juice consumption. Participants who chose to change dietary pattern without consuming significant quantities of vegetable juice achieved 75% of the level of change observed in other intervention participants. CONCLUSIONS: Innovative telephone counseling intervention and dietary targets in the Women's Healthy Eating and Living study were associated with the level of change in circulating carotenoid concentration necessary to test the diet and breast cancer hypothesis suggested by cohort studies.						
Cancer: breast	Hernandez-Valero MA	Comparison of baseline dietary intake of Hispanic and matched non-Hispanic white breast cancer survivors enrolled in the Women's Healthy Eating and Living study. Hernandez-Valero MA, Thomson CA, Hernandez M, Tran T, Detry MA, Theriault RL, Hajek RA, Pierce JP, Flatt SW, Caan BJ, Jones LA. J Am Diet Assoc.	2008	OBJECTIVE: To assess the reported baseline dietary intake of Hispanic and non-Hispanic white breast cancer survivors in the Women's Healthy Eating and Living study, a randomized plant-based dietary intervention clinical trial. DESIGN: Dietary data from 4 days repeated 24-hour recalls within 3 weeks included daily total intake of energy, protein, carbohydrates, cholesterol, total fat, monounsaturated fat, saturated fat, polyunsaturated fat, fruit/vegetable servings, carotenoids, alcohol, caffeine, and percentage of energy from protein, carbohydrates, alcohol, and fats.	CC				Hispanic women ↑ lyco	

		2008 Aug;108(8):1323-9.		SUBJECTS: One hundred sixty-five Hispanic breast cancer survivors age-matched to 165 non-Hispanic white breast cancer survivors diagnosed with Stage I, II, or IIIA primary operable breast cancer. STATISTICAL ANALYSES: Two-sample t tests and Wilcoxon rank sum tests to compare dietary intake, and logistic and ordinal logistic regression analyses to examine the association between ethnicity, alcohol, and lycopene consumption, while controlling for place of birth, education, body mass index, and time since diagnosis. RESULTS: Hispanics were more likely to be foreign-born (P<0.001), less educated (P<0.0001) and to consume higher amounts of lycopene (P=0.029), while non-Hispanic whites were more likely to consume alcohol (P=0.001). However, no differences were observed in the average amounts of alcohol consumed or total percents of energy from alcohol. Both groups consumed more than five servings of fruits and vegetables daily. Being Hispanic remained a significant predictor of lower alcohol use (P=0.004) and higher lycopene consumption (P=0.005) after controlling for place of birth, education, body mass index, and time since diagnosis. CONCLUSIONS: There are more similarities than differences in the dietary intake of Hispanic and non-Hispanic white breast cancer survivors in the Women's Healthy Eating and Living study. Further analysis is needed to determine if higher lycopene consumption shown among the Hispanic participants will translate to greater protection against breast cancer recurrence or increased survival.						

Cancer: breast	Hernández-Valero MA	Comparison of baseline dietary intake of Hispanic and matched non-Hispanic white breast cancer survivors enrolled in the Women's Healthy Eating and Living study. Hernández-Valero MA, Thomson CA, Hernández M, Tran T, Detry MA, Theriault RL, Hajek RA, Pierce JP, Flatt SW, Caan BJ, Jones LA. J Am Diet Assoc. 2008 Aug;108(8):1323-9.	2008	OBJECTIVE: To assess the reported baseline dietary intake of Hispanic and non-Hispanic white breast cancer survivors in the Women's Healthy Eating and Living study, a randomized plant-based dietary intervention clinical trial. DESIGN: Dietary data from 4 days repeated 24-hour recalls within 3 weeks included daily total intake of energy, protein, carbohydrates, cholesterol, total fat, monounsaturated fat, saturated fat, polyunsaturated fat, fruit/vegetable servings, carotenoids, alcohol, caffeine, and percentage of energy from protein, carbohydrates, alcohol, and fats. SUBJECTS: One hundred sixty-five Hispanic breast cancer survivors age-matched to 165 non-Hispanic white breast cancer survivors diagnosed with Stage I, II, or IIIA primary operable breast cancer. STATISTICAL ANALYSES: Two-sample t tests and Wilcoxon rank sum tests to compare dietary intake, and logistic and ordinal logistic regression analyses to examine the association between ethnicity, alcohol, and lycopene consumption, while controlling for place of birth, education, body mass index, and time since diagnosis. RESULTS: Hispanics were more likely to be foreign-born (P<0.001), less educated (P<0.0001) and to consume higher amounts of lycopene (P=0.029), while non-Hispanic whites were more likely to consume alcohol (P=0.001). However, no differences were observed in the average amounts of alcohol consumed or total percents of energy from alcohol. Both groups	CC Descriptive study					

				consumed more than five servings of fruits and vegetables daily. Being Hispanic remained a significant predictor of lower alcohol use (P=0.004) and higher lycopene consumption (P=0.005) after controlling for place of birth, education, body mass index, and time since diagnosis. CONCLUSIONS: There are more similarities than differences in the dietary intake of Hispanic and non-Hispanic white breast cancer survivors in the Women's Healthy Eating and Living study. Further analysis is needed to determine if higher lycopene consumption shown among the Hispanic participants will translate to greater protection against breast cancer recurrence or increased survival.						
Cancer: breast	Hernandez-Valero MA	Comparison of baseline dietary intake of Hispanic and matched non-Hispanic white breast cancer survivors enrolled in the Women's Healthy Eating and Living study. Hernandez-Valero MA, Thomson CA, Hernandez M, Tran T, Detry MA, Theriault RL, Hajek RA, Pierce JP, Flatt SW, Caan BJ, Jones LA. J Am Diet Assoc. 2008 Aug;108(8):1323-9.	2008	OBJECTIVE: To assess the reported baseline dietary intake of Hispanic and non-Hispanic white breast cancer survivors in the Women's Healthy Eating and Living study, a randomized plant-based dietary intervention clinical trial. DESIGN: Dietary data from 4 days repeated 24-hour recalls within 3 weeks included daily total intake of energy, protein, carbohydrates, cholesterol, total fat, monounsaturated fat, saturated fat, polyunsaturated fat, fruit/vegetable servings, carotenoids, alcohol, caffeine, and percentage of energy from protein, carbohydrates, alcohol, and fats. SUBJECTS: One hundred sixty-five Hispanic breast cancer survivors age-matched to 165 non-Hispanic white breast cancer survivors diagnosed	CC					↑ lyco intake in Hispanics vs whie survivors

				with Stage I, II, or IIIA primary operable breast cancer. STATISTICAL ANALYSES: Two-sample t tests and Wilcoxon rank sum tests to compare dietary intake, and logistic and ordinal logistic regression analyses to examine the association between ethnicity, alcohol, and lycopene consumption, while controlling for place of birth, education, body mass index, and time since diagnosis. RESULTS: Hispanics were more likely to be foreign-born (P<0.001), less educated (P<0.0001) and to consume higher amounts of lycopene (P=0.029), while non-Hispanic whites were more likely to consume alcohol (P=0.001). However, no differences were observed in the average amounts of alcohol consumed or total percents of energy from alcohol. Both groups consumed more than five servings of fruits and vegetables daily. Being Hispanic remained a significant predictor of lower alcohol use (P=0.004) and higher lycopene consumption (P=0.005) after controlling for place of birth, education, body mass index, and time since diagnosis. CONCLUSIONS: There are more similarities than differences in the dietary intake of Hispanic and non-Hispanic white breast cancer survivors in the Women's Healthy Eating and Living study. Further analysis is needed to determine if higher lycopene consumption shown among the Hispanic participants will translate to greater protection against breast cancer recurrence or increased survival.						
Cancer: cells	Tang Y	Lycopene enhances	2011	Docetaxel is currently the most effective drug for the treatment of					(-)	

		docetaxel's effect in castration-resistant prostate cancer associated with insulin-like growth factor I receptor levels. Tang Y, Parmakhtiar B, Simoneau AR, Xie J, Fruehauf J, Lilly M, Zi X. Neoplasia. 2011 Feb;13(2):108-19		castration-resistant prostate cancer (CRPC), but it only extends life by an average of 2 months. Lycopene, an antioxidant phytochemical, has antitumor activity against prostate cancer (PCa) in several models and is generally safe. We present data on the interaction between docetaxel and lycopene in CRPC models. The growth-inhibitory effect of lycopene on PCa cell lines was positively associated with insulin-like growth factor I receptor (IGF-IR) levels. In addition, lycopene treatment enhanced the growth-inhibitory effect of docetaxel more effectively on DU145 cells with IGF-IR high expression than on those PCa cell lines with IGF-IR low expression. In a DU145 xenograft tumor model, docetaxel plus lycopene caused tumor regression, with a 38% increase in antitumor efficacy (P = .047) when compared with docetaxel alone. Lycopene inhibited IGF-IR activation through inhibiting IGF-I stimulation and by increasing the expression and secretion of IGF-BP3. Downstream effects include inhibition of AKT kinase activity and survivin expression, followed by apoptosis. Together, the enhancement of docetaxel's antitumor efficacy by lycopene supplementation justifies further clinical investigation of lycopene and docetaxel combination for CRPC patients. CRPC patients with IGF-IR-overexpressing tumors may be most likely to benefit from this combination.						
Cancer: cervical	Marshall JR	Diet and smoking in the epidemiology of cancer of the cervix.	1983	This study of 513 white cervical cancer patients and 490 white hospitalized controls considered, with adjustment for marital history and parity, the effects of smoking and dietary characteristics on the relative	CC				(-) b-carot	

		Marshall JR, Graham S, Byers T, Swanson M, Brasure J. J Natl Cancer Inst. 1983 May;70(5):847-51.		risk of developing cervical cancer. Although smoking was shown to be positively associated with risk, no dose-response relationship was evident. The frequency of consumption of cruciferous vegetables was positively associated with risk. Respondent reports of the frequency of prior ingestion of several food items were used in constructing crude indices of exposure to basic nutrients; the index of beta-carotene exposure was negatively associated with risk, whereas the index of fat consumption was positively associated with risk.					(+) crucif	
Cancer: cervical	De Vet	The role of beta-carotene and other dietary factors in the aetiology of cervical dysplasia: results of a case-control study. de Vet HC, Knipschild PG, Grol ME, Schouten HJ, Sturmans F Int J Epidemiol. 1991 Sep;20(3):603-10.	1991	The effects of beta-carotene and several other dietary factors on the risk of cervical dysplasia were evaluated in a case-control study. Cases (n = 257) were the participants of a randomized trial assessing the effect of beta-carotene on cervical dysplasia. Controls (n = 705) were sampled from the general population. A postal questionnaire was used to obtain information about the frequency of consumption of several food items containing beta-carotene, retinol, vitamin C and dietary fibre. Information was also collected about other risk factors for cervical dysplasia, in order to adjust for possible confounding. To our surprise, we observed an increased risk of cervical dysplasia for women with a high intake of beta-carotene (odds ratio (OR) = 2.31; 95% confidence interval (CI): 1.27-4.19). No relationship was found with the intake of retinol, while both vitamin C and dietary fibre showed a weak and not statistically significant inverse relationship with cervical dysplasia. These findings do not support the hypothesis that beta-carotene protects against cervical dysplasia.	CC				(-) Vit C	

Cancer: cervical	Palan PR	Plasma concentrations of micronutrients during a nine-month clinical trial of beta-carotene in women with precursor cervical cancer lesions. Palan PR, Chang CJ, Mikhail MS, Ho GY, Basu J, Romney SL. Nutr Cancer. 1998; 30(1):46-52.	1998	The effects of oral supplementation of a 30-mg dose of beta-carotene on the plasma levels of carotenoids, tocopherols, and retinol were studied sequentially in 69 patients participating in a nine-month randomized placebo controlled trial conducted to examine efficacy of beta-carotene to induce regression of cervical intraepithelial neoplasia. At each visit (baseline and 1.5, 3, 6, 9, 10.5, and 15 mo), blood samples were collected and the levels of six micronutrients were determined by high-performance liquid chromatography. No limitations or changes were introduced in each participant's dietary habits. Cervico-vaginal lavage samples were also obtained at the same visit and assayed for the presence of human papillomavirus DNA by Southern blot hybridization and polymerase chain reaction. In the supplemented group, mean plasma beta-carotene levels were significantly higher ($p = 0.0001$) than baseline and remained markedly elevated for 15 months. In the longitudinal analysis of the placebo group, there were no variations among individual mean plasma levels of beta-carotene, alpha-carotene, lycopene, retinol, gamma-tocopherol, or alpha-tocopherol, suggesting absence of seasonal or dietary changes. In the placebo group, cigarette smoking and steroid contraceptive use were significantly associated with low levels of plasma beta-carotene ($p = 0.05$ and $p = 0.012$, respectively). However, in contrast, in the beta-carotene-supplemented group, steroid contraceptive use had no influence on the plasma beta-carotene levels. An additional noteworthy finding was that beta-carotene supplementation did not	RCT					

				reverse the depletion effect in smokers. There was no association between the plasma levels of these six micronutrients in women with cervical intraepithelial neoplasia and persistent human papillomavirus infection status in the placebo or the supplemented groups. Functional sequential nutrient interactions with each other or with other essential micronutrients and possible long-term toxicity need to be addressed in clinical trials.						
Cancer: colorectal	Franceschi S	Food groups and risk of colorectal cancer in Italy. Franceschi S, Favero A, La Vecchia C, Negri E, Conti E, Montella M, Giacosa A, Nanni O, Decarli A. Int J Cancer. 1997 Jul 3;72(1):56-61.	1997	The proportion of colorectal cancer attributed to dietary habits is high, but several inconsistencies remain, especially with respect to the influence of some food groups. To further elucidate the role of dietary habits, 1,225 subjects with cancer of the colon, 728 with cancer of the rectum and 4,154 controls, hospitalized with acute non-neoplastic diseases, were interviewed between 1992 and 1996 in 6 different Italian areas. The validated food-frequency questionnaire included 79 questions on food items and recipes, categorised into 16 food groups. After allowance for non-dietary confounding factors and total energy intake, significant trends of increasing risk of colorectal cancer with increasing intake emerged for bread and cereal dishes (odds ratio [OR] in highest vs. lowest quintile = 1.7), potatoes (OR = 1.2), cakes and desserts (OR = 1.1), and refined sugar (OR = 1.4). Intakes of fish (OR = 0.7), raw and cooked vegetables (OR = 0.6 for both) and fruit other than citrus fruit (OR = 0.7) showed a negative association with risk. Consumption of eggs and meat (white, red or processed meats) seemed uninfluential. Most findings	CC					(-) V

				were similar for colon and rectum, but some negative associations (i.e., coffee and tea, and fish) appeared stronger for colon cancer. Our findings lead us to reconsider the role of starchy foods and refined sugar in light of recent knowledge on the digestive physiology of carbohydrates and the insulin/colon cancer hypothesis. The beneficial role of most vegetables is confirmed, with more than 20% reduction in risk of colorectal cancer from the addition of one daily serving.						
Cancer: colorectal	La Vecchia C	Intake of selected micronutrients and risk of colorectal cancer. La Vecchia C, Braga C, Negri E, Franceschi S, Russo A, Conti E, Falcini F, Giacosa A, Montella M, Decarli A. Int J Cancer. 1997 Nov 14;73(4):525-30.	1997	The relationship between various micronutrients and colorectal cancer risk was investigated using data from a case-control study conducted between January 1992 and June 1996 in Italy. Cases were 1,953 incident, histologically confirmed colorectal cancers (1,225 of the colon and 728 of the rectum), admitted to the major teaching and general hospitals in the study areas, and 4,154 controls with no history of cancer, admitted to hospitals in the same catchment areas for acute, non-neoplastic diseases unrelated to the digestive tract and requiring no long-term modifications of the diet. Dietary habits were investigated using a validated food-frequency questionnaire. Odds ratio (ORs) were computed after allowance for age, sex and other potential confounding factors, including physical activity, total energy and fibre intake. For most micronutrients, ORs were below unity with increasing quintile of intake. The most consistent protective effects were for carotene, riboflavin and vitamin C (Multivariate ORs from the continuous model, with unit set as the difference between the upper cut-point of the 4th quintile and that of the 1st one, were 0.65, 0.73 and	CC					(-) carrot, ribo, Vit C

				0.80, respectively). Inverse relationships were observed also for calcium and vitamin D (ORs of 0.85 and 0.93, respectively). When the combined effect of calcium and vitamin D and selected anti-oxidants was considered, the OR reached 0.46 in subjects reporting high calcium/vitamin D and high anti-oxidant intake compared to those reporting low intake of both groups of micronutrients. Most results were apparently stronger for colon cancer and among females. Our results provide further support for a protective effect of several micronutrients on colorectal cancer risk and some indications for a specific and stronger effect of selected anti-oxidants.						
Cancer: colorectal	Voorrips LE	Vegetable and fruit consumption and risks of colon and rectal cancer in a prospective cohort study: The Netherlands Cohort Study on Diet and Cancer. Voorrips LE, Goldbohm RA, van Poppel G, Sturmans F, Hermus RJ, van den Brandt PA. Am J Epidemiol. 2000 Dec 1;152(11):1081-92.	2000	The relation between vegetable and fruit consumption and colorectal cancer risk was comprehensively assessed in the Netherlands Cohort Study on Diet and Cancer using a validated 150-item food frequency questionnaire. After 6.3 years of follow-up (1986-1992), over 1,000 incident cases of colorectal cancer were registered. Using case-cohort analysis, the authors calculated rate ratios and 95% confidence intervals adjusted for age, alcohol intake, and family history of colorectal cancer. For colon cancer, no statistically significant associations with total vegetable intake or total fruit intake were found. However, among women, an inverse association was observed with vegetables and fruits combined (for the highest quintile vs. the lowest, the rate ratio was 0.66 (95% confidence interval: 0.44, 1.01)). Brassica vegetables and cooked leafy vegetables showed inverse associations for both men and women. Among women and, to a	PC					N F/V (-)W F/V

				lesser extent, among men, inverse associations were stronger for distal colonic tumors than for proximal colonic tumors. For rectal cancer, no statistically significant associations were found for vegetable consumption or fruit consumption or for specific groups of vegetables and fruits; only Brassica vegetables showed a positive association in women. As in other cohort studies, the observed inverse relation between vegetable and fruit consumption and occurrence of colorectal cancer was less strong than relations reported in case-control studies.						
Cancer: colorectal	Seow A	Food groups and the risk of colorectal carcinoma in an Asian population. Seow A, Quah SR, Nyam D, Straughan PT, Chua T, Aw TC. Cancer. 2002 Dec 1;95(11):2390-6.	2002	BACKGROUND: Singapore Chinese have experienced a rapid transition toward a pattern of disease in which lifestyle-related, chronic, degenerative diseases are major public health concerns. The rates of colorectal carcinoma have increased 2-fold over the last 3 decades. It has long been known that dietary factors play a role in the risk of this disease, although studies in Asian populations, with their unique dietary intake, have been few. METHODS: The authors conducted a population-based case-control study that included 121 Chinese patients with colorectal carcinoma and 222 healthy control participants who provided information on usual intake of major food groups in the preceding 3 years, physical activity, family history of colorectal carcinoma, and demographic variables through an in-person questionnaire. RESULTS: High intake of red meat, but not other meats, indicated a	CC					N F/S/L

				predisposition to risk of colorectal carcinoma (adjusted odds ratio [OR] for the highest tertile vs. the lowest tertile, 2.2; 95% confidence interval [95%CI], 1.1-4.2). A low vegetable intake also was associated with a higher risk, and the combined effect appeared to be additive. Those in the highest tertile of meat intake and the lowest quartile of vegetable intake had an OR of 2.6 (95%CI, 1.0-6.7). The authors observed a slight, albeit nonsignificant, positive association with foods high in refined sugars. There was no association observed with fruit or soy-legume intake in this study. Among nondietary variables, a family history of colorectal carcinoma conferred a significant increase in risk (OR, 6.7; 95% CI 2.4-18.7). CONCLUSIONS: Meat intake and vegetable intake were associated significantly with risk of colorectal carcinoma in this Asian population, and further studies on the effects of changes in these specific types of food may shed light on how best to reduce the rapid increase in rates in similar populations.						
Cancer: colorectal	Forman MR	Components of variation in serum carotenoid concentrations: the Polyp Prevention Trial. Forman MR, Borkowf CB, Cantwell MM, Steck S, Schatzkin A, Albert PS, Lanza E. Eur J Clin Nutr. 2009 Jun;63(6):763-70. Epub 2008 Apr 16.	2009	OBJECTIVES: The intra- and interindividual variations and season and center effects were estimated from a series of serum carotenoid concentrations in the Polyp Prevention Trial (PPT) participants. SUBJECTS/METHODS: Fasting blood was collected annually for 4 years in all 1905 participants, and a subcohort of 901 participants were selected within each (of eight) center(s), by gender and dietary arm of the study, for measurement of five major carotenoid peaks. Using variance of component methods, the variation in serum carotenoid	PC					Variation testing serum [lyco] ↑intra(-) & inter subject variation

				concentrations about the underlying mean was partitioned into explanatory components attributed to various sources. RESULTS: The contributions of the inter- and intraindividual variances to the overall variation in carotenoid concentrations were in the range of 61-70 and 20-35%, respectively, whereas center and center-by-season effects provided 2.6-9.5 and 0.2-1.4%, respectively. The highest percent (35%) of intraindividual variation was exhibited by lycopene, and the highest percent (70% apiece) of interindividual variation was exhibited by lutein/zeaxanthin and beta-carotene. Serum lycopene had the highest ratio of intra- to interindividual variation of 0.57, whereas lutein had the lowest ratio of 0.29. We estimate that the ratio of intra- to interindividual variance around the mean carotenoid concentration can be reduced greatly by collecting 3-4 compared to 1 blood measurement in large-scale trials like the PPT. CONCLUSION: In the largest study of components of variation in individuals at high risk for colorectal cancer, the largest contributors to variation in serum carotenoid concentrations were intra- and interindividual effects followed by center and center-by-season effects.						
Cancer: edno-meterial	Goodman MT	Diet, body size, physical activity, and the risk of endometrial cancer. Goodman MT, Hankin JH, Wilkens	1997	Endometrial cancer is associated with increased weight and body size, diabetes, and other conditions that may result from an excess in calories or lack of physical activity. Although a few studies have explored the effect of dietary constituents on the risk of endometrial cancer, the	CC					(-) Lutein (-) F/V

