

## Plasma/Serum Lycopene and Disease Risk

### Breast 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: breast | Potischman N | <p>Breast cancer and dietary and plasma concentrations of carotenoids and vitamin A.</p> <p>Potischman N, McCulloch CE, Byers T, Nemoto T, Stubbe N, Milch R, Parker R, Rasmussen KM, Root M, Graham S, et al.</p> <p>Am J Clin Nutr. 1990 Nov;52(5):909-15.</p> | 1990 | <p>A case-control study of breast cancer was conducted in Buffalo. Participants completed a food frequency questionnaire and donated a fasting blood sample before definitive workup for breast masses. Dietary and plasma concentrations of carotenoids and retinol for 83 women found to have breast cancer were compared with those of 113 women found to be free of breast cancer (control subjects). There were no case-control differences in dietary estimates of vitamin A intake or in plasma alpha-carotene and lycopene. However, subjects with breast cancer had lower concentrations of plasma beta-carotene than did control subjects (P = 0.02). There was no overall association between plasma retinol and breast cancer but a positive relationship was observed between retinol and breast cancer in the subgroup with low beta-carotene values. These results suggest that low plasma beta-carotene is associated with increased risk of breast cancer. Other studies will need to determine whether low carotene concentrations are a subtle effect of the disease or might be causally related to breast cancer.</p> | CC         |               |               |               | N            |               |
| Cancer: breast | Zhang S      | <p>Measurement of retinoids and carotenoids in breast adipose tissue and a comparison of concentrations in breast cancer cases and control subjects.</p> <p>Zhang S, Tang G, Russell RM, Mayzel KA, Stampfer MJ, Willett WC, Hunter</p>                          | 1997 | <p>A case-control study of the associations of retinoids and specific carotenoids with breast cancer using concentrations of these nutrients in breast adipose tissue was conducted among women attending a breast clinic in the Boston area in 1989-1992. Breast adipose tissue was collected during breast biopsy. Cases (n = 46) were women whose biopsies revealed invasive or in situ breast cancer; control subjects (n = 63) were women whose biopsies revealed benign disease. We observed inverse associations between breast adipose concentrations of retinoids and carotenoids and risk of breast cancer, although not all were statistically significant. The multivariate-adjusted odds ratio comparing women above the median value of the control</p>  | CC tissue  |               |               |               | (-)          |               |

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|                   |           | DJ.<br>Am J Clin Nutr.<br>1997<br>Sep;66(3):626-32.  |      | group for retinol with those below or equal to the median was 0.71 (95% CI: 0.26, 1.93; NS); corresponding odds ratios were 0.61 (95% CI: 0.23, 1.64; NS) for retinyl palmitate, 0.30 (95% CI: 0.11, 0.85) for beta-carotene, 0.32 (95% CI: 0.11, 0.94) for lycopene, and 0.68 (95% CI: 0.27, 1.73; NS) for lutein/zeaxanthin. There was a nonsignificant positive correlation ( $r = 0.23$ , $P = 0.15$ ) between breast adipose tissue concentrations of retinol and dietary intake of preformed vitamin A, including supplements measured by using a food-frequency questionnaire. No correlation was found between breast adipose concentrations of carotenoids and intake of dietary carotenoids. These data suggest that higher breast adipose concentrations of retinoids and some carotenoids may be associated with decreased risk of breast cancer and that further examination of these relations is warranted.  |              |  |  |  |     |  |
| Cancer:<br>breast | Dorgan JF | Relationships of serum carotenoids, retinol, alpha-tocopherol, and selenium with breast cancer risk: results from a prospective study in Columbia, Missouri (United States)<br><br>Dorgan JF, Sowell A, Swanson CA, Potischman N, Miller R, Schussler N, Stephenson HE Jr.<br><br>Cancer Causes Control.<br>1998 Jan;9(1):89-97. | 1998 | To evaluate relationships of serum carotenoids, alpha-tocopherol, selenium, and retinol with breast cancer prospectively, we conducted a case-control study nested in a cohort from the Breast Cancer Serum Bank in Columbia, Missouri (United States). Women free of cancer donated blood to this bank in 1977-87. During up to 9.5 years of follow-up (median = 2.7 years), 105 cases of histologically confirmed breast cancer were diagnosed. For each case, two women alive and free of cancer at the age of the case's diagnosis and matched on age and date of blood collection were selected as controls. A nonsignificant gradient of decreasing risk of breast cancer with increasing serum beta-cryptoxanthin was apparent for all women. Serum lycopene also was associated inversely with risk, and among women who donated blood at least two years before diagnosis, a significant gradient of decreasing breast cancer risk with increasing lycopene concentration was evident. A marginally significant gradient of decreasing risk with increasing serum lutein/zeaxanthin also was apparent among these women. We did not observe any evidence for protective effects of alpha- and beta-carotene, alpha-tocopherol, retinol, or selenium for breast cancer. Results of this study suggest that the carotenoids beta-cryptoxanthin, lycopene, and lutein/zeaxanthin may protect against breast cancer. | CC<br>nested |  |  |  | (-) |  |
| Cancer:<br>breast | Ito Y     | A study on serum carotenoid levels in breast cancer  | 1999 | Two-hundred and six breast cancer cases were histologically confirmed breast cancer diagnoses at the Cancer Institute in Chennai (Madras), India. One-hundred   | CC<br>serum  |  |  |  | N?  |  |

