

## Dietary Lycopene and Disease Risk

### Gastric Cancer Critical Findings

Disease type	First Author	Study Title and Complete Citation	Date	Abstract	Study Type	G.Tom +, N, -	P.Tom +, N, -	F.Tom +, N, -	Lyco +, N, -	Other +, N, -
Cancer: gastric	Tsugane S	Cross-sectional study with multiple measurements of biological markers for assessing stomach cancer risks at the population level.  Tsugane S, Tsuda M, Gey F, Watanabe S.  Environ Health Perspect. 1992 Nov;98:207-10.	1992	A cross-sectional study to determine correlations between measurable biologic markers and mortality from stomach cancer was performed in various areas of Japan. Blood and urine were collected from randomly selected 40- to 49-year-old men and their spouses in four areas with different rates of mortality from stomach cancer. The samples were analyzed for levels of the micronutrients vitamins A, C, and E, beta-carotene, and lycopene in plasma and for levels of NaCl, nitrate, and N-nitrosamino acids (N-nitrosoproline, N-nitrosothioprolin [NTPRO] and N-nitrosomethylthioprolin [NMTPRO]) in 24-hr urine. A significant, strong correlation was found between the amount of salt excreted in urine and stomach cancer mortality in both men and women. Although the amounts of nitrate and of the three N-nitrosamino acids in 24-hr urine were not correlated with stomach cancer rates, the low excretion levels of NTPRO and NMTPRO in the lowest risk area for stomach cancer were noteworthy, regardless of the high level of nitrate excretion in the same area. This suggests a lesser degree of endogenous nitrosation in the body. No protective effect of micronutrients was observed in this correlation study; there was, however, a negative correlation between plasma lycopene level and stomach cancer mortality. Salt intake was thus confirmed to play an important role in the development of stomach cancer and is likely to be a rate-regulating factor in Japanese populations. N-Nitrosamino acids and lycopene may also be related to stomach cancer mortality.	CS				(-)	
Cancer: gastric	Nomura AM	Serum micronutrients and upper aerodigestive tract cancer.  Nomura AM, Ziegler RG, Stemmermann GN, Chyou PH, Craft NE.	1997	Numerous dietary studies have found that vegetables and fruits protect against upper aerodigestive tract cancer. To evaluate the role of beta-carotene and other specific carotenoids, a nested case-control study using prediagnostic serum was conducted among 6832 American men of Japanese ancestry examined from 1971 to 1975. During a surveillance period of 20 years, the study identified 28 esophageal, 23 laryngeal, and 16 oral-pharyngeal cancer cases in this cohort. The 69 cases were matched to 138 controls. A liquid chromatography technique, designed to optimize recovery and separation of the individual carotenoids, was used to measure serum levels of lutein,	CC nested				N	

		Cancer Epidemiol Biomarkers Prev. 1997 Jun;6(6):407-12.		<p>zeaxanthin, beta-cryptoxanthin, lycopene, alpha-carotene, beta-carotene, retinol, retinyl palmitate, and alpha-, delta-, and gamma-tocopherol. With adjustment for cigarette smoking and alcohol intake, we found that alpha-carotene, beta-carotene, beta-cryptoxanthin, total carotenoids and gamma-tocopherol levels were significantly lower in the 69 upper aerodigestive tract cancer patients than in their controls. Trends in risk by tertile of serum level were significant for these five micronutrients. These significant trends persisted in cases diagnosed 10 or more years after phlebotomy for the three individual carotenoids and total carotenoid measurements. The odds ratios for the highest tertile were 0.19 (95% confidence interval, 0.05-0.75) for alpha-carotene, 0.10 (0.02-0.46) for beta-carotene, 0.25 (0.06-1.04) for beta-cryptoxanthin, and 0.22 (0.05-0.88) for total carotenoids. When the cases were separated into esophageal, laryngeal, and oral-pharyngeal cancer, both alpha-carotene and beta-carotene were consistently and strongly associated with reduced risk at each site. The findings suggest that alpha-carotene and other carotenoids, as well as beta-carotene, may be involved in the etiology of upper aerodigestive tract cancer.</p>						
Cancer: gastric	Tsubono Y	<p>Plasma antioxidant vitamins and carotenoids in five Japanese populations with varied mortality from gastric cancer.</p> <p>Tsubono Y, Tsugane S, Gey KF. Nutr Cancer. 1999;34(1):56-61.</p>	1999	<p>To examine the geographic associations between plasma antioxidant levels and gastric cancer risk, we conducted an ecological study in five regions of Japan representing the threefold variation in the disease mortality within the country. Subjects were 634 men aged 40-49 years sampled randomly from the five regions with 72% response rates. Plasma concentrations of five carotenoids (beta-carotene, alpha-carotene, lycopene, lutein, and zeaxanthin), alpha-tocopherol, and ascorbic acid were measured, and the mean levels were correlated with age-adjusted mortality rates from gastric cancer. beta-Carotene and alpha-tocopherol were inversely correlated with gastric cancer rates (<math>r = -0.31</math> and <math>-0.89</math>, respectively). alpha-Carotene and lycopene showed stronger inverse correlation than did beta-carotene (<math>r = -0.67</math> and <math>-0.56</math>, respectively), but these relations disappeared after the exclusion of one outlying region in Okinawa with the lowest mortality. In contrast, ascorbic acid revealed a negative correlation with the exclusion of this outlier (<math>r = -0.61</math>). Lutein and zeaxanthin were not inversely associated with risk. The results suggest that plasma levels of beta-carotene and alpha-tocopherol, and possibly alpha-carotene, lycopene, and ascorbic acid, may partly account for the regional difference in gastric cancer mortality in Japan.</p>	Eco				N	