		LR, Lyu LC, McDuffie K, Liu LQ, Kolonel LN. Cancer Res. 1997 Nov 15;57(22):5077-85.		nature of the joint association of these constituents and obesity, energy intake, or energy expenditure with risk is unknown. A population-based case-control study was conducted in Hawaii to examine the association of diet, body size, and physical activity with the risk of endometrial cancer. Subjects included 332 histologically confirmed, primary endometrial cancer cases and 511 controls identified between 1985 and 1993. Cases and controls were residents of Oahu, Hawaii who were between 18 and 84 years of age and were from one of the following ethnic groups: Japanese, Caucasian, Native Hawaiian, Filipino, and Chinese. Cases were identified through the Hawaii Tumor Registry and matched to the controls on age (+/-2.5 years) and ethnicity. In-person interviews, conducted in the subjects' homes, included dietary, reproductive, menstrual, and medical histories and use of exogenous hormones, physical activity, and other lifestyle variables. Weight, girth, and skinfold measurements were taken at the time of the interview. We found a strong dose-response relation of increased body size to the development of endometrial cancer after adjustment for energy intake. The odds ratio (OR) for endometrial cancer among women in the highest quartile of body mass index (BMI; kg/m2) was more than four times that among women in the lowest quartile. Waist, hip, midarm, and wrist girths were positively associated with the estimated risk of endometrial cancer after adjustment for total calories and other nondietary risk factors, although the trends in the ORs were attenuated after adjustment for BMI. Physically active women had a						

				modest reduction in their risk of disease compared with inactive women. Cases consumed a greater percentage of their calories from fat and a lower percentage of their calories from carbohydrates than did controls. Adjustment for BMI reduced the ORs for the highest compared with the lowest quartile of fat calorie intake from 2.0 (95% confidence interval, 1.3-3.2) to 1.6 (95% confidence interval, 1.0-2.6), suggesting that part of the association is explained by obesity. There was a differential effect of fat on endometrial cancer according to BMI. For all components of fat, the associations with endometrial cancer were either minimal or absent among leaner women (i.e., those with BMI below the median), whereas, among more obese women, two-fold differences in risk were observed between women above and below the median of fat intake. Foods that are high in fat and cholesterol, such as red meat, margarine, and eggs, were positively associated with endometrial cancer, whereas cereals, legumes, vegetables, and fruits, particularly those high in lutein, were inversely associated. These findings suggest that women who avoid being overweight and who consume a diet low in plant and animal fats and high in complex carbohydrates are at a reduced risk of endometrial cancer.						
Cancer: edno-meterial	Goodman MT	Association of soy and fiber consumption with the risk of endometrial cancer. Goodman MT, Wilkens LR, Hankin	1997	The authors conducted a case-control study among the multi-ethnic population of Hawaii to examine the role of dietary soy, fiber, and related foods and nutrients on the risk of endometrial cancer. Endometrial cancer cases (n = 332) diagnosed between 1985 and 1993 were identified from the five main ethnic	CC					(-) S/L (-)

		JH, Lyu LC, Wu AH, Kolonel LN. Am J Epidemiol. 1997 Aug 15;146(4):294-306.		groups in the state (Japanese, Caucasian, Native Hawaiian, Filipino, and Chinese) through the rapid-reporting system of the Hawaii Tumor Registry. Population controls (n = 511) were selected randomly from lists of female Oahu residents and matched to cases on age (+/-2.5 years) and ethnicity. All subjects were interviewed using a diet history questionnaire that included over 250 food items. Non-dietary risk factors for endometrial cancer included nulliparity, never using oral contraceptives, fertility drug use, use of unopposed estrogens, a history of diabetes mellitus or hypertension, and a high Quetelet's index (kg/cm2). Energy intake from fat, but not from other sources, was positively associated with the risk of endometrial cancer. The authors also found a positive, monotonic relation of fat intake with the odds ratios for endometrial cancer after adjustment for energy intake. The consumption of fiber, but not starch, was inversely related to risk after adjustment for energy intake and other confounders. Similar inverse gradients in the odds ratios were obtained for crude fiber, non-starch polysaccharide, and dietary fiber. Sources of fiber, including cereal and vegetable and fruit fiber, were associated with a 29-46% reduction in risk for women in the highest quartiles of consumption. Vitamin A and possibly vitamin C, but not vitamin E, were also inversely associated with endometrial cancer, although trends were not strong. High consumption of soy products and other legumes was associated with a decreased risk of endometrial cancer (p for trend = 0.01; odds ratio = 0.46, 95% confidence interval 0.26-0.83) for the highest compared with the lowest						F/V

				quartile of soy intake. Similar reductions in risk were found for increased consumption of other sources of phytoestrogens such as whole grains, vegetables, fruits, and seaweeds. Ethnic-specific analyses were generally consistent with these results. The observed dietary associations appeared to be largely independent of other risk factors, although the effects of soy and legumes on risk were limited to women who were never pregnant or who had never used unopposed estrogens. These data suggest that plant-based diets low in calories from fat, high in fiber, and rich in legumes (especially soybeans), whole grain foods, vegetables, and fruits reduce the risk of endometrial cancer. These dietary associations may explain in part the reduced rates of uterine cancer in Asian countries compared with those in the United States.						
Cancer: gastric	Correa P	Dietary determinants of gastric cancer in south Louisiana inhabitants. Correa P, Fontham E, Pickle LW, Chen V, Lin YP, Haenszel W. J Natl Cancer Inst. 1985 Oct;75(4):645-54.	1985	In south Louisiana, 391 recently diagnosed gastric cancer patients and an equal number of controls were interviewed. Questions asked covered residential and occupational histories, environmental exposures, tobacco use, diet, alcohol consumption, and pertinent demographic characteristics. Elevated relative risks were found for use of tobacco and alcohol products. Diet was found to be the main determinant of gastric cancer risk in south Louisiana. Both dietary patterns and dietary risk factors differed for blacks and whites, although fruits as a group and dietary vitamin C were found to exert strong protective effects for both blacks and whites. Consumption of smoked foods and homemade or home-cured meats increased risk of gastric cancer for blacks but not for	CC				(-) Vit C	

				whites. The findings are discussed in the light of the prevailing etiologic hypotheses.						
Cancer: gastric	La Vecchia C	A case-control study of diet and gastric cancer in northern Italy. La Vecchia C, Negri E, Decarli A, D'Avanzo B, Franceschi S. Int J Cancer. 1987 Oct 15;40(4):484-9.	1987	Dietary factors in the aetiology of stomach cancer were investigated using data from a case-control study conducted in Northern Italy on 206 histologically confirmed carcinomas and 474 control subjects in hospital for acute, non-digestive conditions, unrelated to any of the potential risk factors for gastric cancer. Dietary histories concerned the frequency of consumption per week of 29 selected food items (including the major sources of starches, proteins, fats, fibres, vitamins A and C, nitrates and nitrites in the Italian diet) and subjective scores for condiments and salt intake. Pasta and rice (the major sources of starch), polenta (a porridge made of maize) and ham were positively related with gastric cancer risk, whereas green vegetables and fresh fruit as a whole (and specifically citrus fruit) and selected fibre-rich aliments (such as whole-grain bread or pasta) showed protective effects on gastric cancer risk. Allowance for major identified potential distorting factors (chiefly indicators of socio-economic status) reduced the positive association with pasta or rice consumption, but did not appreciably modify any of the other risk estimates. When a single logistic model was fitted including all food items significant in univariate analysis, the 3 items remaining statistically significant were green vegetables (relative risk, RR = 0.27 for upper vs. lower tertile), polenta (RR = 2.32) and ham (RR = 1.60). Indices of beta-carotene and ascorbate intake were negatively and strongly related with gastric cancer risk, but the association with these micronutrients	CC				(-) veg	

				was no longer evident after simultaneous allowance for various food items. An approximately 7-fold difference in risk was found between extreme quintiles of a scale measuring major positive and negative associations.						
Cancer: gastric	Boeing H	Dietary risk factors in intestinal and diffuse types of stomach cancer: a multicenter case-control study in Poland. Boeing H, Jedrychowski W, Wahrendorf J, Popiela T, Tobiasz-Adamczyk B, Kulig A. Cancer Causes Control. 1991 Jul;2(4):227-33.	1991	A hospital-based, multicenter, case-control study has been performed in Poland covering 741 incident stomach-cancer cases (520 males and 221 females) and the same number of controls. All stomach-cancer diagnoses were evaluated for histologic type according to the Lauren criteria. Fifty-one percent were of the intestinal type, 35 percent of the diffuse type, and 8.5 percent of the mixed type. The frequency of consumption of individual food items and several food groups was analyzed and the association of various foods with stomach cancer risk was evaluated after controlling for sex, age, occupation, education, and residency. Increased consumption of sausages was related significantly to gastric cancer risk, whereas increased consumption of cheese products, nonwhite bread, vegetables, and fruit was associated with decreased risk. A particularly strong decrease in risk was associated with consumption of radishes and onions. When consumption of fruits and vegetables, sausages, nonwhite bread, and cheese were introduced simultaneously in a multivariate model, independent effects were found only for fruit and vegetables, sausages, and nonwhite bread. The use of table salt, the frequency of eating hot meals, and an irregular eating pattern were also associated with increased risk, while additional	CC				(-) F/V	

				consumption of fruit between meals showed reduced risk. If a reduction in vegetable and fruit consumption took place after marriage, an increased risk for stomach cancer was found, whereas augmented consumption of these food items after marriage decreased the risk. Separate risk models were calculated for stomach cancer of the intestinal and diffuse types, but both histologic varieties showed the same pattern of associations with dietary risk factors.						
Cancer: gastric	Tuyns AJ	Diet and gastric cancer. A case-control study in Belgium. Tuyns AJ, Kaaks R, Haelterman M, Riboli E. Int J Cancer. 1992 Apr 22;51(1):1-6.	1992	A case-control study was carried out in 2 Belgian provinces with contrasting gastric-cancer mortality. The results were analyzed for the total study group and also separately in each of the 4 sub-groups: men and women in each province. Only risks which appeared consistently in at least 3 of these 4 sub-groups were retained in the discussion. Consumption of most vegetables, either cooked or raw, and of fresh fruit was found to be protective. There was an increased risk associated with meal and flour products, including white bread. Added sugar also increased the risk of gastric cancer. Consumption of lean meat was associated with a decreased risk. There was no clear effect for most sources of fat, but for oils with a high P/S ratio there was a decreased risk. Together with our earlier finding on salt, these results are to a large extent similar to those of other recent studies on gastric cancer.	CC					(-) F/V
Cancer: gastric	Ramon J M	Dietary factors and gastric cancer risk. A case-control study in Spain.	1993	BACKGROUND. Evidence supports that gastric cancer has an environmental etiology, of which diet appears to be the most important component. The authors examined	CC					

		Ramon JM, Serra L, Cerdo C, Oromi J. Cancer. 1993 Mar 1;71(5):1731-5.		the effect of diet on the risk of gastric cancer. METHODS. A case-control study of dietary factors and gastric cancer was conducted between September 1986 and March 1989 in the Barcelona metropolitan area, Spain. One hundred seventeen cases with histologically confirmed diagnosis of gastric adenocarcinoma were matched by age, gender, and whether they possessed a telephone to 234 community controls. One hundred eighty-eight (80.3%) controls were selected by random-digit telephone dialing and 46 (19.7%) by neighborhood of residence. Information about frequency and amount of consumption of 89 food items in one year was gathered by using a questionnaire, and cases and controls were interviewed in their homes by trained interviewers. Unconditional logistic regression was used for the analysis. RESULTS. Gastric cancer risk rose with increasing intake of smoked and pickled foods (OR 3.67 for upper tertile) and salt (OR 2.11 for upper quartile). Intake of citrus fruits (OR 0.47 for upper tertile) and raw-green vegetables (OR 0.56 for upper quartile) appeared to be protective. Gastric cancer risk was not associated with intake of cereals, rice, total vegetables, and fruits as a whole. CONCLUSIONS. These data suggest that high intake of salt and smoked and pickled food may be associated with a high risk of gastric cancer, and this association could be due to intragastric formation of nitrosamines. The negative association with citric					(-) Fcitrus (-) Vgreen	

				and green vegetables consumption to be associated with the inhibition of nitrosation process.						
Cancer: gastric	Gao C	Protective effect of allium vegetables against both esophageal and stomach cancer: a simultaneous case-referent study of a high-epidemic area in Jiangsu Province, China. Gao CM, Takezaki T, Ding JH, Li MS, Tajima K. Jpn J Cancer Res. 1999 Jun;90(6):614-21.	1999	To study the relation between allium vegetable intake and cancer of the esophagus (EC) and stomach (SC) in Yangzhong city, which is one of the highest-risk areas for these cancers in Jiangsu province, China, a simultaneous case-referent study was conducted using histopathologically confirmed cases (EC: n = 81, SC: n = 153) and population-based referents (n = 234). A questionnaire was used to collect information on the general status of subjects, their dietary habits, frequency intake of allium vegetables and other foods, tea consumption, smoking and alcohol drinking. The odds ratios (ORs) and 95% confidence intervals (CIs) were estimated by a multiple logistic regression model. The results showed that frequent intake of allium vegetables (including garlic, onion, Welsh onion and Chinese chives), raw vegetables, tomatoes and snap beans, and tea consumption were inversely associated with the risk for EC and SC. In the highest consumption category (> or = 1 time/week) of garlic, onion, Welsh onion and Chinese chives, the adjusted ORs compared with the lowest category (< 1 time/month) were 0.30 (CI = 0.19-0.47), 0.25 (CI = 0.11-0.54), 0.15 (CI = 0.08-0.26), and 0.57 (CI = 0.23-1.42) for EC, and 0.31 (CI = 0.22-0.44), 0.17 (CI = 0.08-0.36), 0.22 (CI = 0.15-0.31) and 0.40 (CI = 0.17-0.94) for SC, respectively. The main results in the present study suggested that allium vegetables, like raw vegetables, may have an important protecting effect against not only stomach cancer, but also esophageal cancer.	CC					

Cancer: head & neck	Djuric Z	Levels of fat-soluble micronutrients and 2,6-cyclolycopene-1,5-diol in head and neck cancer patients. Djuric Z, Ronis DL, Fowler KE, Ren J, Duffy SA. Int J Vitam Nutr Res. 2007 Nov;77(6):382-8.	2007	Smoking negatively affects serum carotenoid levels, and it is a negative prognostic factor for head and neck cancer. In this study, micronutrient levels were examined in 60 smoking and non-smoking head and neck cancer patients. The goal was to determine if oxidation of the carotenoid lycopene would occur to a greater extent in smokers. Subjects were drawn from a prospective cohort study and matched on seven demographic factors. Serum levels of alpha-carotene, zeaxanthin, and 2,6-cyclolycopene-1,5-diol A, an oxidation product of lycopene, were all lower in smokers versus non-smokers (18%, 22%, and 8%, respectively) while beta-carotene, beta-cryptoxanthin, and lutein were about the same in the two groups. Levels of lycopene, gamma-tocopherol, and alpha-tocopherol were higher in smokers, and notably serum alpha-tocopherol was 48% higher in smokers. The majority of vitamin E intake was from supplements. The higher levels of alpha-tocopherol in smokers were interesting in that higher alpha-tocopherol levels have been associated with higher mortality in head and neck cancer. Although this was a pilot investigation, there was no evidence that 2,6-cyclolycopene-1,5-diol A formation was appreciably affected by smoking status, but alpha-tocopherol levels were higher in smokers.	CS						Smokers had ↓ 2,6-cyclopene-1,5-diol A ↑ serum [lyco]
Cancer: liver	Nishino H.	Phytochemicals in hepatocellular cancer prevention. Nishino H. Nutr Cancer. 2009;61(6):789-91	2009	Since the incidence of liver cancer is increasing in the world, it is valuable to develop an effective method for its prevention. Various phytochemicals have been shown to suppress liver carcinogenesis in experimental studies. Using these phytochemicals, a clinical trial was						

				conducted. Combination of carotenoids and myo-inositol was found to prevent hepatocellular carcinoma development in patients with chronic viral hepatitis and cirrhosis.						
Cancer: lung	Kvale G	Dietary habits and lung cancer risk. Kvale G, Bjelke E, Gart JJ. Int J Cancer. 1983 Apr 15;31(4):397-405.	1983	A previously reported negative association between a high index of dietary vitamin A and lung cancer incidence was confirmed in an extended follow-up, covering 11 1/2 years, of 13,785 men and 2,928 women, Responses to a postal questionnaire provided the dietary information. Relationships between the major dietary items and lung cancer were explored for various diagnostic subsets of the 168 lung cancer cases diagnosed among the study subjects. Analyses were stratified for sex, age, residence characteristics, cigarette smoking and, at times, socioeconomic group. Although the data do not permit a firm interpretation in terms of risk enhancement by a marginal retinoid deficiency, we found that the apparent protection afforded by higher intakes of vitamin A or its provitamins was particularly strong for lung cancer appearing as squamous-cell carcinoma and among those with higher alcohol intakes. The individual food items which showed the strongest negative association with lung cancer were carrots and milk. These two items made a major contribution to the vitamin A index and its variation among the respondents.	PC					(-) Vit A
Cancer: lung	Bond GG	Dietary vitamin A and lung cancer: results of a case-control study among chemical workers.	1987	A nested case-control study conducted among a cohort of chemical manufacturing employees provided an opportunity to test the hypothesis that lung cancer risk is inversely related to dietary intake of	CC nested					(-) Vit A