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|                |          | <p>patients of Indian women in Chennai (Madras), India.</p> <p>Ito Y, Gajalakshmi KC, Sasaki R, Suzuki K, Shanta V.</p> <p>J Epidemiol. 1999 Nov;9(5):306-14.</p>  |      | <p>and fifty hospital controls were patients who had cancer at any site other than breast and gynecological organs, and 61 healthy controls were persons accompanying patients in the Cancer Institute. Serum levels of carotenoids such as beta-carotene, lycopene, cryptoxanthin, and zeaxanthin &amp; lutein were determined by HPLC. Serum levels of total carotenes and total carotenoids including beta-carotene, which reflects food intake of colored vegetables and fruits and has a protective role for certain sites of cancer, were significantly lower among breast cancer cases and hospital controls compared to healthy controls, especially in post-menopausal women. Serum carotenoid levels appeared to change with menopausal status. Serum beta-carotene levels tended to be lower among breast cancer cases than among hospital controls in premenopausal women. Serum xanthophyll levels were significantly lower among breast cancer cases than among healthy controls in post-menopausal women, but not in premenopausal women. Serum levels of retinol and alpha-tocopherol among breast cancer cases were not significantly different from those in post-menopausal healthy controls, but were higher than those in hospital controls. Serum estrone levels were significantly higher among breast cancer cases than among healthy controls, but serum levels of estradiol and estriol were not. In conclusion, Indian women with cancer of breast or of other sites might have low intake of green-yellow vegetables rich in fiber and carotenoids such as beta-carotene and zeaxanthin &amp; lutein.</p> |    |  |  |  |   |  |
| Cancer: breast | Simon MS | <p>An Evaluation of Plasma Antioxidant Levels and the Risk of Breast Cancer: A Pilot Case Control Study.</p> <p>Simon MS, Djuric Z, Dunn B, Stephens D, Lababidi S, Heilbrun LK.</p> <p>Breast J. 2000 Nov;6(6):388-395.</p> | 2000 | <p>Antioxidant micronutrients found in fruits and vegetables have been shown in numerous studies to be protective against cancer. There is limited information on the relationship between blood antioxidant micronutrient levels and cancer among ethnic minorities. We conducted a pilot case-control study to evaluate the potential for accrual to a study of the association of plasma levels of beta-carotene, retinol, lycopene, alpha-tocopherol, and gamma-tocopherol with breast cancer risk among African American and Caucasian women seen at a large university medical center in Detroit. Cases included women with newly diagnosed invasive breast cancer who had not yet had any cancer-related therapy and who were age-matched to controls within 5 years. Plasma levels of micronutrients were analyzed by high-pressure liquid chromatography. Compared to the expected accrual based on cancer registry data, only</p>   | CC |  |  |  | N |  |