Cancer: gastric	Nagao T	<p>Serum antioxidant micronutrients and the risk of oral leukoplakia among Japanese.</p> <p>Nagao T, Ikeda N, Warnakulasuriya S, Fukano H, Yuasa H, Yano M, Miyazaki H, Ito Y.</p> <p>Oral Oncol. 2000 Sep;36(5):466-70.</p>	2000	<p>A population-based case-control study was designed for the investigation of any association between serum micronutrient levels and oral leukoplakia. Out of a total of 9536 subjects over the age of 40 years who participated in the oral mucosal screening programme in Tokoname city, 48 cases detected with oral leukoplakia (38 male:10 female) were recruited. For each case, four controls matched by age and sex were selected from the same cohort. We examined the fasting serum levels of retinol, alpha-tocopherol, zeaxanthin and lutein, cryptoxanthin, lycopene and carotenoids (alpha-carotene and beta-carotene) by high-performance liquid chromatography. Among males with leukoplakia mean serum lycopene and beta-carotene levels (0.175+/-0.202, 0.357+/-0.295 micromol/l) were significantly lower than those of controls (0.257+/-0.252, 0.555+/-0.408 micromol/l) (P&lt;0.05, P&lt;0.005). Logistic regression analysis with leukoplakia as the dependent variable showed that high serum levels of beta-carotene were related to low risk of oral leukoplakia (odds ratio 0.160, 95% C.I.: 0.029-0.866, P&lt;0.05). There were no significant differences in any of the serum nutrients estimated in female subjects. Our results suggest for the first time that high serum levels of beta-carotene may provide protection against oral precancer for the Japanese male.</p>	CC				(-)/N risk est	
Cancer: gastric	Yuan JM	<p>Prediagnostic levels of serum micronutrients in relation to risk of gastric cancer in Shanghai, China.</p> <p>Yuan JM, Ross RK, Gao YT, Qu YH, Chu XD, Yu MC.</p> <p>Cancer Epidemiol Biomarkers Prev. 2004 Nov;13(11 Pt 1):1772-80.</p>	2004	<p>Data on blood levels of specific carotenoids and vitamins in relation to gastric cancer are scarce. Little is known about the relationship between prediagnostic serum levels of carotenoids other than beta-carotene and risk of gastric cancer especially in non-Western populations. Prediagnostic serum concentrations of alpha-carotene, beta-carotene, beta-cryptoxanthin, lycopene, lutein/zeaxanthin, retinol, alpha-tocopherol, gamma-tocopherol, and vitamin C were determined on 191 cases and 570 matched controls within a cohort of 18,244 middle-aged or older men in Shanghai, China, with a follow-up of 12 years. High serum levels of alpha-carotene, beta-carotene, and lycopene were significantly associated with reduced risk of developing gastric cancer (all Ps for trend &lt;= 0.05); the odds ratios (95% confidence intervals) for the highest versus the lowest quartile of alpha-carotene, beta-carotene, and lycopene were 0.38 (0.13-1.11), 0.54 (0.32-0.89), and 0.55 (0.30-1.00), respectively. Increased serum level of vitamin C was significantly associated with reduced risk of gastric cancer among men who neither smoked cigarettes over lifetime nor consumed &gt;=3 drinks of alcohol per day; the odds ratios (95% confidence intervals) for the second, third, and fourth quartile categories were 0.69 (0.28-1.70), 0.36 (0.14-0.94),</p>	CC nested				(-) modest  ↓ risk with ↑ serum [lyco]	