		Bond GG, Thompson FE, Cook RR. Nutr Cancer. 1987;9(2-3):109-21.		vitamin A. Eligible for study were 308 former male employees who had died of lung cancer between 1940 and 1980. Two control groups, one a decedent and the other a "living" series, were individually matched to the cases one-for-one. Interviews were completed with 734 subjects or their next-of-kin and included a food frequency list. A vitamin A index was developed for each subject based on the frequency of consumption of 29 food items. After adjustment for a number of potentially confounding variables (e.g., smoking, educational level, and use of vitamin supplements), there was evidence that vitamin A intake was inversely associated with lung cancer risk. The effect was most pronounced in the comparisons with the "living" controls and appeared strongest among cigarette smokers. Subjects in the lowest tertile of vitamin A intake had approximately twice the risk of lung cancer as those in the highest. Analyses of an index of carotenoids and of individual food items suggested that plant sources of vitamin A may play a more important role in producing the effect than do animal sources.						
Cancer: lung	Fraser GE	Diet and lung cancer in California Seventh-day Adventists. Fraser GE, Beeson WL, Phillips RL. Am J Epidemiol. 1991 Apr 1;133(7):683-93.	1991	The Adventist Health Study, a cohort study of 34,198 California Seventh-day Adventists, identified 61 cases of new primary lung cancer over 6 years of follow-up (1977-1982). The population studied was unique in that only 4% admitted to current cigarette smoking and about half were lacto-ovovegetarians. A total of 36% of the lung tumors were adenocarcinomas, and 19% were squamous cell carcinomas. The expected associations with cigarette smoking were noted for Kreyberg group I tumors (squamous cell, large	PC					(-) F

				cell, and small cell carcinoma; relative risk (RR) = 53.2 for current smokers and 7.07 for past smokers), but much lesser associations were noted for Kreyberg group II tumors (adenocarcinoma and bronchoalveolar carcinoma; RR = 1.99 for current smokers and 1.59 for past smokers). In this study, fruit consumption was the dietary constituent that showed a strong, statistically significant protective association with lung cancer that was independent of smoking (fruit consumption less than 3 times/week, RR = 1.0; 3-7 times/week, RR = 0.30; greater than or equal to 2 times/day, RR = 0.26). This association was somewhat stronger for Kreyberg group II tumors, but similar trends were also noted for Kreyberg group I tumors. Confounding with smoking seems unlikely in a population with very few current smokers and where both stratification and Cox modeling methods of analysis led to similar conclusions.						
Cancer: lung	Harris RW	A case-control study of dietary carotene in men with lung cancer and in men with other epithelial cancers. Harris RW, Key TJ, Silcocks PB, Bull D, Wald NJ. Nutr Cancer. 1991;15(1):63-8.	1991	Dietary carotene intake during the year before diagnosis was estimated for 96 men with lung cancer, 75 men with other epithelial cancers, and 97 hospital controls. Relative to those of men in the lowest third of carotene intake (less than 1,683 micrograms/day), the smoking-adjusted odds ratios for men in the middle (1,683-2,698 micrograms/day) and upper (greater than 2,698 micrograms/day) thirds of carotene intake were 0.67 and 0.45, respectively, for lung cancer (one-sided test for trend, p = 0.048) and 0.63 and 0.65, respectively, for other epithelial cancers (one-sided test for trend p = 0.074). The protective effect of estimated dietary carotene intake was considerably stronger	CC					(-) carotene

				than was the effect of total intake of carotene-rich vegetables and fruits (grams per day), providing some evidence that the protective factor is carotene itself rather than another component of vegetables and fruits.						
Cancer: lung	Knekt P	Dietary antioxidants and the risk of lung cancer Knekt P, Jarvinen R, Seppanen R, Rissanen A, Aromaa A, Heinonen OP, Albanes D, Heinonen M, Pukkala E, Teppo L. Am J Epidemiol. 1991 Sep 1;134(5):471-9	1991	The relation between the intake of retinoids, carotenoids, vitamin E, vitamin C, and selenium and the subsequent risk of lung cancer was studied among 4,538 initially cancer-free Finnish men aged 20-69 years. During a follow-up of 20 years beginning in 1966-1972, 117 lung cancer cases were diagnosed. Inverse gradients were observed between the intake of carotenoids, vitamin E, and vitamin C and the incidence of lung cancer among nonsmokers, for whom the age-adjusted relative risks of lung cancer in the lowest tertile of intake compared with that in the highest tertile were 2.5 (p value for trend = 0.04), 3.1 (p = 0.12), and 3.1 (p less than 0.01) for the three intakes, respectively. Adjustment for various potential confounding factors did not materially alter the results, and the associations did not seem to be due to preclinical cancer. In the total cohort, there was an inverse association between intake of margarine and fruits and risk of lung cancer. The relative risk of lung cancer for the lowest compared with the highest tertile of margarine intake was 4.0 (p less than 0.001), and that for fruits was 1.8 (p = 0.01). These associations persisted after adjustment for the micronutrient intakes and were stronger among nonsmokers. The results suggest that carotenoids, vitamin E, and vitamin C may be protective against lung cancer among nonsmokers. Food sources rich in these micronutrients	PC					(-) carotenoids

				may also have other constituents with independent protective effects against lung cancer.						
Cancer: lung	Sankaranarayanan R	A case-control study of diet and lung cancer in Kerala, south India. Sankaranarayanan R, Varghese C, Duffy SW, Padmakumary G, Day NE, Nair MK. Int J Cancer. 1994 Sep 1;58(5):644-9.	1994	A total of 281 male lung-cancer patients were identified from the hospital cancer registry in the Regional Cancer Centre in Trivandrum. The controls were selected from the visitors and patients' bystanders in the hospital. The recruitment of cases and controls started in 1990, and the present study used the cases registered in the first year. The questionnaire administered to cases and controls collected information on tobacco smoking and alcohol habits. Dietary data were collected using a food frequency questionnaire and were analyzed by multiple logistic regression producing odds ratio estimates of the relative risk and deviance chi-squared tests of significance. Analysis was done on the computer package, EGRET. All models included age, education, religion and smoking to adjust for the effect of confounding. Green vegetables and bananas were found to have a protective association with lung cancer. The odds ratio associated with the highest quartile of vegetable consumption compared with the lowest was 0.32 (95% confidence interval 0.13, 0.78). Forward stepwise regression analysis indicated pumpkins and onions as the most consistently significant protective factors. Animal protein foods and dairy products were found to have a predisposing effect on lung cancer in this study. The expected influence of smoking on lung cancer (a considerable increase in risk among smokers) provided evidence of the reliability of the data. In conclusion the results from this study show that diet has a role in lung	CC					(-) veg

				cancer aetiology, although the association is weak compared to the effects of smoking.						
Cancer: lung	Axelsson G	Dietary factors and lung cancer among men in west Sweden. Axelsson G, Liljeqvist T, Andersson L, Bergman B, Rylander R. Int J Epidemiol. 1996 Feb;25(1):32-9.	1996	BACKGROUND: Previous studies have reported an association between tea drinking and lung cancer. In view of these data, the relationship between tea drinking as well as other dietary factors and lung cancer was investigated in a case-control study in the west of Sweden. METHODS: Patients with suspected lung cancer were collected from pulmonary units at central hospitals in the area investigated, and population controls were matched for age. The material reported here comprises 308 male cases with a confirmed diagnosis of lung cancer and 504 controls. The participants were interviewed by specially trained nurses, using a questionnaire to assess smoking, dietary habits, occupational exposures and conditions in the residential area (local air pollution). This paper reports the results from dietary factors studied with a food frequency technique. RESULTS: The results demonstrated a strong protective effect of vegetables (odds ratio [OR] = 0.69, 95% confidence interval [CI]: 0.46-1.05, and OR = 0.37, 95% CI: 0.23-0.61 for intermediate and high consumption classes respectively). A low OR was consistent for all histological types of lung cancer. High consumption of fruits did not show any similar protective effect. Drinking milk was associated with a dose-response related risk increase after adjustment for smoking and vegetable consumption (P for trend = 0.07). Odds ratio was 1.73, 95% CI:	CC					(-) veg

				1.00-3.01 for high consumption of milk. CONCLUSIONS: High intake of vegetables had a strong protective effect among males. Diet is thus a potential confounding factor in studies on lung cancer and environmental factors and should thus be taken into consideration in the planning of such studies.						
Cancer: lung	Omenn GS	Effects of a combination of beta carotene and vitamin A on lung cancer and cardiovascular disease. Omenn GS, Goodman GE, Thornquist MD, Balmes J, Cullen MR, Glass A, Keogh JP, Meyskens FL, Valanis B, Williams JH, Barnhart S, Hammar S. N Engl J Med. 1996 May 2;334(18):1150-5.	1996	BACKGROUND. Lung cancer and cardiovascular disease are major causes of death in the United States. It has been proposed that carotenoids and retinoids are agents that may prevent these disorders. METHODS. We conducted a multicenter, randomized, double-blind, placebo-controlled primary prevention trial -- the Beta Carotene and Retinol Efficacy Trial -- involving a total of 18,314 smokers, former smokers, and workers exposed to asbestos. The effects of a combination of 30 mg of beta carotene per day and 25,000 IU of retinol (vitamin A) in the form of retinyl palmitate per day on the primary end point, the incidence of lung cancer, were compared with those of placebo. RESULTS. A total of 388 new cases of lung cancer were diagnosed during the 73,135 person-years of follow-up (mean length of follow-up, 4.0 years). The active-treatment group had a relative risk of lung cancer of 1.28 (95 percent confidence interval, 1.04 to 1.57; P=0.02), as compared with the placebo group. There were no statistically significant differences in the risks of other types of cancer. In	RCT					Study that was stopped due to increase death w/ supple.

				the active-treatment group, the relative risk of death from any cause was 1.17 (95 percent confidence interval, 1.03 to 1.33); of death from lung cancer, 1.46 (95 percent confidence interval, 1.07 to 2.00); and of death from cardiovascular disease, 1.26 (95 percent confidence interval, 0.99 to 1.61). On the basis of these findings, the randomized trial was stopped 21 months earlier than planned; follow-up will continue for another 5 years. CONCLUSIONS. After an average of four years of supplementation, the combination of beta carotene and vitamin A had no benefit and may have had an adverse effect on the incidence of lung cancer and on the risk of death from lung cancer, cardiovascular disease, and any cause in smokers and workers exposed to asbestos.						
Cancer: lung	Speizer B	Prospective study of smoking, antioxidant intake, and lung cancer in middle-aged women (USA). Speizer FE, Colditz GA, Hunter DJ, Rosner B, Hennekens C. Cancer Causes Control. 1999 Oct;10(5):475-82.	1999	BACKGROUND: Although substantial evidence suggests that higher intake of fruits and vegetables can reduce the adverse impact of smoking on lung cancer risk, great uncertainty exists regarding the specific foods and their constituents that are protective. We therefore examine prospectively the relation between cigarette smoking and lung cancer incidence among women, and quantify the associations between dietary antioxidants, other nutrients, and lung cancer risk. METHODS: In a 16-year prospective cohort study (the Nurses' Health Study), 593 cases of lung cancer were confirmed during 1,793,327 person-years of follow-up. Dietary data, including vitamin supplement use and food intake, were collected	PC					(-) carrots

				in 1980 using a validated semiquantitative food frequency questionnaire. RESULTS: The risk of lung cancer increased with the number of cigarettes smoked and with early onset of cigarette smoking. The risk decreased rapidly with the discontinuation of smoking but took 15 years to fall to about the level of risk for women who had never smoked. Dietary intake of fat was not related to the risk of lung cancer. Although beta-carotene intake was not related to risk, intake of carrots showed a strong inverse relation: women who reported consuming five or more carrots per week had a relative risk of 0.4 (95% CI = 0.2-0.8) compared with the risk for women who never ate carrots. CONCLUSIONS: Smoking is the most important risk factor for lung cancer in women, as it is in men. Higher vegetable consumption, particularly of carrots, may significantly reduce the risk of lung cancer, but dietary modification cannot be considered a substitute for smoking prevention and cessation.						
Cancer: lung	Voorrips LE	Vegetable and fruit consumption and lung cancer risk in the Netherlands Cohort Study on diet and cancer. Voorrips LE, Goldbohm RA, Verhoeven DT, van Poppel GA, Sturmans F, Hermus RJ, van den Brandt	2000	OBJECTIVE: The purpose was to study the association between vegetable and fruit consumption and lung cancer incidence using 1074 cases after 6.3 years of follow-up in the Netherlands Cohort Study. METHODS: Dietary intake was assessed using a 150-item food-frequency questionnaire. Multivariate models were used including age, sex, family history of lung cancer, highest	PC					(-) F/V

		PA. Cancer Causes Control. 2000 Feb;11(2):101-15.		educational level attained, and smoking history. RESULTS: Statistically significant inverse associations were found with total vegetables and most vegetable groups. Rate r atios (RRs) based on consumption frequency showed the strongest effect of vegetables from the Brassica group (RR 0.5, 95% confidence interval (95% CI) 0.3-0.9, for consumption > or = 3 times per week versus < or = once a month). RR of highest versus lowest quintile of total vegetable consumption was 0.7 (95% CI 0.5-1.0, p-trend 0.001). Statistically significant inverse associations were found for all fruits listed in the questionnaire. RRs for quintiles of total fruit intake were 1.0, 0.7, 0.6, 0.6 and 0.8 respectively (p-trend < 0.0001). Protective effects of fruits and vegetables were stronger in current than in former smokers, and weaker for adenocarcinomas than for other types of tumors. CONCLUSIONS: Inverse associations with lung cancer are found for both vegetable and fruit intake, but no specific type of vegetable or fruit seems to be particularly responsible.						
Cancer: lung	Wright ME	Dietary carotenoids, vegetables, and lung cancer risk in women: the Missouri women's health study (United States). Wright ME, Mayne ST, Swanson CA, Sinha R, Alavanja MC.	2003	OBJECTIVE: To examine the effect of specific dietary carotenoids and their primary plant food sources on lung cancer risk in a population-based case-control study of women. METHODS: Data were available for 587 incident primary lung cancer cases and 624 controls frequency matched to cases based on age. A modified version of the 100-item NCI-Block food-frequency questionnaire was used to obtain information	CC					

		Cancer Causes Control. 2003 Feb;14(1):85-96.		concerning usual diet 2-3 years prior to interview. RESULTS: In models adjusted for age, total calorie intake, pack-years of smoking, and education, beta-carotene, beta-cryptoxanthin, lutein + zeaxanthin, and total carotenoid intake were each associated with a significantly lower risk of lung cancer. Several vegetable groups were predictive of lower lung cancer risk, particularly the frequency of total vegetable intake. Individual and total carotenoids were no longer significantly associated with lower lung cancer risk in models adjusted for total vegetable intake. However, total vegetable intake remained significantly inversely associated with risk in models adjusted for total carotenoids. CONCLUSIONS: These results indicate that consumption of a wide variety of vegetables has a greater bearing on lung cancer risk in a population of smoking and nonsmoking women than intake of any specific carotenoid or total carotenoids.						
Cancer: lung and colorectal	Suzuki K	Association of serum retinol and carotenoids with insulin-like growth factors and insulin-like growth factor binding protein-3 among control subjects of a nested case-control study in the Japan Collaborative Cohort Study. Suzuki K, Ito Y,	2009	Insulin-like growth factor (IGF)-I and its main binding protein, IGFBP-3, modulate cell growth and survival, and thus are thought to be important for tumor development. Carotenoids and retinol have been linked to the prevention of several cancers. We here evaluated associations of serum levels of carotenoids and retinol with IGF-I, IGF-II, and IGFBP-3 within the context of the JACC Study. The study subjects were 924 controls (578 men and 346 women) of a nested case-control study of lung and colorectal cancer risk. Using frozen-stored sera, serum levels of a-carotene, b-	CC nested				N IGF-1 IGF-11 ~~~~~ (-) IGFBP-3	

		Hashimoto S, Kawado M, Inoue T, Ando M, Watanabe Y, Inaba Y, Tajima K, Nakachi K, Tamakoshi A; JACC Study Group. Asian Pac J Cancer Prev. 2009 Dec;10 Suppl:29-35.		carotene, lycopene, b-cryptoxanthin, zeaxanthin/lutein, and retinol were separately determined using high-performance liquid chromatography. Serum levels of IGF-I, IGF-II, and IGFBP-3 were measured by immuno-radiometric assay. Confounding factors-adjusted least squares mean levels of serum IGF-I, IGF-II, and IGFBP-3 for each quartile of serum levels of carotenoids and retinol were estimated. Serum IGF-I, IGF-II, and IGFBP-3 levels increased with increasing serum retinol levels. Moreover, serum IGF-I levels were significantly higher in highest quartile of serum provitamin A, such as a-carotene, b-carotene, and b-cryptoxanthin, among women. Serum IGFBP-3 levels decreased with increasing serum lycopene levels in women and with increasing serum zeaxanthin/lutein levels in men. The current study indicates that positive associations exist for serum retinol levels with serum levels of IGF-I, IGF-II, and IGFBP-3 independent of age, BMI, smoking habits, drinking habits, and intake of energy and protein among Japanese healthy men and women.						
Cancer: pancreatic	Mills P K	Dietary habits and past medical history as related to fatal pancreas cancer risk among Adventists. Mills PK, Beeson WL, Abbey DE, Fraser GE, Phillips RL. Cancer. 1988 Jun 15;61(12):2578-85.	1988	Epidemiologic studies of diet and pancreas cancer are few, and include ecologic comparisons and a limited number of prospective and case-control studies. Foods and/or nutrients that have been suggested to be associated with increased risk of this cancer include total fat intake, eggs, animal protein, sugar, meat, coffee and butter. Consumption of raw fruits and vegetables has been consistently associated with decreased risk. Dietary habits and medical history variables were evaluated in a prospective study of fatal pancreas cancer among 34,000	PC				(-) Veg (-) L	

				California Seventh-day Adventists between 1976 and 1983. Forty deaths from pancreas cancer occurred during the follow-up period. Compared to all US whites, Adventists experienced decreased risk from pancreas cancer death (standardized mortality ratio [SMR] = 72 for men; 90 for women), which was not statistically significant. Although there was a suggestive relationship between increasing meat, egg, and coffee consumption and increased pancreatic cancer risk, these variables were not significantly related to risk after controlling for cigarette smoking. However, increasing consumption of vegetarian protein products, beans, lentils, and peas as well as dried fruit was associated with highly significant protective relationships to pancreas cancer risk. A prior history of diabetes was associated with increased risk of subsequent fatal pancreas cancer, as was a history of surgery for peptic or duodenal ulcer. A history of tonsillectomy was associated with a slight, nonsignificant protective relationship as was history of various allergic reactions. These findings suggest that the protective relationships associated with frequent consumption of vegetables and fruits high in protease-inhibitor content are more important than any increase in pancreas cancer risk attendant on frequent consumption of meat or other animal products. Furthermore, the previously reported positive associations between diabetes and abdominal surgery and pancreas cancer risk are supported in these data.						
Cancer: prostate	Meyer F	Dietary energy and nutrients in relation to	1997	Previous studies of diet and prostate cancer have focused on advanced disease and have suggested a	CC					

		preclinical prostate cancer. Meyer F, Bairati I, Fradet Y, Moore L. Nutr Cancer. 1997;29(2):120-6.		positive association with saturated fat intake. We report a study assessing the relationship between diet and preclinical prostate cancer. A total of 215 men with preclinical prostate cancer and 593 controls with no evidence of cancer participated in a case-control study conducted in Quebec City between October 1990 and May 1993. The study population comprised two groups: men treated surgically for benign prostatic hypertrophy and participants in a prostate cancer screening program. Trained nutritionists interviewed the participants on their usual diet using a diet history questionnaire. Odds ratios for prostate cancer associated with quartiles of dietary intake and P values for trend were estimated by logistic regression while controlling for age, education, group, and family history of prostate cancer. A positive association was observed between total energy intake and preclinical prostate cancer (p = 0.004). The odds ratios for prostate cancer increased with each quartile of energy intake: 1.00, 1.77, 1.90, and 2.67. After adjustment for energy, nutrients were not associated with prostate cancer. This study provides some evidence that total energy intake is related to preclinical prostate cancer and suggests that diet could be involved earlier than thought in the occurrence of prostate cancer.						
Cancer: prostate	Schuurman AG	Vegetable and fruit consumption and prostate cancer risk: a cohort study in The Netherlands. Schuurman AG, Goldbohm RA, Dorant E, van den	1998	The association between 21 vegetables and eight fruits and prostate cancer risk was assessed in the Netherlands Cohort Study among 58,279 men of ages 55-69 years at baseline in 1986. After 6.3 years of follow-up, 610 cases with complete vegetable data and 642 cases with complete fruit data were available for analysis. In multivariate case-	PC					N F/V

		Brandt PA. Cancer Epidemiol Biomarkers Prev. 1998 Aug;7(8):673-80.		cohort analyses, the following rate ratios (RRs) and 95% confidence intervals (CIs) for vegetable consumption were found (comparing highest versus lowest quintile): total vegetables (RR, 0.80; CI, 0.57-1.12); prepared vegetables (RR, 0.85; CI, 0.61-1.19); and raw vegetables (RR, 0.96; CI, 0.69-1.34). For vegetables categorized in botanical groups, no associations were found except for consumption of pulses (RR, 0.71; CI, 0.51-0.98; P for trend, 0.01). The RRs for total fruit and citrus fruit were 1.31 (CI, 0.96-1.79) and 1.27 (CI, 0.93-1.73), respectively; the corresponding Ps for trend were 0.02 and 0.01, respectively. In a continuous model, no association for total fruit was observed. Individual vegetables and fruits were evaluated as continuous variables (g/day). Nonsignificant inverse associations (RRs per increment of 25 g/day) were found for consumption of kale (RR, 0.74), raw endive (RR, 0.72), mandarins (RR, 0.75), and raisins or other dried fruit (RR, 0.49). Observed positive associations were significant for consumption of leek (RR, 1.38) and oranges (RR, 1.07) and nonsignificant for sweet peppers (RR, 1.60) and mushrooms (RR, 1.49). Results in subgroups of cases were more or less consistent with the overall results. From our study, we cannot conclude that vegetable consumption is important in prostate cancer etiology, but for certain vegetables or fruits, an association cannot be excluded.						
Cancer: prostate	Deneo-Pellegrini H	Foods, nutrients and prostate cancer: a case-control study in Uruguay.	1999	A case-control study of diet and prostate cancer was conducted in Montevideo, Uruguay involving 175 cases and 233 controls. When the highest quartile of intake was compared with the lowest, positive	CC					(-) F/V

		Deneo-Pellegrini H, De Stefani E, Ronco A, Mendilaharsu M. Br J Cancer. 1999 May;80(3-4):591-7.		findings were obtained for red meat intake (OR 2.0, 95% CI 1.1-3.8), desserts (OR 1.8, 95% CI 0.9-3.3), total energy (OR 1.9, 95% CI 1.0-3.4) and total fat intake (OR 1.8, 95% CI 0.9-3.4). On the other hand, vegetables and fruits (OR 0.5, 95% CI 0.3-0.9), vitamin C (OR 0.4, 95% 0.2-0.8) and vitamin E (OR 0.6, 95% CI 0.3-1.1) were associated with reduced risks of prostate cancer. Possible mechanisms are discussed.						
Cancer: prostate	Norrish AE	Men who consume vegetable oils rich in monounsaturated fat: their dietary patterns and risk of prostate cancer (New Zealand). Norrish AE, Jackson RT, Sharpe SJ, Skeaff CM. Cancer Causes Control. 2000 Aug;11(7):609-15.	2000	OBJECTIVES: To investigate (i) dietary patterns associated with consumption of vegetable oils rich in monounsaturated fatty acids (MUFA), and (ii) the risk of prostate cancer associated with consumption of these oils. METHODS: A population-based case-control study was conducted in Auckland, New Zealand, involving 317 prostate cancer cases and 480 controls. A food-frequency questionnaire was used to collect data concerning consumption of MUFA-rich vegetable oils (including olive oil, canola or peanut oil) and other dietary variables. Biomarkers for fatty acids were measured n erythrocytes. RESULTS: The group of participants who reported regular consumption of greater than 5.5 ml of MUFA-rich vegetable oils per day had a diet relatively high in monounsaturated fat, vegetables, lycopene, vitamin E, selenium, and n-3 fish oils. Increasing levels of MUFA-rich vegetable oil intake were associated with a progressive reduction in prostate cancer risk (multivariate relative risk = 0.5; 95% confidence interval 0.3-0.9; > 5.5 ml per day vs. nonconsumption, p	CC					(-) Veg & oil

				trend = 0.005), and similar trends were observed across all strata of socioeconomic status. Prostate cancer risk was not associated with intake of total MUFA or the major animal food sources of MUFA. CONCLUSION: This finding may be explained by the protective effect of an associated dietary pattern high in antioxidants and fish oils, an independent protective effect of MUFA-rich vegetable oils unrelated to the MUFA component, or a combination of these factors.						
Cancer: prostate	Miyata Y	Serum insulin-like growth factor binding protein-3/prostate-specific antigen ratio is a useful predictive marker in patients with advanced prostate cancer. Miyata Y, Sakai H, Hayashi T, Kanetake H. Prostate. 2003 Feb 1;54(2):125-32.	2003	BACKGROUND: Insulin-like growth factor-1 (IGF-1) and insulin-like growth factor binding protein-3 (IGFBP-3) play an important role in regulation of prostate cancer cell growth. We studied the prognostic significance of serum IGF-1 and IGFBP-3 levels, and IGF-1/prostate-specific antigen (PSA) and IGFBP-3/PSA ratios in patients with prostate cancer. METHODS: Serum levels of IGF-1, IGFBP-3, and PSA were determined in 112 patients diagnosed with prostate cancer. Serum samples from 32 patients with histologically confined benign prostatatic hyperplasia (BPH) served as control. RESULTS: Serum IGF-1 levels were significantly higher in advanced prostate cancer (n = 84) than in BPH patients (P < 0.01). IGFBP-3 levels were significantly lower in patients with advanced prostate cancer than in localized tumor (n = 28) or BPH (P < 0.05, each). Univariate analysis showed that serum PSA, IGF-1/PSA ratio, IGFBP-3/PSA ratio, T, N and M classifications correlated significantly with relapse-free survival of advanced prostate cancer patients treated with hormonal therapy. Multivariate analysis identified IGFBP-	CC					

				3/PSA ratio as the only significant variable for relapse-free survival (odds ratio 5.81, 95% CI 1.57-21.51). IGFBP-3/PSA ratio was also an independent predictor of cause-specific survival (stepwise analysis, odds ratio 4.86, P < 0.01). CONCLUSIONS: Our results suggested that IGFBP-3/PSA ratio might be a useful prognostic marker of advanced prostate cancer.						
Cancer: prostate	Dewell A	A very-low-fat vegan diet increases intake of protective dietary factors and decreases intake of pathogenic dietary factors. Dewell A, Weidner G, Sumner MD, Chi CS, Ornish D. J Am Diet Assoc. 2008 Feb;108(2):347-56.	2008	There is increasing evidence that dietary factors in plant-based diets are important in the prevention of chronic disease. This study examined protective (eg, antioxidant vitamins, carotenoids, and fiber) and pathogenic (eg, saturated fatty acids and cholesterol) dietary factors in a very-low-fat vegan diet. Ninety-three early-stage prostate cancer patients participated in a randomized controlled trial and were assigned to a very-low-fat (10% fat) vegan diet supplemented with soy protein and lifestyle changes or to usual care. Three-day food records were collected at baseline (n=42 intervention, n=43 control) and after 1 year (n=37 in each group). Analyses of changes in dietary intake of macronutrients, vitamins, minerals, carotenoids, and isoflavones from baseline to 1 year showed significantly increased intake of most protective dietary factors (eg, fiber increased from a mean of 31 to 59 g/day, lycopene increased from 8,693 to 34,464 mug/day) and significantly decreased intake of most pathogenic dietary factors (eg, saturated fatty acids decreased from 20 to 5 g/day, cholesterol decreased from 200 to 10 mg/day) in the intervention group compared to controls. These results suggest that a very-low-fat vegan diet can be useful	RCT					dietary interv feasibility

				in increasing intake of protective nutrients and phytochemicals and minimizing intake of dietary factors implicated in several chronic diseases.						
Cancer: prostate	Liu X	Lycopene inhibits IGF-I signal transduction and growth in normal prostate epithelial cells by decreasing DHT-modulated IGF-I production in co-cultured reactive stromal cells. Liu X, Allen JD, Arnold JT, Blackman MR. Carcinogenesis. 2008 Apr;29(4):816-23. Epub 2008 Feb 17.	2008	Prostate stromal and epithelial cell communication is important in prostate functioning and cancer development. Primary human stromal cells from normal prostate stromal cells (PRSC) maintain a smooth muscle phenotype, whereas those from prostate cancer (6S) display reactive and fibroblastic characteristics. Dihydrotestosterone (DHT) stimulates insulin-like growth factor-I (IGF-I) production by 6S but not PSRC cells. Effects of reactive versus normal stroma on normal human prostate epithelial (NPE or PREC) cells are poorly understood. We co-cultured NPE plus 6S or PRSC cells to compare influences of different stromal cells on normal epithelium. Because NPE and PREC cells lose androgen receptor (AR) expression in culture, DHT effects must be modulated by associated stromal cells. When treated with camptothecin (CM), NPE cells, alone and in stromal co-cultures, displayed a dose-dependent increase in DNA fragmentation. NPE/6S co-cultures exhibited reduced CM-induced cell death with exposure to DHT, whereas NPE/PRSC co-cultures exhibited CM-induced cell death regardless of DHT treatment. DHT blocked CM-induced, IGF-I-mediated, NPE death in co-cultured NPE/6S cells without, but not with, added anti-IGF-I and anti-IGF-R antibodies. Lycopene consumption is inversely related to human prostate cancer risk and inhibits IGF-I and androgen signaling in rat prostate cancer. In this study, lycopene, in dietary concentrations,	Cell culture				(-) ↓ NPE & PREC cell growth ↓ IGF-1	

				reversed DHT effects of 6S cells on NPE cell death, decreased 6S cell IGF-I production by reducing AR and beta-catenin nuclear localization and inhibited IGF-I-stimulated NPE and PREC growth, perhaps by attenuating IGF-I's effects on serine phosphorylation of Akt and GSK3beta and tyrosine phosphorylation of GSK3. This study expands the understanding of the preventive mechanisms of lycopene in prostate cancer.						
Cancer: prostate	Wilkinson S	The use of complementary therapy by men with prostate cancer in the UK. Wilkinson S, Farrelly S, Low J, Chakraborty A, Williams R, Wilkinson S. Eur J Cancer Care (Engl). 2008 Sep;17(5):492-9. Epub 2008 Jul 10.	2008	The study aims were to determine the use of complementary therapies (CT) by men with prostate cancer, and to explore factors influencing CT use and attitudes toward CT use. A cross-sectional survey design was used in which a postal questionnaire was mailed to an eligible sample of 405 patients with prostate cancer receiving outpatient treatment in a London teaching hospital. The primary outcomes were the prevalence of CT use and the relationship between CT use and mental health status. Two hundred and ninety-four patients (73%) responded, of whom 25% were using CT. The most frequently used CTs were vitamins, low-fat diets, lycopene and green tea. Multivariate analyses revealed no differences in mental health scores between CT users and non-users. CT users were younger (OR 0.93, 95% CI 0.89-0.97) and were more likely to be receiving conservative management in the form of 'active surveillance' (OR 5.23, 95% CI 1.78-15.41) compared with non-users. Over half of the participants (55%) wanted to learn more about CT. Forty-three per cent of CT users had not informed any doctor about their CT use. Clinicians need to be aware of the prevalence	CS					N

				of CT use amongst patients with prostate cancer, considering the potential harm that could be caused by interactions with conventional treatments.						
Diabetes	Ratnam DV	Role of antioxidants in prophylaxis and therapy: A pharmaceutical perspective. Ratnam DV, Ankola DD, Bhardwaj V, Sahana DK, Kumar MN. J Control Release. 2006 Jul 20;113(3):189-207. Epub 2006 May 13.	2006	Antioxidants are emerging as prophylactic and therapeutic agents. These are the agents, which scavenge free radicals otherwise reactive oxygen species and prevent the damage caused by them. Free radicals have been associated with pathogenesis of various disorders like cancer, diabetes, cardiovascular diseases, autoimmune diseases, neurodegenerative disorders and are implicated in aging. Several antioxidants like SOD, CAT, epigallocatechin-3-O-gallate, lycopene, ellagic acid, coenzyme Q10, indole-3-carbinol, genistein, quercetin, vitamin C and vitamin E have been found to be pharmacologically active as prophylactic and therapeutic agents for above mentioned diseases. Antioxidants are part of diet but their bioavailability through dietary supplementation depends on several factors. This major drawback of dietary agents may be due to one or many of the several factors like poor solubility, inefficient permeability, instability due to storage of food, first pass effect and GI degradation. Conventional dosage forms may not result in efficient formulation owing to their poor biopharmaceutical properties. Principles of novel drug delivery systems need to be applied to significantly improve the performance of antioxidants. Novel drug delivery systems (NDDS) would also help in delivery of these antioxidants by oral route, as this route is of prime importance when antioxidants are intended for						

				prophylactic purpose. Implication of NDDS for the delivery of antioxidants is largely governed by physicochemical characteristics, biopharmaceutical properties and pharmacokinetic parameters of the antioxidant to be formulated. Recently, chemical modifications, coupling agents, liposomes, microparticles, nanoparticles and gel-based systems have been explored for the delivery of these difficult to deliver molecules. Results from several studies conducted across the globe are positive and provided us with new anticipation for the improvement of human healthcare.						
Diabetes	Sugiura M	The homeostasis model assessment-insulin resistance index is inversely associated with serum carotenoids in non-diabetic subjects. Sugiura M, Nakamura M, Ikoma Y, Yano M, Ogawa K, Matsumoto H, Kato M, Ohshima M, Nagao A. J Epidemiol. 2006 Mar;16(2):71-8.	2006	BACKGROUND: Carotenoids may reduce the risk for diabetes mellitus, but little is known about the association of insulin resistance with serum carotenoids in non-diabetic subjects. This study aimed to investigate whether the homeostasis model assessment-insulin resistance (HOMA-IR) index would be lower in the presence of high serum carotenoid concentrations in non-diabetic subjects. METHODS: A total of 812 subjects (256 males and 556 females) who had received health examinations in 2003 participated in the study. The associations of the serum-carotenoid concentrations and HOMA-IR were evaluated cross-sectionally. The multivariate-adjusted geometric means of HOMA-IR by the tertiles of the serum carotenoid concentration were calculated after adjusting for age, body mass index, systolic blood pressure, total cholesterol, triacylglycerols, current tobacco use, regular alcohol intake, exercise	CS				(-)	HOMA-IR

				habits and total energy intake. Associations among high HOMA-IR (3.0+mUxmmol/L2) across tertiles of serum carotenoid concentration were assessed by tests for logistic regression analysis. RESULTS: In male subjects, the multivariate adjusted geometric mean of HOMA-IR was inversely associated with the serum beta-cryptoxanthin concentrations. In female subjects, an inverse association of the serum carotenoid concentration and HOMA-IR was observed in lycopene, beta-cryptoxanthin, and zeaxanthin. The confounding factor-adjusted odds ratios (OR) for high HOMA-IR on the highest tertiles of serum alpha-carotene, beta-carotene, beta-cryptoxanthin, and zeaxanthin were 0.18 [95% confidence interval (CI): 0.06-0.52], 0.22 (95% CI: 0.07-0.67), 0.34 (95% CI: 0.12-0.96), and 0.30 (95% CI: 0.11-0.79), respectively, in male subjects. On the other hand, in female subjects, the adjusted OR for high HOMA-IR on the highest tertiles of serum lycopene and beta-cryptoxanthin were 0.39 (95% CI: 0.21-0.73) and 0.51 (95% CI: 0.28-0.95), respectively. CONCLUSIONS: The serum antioxidant carotenoids were inversely associated with HOMA-estimated insulin resistance in non-diabetic subjects.						
Diabetes Vit C	Davison GW	Molecular detection of exercise-induced free radicals following ascorbate prophylaxis in type 1 diabetes mellitus: a randomised	2008	AIMS/HYPOTHESIS: Patients with type 1 diabetes mellitus are more susceptible than healthy individuals to exercise-induced oxidative stress and vascular endothelial dysfunction, which has important implications for the progression of disease. Thus, in the present study, we designed a	RCT					

		controlled trial. Davison GW, Ashton T, George L, Young IS, McEneny J, Davies B, Jackson SK, Peters JR, Bailey DM. Diabetologia. 2008 Nov;51(11):2049-59. Epub 2008 Sep 4.		randomised double-blind, placebo-controlled trial to test the original hypothesis that oral prophylaxis with vitamin C attenuates rest and exercise-induced free radical-mediated lipid peroxidation in type 1 diabetes mellitus. METHODS: All data were collected from hospitalised diabetic patients. The electron paramagnetic resonance spectroscopic detection of spin-trapped alpha-phenyl-tert-butylnitrone (PBN) adducts was combined with the use of supporting markers of lipid peroxidation and non-enzymatic antioxidants to assess exercise-induced oxidative stress in male patients with type 1 diabetes (HbA(1c) 7.9 +/- 1%, n = 12) and healthy controls (HbA(1c) 4.6 +/- 0.5%, n = 14). Following participant randomisation using numbers in a sealed envelope, venous blood samples were obtained at rest, after a maximal exercise challenge and before and 2 h after oral ingestion of 1 g ascorbate or placebo. Participants and lead investigators were blinded to the administration of either placebo or ascorbate treatments. Primary outcome was the difference in changes in free radicals following ascorbate ingestion. RESULTS: Six diabetic patients and seven healthy control participants were randomised to each of the placebo and ascorbate groups. Diabetic patients (n = 12) exhibited an elevated concentration of PBN adducts ($p < 0.05$ vs healthy, n = 14), which were confirmed as secondary, lipid-derived oxygen-centred alkoxyl (RO.) radicals (a(nitrogen) = 1.37 mT and abeta(hydrogen) = 0.18 mT). Lipid hydroperoxides were also selectively elevated and associated with a depression of retinol and lycopene ($p < 0.05$ vs healthy).						

				Vitamin C supplementation increased plasma vitamin C concentration to a similar degree in both groups ($p < 0.05$ vs pre-supplementation) and attenuated the exercise-induced oxidative stress response ($p < 0.05$ vs healthy). There were no selective treatment differences between groups in the primary outcome variable. CONCLUSIONS/INTERPRETATION: These findings are the first to suggest that oral vitamin C supplementation provides an effective prophylaxis against exercise-induced free radical-mediated lipid peroxidation in human diabetic blood. Clinical trials registration number:						
Diabetes Rats	Ali MM	Amelioration of streptozotocin-induced diabetes mellitus, oxidative stress and dyslipidemia in rats by tomato extract lycopene. Ali MM, Agha FG. Scand J Clin Lab Invest. 2009;69(3):371-9.	2009	The effects of various doses of lycopene were studied in streptozotocin (STZ)-induced hyperglycaemic rats to evaluate its possible hypoglycaemic, hypolipidaemic and antioxidant activity in diabetes. Compared to the normoglycaemic group, the treatment of rats with a single dose of STZ (65 mg/kg body weight) revealed a significant increase ($p<0.05$) only in plasma hydrogen peroxide ($H(2)O(2)$), i.e. by 230%; it increased the thiobarbituric acid reactive substances (TBARS) as index of the lipid peroxidation level by 69%, while total antioxidant activity was decreased by 36%, with a consistently significant decrease ($p<0.05$) in the activity of erythrocytes antioxidative enzymes catalase (CAT), superoxide dismutase (SOD) and glutathione peroxidase (GPx). The levels of total lipid, triglycerides and total cholesterol in serum of hyperglycaemic rats were increased by 14%, 65% and 36%, respectively,					(-) Glucose Insulin Ox Stress Lipids	

				while HDL-C decreased by 22% compared to the normoglycaemic group. Exogenous administration of individual gradual doses of lycopene to hyperglycaemic rats causes a dose-dependent decrease in glucose level, an increase of insulin concentration, a decrease of H(2)O(2) and TBARS levels, as well as increased total antioxidant status with increased antioxidant enzyme activities (CAT, SOD and GPx) with improvement in serum lipid profile. It is obvious from this study that lycopene acts as an antidiabetic agent through lowering the free radical and has an improving effect on serum that reaches the normal level; the greatest effect of lycopene was observed at 90 mg/kg body weight.						
Dietary Intake	Chaiter Y	Dietary intake of carotenoid isomers in Israel. Chaiter Y, Rennert G, Fischler R, Rennert HS, Rozen G, Gruber SB, Amotz AB. Int J Vitam Nutr Res. 2007 Nov;77(6):398-405.	2007	Controversy exists regarding the possible protective role of carotenoids against cancer. Evidence is mainly against all-E-beta-carotene, while there is no evidence against other carotenoids or against mixtures of beta-carotene stereoisomers. Carotenoid isomers could account for the variability in study results but are rarely estimated, and reference to the degree of their consumption is lacking. The aim of our study was to create a comprehensive database of carotenoid isomers content in food items commonly consumed in Israel. Food items were analyzed using a liquid chromatography system to determine the content of carotenoid isomers in Israeli food. The main sources of carotenoids detected in Israeli foods were tomato juice, tomato, watermelon, parsley, coriander, spinach, carrot, sweet potato, banana, zucchini, mango, loquat, pepper, eggplant, and						

				chickpeas. Data were used to measure consumption in healthy participants of a case-control study, using a semi-quantitative food-frequency 187-item questionnaire. Compared to reference studies, the median carotenoid isomers intake in 712 Israeli healthy controls (age range 23-95 years, mean 71 +/- 10.9 years, median 73 years) was higher for beta-carotene, alpha-carotene, beta-cryptoxanthin, and zeaxanthin, while the intake of lycopene was lower. Major differences in consumption were noticed between ethnic groups consuming Mediterranean diets and those consuming Western-type diets. Population consumption patterns of carotenoid isomers using a comprehensive database are used to improve our understanding in disease prevention. Consumption in Israel seems to be generally higher than that reported in studies conducted elsewhere, and varies by ethnic group.						
Dietary Patterns	Lopez-Garcia E	Major dietary patterns are related to plasma concentrations of markers of inflammation and endothelial dysfunction. Lopez-Garcia E, Schulze MB, Fung TT, Meigs JB, Rifai N, Manson JE, Hu FB. Am J Clin Nutr. 2004 Oct;80(4):1029-35.	2004	BACKGROUND: Endothelial dysfunction is one of the mechanisms linking diet and the risk of cardiovascular disease. OBJECTIVE: We evaluated the hypothesis that dietary patterns (summary measures of food consumption) are directly associated with markers of inflammation and endothelial dysfunction, particularly C-reactive protein (CRP), interleukin 6, E-selectin, soluble intercellular adhesion molecule 1 (sICAM-1), and soluble vascular cell adhesion molecule 1 (sVCAM-1). DESIGN: We conducted a cross-sectional study of 732 women from the Nurses' Health Study I cohort who were 43-69 y of age and free of cardiovascular disease, cancer, and diabetes mellitus at the time of blood	CS					(-) F/V

				drawing in 1990. Dietary intake was documented by using a validated food-frequency questionnaire in 1986 and 1990. Dietary patterns were generated by using factor analysis. RESULTS: A prudent pattern was characterized by higher intakes of fruit, vegetables, legumes, fish, poultry, and whole grains, and a Western pattern was characterized by higher intakes of red and processed meats, sweets, desserts, French fries, and refined grains. The prudent pattern was inversely associated with plasma concentrations of CRP (P = 0.02) and E-selectin (P = 0.001) after adjustment for age, body mass index (BMI), physical activity, smoking status, and alcohol consumption. The Western pattern showed a positive relation with CRP (P < 0.001), interleukin 6 (P = 0.006), E-selectin (P < 0.001), sICAM-1 (P < 0.001), and sVCAM-1 (P = 0.008) after adjustment for all confounders except BMI; with further adjustment for BMI, the coefficients remained significant for CRP (P = 0.02), E-selectin (P < 0.001), sICAM-1 (P = 0.002), and sVCAM-1 (P = 0.02). CONCLUSION: Because endothelial dysfunction is an early step in the development of atherosclerosis, this study suggests a mechanism for the role of dietary patterns in the pathogenesis of cardiovascular disease.						
Food intake methods	Ishihara J	Food frequency questionnaire is a valid tool in the nutritional assessment of Brazilian women of diverse ethnicity. Ishihara J, Iwasaki M, Kunieda CM,	2009	The objective of this study was to validate a food frequency questionnaire (FFQ) used to estimate energy and selected nutrient intake in a Brazilian population with various ethnic backgrounds. Validity of intake estimated using the FFQ was tested among 55 Brazilian women, namely 26 Caucasians, 15 of Japanese descent, and 14 others.	CS					Validity testing lyco intake was underestimated