				and 0.39 (0.15-0.98), respectively, compared with the lowest quartile of vitamin C (P for trend = 0.02). There were no statistically significant relationships of serum levels of beta-cryptoxanthin, lutein/zeaxanthin, retinol, alpha-tocopherol, and gamma-tocopherol with gastric cancer risk. The present study implicates that dietary carotenoids, lycopene, and vitamin C are potential chemopreventive agents for gastric cancer in humans.						
Cancer: gastric	Persson C	<p>Plasma levels of carotenoids, retinol and tocopherol and the risk of gastric cancer in Japan: a nested case-control study.</p> <p>Persson C, Sasazuki S, Inoue M, Kurahashi N, Iwasaki M, Miura T, Ye W, Tsugane S; JPHC Study Group.</p> <p>Carcinogenesis. 2008 May;29(5):1042-8. Epub 2008 Mar 13.</p>	2008	<p>Fruits and vegetables have been suggested to confer protection against diseases such as cancer through the effects of antioxidants, often represented by carotenoids. We investigated the impact of carotenoids, retinol and tocopherol on gastric cancer development in a large nested case-control study among Japanese with known Helicobacter pylori infection status. A total of 36 745 subjects aged 40-69 in the Japan Public Health Center-based Prospective Study who responded to the baseline questionnaire and provided blood samples in 1990-1995 were followed until 2004. Plasma levels of carotenoids in 511 gastric cancer cases and 511 matched controls were measured by high-performance liquid chromatography. Odds ratios (ORs) and their corresponding 95% confidence intervals (CIs) were estimated using conditional logistic regression models. Plasma level of beta-carotene was inversely associated with the risk of gastric cancer (compared with the lowest quartile: OR = 0.63, 95% CI = 0.31-0.75; OR = 0.48, 95% CI = 0.31-0.75 and OR = 0.46, 95% CI = 0.28-0.75, for quartile 2, 3 and 4, respectively, P(trend) &lt; 0.01). Inverse associations were evident in men for alpha-carotene (P(trend) = 0.04) and beta-carotene (P(trend) &lt; 0.01), but not in women, who had relatively higher plasma levels compared with men. We found no statistically significant association between plasma levels of lutein/zeaxanthin, lycopene, retinol, alpha- or gamma-tocopherol and gastric cancer risk. Our findings suggest that those who have very low plasma levels of alpha-carotene and beta-carotene are at a higher risk of gastric cancer.</p> <p>Collaborators (100): Sobue T, Hanaoka T, Ogata J, Baba S, Mannami T, Okayama A, Kokubo Y, Miyakawa K, Saito F, Koizumi A, Sano Y, Hashimoto I, Ikuta T, Miyajima Y, Suzuki N, Nagasawa S, Furusugi Y, Nagai N, Sanada H, Hatayama Y, Kobayashi F, Uchino H, Shirai Y, Kondo T, Sasaki R, Watanabe Y, Miyagawa Y, Kobayashi Y, Kishimoto Y, Takara E, Fukuyama T, Kinjo M, Irei M, Sakiyama H, Imoto K, Yazawa H, Seo T, Seiko A, Ito F, Shoji F, Murata A, Minato K, Motegi K, Fujieda T, Matsui K, Abe T, Katagiri M, Suzuki M, Doi M, Terao A, Ishikawa Y,</p>	CC nested				N	

			<p>Tagami T, Sueta H, Doi H, Urata M, Okamoto N, Ide F, Sakiyama H, Onga N, Takaesu H, Uehara M, Horii F, Asano I, Yamaguchi H, Aoki K, Maruyama S, Ichii M, Takano M, Tsubono Y, Suzuki K, Honda Y, Yamagishi K, Sakurai S, Kabuto M, Yamaguchi M, Matsumura Y, Sasaki S, Watanabe S, Akabane M, Kadowaki T, Noda M, Kawaguchi Y, Takashima Y, Nakamura K, Matsushima S, Natsukawa S, Shimizu H, Sugimura H, Tominaga S, Iso H, Iida M, Ajiki W, Ioka A, Sato S, Maruyama E, Konishi M, Okada K, Saito I, Yasuda N, Kono S.</p>						
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