		Hamada GS, Tsugane S. Asia Pac J Clin Nutr. 2009;18(1):76-80.		The FFQ was originally developed for use in a case-control study of breast cancer conducted in Sao Paulo. Dietary records (DRs) recorded in two seasons were used as references. Intake of energy and 24 nutrients were calculated using the USDA and Japanese food composition tables. Validity and reproducibility were evaluated using Spearman's correlation coefficients. Results showed that intake of chicken/poultry, eggs and legumes were overestimated by the FFQ compared to the DR, whereas that of pork and fat was underestimated. Further, intake of folate, fiber and isoflavones was overestimated by the FFQ whereas that of energy, fat, carbohydrate alpha-carotene and lycopene was underestimated. Energy-adjusted correlation coefficients between nutrient intakes estimated with the FFQ and DR were high for isoflavones (0.76), calcium (0.50), and vitamin C (0.49). In contrast, validity varied from moderately high to low for energy and other nutrients. In conclusion, validity of the FFQ for estimation of the intake of selected nutrients among Brazilian women with varied ethnic background was moderately high.						
Food intake methods	Wawrzyniak A	[Comparative assessment of carotenoids intake by food frequency questionnaire and 4-day dietary food records method] Wawrzyniak A, Hamuaka J. Rocz Panstw Zakl	2009	The aim of the work was comparative assessment of beta-carotene, lycopene and lutein intake by two methods: food frequency questionnaire and 4-day dietary food records. Subjects were 130 female volunteers, aged 18 to 25 years, Warsaw University of Life Sciences students. Data were collected in spring/summer 2005. Intakes of beta-carotene (3.62 vs. 3.49 mg/day per person), lycopene (4.54 vs. 4.05 mg/day per person) and lutein (2.50	CS				N Diff between FFQ and FR no sig	

		Hig. 2009;60(1):25-9.		vs. 2.12 mg/day per person, respectively) estimated these methods were not statistically significant. The mean differences in intakes assessed were higher for food frequency questionnaire (respectively 3.7% for beta-carotene; 12.1% for lycopene; 1.9% for lutein). Statistically significant Pearson correlations were observed between estimation of carotenoids intake by two methods (r = 0.82 for beta-carotene, r = 0.75 for lycopene, r = 0.73 for lutein; p < 0.001). Main sources of beta-carotene were vegetables supplied 90% of this carotenoid (therein carrot 54%). Tomato products and fresh tomatoes contributed 60-61% and 30% of lycopene/day respectively. Sources of lutein were fresh vegetables contributed to diet 54-60% of lutein (therein leafy vegetables 25-30%).						
Food intake Patterns	Kant AK	A comparison of three dietary pattern indexes for predicting biomarkers of diet and disease. Kant AK, Graubard BI. J Am Coll Nutr. 2005 Aug;24(4):294-303.	2005	OBJECTIVE: Examination of dietary indexes in association with objective biomarkers of dietary intake and chronic disease risk is an important step in their validation. We compared three dietary pattern indexes-Healthy Eating Index (HEI), Recommended Foods Score (RFS-24 hour recall), and Dietary Diversity Score for recommended foods (DDS-R)-for their ability to predict biomarkers of dietary intake, obesity, cardiovascular disease, and diabetes. METHODS: We used dietary and laboratory data from the third National Health and Nutrition Examination Survey to study these associations in 8719 disease-free adults aged > or =20 y. The HEI, developed by the USDA, was a sum of scores on consideration of ten	CS					N no corr of serum [lyco] with F.I.

				individual components; the RFS was a sum of all recommended foods (lean meat, poultry and fish, whole grains, fruits and juices, low-fat dairy, and vegetables) mentioned in the recall; the DDS-R examined whether or not a recommended food was mentioned from each of the five major food groups. The independent association of the dietary pattern indexes with body mass index (BMI), blood pressure, and serum concentrations of several biomarkers were examined using regression methods to adjust for multiple covariates. RESULTS: All indexes were strong independent positive predictors of serum concentrations of vitamin C, E, folate, and all carotenoids ($p < or = 0.00001$), except lycopene, and were negative predictors of BMI, serum homocysteine, C-reactive protein, plasma glucose, and hemoglobin A1C ($p < 0.05$). The RFS and DDS-R were inversely associated with blood pressure and serum cholesterol ($p < or = 0.03$). CONCLUSIONS: The RFS and DDS-R performed as well or better than the HEI for predicting serum concentration of nutrients and biomarkers of disease risk.						
Food intake patterns	Chaiter Y	Dietary intake of carotenoid isomers in Israel. Chaiter Y, Rennert G, Fischler R, Rennert HS, Rozen G, Gruber SB, Amotz AB. Int J Vitam Nutr	2007	Controversy exists regarding the possible protective role of carotenoids against cancer. Evidence is mainly against all-E-beta-carotene, while there is no evidence against other carotenoids or against mixtures of beta-carotene stereoisomers. Carotenoid isomers could account for the variability in study results but are rarely estimated, and reference to the degree of their	CC					(-) ↓ lyco intake in this aged Israeli population

		Res. 2007 Nov;77(6):398-405.		consumption is lacking. The aim of our study was to create a comprehensive database of carotenoid isomers content in food items commonly consumed in Israel. Food items were analyzed using a liquid chromatography system to determine the content of carotenoid isomers in Israeli food. The main sources of carotenoids detected in Israeli foods were tomato juice, tomato, watermelon, parsley, coriander, spinach, carrot, sweet potato, banana, zucchini, mango, loquat, pepper, eggplant, and chickpeas. Data were used to measure consumption in healthy participants of a case-control study, using a semi-quantitative food-frequency 187-item questionnaire. Compared to reference studies, the median carotenoid isomers intake in 712 Israeli healthy controls (age range 23-95 years, mean 71 +/- 10.9 years, median 73 years) was higher for beta-carotene, alpha-carotene, beta-cryptoxanthin, and zeaxanthin, while the intake of lycopene was lower. Major differences in consumption were noticed between ethnic groups consuming Mediterranean diets and those consuming Western-type diets. Population consumption patterns of carotenoid isomers using a comprehensive database are used to improve our understanding in disease prevention. Consumption in Israel seems to be generally higher than that reported in studies conducted elsewhere, and varies by ethnic group.						
Food intake patterns	Reyes-Ortiz CA	Acculturation and serum nutrients thought to be involved with cancer prevention	2009	BACKGROUND: Mexican American men living in the United States who are more acculturated exhibit higher rates of cancer compared to those less acculturated. This study explored	CS				[Lyco] w/ aculturation	

		among Mexican American men in the United States. Reyes-Ortiz CA, Ju H, Inniss A, Eschbach K, Kuo YF, Goodwin JS. Cancer Control. 2009 Apr;16(2):169-75.		the association between acculturation and serum levels of nutrients thought to be involved with cancer prevention among Mexican American men. METHODS: Our sample included 2,479 Mexican American men from the Third National Health and Nutrition Examination Survey (1988-1994). Outcomes were serum levels of micronutrients. Acculturation in Mexican American men was assessed by a combined measure including country of origin, language of interview, and years of residence in the United States and was categorized as follows: (1) foreign-born, 0-5 years in the United States (lowest acculturation), (2) foreign-born, 6-15 years in the United States, (3) foreign-born, > 15 years in the United States, (4) US-born Spanish-speaking, and (5) US-born English-speaking (highest acculturation). RESULTS: Adjusted analyses showed that acculturation decreased the serum levels for vitamin E, vitamin C, and folate and also for some carotenoids (alpha and beta carotenes, beta cryptoxanthin, and lutein-zeaxanthin). By contrast, acculturation increased the serum levels for selenium and lycopene. CONCLUSIONS: With the exception of selenium and lycopene, acculturation among Mexican American men decreased the serum levels for most carotenoids and for vitamin E, vitamin C, and folate. These changes in nutrient profiles, reflecting altered patterns in food consumption or other behaviors, may explain in part why Mexican American men who are more						

				acculturated have an increased risk for diet-related cancer.						
General population	Fraser GE.	Associations between diet and cancer, ischemic heart disease, and all-cause mortality in non-Hispanic white California Seventh-day Adventists. Fraser GE. Am J Clin Nutr. 1999 Sep;70(3 Suppl):532S-538S.	1999	Seventh-day Adventists are summarized. Most Seventh-day Adventists do not smoke cigarettes or drink alcohol, and there is a wide range of dietary exposures within the population. About 50% of those studied ate meat products <1 time/wk or not at all, and vegetarians consumed more tomatoes, legumes, nuts, and fruit, but less coffee, doughnuts, and eggs than did nonvegetarians. Multivariate analyses showed significant associations between beef consumption and fatal ischemic heart disease (IHD) in men [relative risk (RR) = 2.31 for subjects who ate beef > or =3 times/wk compared with vegetarians], significant protective associations between nut consumption and fatal and nonfatal IHD in both sexes (RR approximately 0.5 for subjects who ate nuts > or =5 times/wk compared with those who ate nuts <1 time/wk), and reduced risk of IHD in subjects preferring whole-grain to white bread. The lifetime risk of IHD was reduced by approximately 31% in those who consumed nuts frequently and by 37% in male vegetarians compared with nonvegetarians. Cancers of the colon and prostate were significantly more likely in nonvegetarians (RR of 1.88 and 1.54, respectively), and frequent beef consumers also had higher risk of bladder cancer. Intake of legumes was negatively associated with risk of colon cancer in nonvegetarians and risk of pancreatic cancer. Higher consumption of all fruit or dried fruit was associated with lower risks of lung, prostate, and pancreatic cancers. Cross-sectional data	CS					

				suggest vegetarian Seventh-day Adventists have lower risks of diabetes mellitus, hypertension, and arthritis than nonvegetarians. Thus, among Seventh-day Adventists, vegetarians are healthier than nonvegetarians but this cannot be ascribed only to the absence of meat.						
General population	Olmedilla B	Serum concentrations of carotenoids and vitamins A, E, and C in control subjects from five European countries. Olmedilla B, Granado F, Southon S, Wright AJ, Blanco I, Gil-Martinez E, Berg H, Corridan B, Roussel AM, Chopra M, Thurnham DI. Br J Nutr. 2001 Feb;85(2):227-38.	2001	High intakes of fruits and vegetables, or high circulating levels of their biomarkers (carotenoids, vitamins C and E), have been associated with a relatively low incidence of cardiovascular disease, cataract and cancer. Exposure to a high fruit and vegetable diet increases antioxidant concentrations in blood and body tissues, and potentially protects against oxidative damage to cells and tissues. This paper describes blood concentrations of carotenoids, tocopherols, ascorbic acid and retinol in well-defined groups of healthy, non-smokers, aged 25-45 years, 175 men and 174 women from five European countries (France, UK (Northern Ireland), Republic of Ireland, The Netherlands and Spain). Analysis was centralised and performed within 18 months. Within-gender, vitamin C showed no significant differences between centres. Females in France, Republic of Ireland and Spain had significantly higher plasma vitamin C concentrations than their male counterparts. Serum retinol and alpha- tocopherol levels were similar between centres, but gamma-tocopherol showed a great variability being the lowest in Spain and France, and the highest in The Netherlands. The provitamin A: non-provitamin A carotenoid ratio was similar among countries, whereas the xanthophylls (lutein, zeaxanthin,	CS				N	Charact-erization study

				beta-cryptoxanthin) to carotenes (alpha-carotene, beta-carotene, lycopene) ratio was double in southern (Spain) compared to the northern areas (Northern Ireland and Republic of Ireland). Serum concentrations of lutein and zeaxanthin were highest in France and Spain; beta-cryptoxanthin was highest in Spain and The Netherlands; trans-lycopene tended to be highest in Irish males and lowest in Spanish males; alpha-carotene and beta-carotene were higher in the French volunteers. Due to the study design, the concentrations of carotenoids and vitamins A, C and E represent physiological ranges achievable by dietary means and may be considered as 'reference values' in serum of healthy, non-smoking middle-aged subjects from five European countries. The results suggest that lutein (and zeaxanthin), beta-cryptoxanthin, total xanthophylls and gamma-tocopherol (and alpha- : gamma-tocopherol) may be important markers related to the healthy or protective effects of the Mediterranean-like diet.						
General population	Subar AF	Comparative validation of the Block, Willett, and National Cancer Institute food frequency questionnaires : the Eating at America's Table Study. Subar AF, Thompson FE, Kipnis V, Midthune D, Hurwitz P, McNutt S, McIntosh A, Rosenfeld S.	2001	Researchers at the National Cancer Institute developed a new cognitively based food frequency questionnaire (FFQ), the Diet History Questionnaire (DHQ). The Eating at America's Table Study sought to validate and compare the DHQ with the Block and Willett FFQs. Of 1,640 men and women recruited to participate from a nationally representative sample in 1997, 1,301 completed four telephone 24-hour recalls, one in each season. Participants were randomized to receive either a DHQ and Block FFQ or a DHQ and Willett FFQ. With a standard measurement error model,	CS					FFQ's in Epi Studies for tool validation.

		Am J Epidemiol. 2001 Dec 15;154(12):1089-99.		correlations for energy between estimated truth and the DHQ, Block FFQ, and Willett FFQ, respectively, were 0.48, 0.45, and 0.18 for women and 0.49, 0.45, and 0.21 for men. For 26 nutrients, correlations and attenuation coefficients were somewhat higher for the DHQ versus the Block FFQ, and both were better than the Willett FFQ in models unadjusted for energy. Energy adjustment increased correlations and attenuation coefficients for the Willett FFQ dramatically and for the DHQ and Block FFQ instruments modestly. The DHQ performed best overall. These data show that the DHQ and the Block FFQ are better at estimating absolute intakes than is the Willett FFQ but that, after energy adjustment, all three are more comparable for purposes of assessing diet-disease risk.						
General population	Al Delaimy W.K.	Plasma levels of six carotenoids in nine European countries: report from the European Prospective Investigation into Cancer and Nutrition (EPIC). Al-Delaimy WK, van Kappel AL, Ferrari P, Slimani N, Steghens JP, Bingham S, Johansson I, Wallstrom P, Overvad K, Tjonneland A, Key TJ, Welch AA, Bueno-de-Mesquita HB, Peeters PH, Boeing H, Linseisen J,	2004	BACKGROUND: In addition to their possible direct biological effects, plasma carotenoids can be used as biochemical markers of fruit and vegetable consumption for identifying diet-disease associations in epidemiological studies. Few studies have compared levels of these carotenoids between countries in Europe. OBJECTIVE: Our aim was to assess the variability of plasma carotenoid levels within the cohort of the European Prospective Investigation into Cancer and Nutrition (EPIC). METHODS: Plasma levels of six carotenoids--alpha-carotene, beta-carotene, beta-cryptoxanthin, lycopene, lutein and zeaxanthin--were measured cross-sectionally in 3043 study subjects from 16 regions in	CS					

		Clavel-Chapelon F, Guibout C, Navarro C, Quiros JR, Palli D, Celentano E, Trichopoulou A, Benetou V, Kaaks R, Riboli E. Public Health Nutr. 2004 Sep;7(6):713-22.		nine European countries. We investigated the relative influence of gender, season, age, body mass index (BMI), alcohol intake and smoking status on plasma levels of the carotenoids. RESULTS: Mean plasma level of the sum of the six carotenoids varied twofold between regions (1.35 micromol l(-1) for men in Malmo, Sweden vs. 2.79 micromol l(-1) for men in Ragusa/Naples, Italy; 1.61 micromol l(-1) for women in The Netherlands vs. 3.52 micromol l(-1) in Ragusa/Naples, Italy). Mean levels of individual carotenoids varied up to fourfold (alpha-carotene: 0.06 micromol l(-1) for men in Murcia, Spain vs. 0.25 micromol l(-1) for vegetarian men living in the UK). In multivariate regression analyses, region was the most important predictor of total plasma carotenoid level (partial R(2)=27.3%), followed by BMI (partial R(2)=5.2%), gender (partial R(2)=2.7%) and smoking status (partial R(2)=2.8%). Females had higher total carotenoid levels than males across Europe. CONCLUSIONS: Plasma levels of carotenoids vary substantially between 16 different regions in Italy, Greece, Spain, France, Germany, the UK, Sweden, Denmark and The Netherlands. Compared with region of residence, the other demographic and lifestyle factors and laboratory measurements have limited predictive value for plasma carotenoid levels in Europe.						
General population	Bingham S	Diet and cancer--the European Prospective Investigation into	2004	Diet is thought to be one of the most important contributing factors to cancer risk. The contribution of diet to cancer is linked to genetic factors,	PC					

		Cancer and Nutrition. Bingham S, Riboli E. Nat Rev Cancer. 2004 Mar;4(3):206-15.		and uncovering the details of this linkage requires that very large studies be carried out over long time periods, with a detailed analysis of food intake. For this reason, the European Prospective Investigation into Cancer and Nutrition — a study of over 500,000 people in 10 European countries — was devised, to investigate the relationship between diet, metabolic and genetic factors, and cancer. How will this study be run, and will it be able to avoid some of the problems of measurement error that were previously encountered with other dietary studies?						
General population	Vrieling A	Dietary determinants of circulating insulin-like growth factor (IGF)-I and IGF binding proteins 1, -2 and -3 in women in the Netherlands. Vrieling A, Voskuil DW, Bueno de Mesquita HB, Kaaks R, van Noord PA, Keinan-Boker L, van Gils CH, Peeters PH. Cancer Causes Control. 2004 Oct;15(8):787-96.	2004	OBJECTIVE: Epidemiological studies suggest that individuals with elevated plasma concentrations of insulin-like growth factor (IGF-I) are at increased risk of developing cancer. We assessed whether dietary intake of total energy, protein, alcohol, phytoestrogens and related foods, and tomatoes and lycopene was associated with plasma levels of IGF-I and IGF binding proteins (IGFBPs) in Dutch women. METHODS: A cross-sectional study was conducted in 224 premenopausal and 162 postmenopausal women, aged 49-69, participating in the Prospect-EPIC study in the Netherlands. Diet was assessed using a food frequency questionnaire. RESULTS: In postmenopausal women, higher alcohol intake was associated with lower plasma IGFBP-1 concentrations (alcohol 1.4 to 20 g/day: 20% decrease in IGFBP-1; p = 0.04), and higher intake of plant lignans was associated with higher IGFBP-1 concentrations (plant lignans 0 to 1 mg/day: 59% increase in IGFBP-1; p =0.02). Higher soy intake was associated with higher plasma IGFBP-	CS			N		

				2 concentrations in premenopausal women (soy 0 to 2.5 g/day: 3% increase in IGFBP-2; p = 0.04). No independent associations of dietary factors with IGF-I or IGFBP-3 concentrations were observed. However, in premenopausal women alcohol intake was inversely associated with IGF-I and positively associated with IGFBP-3 after mutual adjustment. CONCLUSIONS: In this study population, with limited variation in dietary intake, total energy, protein, phytoestrogens and lycopene were not associated with IGF-I and IGFBP-3. Alcohol was inversely, and some measures of phytoestrogenintake were positively associated with plasma IGFBP-1 or -2 concentrations. The roles of IGFBP-1 and -2 in relation to IGF-I bioactivity and cancer deserve further investigation. Further research on the bioavalability, pharmacology, biochemistry, and physiology must be done to reveal the mechanism of lycopene in human diet, and the in vivo metabolism of lycopene. Consumer demand for healthy food products provides an opportunity to develop lycopene-rich food as new functional foods, as well as food-grade and pharmaceutical-grade lycopene as new nutraceutical products. An industrial scale, environmentally friendly lycopene extraction and purification procedure with minimal loss of bioactivities is highly desirable for the foods, feed, cosmetic, and pharmaceutical industries. High-quality lycopene products that meet food safety regulations will offer potential benefits to the food industry.						
General population	Ferrari P	An approach to estimate between-	2005	In a multicenter study, the overall correlation between two variables	CS					

		and within-group correlation coefficients in multicenter studies: plasma carotenoids as biomarkers of intake of fruits and vegetables. Ferrari P, Al-Delaimy WK, Slimani N, Boshuizen HC, Roddam A, Orfanos P, Skeie G, Rodriguez-Barranco M, Thiebaut A, Johansson G, Palli D, Boeing H, Overvad K, Riboli E. Am J Epidemiol. 2005 Sep 15;162(6):591-8. Epub 2005 Aug 10.		can be broken down into a within- and a between-group correlation reflecting associations at the individual and aggregate levels, respectively. A random-effects model is used to estimate variance components of nutrition-related variables and the within- and between-group correlation coefficients. Using data from the European Prospective Investigation into Cancer and Nutrition (EPIC), the authors analyzed the association between levels of three plasma carotenoids (alpha-carotene, beta-cryptoxanthin, and lycopene) and dietary intake of three items (total fruits, carrots, and tomatoes), assessed through dietary questionnaire and single 24-hour dietary recall measurements, in a cross-sectional study involving 3,089 subjects from nine European countries. Intraclass correlation coefficients were 0.178 for alpha-carotene, 0.216 for beta-cryptoxanthin, and 0.299 for lycopene. The between-group correlation coefficients were higher than the within-group coefficients for all three carotenoids. For beta-cryptoxanthin and fruit intake, the between-group versus the within-group correlations were 0.78 and 0.26 for the dietary questionnaire and 0.85 and 0.19 for the 24-hour dietary recall. Results indicate that variability of exposure is driven mainly by the individual compared with the aggregate variation and that biomarker levels perform fairly accurately in discriminating population-level consumption of fruits and vegetables.						
General population	Jansen MC	Plasma carotenoid levels in Dutch men and women,	2004	OBJECTIVE: Fruit and vegetable intake is inversely associated with cancer risk in many epidemiological	PC subset					Markers of vegetable

(EPIC)		and the relation with vegetable and fruit consumption. Jansen MC, Van Kappel AL, Ocke MC, Van 't Veer P, Boshuizen HC, Riboli E, Bueno-de-Mesquita HB Eur J Clin Nutr. 2004 Oct;58(10):1386-95.		studies. Accurate assessment of consumption of these foods is difficult, and biomarkers of intake would overcome several drawbacks of currently used dietary assessment methods. Therefore, we investigated the relation between plasma carotenoids and usual vegetable and fruit intake. DESIGN: Plasma carotenoid concentrations were measured and vegetable, fruit and juice consumption was assessed by a food frequency questionnaire (FFQ) in a random sample of 591 Dutch men and women aged 20-59 y from the MORGEN- project, one of the contributions to the European Prospective Investigation into Cancer and Nutrition (EPIC)-study. RESULTS: In this sample of the general Dutch population, in both genders, relative to the other carotenoids, plasma beta-cryptoxanthin was the best indicator for fruit intake, and for the sum of vegetable, fruit and juice intake, while lutein concentrations best reflected intake of vegetables, although quartiles of intake were not consistently separated. Since levels of lycopene were not associated with any of the main food groups examined, associations with total carotenoids improved when excluding lycopene, and monotonously increasing plasma levels were seen for intakes of vegetables, of fruits, and of the sum of vegetables, fruits and juices. Several vegetable types and orange/grapefruit juice were associated with plasma levels of one of the carotenoids. CONCLUSION: Plasma carotenoids were only crude indicators of						& fruit intake

				vegetable and fruit intake as assessed by a FFQ; beta-cryptoxanthin for fruit intake and lutein for vegetable intake. None of the plasma carotenoids could distinguish all four quartiles of vegetables, fruit and/or juice intake.						
General population	Gomez-Aracena J	Vegetable consumption and carotenoids in plasma and adipose tissue in Malaga, Spain. Gomez-Aracena J, Bogers R, Van't Veer P, Gomez-Gracia Garcia-Rodriguez A, Wedel H, Fernandez-Crehuet Navajas J. Int J Vitam Nutr Res. 2003 Feb;73(1):24-31.	2003	OBJECTIVE: To study relationships between habitual dietary intake, adipose tissue concentrations of alpha-carotene, beta-carotene and lycopene, and plasma concentrations of alpha- and beta-carotene. DESIGN: Cross-sectional study including assessment of food habits by a food frequency questionnaire and 48-hour recall and determination of carotenoid concentrations in adipose tissue and plasma. SUBJECTS: 51 women (mean age of 62 years) from the control group of the European Community Multicentre Study on Antioxidants, Myocardial Infarction, and Breast Cancer (EURAMIC), Malaga, Spain. RESULTS: In adipose tissue, beta-carotene was correlated with consumption of green pepper ($r = 0.36$; $p < 0.05$) and lycopene with total fruit/vegetable intake ($r = 0.28$; $p < 0.05$), green pepper ($r = 0.31$; $p < 0.05$), and carrot ($r = 0.25$; $p < 0.10$). In plasma, beta-carotene was correlated with total fruit/vegetable intake ($r = 0.29$; $p < 0.10$), lettuce ($r = 0.34$; $p < 0.05$), tomato ($r = 0.26$; $p < 0.10$), and lycopene with total fruit/vegetable intake ($r = 0.27$; $p < 0.10$). Age-, BMI- and waist circumference-adjusted regression coefficients for the regression of logn-	CS					F/V + lyco

				transformed adipose and plasma concentrations on consumption of specific fruits and vegetables (per 100 g/day) were calculated. In adipose tissue, coefficients were: 1.50 ($p < 0.05$) for alpha-carotene/carrot; 1.90 ($p < 0.10$) and 0.51 ($p < 0.10$) for beta-carotene/green pepper and lettuce; 2.02 ($p < 0.05$), 1.25 ($p < 0.05$) and 0.18 ($p < 0.05$) for lycopene/green pepper, carrot and total fruit/vegetable intake. In plasma, coefficients were 1.14 ($p < 0.05$) and 0.21 ($p < 0.05$) for beta-carotene/lettuce and total fruit/vegetable intake. CONCLUSIONS: Consumption of fruit and vegetables could be linked directly to carotenoid concentrations in adipose tissue and plasma. Although associations with individual food items are related to their carotenoid contents, the absorption and distribution of carotenoids needs more attention to improve their usefulness as biomarkers of exposure.						
Geno-typing	Goodman M	Lycopene intake and prostate cancer risk: effect modification by plasma antioxidants and the XRCC1 genotype. Goodman M, Bostick RM, Ward KC, Terry PD, van Gils CH, Taylor JA, Mandel JS Nutr Cancer. 2006;55(1):13-20.	2006	Lycopene has been associated with reduced prostate cancer risk, although the results of epidemiological studies have varied. We hypothesize that an effect of lycopene may be modified by XRCC1 genotype and other antioxidants. We used a food-frequency questionnaire to assess lycopene intake in a case-control study of prostate cancer in North Carolina. Plasma alpha-tocopherol and beta-carotene levels were measured using high-performance liquid chromatography. XRCC1 genotypes were detected using polymerase chain reaction-restriction fragment length polymorphism. The final dataset included 77 cases and	CC				(-)	

				174 controls with complete questionnaires, genotyping, and plasma analyses. Among men with the Arg/Arg genotype at codon 399, odds ratios (ORs) for prostate cancer risk associated with medium (732-1,529 microg/day) and high (>1,529 microg/day) lycopene intake were 0.59 (95% confidence interval = 0.23-1.50) and 0.21 (0.06-0.71), respectively (P(trend) < 0.01). Similar analyses for persons with Arg/Gln or Gln/Gln genotypes produced null results. Above-median (1,048 microg/day) lycopene intake combined with above-median levels of alpha-tocopherol and beta-carotene was associated with an OR of 0.11 (0.02-0.65) among men with the Arg/Arg genotype but not those with at least one Gln allele (P(interaction) = 0.01). Although limited by small sample size, these findings indicate that the association between lycopene and prostate cancer is complex and may be modified by other antioxidants and by XRCC1 genotype.						
Healthy	Gartner C	Lycopene is more bioavailable from tomato paste than from fresh tomatoes. Gartner C, Stahl W, Sies H. Am J Clin Nutr. 1997 Jul;66(1):116-22.	1997	Lycopene bioavailability from a single dose of fresh tomatoes or tomato paste (23 mg lycopene) ingested together with 15 g corn oil was compared by analyzing carotenoid concentrations in the chylomicron fraction. The lycopene isomer pattern was the samein both fresh tomatoes and tomato paste. The triacylglycerol response in chylomicrons was not significantly different after both treatments. Ingestion of tomato paste was found to yield 2.5-fold higher total and all-trans-lycopene peak concentrations (P < 0.05 and P < 0.005, respectively) and 3.8-fold higher area under the curve (AUC) responses (P < 0.001) than ingestion of fresh tomatoes. The	Interv					Fresh vs. Processed (paste) TG + lycopene bioavail-ability

				same was calculated for lycopene cis-isomers, but only the AUC response for the cis-isomers was significantly higher after ingestion of tomato paste ($P < 0.005$). No difference was observed in the alpha- and beta-carotene response. Thus, in humans, the bioavailability of lycopene is greater from tomato paste than from fresh tomatoes.						
Healthy - IGF	Vrieling A	Dietary determinants of circulating insulin-like growth factor (IGF)-I and IGF binding proteins 1, -2 and -3 in women in the Netherlands. Vrieling A, Voskuil DW, Bueno de Mesquita HB, Kaaks R, van Noord PA, Keinan-Boker L, van Gils CH, Peeters PH. Cancer Causes Control. 2004 Oct;15(8):787-96.	2004	OBJECTIVE: Epidemiological studies suggest that individuals with elevated plasma concentrations of insulin-like growth factor (IGF-I) are at increased risk of developing cancer. We assessed whether dietary intake of total energy, protein, alcohol, phytoestrogens and related foods, and tomatoes and lycopene was associated with plasma levels of IGF-I and IGF binding proteins (IGFBPs) in Dutch women. METHODS: A cross-sectional study was conducted in 224 premenopausal and 162 postmenopausal women, aged 49-69, participating in the Prospect-EPIC study in the Netherlands. Diet was assessed using a food frequency questionnaire. RESULTS: In postmenopausal women, higher alcohol intake was associated with lower plasma IGFBP-1 concentrations (alcohol 1.4 to 20 g/day: 20% decrease in IGFBP-1; $p = 0.04$), and higher intake of plant lignans was associated with higher IGFBP-1 concentrations (plant lignans 0 to 1 mg/day: 59% increase in IGFBP-1; $p = 0.02$). Higher soy intake was associated with higher plasma IGFBP-2 concentrations in premenopausal women (soy 0 to 2.5 g/day: 3% increase in IGFBP-2; $p = 0.04$). No	CS				N	

				independent associations of dietary factors with IGF-I or IGFBP-3 concentrations were observed. However, in premenopausal women alcohol intake was inversely associated with IGF-I and positively associated with IGFBP-3 after mutual adjustment. CONCLUSIONS: In this study population, with limited variation in dietary intake, total energy, protein, phytoestrogens and lycopene were not associated with IGF-I and IGFBP-3. Alcohol was inversely, and some measures of phytoestrogen intake were positively associated with plasma IGFBP-1 or -2 concentrations. The roles of IGFBP-1 and -2 in relation to IGF-I bioactivity and cancer deserve further investigation.						
Heart	Lin Y	Estimating the concentration of beta-carotene required for maximal protection of low-density lipoproteins in women. Lin Y, Burri BJ, Neidlinger TR, Maller HG, Dueker SR, Clifford AJ. Am J Clin Nutr. 1998 May;67(5):837-45.	1998	The reportedly inconsistent antioxidant protective effect of beta-carotene on plasma LDL may depend on LDL's beta-carotene concentration. We measured carbonyl production by CuSO4-challenged LDL from nine healthy women living at the US Department of Agriculture-Western Human Nutrition Research Center and consuming a natural food diet that provided only 0.14 micromol beta-carotene/d for 120 d. During the first 60 d, four women received a placebo and the remaining five women received too small a supplement (0.93 micromol beta-carotene/d) to increase plasma or LDL beta-carotene; therefore, the data for all nine women during this time were pooled. From days 61 to 120, all subjects received the small supplement. From days 101 to 120 they all received an additional, larger, mixed carotenoid supplement	CT/RCT					plasma [lyco] ↓ during supple-mentation with b-carotene and there was ↓ LDL carbonyl production

				(6.16 micromol beta-carotene/d). Plasma beta-carotene dropped from 0.76 +/- 0.21 micromol/L (x +/- SEM) on day 2 to 0.33 +/- 0.08 on day 60 (P = 0.035) and rose to 1.73 +/- 0.18 (P = 0.001) on day 120. LDL beta-carotene dropped from 1.67 +/- 0.53 micromol/g LDL protein on day 2 to 1.27 +/- 0.28 micromol/g LDL protein on day 60 (P = 0.650) and rose to 10.04 +/- 1.07 micromol/g LDL protein (P = 0.001) on day 120. Plasma lycopene dropped from 0.20 micromol/L on day 2 to 0.02 micromol/L on day 60 and did not increase by day 120. Carbonyl production rose from 24 +/- 6 micromol/g LDL protein on day 2 to 42 +/- 4 micromol/g LDL protein (P = 0.001) on day 60 and dropped to 6 +/- 1 micromol/g LDL protein (P = 0.001) on day 120. LDL seemed fully protected with 9.7 +/- 2.5 micromol beta-carotene/g LDL protein, or 2.3 +/- 1.8 micromol beta-carotene/L plasma.						
Heart	Gitenay D	Comparison of lycopene and tomato effects on biomarkers of oxidative stress in vitamin E deficient rats. Gitenay D, Lyan B, Rambeau M, Mazur A, Rock E. Eur J Nutr. 2007 Dec;46(8):468-75. Epub 2007 Nov 17.	2008	BACKGROUND: Cohort studies suggested that individuals with higher intake of tomatoes and tomato products have a lower risk of degenerative diseases. Lycopene, an antioxidant and antiproliferative carotenoid, has been hypothesized to be responsible for the health benefits of tomatoes. However, studies demonstrated a higher potential of tomatoes compared to lycopene to reduce oxidative stress or carcinogenesis. AIM OF THE STUDY: Our study aimed at distinguishing lycopene effect from that of tomato on oxidative stress, by using yellow tomato, a tomato variety devoid of lycopene. METHODS: Effects of feeding with none (control), 16% freeze-dried yellow tomato (YT), 16% freeze-dried red tomato (RT) or 0.05%	RAT RCT	(-) ↓ ox stress			N	

				lycopene beadlets (LB) were compared in a rat model with mild oxidative stress induced by low vitamin E diet (LVED). Four groups of 10 rats were fed ad libitum for 6 weeks. Physiological parameters such as ingesta, body, spleen and liver weights, cholesterol and triglycerides (TG) levels were assessed. Lycopene and vitamin E concentrations and oxidative stress biomarkers were measured in the plasma and/or liver and/or heart tissue of the rats. RESULTS: RT, YT, and LB had no effect on rats' ingesta, body and spleen weights. RT, YT and LB had no effect on plasma cholesterol concentration. RT decreased TG level compared to control, YT and LB ($P < 0.05$). Rats fed RT or LB accumulated lycopene in plasma in contrast with rats fed YT. Heart level of thiobarbituric reactive species (TBARS) in rats fed RT or YT was lower than that in the control and the LB fed rats ($P < 0.05$). Despite similar concentrations of lycopene in plasma and liver, rats fed LB showed a significantly higher heart level of TBARS than rats fed tomatoes. RT increased erythrocyte superoxide dismutase (eSOD) activity compared with LB and nitric oxide (NO) level compared with control and LB. LB decreased ferric reducing ability of plasma (FRAP) level compared with control, RT and LB ($P < 0.05$). CONCLUSION: Our study showed for the first time that tomatoes, containing or not containing lycopene, have a higher potential than lycopene to attenuate and or to reverse oxidative stress-related parameters in a mild oxidative stress context.						
Heart	Misra R	LycoRed as an alternative to	2006	AIM: Menopause is a pro-atherogenic state with a sharp rise in	RCT					N

		hormone replacement therapy in lowering serum lipids and oxidative stress markers: a randomized controlled clinical trial. Misra R, Mangi S, Joshi S, Mittal S, Gupta SK, Pandey RM. J Obstet Gynaecol Res. 2006 Jun;32(3):299-304.		the incidence of coronary artery disease. This pilot study was designed as an equivalence randomized clinical trial to explore the potential of LycoRed (containing 2000 microg lycopene) as an alternative to hormone replacement therapy (HRT) for the prevention of coronary artery disease in postmenopausal women. METHODS: Forty-one healthy postmenopausal women were randomly allocated to receive either continuous combined HRT (n = 21) or LycoRed (n = 20) for six months. Serum lipid profile, marker of lipid peroxidation (malondialdehyde), and the level of endogenous antioxidant (glutathione) were measured at the baseline, and 3 and 6 months after the intervention in both groups. RESULTS: At 6 months, HRT resulted in a significant decrease in total cholesterol (TC) level by 23.5%, low-density lipoproteins (LDL) by 19.6%, and an increase in high-density lipoproteins (HDL) by 38.9%. The LycoRed group showed similar changes in TC (-24.2%), LDL (-14.9%) and HDL (+26.1%). Triglyceride levels showed a smaller though significant increase at 6 months, but not at 3 months, in both groups. There was no significant change in the very LDL (VLDL) level in either group. Malondialdehyde levels decreased significantly by 16.3% and 13.3%, whereas glutathione levels increased significantly by 5.9% and 12.5% in HRT and LycoRed groups, respectively. CONCLUSION: Both HRT and LycoRed had a favorable effect on serum lipids and oxidative stress markers which were comparable. LycoRed						

				can be used as an alternative to HRT to reduce the risk of atherosclerosis in postmenopausal women.						
Heart: endothelial fxn	Cuevas AM	A high-fat diet induces and red wine counteracts endothelial dysfunction in human volunteers. Cuevas AM, Guasch V, Castillo O, Irribarra V, Mizon C, San Martin a, Strobel P, Perez D, Germain AM, Leighton F. Lipids. 2000 Feb;35(2): 143-8.	2000	Endothelial dysfunction is associated with atherogenesis and oxidative stress in humans. In rat and rabbit blood vessels, wine polyphenol antioxidants induce vascular relaxation in vitro through the NO-cGMP pathway. To assess the effect of a regular high-fat diet (HFD) and moderate red wine consumption on endothelial function (EF), a study was performed in healthy male volunteers. EF was measured as flow-mediated dilatation of the brachial artery, employing high-resolution ultrasound after an overnight fast. Other clinical and biochemical parameters related to EF were also measured. Six volunteers received a control diet, rich in fruits and vegetables (27% calories as fat) and five volunteers received an HFD (39.5% calories as fat). Measurements were done twice on each volunteer: after a period of 30 d with diet plus 240 mL of red wine/d, and after a period of 30 d with diet, without wine. In the absence of wine, there is a reduction of EF with HFD when compared to the control diet (P = 0.014). This loss of EF is not seen when both diets are supplemented with wine for 30 d (P = 0.001). Plasma levels of n-3 fatty acids (R2 = 0.232, P = 0.023) and lycopene (R2 = 0.223, P = 0.020) show a positive correlation with individual EF measurements, but they do not account for the significant differences observed among dietary groups or after wine supplementation. These results help elucidate the deleterious effect of a high-fat diet and the protective role of wine, n-3 fatty acids and dietary	Interv					

				antioxidants in cardiovascular disease.						
Heart: oxidation	Ahuja KD	Effects of olive oil and tomato lycopene combination on serum lycopene, lipid profile, and lipid oxidation. Ahuja KD, Pittaway JK, Ball MJ. Nutrition. 2006 Mar;22(3):259-65. Epub 2006 Jan 18.	2006	OBJECTIVE: We compared the effect of two diets (a diet high in olive oil and a diet high in carbohydrate and low in olive oil) with high lycopene content and other controlled carotenoids on serum lycopene, lipids, and in vitro oxidation. METHODS: This was a randomized crossover dietary intervention study carried out in Launceston, Tasmania, Australia in healthy free-living individuals. Twenty-one healthy subjects who were 22 to 70 y old were recruited by advertisements in newspapers and a university newsletter. A randomized dietary intervention was done with two diets of 10 d each. One diet was high in olive oil and the other was high in carbohydrate and low in olive oil; the two diets contained the same basic foods and a controlled carotenoid content high in lycopene. RESULTS: Significant increases (P<0.001) in serum lycopene concentration on both diets were to similar final concentrations. Higher serum high-density lipoprotein cholesterol (P<0.01), lower ratio of total cholesterol to high-density lipoprotein (P<0.01), and lower triacylglycerols (P<0.05) occurred after the olive oil diet compared with the high-carbohydrate, low-fat diet. There was no difference in total antioxidant status and susceptibility of serum lipids to oxidation. CONCLUSIONS: Serum lycopene level changes with dietary lycopene intake irrespective of the amount of	Interv					N

				fat intake. However, a diet high in olive oil and rich in lycopene may decrease the risk of coronary heart disease by improving the serum lipid profile compared with a high-carbohydrate, low-fat, lycopene-rich diet.						
Heart: oxidative stress and inflammation	Farwell WR	The relationship between total plasma carotenoids and risk factors for chronic disease among middle-aged and older men. Farwell WR, Michael Gaziano J, Norkus EP, Sesso HD Br J Nutr. 2008 Oct;100(4):883-9. Epub 2008 Mar 12.	2008	Individual plasma carotenoids have been associated with various chronic diseases but little is known about the relationship between total plasma carotenoids and risk factors for chronic diseases. In the Physicians' Health Study, we examined 492 men free of CVD and cancer for the relationship between total plasma carotenoids (the sum of alpha-carotene, beta-carotene, lycopene, zeaxanthin, lutein and beta-cryptoxanthin) and a wide variety of factors that predict chronic disease. Multivariate linear and logistic regression was performed to calculate parameter estimates (95% CI) and OR (95% CI) for total plasma carotenoids. In linear regression models, BMI, hypertension, alcohol intake and plasma levels of each lipid parameter and a-tocopherol significantly predicted levels of total plasma carotenoids. Upon adjustment for multiple chronic disease risk factors, the OR for levels of total plasma carotenoids greater than or equal to the median (> or=1.301 micromol/l) was statistically significant for current smoking (OR 0.21; 95% CI 0.06, 0.77), weekly alcohol ingestion (OR 2.30; 95% CI 1.06, 4.99), daily alcohol ingestion (OR 2.46; 95% CI 1.29, 4.67), each 100 mg/l increase in total cholesterol (OR 0.73; 95% CI 0.58, 0.91), LDL-cholesterol (OR 1.48; 95% CI 1.17, 1.89) and HDL-cholesterol (OR 1.58; 95% CI 1.26, 1.99), each 100 mg/ml increase in intercellular adhesion	CS					

				molecule-1 (OR 0.70; 95% CI 0.53, 0.93) and each 10 micromol/l increase in alpha-tocopherol (OR 1.33; 95% CI 1.12, 1.57), using logistic regression. Few lifestyle and clinical risk factors appear to be related to levels of total plasma carotenoids; however, levels of biomarkers such as plasma lipids and alpha-tocopherol may be strongly related.						
IBS	Friedman G	Diet and the irritable bowel syndrome. Friedman G. Gastroenterol Clin North Am. 1991 Jun;20(2):313-24.	1991	Food intake plays a key role in triggering or perpetuating symptoms in patients with IBS. Evaluation of the impact of diet in the individual patient requires a precise dietary history and a 7-day prospective dietary analysis, which should include the quality and quantity of food consumed, chronologic sequence and nature of symptoms, and the frequency and consistency of bowel movements. The caloric density of the meal, total fat intake, the quantity and quality of lactose-containing foods, sorbitol, fructose, and the nature and quantity of soluble and insoluble fiber intake must be noted. Patients with reflux esophageal symptoms should eliminate foods that decrease LES pressure, such as chocolate, peppermint, alcohol, and coffee. Direct esophageal mucosal irritants such as tomatoes, citrus juices, sharp condiments, and alcohol should be limited. Gastric emptying is slowed with the ingestion of fats and soluble fiber. Small bowel motility is slowed by soluble fiber and fatty foods. Gaseous syndromes may be reduced by avoidance of smoking, chewing gum, excessive liquid intake, and carbonated drinks. The reduced intake of large amounts of lactose-containing foods, sorbitol, and fructose may limit postprandial bloating. Flatus production can be	Review	(+) ↑ mucosal irritant				

				lowered by reducing fermentable carbohydrates such as beans, cabbage, lentils, brussel sprouts, and legumes. Soluble and insoluble fiber ingestion will reduce sigmoidal intraluminal pressures and overcome spastic constipation when given in progressive graded doses. Effective dietary manipulations remain a key factor in reducing symptoms in IBS.						
IGF	Gunnell D	Are diet-prostate cancer associations mediated by the IGF axis? A cross-sectional analysis of diet, IGF-I and IGFBP-3 in healthy middle-aged men. Gunnell D, Oliver SE, Peters TJ, Donovan JL, Persad R, Maynard M, Gillatt D, Pearce A, Hamdy FC, Neal DE, Holly JM Br J Cancer. 2003 Jun 2;88(11):1682-6	2003	We examined the association of diet with insulin-like growth factors (IGF) in 344 disease-free men. Raised levels of IGF-I and/or its molar ratio with IGFBP-3 were associated with higher intakes of milk, dairy products, calcium, carbohydrate and polyunsaturated fat; lower levels with high vegetable consumption, particularly tomatoes. These patterns support the possibility that IGFs may mediate some diet-cancer associations.	CS	(-)				
Plasma lycopene	Al-Delaimy WK	Reliability of plasma carotenoid biomarkers and its relation to study power. Al-Delaimy WK, Natarajan L, Sun X, Rock CL, Pierce JP; Women's Healthy Eating and Living (WHEL) Study Group. Epidemiology.	2008	BACKGROUND: The reliability of biomarkers profoundly impacts validity of their use in epidemiology and can have serious implications for study power and the ability to find true associations. We assessed reliability of plasma carotenoid levels over time and how it could influence study power through sample size and effect-size. METHODS: Plasma carotenoid levels were measured in a cohort study of 1323 women participating in the	PC				N	

		2008 Mar;19(2):338-44.		control arm of the Women's Healthy Eating and Living Study. We compared mean plasma levels at baseline, year 1, and year 4 of the study for alpha-carotene, beta-carotene, lycopene, lutein, and beta-cryptoxanthin. Reliability of these levels over time was assessed by Spearman correlations and intraclass correlation. RESULTS: We found limited variation in mean levels between any 2 time points. Variation did not exceed 8% for lycopene, lutein, and beta-cryptoxanthin, 15% for alpha-carotene, and 18% for beta-carotene. Spearman correlations for individual carotenoids over time varied between 0.50 and 0.80, with lycopene having the lowest correlation. Intraclass correlations ranged from 0.47 to 0.66 for carotenoids. CONCLUSION: Intraclass correlations for plasma carotenoids over a period of several years are acceptable for epidemiologic studies. However, such variation is enough to decrease statistical power and increase the sample size needed to detect a given effect. Additional members of the Women's Healthy Eating and Living (WHEL) Study Group: Pierce JJ, Al-Delaimy WK, Rock CL, Faerber S, Newman VA, Flatt SW, Kealey S, Natarajan L, Parker BA, Karanja N, Rarick M, Caan BJ, Fehrenbacher L, Stefanick ML, Carlson RW, Thomson CA, Warnecke J, Gold EB, Scudder S, Wasserman L, Hollenbach KA, Jones LA, Theriault R.						
Review/report		Food, Nutrition, Physical Activity,	2007	This Report has a number of inter-related general purposes. One is to	Special Interest					

		and the Prevention of Cancer: a Global Perspective. World Cancer Research Fund / American Institute for Cancer Research. Washington DC: AICR, 2007		explore the extent to which food, nutrition, physical activity, and body composition modify the risk of cancer, and to specify which factors are most important. To the extent that environmental factors such as food, nutrition, and physical activity influence the risk of cancer, it is a preventable disease. The Report specifies recommendations based on solid evidence which, when followed, will be expected to reduce the incidence of cancer. Only "TOMATO" REFERENCES ARE RECOMMENDATION 4 and Chapter 12 (repeats Rec 4) which is a foot note PUBLIC HEALTH GOALS Population average consumption of non-starchy1 1 This is best made up from a range of various amounts of non-starchy vegetables and fruits of different colours including red, green, yellow, white, purple, and orange, including tomato-based products and allium vegetables such as garlic						
Skin	Ermakov IV	Resonance Raman detection of carotenoid antioxidants in living human tissue. Ermakov IV, Sharifzadeh M, Ermakova M, Gellermann W. J Biomed Opt. 2005 Nov-Dec;10(6):064028.	2005	Increasing evidence points to the beneficial effects of carotenoid antioxidants in the human body. Several studies, for example, support the protective role of lutein and zeaxanthin in the prevention of age-related eye diseases. If present in high concentrations in the macular region of the retina, lutein and zeaxanthin provide pigmentation in this most light sensitive retinal spot, and as a result of light filtering and/or antioxidant action, delay the onset of macular degeneration with increasing age. Other carotenoids, such as lycopene and beta-carotene, play an important role as well in the protection of skin from UV and short-wavelength visible radiation. Lutein and lycopene may also have protective function for cardiovascular health, and lycopene	CS						skin caro-tenoids with ↑ uv exposure

				may play a role in the prevention of prostate cancer. Motivated by the growing importance of carotenoids in health and disease, and recognizing the lack of any accepted noninvasive technology for the detection of carotenoids in living human tissue, we explore resonance Raman spectroscopy as a novel approach for noninvasive, laser optical carotenoid detection. We review the main results achieved recently with the Raman detection approach. Initially we applied the method to the detection of macular carotenoid pigments, and more recently to the detection of carotenoids in human skin and mucosal tissues. Using skin carotenoid Raman instruments, we measure the carotenoid response from the stratum corneum layer of the palm of the hand for a population of 1375 subjects and develop a portable skin Raman scanner for field studies. These experiments reveal that carotenoids are a good indicator of antioxidant status. They show that people with high oxidative stress, like smokers, and subjects with high sunlight exposure, in general, have reduced skin carotenoid levels, independent of their dietary carotenoid consumption. We find the Raman technique to be precise, specific, sensitive, and well suitable for clinical as well as field studies. The noninvasive laser technique may become a useful method for the correlation between tissue carotenoid levels and risk for malignancies or other degenerative diseases associated with oxidative stress.						
Skin	Offord EA	Photoprotective potential of lycopene, beta-	2002	The photoprotective potential of the dietary antioxidants vitamin C, vitamin E, lycopene, beta-carotene,	Cell culture				(+) ↑ UVA	

MOA		carotene, vitamin E, vitamin C and carnosic acid in UVA-irradiated human skin fibroblasts. Offord EA, Gautier JC, Avanti O, Scaletta C, Runge F, KrÃ¤mer K, Applegate LA. Free Radic Biol Med. 2002 Jun 15;32(12):1293-303.		and the rosemary polyphenol, carnosic acid, was tested in human dermal fibroblasts exposed to ultraviolet-A (UVA) light. The carotenoids were prepared in special nanoparticle formulations together with vitamin C and/or vitamin E. Nanoparticle formulations, in contrast to dimethylsulphoxide, stablized lycopene in the cell culture medium and allowed efficient cellular uptake. The presence of vitamin E in the formulation further increased the stability and cellular uptake of lycopene. UVA irradiation of the human skin fibroblasts led to a 10-15-fold rise in metalloproteinase 1 (MMP-1) mRNA. This rise was suppressed in the presence of low microM concentrations of vitamin E, vitamin C, or carnosic acid but not with beta-carotene or lycopene. Indeed, in the presence of 0.5-1.0 microM beta-carotene or lycopene, the UVA-induced MMP-1 mRNA was further increased by 1.5-2-fold. This increase was totally suppressed when vitamin E was included in the nanoparticle formulation. Heme-oxygenase 1 (HO-1) mRNA expression was strongly induced by UVA irradiation but none of the antioxidants inhibited this effect at the concentrations used in this study. Indeed, beta-carotene or lycopene (0.5-1.0 microM) led to a further 1.5-fold rise in the UVA-induced HO-1 mRNA levels. In conclusion, vitamin C, vitamin E, and carnosic acid showed photoprotective potential. Lycopene and beta-carotene did not protect on their own but in the presence of vitamin E, their stability in culture was improved and the rise in MMP-1 mRNA expression was suppressed, suggesting a requirement for antioxidant protection of the carotenoids against					induced exp of MMP-1 mRNA and HO-1 mRNA ~~~~~ N Add Vit E = supprssd MMP-1 mRNA exp	

				formation of oxidative derivatives that can influence the cellular and molecular responses.						
Skin MOA	Eichler O	Divergent optimum levels of lycopene, beta-carotene and lutein protecting against UVB irradiation in human fibroblastst. Eichler O, Sies H, Stahl W. Photochem Photobiol. 2002 May;75(5):503-6.	2002	Exposure of living organisms to UV light leads to photooxidative reactions. Peroxyl radicals are involved in the propagation of lipid peroxidation. Carotenoids are dietary antioxidants and show photoprotective effects in human skin, efficiently scavenging peroxyl radicals and inhibiting lipid peroxidation. Cultured human skin fibroblasts were used to examine the protective effects of the carotenoids, lycopene, beta-carotene and lutein on UVB-induced lipid peroxidation. The carotenoids were delivered to the cells using liposomes as the vehicle. The cells were exposed to UVB light for 20 min. Lycopene, beta-carotene and lutein were capable of decreasing UV-induced formation of thiobarbituric acid-reactive substances at 1 h to levels 40-50% of controls free of carotenoids. The amounts of carotenoid needed for optimal protection were divergent at 0.05, 0.40 and 0.30 nmol/mg protein for lycopene, beta-carotene and lutein, respectively. Beyond the optimum levels, further increases of carotenoid levels in cells led to prooxidant effects.	Cell culture				(-) ↓ TBARS	
Skin MOA	Chiang HS	Lycopene inhibits PDGF-BB-induced signaling and migration in human dermal fibroblasts through interaction with PDGF-BB. Chiang HS, Wu WB, Fang JY, Chen DF, Chen BH, Huang	2007	In melanoma development and progression, platelet-derived growth factor (PDGF) has been suggested to modulate the microenvironment, especially stromal fibroblasts, to the benefit of melanoma growth, invasion, and metastasis. Lycopene, a natural carotenoid that is abundant in tomato, has been shown to inhibit proliferation of several types of cancer cells. However, little attention has been	Cell culture				(-) ↓ cell proliferation	

		CC, Chen YT, Hung CF. Life Sci. 2007 Nov 10;81(21-22):1509-17. Epub 2007 Oct 2.		paid to skin fibroblasts and melanoma cells. In the present study, we determined the effects of lycopene on stromal fibroblasts and their interactions with melanoma cells. We found that lycopene inhibited PDGF-BB-induced human Hs68 skin fibroblast migration on gelatin and collagen. Further analysis showed that lycopene inhibited PDGF-BB-induced signaling in human Hs68 and primary cultured skin fibroblasts. PDGF-BB-induced phosphorylation of PDGF receptor beta (PDGFR-beta), extracellular signal-regulated kinase 1/2 (ERK1/2), p38, and c-Jun N-terminal kinase (JNK) was attenuated by lycopene in a concentration-dependent manner, whereas the total expression of each protein was not affected. Interestingly, dot binding assay revealed that lycopene could directly bind to human PDGF-BB in PBS and human plasma, indicating that lycopene can bind to PDGF-BB in both in vitro and in vivo conditions. In functional studies, lycopene inhibited melanoma-induced fibroblast migration in a noncontact coculture system and attenuated signaling in fibroblasts simulated by melanoma-derived conditioned medium. Our results provide the first evidence showing that lycopene is an effective inhibitor of migration of stromal fibroblasts and this effect may contribute to its antitumor activity.						
Skin MOA	Wu WB	Inhibitory effect of lycopene on PDGF-BB-induced signalling and migration in human dermal fibroblasts: a possible target for	2007	Tumours are complex tissues composed of both matrix proteins and stromal cells such as fibroblasts and inflammatory cells. Tumour progression is often the result of dynamic interactions between the tumour cells and their surroundings. Lycopene, a natural carotenoid that	Cell culture				(-) ↓ tumor cell actions	

		cancer. Wu WB, Chiang HS, Fang JY, Hung CF. Biochem Soc Trans. 2007 Nov;35(Pt 5):1377-8.		is abundant in tomato, has been shown to inhibit proliferation of several types of cancer cells through arrest of tumour cell-cycle progression, IGF-1 (insulin-like growth factor 1) signalling transduction, induction of apoptosis etc. However, in our recent study, we found that lycopene inhibited PDGF-BB (platelet-derived growth factor-BB)-induced signalling and cell migration in human cultured skin fibroblasts through a novel mechanism of action, i.e. direct binding to PDGF-BB. Trapping of PDGF by lycopene also compromised melanoma-induced fibroblast migration and attenuated signalling transduction in fibroblasts simulated by melanoma-derived conditioned medium, suggesting that lycopene may interfere with tumour-stroma interactions. The trapping activity of lycopene on PDGF suggests that it may act as an inhibitor on stromal cells, tumour cells and their interactions, which may contribute to its anti-tumour activity.						
Skin MOA	Zefferino R	Mercury modulates interplay between IL-1beta, TNF-alpha, and gap junctional intercellular communication in keratinocytes: mitigation by lycopene. Zefferino R, Leone A, Piccaluga S, Cincione R, Ambrosi L. J Immunotoxicol. 2008 Oct;5(4):353-60.	2008	Gap junctional intercellular communication (GJIC) is used to control cell proliferation. It is not surprising then that a lack of GJIC (i.e., during loss of contact inhibition among adjacent cells) is associated with cancer promotion/progression. There also seems to be a link between ineffective GJIC and increases in inflammatory events. Interestingly, many cytokines released during an inflammatory response also have critical roles in cancer cell survival. Specifically, TNFalpha and IL-1beta are important for initiating/augmenting CD8(+)- and NK-cell mediated killing; however, in what appears counterintuitive, each--at times--can act to protect cancer cells against	Cell culture				(-) oleoresin	

				apoptosis, a major mechanism for cell killing from within. It is thus plausible to assume that certain toxicants might act as cancer promoters in manners distinct from/augmentive of direct effects on DNA, i.e., by concurrently altering GJIC and cytokine formation in host or microenvironment of a cancer cell. Our research has evaluated effects of many toxicants upon keratinocytes; in particular, we have examined effects of mercury on GJIC and on TNFalpha and IL-1beta levels in (and secretion by) these cells. In the studies here, a tomato preparation (i.e., an oleoresin) bearing the antioxidant carotenoid lycopene was examined for its effects on GJIC and cytokine formation by keratinocytes in general, and its potential ability to mitigate/reverse the toxic effects of mercury in the cells in particular. It was shown that a 4-hr treatment with the oleoresin (containing 56, 6 nM lycopene) re-established GJIC among--and increased the formation of IL-1beta and TNFalpha that had been significantly reduced within--keratinocytes that had been pre-treated for 24 hr with 10 nM HgCl(2). These results show that effects of mercury likely depend on some level of oxidative stress and that its potential effects on keratinocyte GJIC and cytokine concentrations could, in an exposed host, be mitigated/reversed by increased dietary intake of carotenoids like lycopene.					
Skin Special Interest	Bogdan Allemann I	Antioxidants used in skin care formulations. Bogdan Allemann I, Baumann L.	2008	The formation of free radicals is a widely accepted pivotal mechanism leading to skin aging. Free radicals are highly reactive molecules with unpaired electrons that can directly damage various cellular structural	Discussion					

		Skin Therapy Lett. 2008 Sep;13(7):5-9.		membranes, lipids, proteins, and DNA. The damaging effects of these reactive oxygen species are induced internally during normal metabolism and externally through various oxidative stresses. The production of free radicals increases with age, while the endogenous defense mechanisms that counter them decrease. This imbalance leads to the progressive damage of cellular structures, and thus, results in accelerated aging. Antioxidants are substances that can provide protection from endogenous and exogenous oxidative stresses by scavenging free radicals. Topical antioxidants are available in multivariate combinations through over-the-counter skin care products that are aimed at preventing the clinical signs of photoaging.						
Smokers	Gabriel HE	A comparison of carotenoids, retinoids, and tocopherols in the serum and buccal mucosa of chronic cigarette smokers versus nonsmokers. Gabriel HE, Liu Z, Crott JW, Choi SW, Song BC, Mason JB, Johnson EJ Cancer Epidemiol Biomarkers Prev. 2006 May;15(5):993-9	2006	BACKGROUND: Cigarette smoking, a major risk factor for oropharyngeal cancer, is reported to alter oral levels of carotenoids and tocopherols. Such effects may be important because these nutrients, as well as retinoids, are putative chemoprotective agents. OBJECTIVES: To determine whether chronic smoking is associated with altered concentrations of these nutrients in serum and buccal mucosa; to distinguish whether such effects are ascribable to diet; and to determine whether oral concentrations of these nutrients correlate with a putative biomarker of oral cancer risk. METHODS: Serum and buccal mucosal cells (BMC) were analyzed for these nutrients and for BMC micronuclei in smokers (n = 35) and	CC					

				nonsmokers (n = 21). RESULTS: General linear regression with adjustments for dietary intake showed that smokers possess lower serum concentrations of beta- and alpha-carotene, cryptoxanthin, lutein, and zeaxanthin (P </= 0.01) and a significantly higher serum gamma-tocopherol (P = 0.03). In BMCs, smokers had significantly lower concentrations of beta- and alpha-carotene, lycopene, and alpha-tocopherol (P < 0.05) but significantly higher gamma-tocopherol (P < 0.01). Among nonsmokers, many serum carotenoid concentrations correlated with concentrations of the corresponding nutrient in BMCs whereas no such correlations existed among smokers. BMC micronuclei did not correlate with the oral concentration of any micronutrient. CONCLUSIONS: Chronic cigarette smokers have lower concentrations of many dietary antioxidants in serum and BMCs compared with nonsmokers, an effect which is not entirely ascribable to diet. Nevertheless, the lack of concordance between oral concentrations of these nutrients and genetic damage in the BMCs of smokers does not support a protective role for these nutrients in oral carcinogenesis.						
Special interest	Ratnam DV	Role of antioxidants in prophylaxis and therapy: A pharmaceutical perspective. Ratnam DV, Ankola DD, Bhardwaj V,	2006	Antioxidants are emerging as prophylactic and therapeutic agents. These are the agents, which scavenge free radicals otherwisereactive oxygen species and prevent the damage caused by them. Free radicals have been associated with pathogenesis of various disorders like cancer, diabetes, cardiovascular diseases,	Review					

		Sahana DK, Kumar MN. J Control Release. 2006 Jul 20;113(3):189-207. Epub 2006 May 13.		autoimmune diseases, neurodegenerative disorders and are implicated in aging. Several antioxidants like SOD, CAT, epigallocatechin-3-O-gallate, lycopene, ellagic acid, coenzyme Q10, indole-3-carbinol, genistein, quercetin, vitamin C and vitamin E have been found to be pharmacologically active as prophylactic and therapeutic agents for above mentioned diseases. Antioxidants are part of diet but their bioavailability through dietary supplementation depends on several factors. This major drawback of dietary agents may be due to one or many of the several factors like poor solubility, inefficient permeability, instability due to storage of food, first pass effect and GI degradation. Conventional dosage forms may not result in efficient formulation owing to their poor biopharmaceutical properties. Principles of novel drug delivery systems need to be applied to significantly improve the performance of antioxidants. Novel drug delivery systems (NDDS) would also help in delivery of these antioxidants by oral route, as this route is of prime importance when antioxidants are intended for prophylactic purpose. Implication of NDDS for the delivery of antioxidants is largely governed by physicochemical characteristics, biopharmaceutical properties and pharmacokinetic parameters of the antioxidant to be formulated. Recently, chemical modifications, coupling agents, liposomes, microparticles, nanoparticles and gel-based systems have been explored for the delivery of these difficult to deliver molecules. Results from several studies conducted across the globe are positive and						

				provided us with new anticipation for the improvement of human healthcare.						
Special interest	Gomez-Romero M	Analytical determination of antioxidants in tomato: typical components of the Mediterranean diet. Gomez-Romero M, Arraez-Roman D, Segura-Carretero A, Fernandez-Gutiarrez A. J Sep Sci. 2007 Mar;30(4):452-61.	2007	Diets in the countries of the Mediterranean basin are characterised by abundant plant foods (fruits, vegetables, breads, nuts, seeds, wine, and olive oil) and include fish and low-fat dairy products. Among the vegetables, tomatoes are a main component of the traditional Mediterranean diet, which has been associated with health protection and longevity. Eating tomatoes has been associated with reduced risks of some types of cancer and other diseases. These beneficial properties appear to be related to the antioxidant content of the fruit, particularly carotenoids (lycopene and beta-carotene), ascorbic acid, and phenols, which may play a role in inhibiting reactions mediated by reactive oxygen species. Due to the importance of antioxidant compounds in tomatoes and tomato products, we present here an overview of current analytical methods (from 2000 until the present date) for determining the different antioxidants. The analytical procedures used to determine individual compounds involve extraction from the sample, analytical separation, and quantification. The choice of analytical method depends on the particular focus of the analysis and the kind of product analysed. High-performance liquid chromatography is the technique of choice for the analysis of tomato antioxidants.	Review					
Special interest	Darmon P	Oral nutritional supplements and taste preferences:	2008	BACKGROUND & AIMS: Acceptability and intake of oral nutritional supplements are often suboptimal,	Interv					(+) In patients

		545 days of clinical testing in malnourished in-patients. Darmon P, Karsegard VL, Nardo P, Dupertuis YM, Pichard C. Clin Nutr. 2008 Aug;27(4):660-5. Epub 2008 Jul 14.		partly because patients dislike flavour, texture or smell. We assessed the taste preferences about milk-based and fruit-juice typed supplements in malnourished in-patients. METHODS: One hundred and nine in-patients requiring oral nutritional support were assigned to consume four given supplements on four consecutive days, to answer a questionnaire based on a 10-point visual analogue scale (VAS) on acceptance/tolerance, and to choose their preferred product for the fifth day. RESULTS: Overall pleasantness was significantly better for milk-based supplements than for sweet and salty fruit-juice typed products (on VAS: 6.2+/-3.1 versus 4.4+/-3.9, p<0.01 and 3.5+/-3.4, p<0.0001, respectively, when 1 meant "not at all" and 10 "very much"), whereas digestive tolerance was comparable. When offered together on day 5, milk-based products were more frequently preferred (81.6%) than fruit-juice typed supplements (18.4%, p<0.001). Among milk-based products, vanilla, coffee and strawberry had comparable good results, whereas chocolate was less chosen and neutral never. For fruit-juice typed products, tomato obtained better results than orange or apple. CONCLUSIONS: Oral nutritional supplements are globally well-accepted and tolerated, but with variations according to categories and flavours that must be considered to improve compliance.						needing oral nutrition, tomato flavor best
Special interest	Martin L	Food products as vehicles for n-3	2008	PURPOSE: An n-3 polyunsaturated fatty acid (PUFA) supplement was						

		fatty acid supplementation. Martin L, Zarn D, Hansen AM, Wismer W, Mazurak V. Can J Diet Pract Res. 2008 Winter;69(4):203-7.		incorporated into three food products previously determined to be preferred by cancer patients, and overall acceptability of these foods was evaluated. METHODS: Preliminary testing was performed; an internal panel determined initial acceptability of foods with the supplement added. Taste panel evaluations were held at the Cross Cancer Institute in Edmonton, Alberta. Each participant completed a questionnaire rating aroma, flavour, and overall acceptance on a seven-point hedonic scale (1 = dislike extremely, 7 = like extremely), as well as ability to consume each food daily. RESULTS: Foods were well-liked by patients and non-patients. Mean +/- standard deviation acceptance scores for the three foods were pasta sauce 5.9 +/- 0.94 (n=90), oatmeal 6.1 +/- 0.88 (n=79), and smoothie 5.9 +/- 1.12 (n=126). Overall, 94% of patients and non-patients gave tomato pasta sauce, oatmeal, and the smoothie an acceptance score of at least 5. CONCLUSIONS: The supplement was incorporated successfully into three foods, which were highly accepted by patients with cancer. Further research should focus on incorporating the supplement into flavoured or sweet foods, as these appear most effective. Microencapsulated fish oil in food products may be used as an alternative to fish oil capsules for delivering n-3 PUFA in clinical trials.						
Special interest	Najm W	Dietary supplements	2008	The use of complimentary and alternative medicine is on the rise.						

		commonly used for prevention. Najm W, Lie D. Prim Care. 2008 Dec;35(4):749-67.		This article reviews some of the commonly used herbal supplements and others focusing mainly on disease prevention. A summary table of medical conditions is provided, and when possible, a summary of efficacy and safety is provided to facilitate decision making.						
Special Interest	Wilkinson S	The use of complementary therapy by men with prostate cancer in the UK. Wilkinson S, Farrelly S, Low J, Chakraborty A, Williams R, Wilkinson S. Eur J Cancer Care (Engl). 2008 Sep;17(5):492-9. Epub 2008 Jul 10	2008	The study aims were to determine the use of complementary therapies (CT) by men with prostate cancer, and to explore factors influencing CT use and attitudes toward CT use. A cross-sectional survey design was used in which a postal questionnaire was mailed to an eligible sample of 405 patients with prostate cancer receiving outpatient treatment in a London teaching hospital. The primary outcomes were the prevalence of CT use and the relationship between CT use and mental health status. Two hundred and ninety-four patients (73%) responded, of whom 25% were using CT. The most frequently used CTs were vitamins, low-fat diets, lycopene and green tea. Multivariate analyses revealed no differences in mental health scores between CT users and non-users. CT users were younger (OR 0.93, 95% CI 0.89-0.97) and were more likely to be receiving conservative management in the form of 'active surveillance' (OR 5.23, 95% CI 1.78-15.41) compared with non-users. Over half of the participants (55%) wanted to learn more about CT. Forty-three per cent of CT users had not informed any doctor about their CT use. Clinicians need to be aware of the prevalence of CT use amongst patients with prostate cancer, considering the potential harm that could be caused by interactions with conventional treatments.	CS					

Special Interest	Djuric Z	A Mediterranean dietary intervention in healthy American women changes plasma carotenoids and fatty acids in distinct clusters. Djuric Z, Ren J, Blythe J, VanLoon G, Sen A. Nutr Res. 2009 Mar;29(3):156-63.	2009	This study examined patterns of changes in plasma fatty acids and carotenoids when women were asked to follow a novel, Greek-Mediterranean exchange list diet. A total of 69 healthy, nonobese women ages 25 to 59 years were randomized either to continue their own usual diet or to follow a modified Mediterranean diet for 6 months. There were no significant changes in blood lipids, triacylglycerol, insulin, glucose, or C-reactive protein. Mean plasma carotenoids increased by 55%, which is consistent with a large increase in fruit and vegetable consumption. Likewise, changes in fat intakes were reflected in blood fatty acids, with a 25% increase in mean plasma monounsaturated fatty acids. Principal component analysis was conducted to examine the sources of interindividual variation for changes in carotenoid and fatty acid levels. Changes in the Mediterranean diet were clustered together in 4 components that accounted for 78% of the variance in plasma levels. Increases in plasma lutein, alpha-carotene, and beta-carotene clustered together in a "vegetable" pattern, and increases in carotenoids found in fruit, beta-cryptoxanthin and zeaxanthin also clustered together but accounted for less of the variance. Increases in plasma monounsaturated fatty acids were clustered with a decrease in plasma polyunsaturated fatty acids, consistent with substitution in the type of oils consumed. The only association of fatty acid levels with carotenoids was that of lycopene, which clustered together with an increase in saturated fatty acids. The changes in blood levels indicate the exchange list diet was effective for targeting Mediterranean nutrient						

				intakes using foods available in the United States.						
Special interest	Epriliati I	Nutriomic analysis of fresh and processed fruit products. 1. During in vitro digestions. Epriliati I, D'Arcy B, Gidley M. J Agric Food Chem. 2009 Apr 22;57(8):3363-76.	2009	Nutriomic analysis is a postgenomic-based study of nutritious components (nutriome). There is a need for an in vitro digestion and absorption model to unravel interactive factors varying nutriome release from various food materials that cannot be directly studied in humans. Effects of processing and in vitro digestion steps on carotenoid, sugar, and organic acid release from tomato, papaya, and mango products were comprehensively studied for the first time in this research. In vivo chewing experiments using 24 healthy adult volunteers was carried out prior to chewing simulation. Microscopy showed that cutting and blending alone were unlikely to mimic chewing at swallowing point. Using general linear model (GLM) ANOVA and principal component analysis (PCA), effects of interaction between digestion steps and processing types on the nutriome release were significant ($p < 0.05$) when 90% particles of 0.5 (dried) and 1.5 cm (fresh) were digested in vitro. Generally, dried and fresh fruits released lower levels of nutriome components than juices. PCA indicated nutriome release from tomato products was affected by the factors studied more than those from papaya and mango products. Fruit type is the main determinant factor relative to processing and digestion steps because it determines the extent of matrix that breaks down and consequent nutriome diffusion rates. It is predicted that pectin plays a role in determining the rate of nutriome release and absorption, which requires further investigation.	Interv					↓ nutrinome components released from dried/fresh fruit vs juice

Special interest	Al-Delaimy WK	Reliability of plasma carotenoid biomarkers and its relation to study power. Al-Delaimy WK, Natarajan L, Sun X, Rock CL, Pierce JP; Women's Healthy Eating and Living (WHEL) Study Group. Epidemiology. 2008 Mar;19(2):338-44.	2008	The reliability of biomarkers profoundly impacts validity of their use in epidemiology and can have serious implications for study power and the ability to find true associations. We assessed reliability of plasma carotenoid levels over time and how it could influence study power through sample size and effect-size. METHODS: Plasma carotenoid levels were measured in a cohort study of 1323 women participating in the control arm of the Women's Healthy Eating and Living Study. We compared mean plasma levels at baseline, year 1, and year 4 of the study for alpha-carotene, beta-carotene, lycopene, lutein, and beta-cryptoxanthin. Reliability of these levels over time was assessed by Spearman correlations and intraclass correlation. RESULTS: We found limited variation in mean levels between any 2 time points. Variation did not exceed 8% for lycopene, lutein, and beta-cryptoxanthin, 15% for alpha-carotene, and 18% for beta-carotene. Spearman correlations for individual carotenoids over time varied between 0.50 and 0.80, with lycopene having the lowest correlation. Intraclass correlations ranged from 0.47 to 0.66 for carotenoids. CONCLUSION: Intraclass correlations for plasma carotenoids over a period of several years are acceptable for epidemiologic studies. However, such variation is enough to decrease statistical power and increase the sample size needed to detect a given effect.						

Validation Study	Dixon LB	Carotenoid and tocopherol estimates from the NCI diet history questionnaire are valid compared with multiple recalls and serum biomarkers. Dixon LB, Subar AF, Wideroff L, Thompson FE, Kahle LL, Potischman N. J Nutr. 2006 Dec;135(12):3054-61.	2006	To improve the measurement of usual dietary intake, the National Cancer Institute developed a cognitively based Diet History Questionnaire (DHQ), which has been validated against four 24-h dietary recalls (4 24-HR) for energy, macronutrients, and several vitamins and minerals. This analysis used data from The Eating at America's Table Study (EATS) to determine the validity of estimates for carotenoids and tocopherols from the DHQ. Over the course of a year, 163 participants provided 1 or 2 blood samples and completed the DHQ and 4 24-HR. For both the DHQ and the 4 24-HR, crude correlations between serum and diet were modest to strong for the provitamin A carotenoids (alpha-carotene, beta-carotene, beta-cryptoxanthin), low to modest for lycopene, and very low for lutein. The individual dietary tocopherols were weakly correlated with the serum tocopherols, but vitamin E from food and dietary supplements was strongly and positively correlated with serum alpha-tocopherol and strongly and inversely correlated with serum gamma-tocopherol for both instruments. Adjustment for energy, BMI, smoking status, serum total cholesterol, and serum triacylglycerol did not appreciably change the correlations. Using the method of triads, validity coefficients for the DHQ were comparable to the 4 24-HR and were especially strong for alpha-carotene, beta-cryptoxanthin, lutein + zeaxanthin, and total vitamin E in men and gamma-tocopherol and total vitamin E in women. In this study, there was no advantage of 2 blood samples over 1, suggesting reasonably stable ranking of individuals for these biomarkers, which is important for large						

				epidemiologic studies that typically obtain only 1 blood sample for biomarker status.						
Vitamin status	Rock CL	Demographic, dietary and lifestyle factors differentially explain variability in serum carotenoids and fat-soluble vitamins: baseline results from the sentinel site of the Olestra Post-Marketing Surveillance Study. Rock CL, Thornquist MD, Kristal AR, Patterson RE, Cooper DA, Neuhouser ML, Neumark-Sztainer D, Cheskin LJ. J Nutr. 1999 Apr;129(4):855-64.	1999	Biochemical measures of nutrients or other dietary constituents can be an important component of nutritional assessment and monitoring. However, accurate interpretation of the nutrient concentration is dependent on knowledge of the determinants of the body pool measured. The purpose of this study was to identify the determinants of serum carotenoid and fat-soluble vitamin concentrations in a large, community-based sample (n = 1042). Multiple linear regression analysis was used to examine effects of demographic characteristics (age, sex, race/ethnicity, education), health-related behavior (exercise, sun exposure, smoking, alcohol consumption), and intake (diet, supplements) on serum retinol, 25-hydroxyvitamin D, alpha-tocopherol, phylloquinone, and carotenoid concentrations. Age, sex, race/ethnicity, vitamin A intake, and alcohol consumption were found to be determinants of serum retinol concentration. Race/ethnicity, vitamin D intake, body mass index, smoking status, and sun exposure were determinants of serum 25-hydroxyvitamin D concentration. Determinants of serum alpha-tocopherol were age, sex, race/ethnicity, alpha-tocopherol intake, serum cholesterol, percentage of energy from fat (inversely related), supplement use, and body mass index. Age, sex, phylloquinone intake, serum triglycerides, and supplement use were determinants of serum phylloquinone concentration. Primary determinants of serum carotenoids	CS					(+) ↑ serum carotenoids

				were age, sex, race/ethnicity, carotenoid intake, serum cholesterol, alcohol consumption, body mass index, and smoking status. Overall, the demographic, dietary, and other lifestyle factors explained little of the variability in serum concentrations of retinol (R2 = 0.20), 25-hydroxyvitamin D (R2 = 0.24), and the carotenoids (R2 = 0.15-0.26); only modest amounts of the variability in serum phylloquinone concentration (R2 = 0.40); and more substantial amounts of the variability in serum alpha-tocopherol concentration (R2 = 0.62).						