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|                |          |   |      | <p>26% (11/42) of African American women with breast cancer enrolled, while 100% (16/16) of Caucasian cases enrolled. Control women were quickly accrued with only a 6% refusal rate. Among African American women, there was a weak inverse association between plasma lycopene levels and breast cancer risk, with a mean level of 0.17 <math>\mu\text{mol/L}</math> (SD = 0.18) among cases, and 0.24 <math>\mu\text{mol/L}</math> (SD = 0.18) among controls (p = 0.09). There was a weak direct association between plasma retinol levels and breast cancer risk among African American women, with a mean retinol level of 2.37 <math>\mu\text{mol/L}</math> (SD = 0.73) among cases and 1.98 <math>\mu\text{mol/L}</math> (SD = 0.49) among controls (p = 0.132). The interaction effect of race and lycopene was statistically significant (p = 0.048). Among the lowest lycopene tertile, the risk of breast cancer among Caucasian women was 0.76 and the risk of breast cancer among African American women was 2.29, although these odds ratios were not statistically significant. Our recruitment efforts were largely successful among Caucasian cases and controls, and African American controls, but were unsuccessful among African American cases. The results suggest a possible relationship between plasma lycopene level and breast cancer among African American women, but these results should be confirmed by a larger, more definitive study.</p> |           |  |  |  |  |     |
| Cancer: breast | Hulten K | <p>Carotenoids, alpha-tocopherols, and retinol in plasma and breast cancer risk in northern Sweden.</p> <p>Hulten K, Van Kappel AL, Winkvist A, Kaaks R, Hallmans G, Lenner P, Riboli E.</p> <p>Cancer Causes Control. 2001 Aug;12(6):529-37.</p> | 2001 | <p>OBJECTIVE: Using a nested case-referent design we evaluated the relationship between plasma levels of six carotenoids, alpha-tocopherol, and retinol, sampled before diagnosis, and later breast cancer risk.</p> <p>METHODS: In total, 201 cases and 290 referents were selected from three population-based cohorts in northern Sweden, where all subjects donated blood samples at enrolment. All blood samples were stored at -80 degrees C. Cases and referents were matched for age, age of blood sample, and sampling centre. Breast cancer cases were identified through the regional and national cancer registries.</p> <p>RESULTS: Plasma concentrations of carotenoids were positively intercorrelated. In analysis of three cohorts as a group none of the carotenoids was found to be significantly related to the risk of developing breast cancer. Similarly, no significant associations between breast cancer risk and plasma levels of alpha-tocopherol or retinol were found. However, in postmenopausal women from a mammography cohort with a high number of prevalent cases, lycopene was significantly associated</p>   | CC nested |  |  |  |  | (-) |

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|----------------|-----------|--|------|---|-----------|--|--|--|----|--|
|                |           |  |      | <p>with a decreased risk of breast cancer. A significant trend of an inverse association between lutein and breast cancer risk was seen in premenopausal women from two combined population-based cohorts with only incident cases. A non-significant reduced risk with higher plasma alpha-carotene was apparent throughout all the sub-analyses.</p> <p>CONCLUSION: In conclusion, no significant associations were found between plasma levels of carotenoids, alpha-tocopherol or retinol and breast cancer risk in analysis of three combined cohorts. However, results from stratified analysis by cohort membership and menopausal status suggest that lycopene and other plasma-carotenoids may reduce the risk of developing breast cancer and that menopausal status has an impact on the mechanisms involved.</p>  |           |  |  |  |    |  |
| Cancer: breast | Toniolo P | <p>Serum carotenoids and breast cancer.</p> <p>Toniolo P, Van Kappel AL, Akhmedkhanov A, Ferrari P, Kato I, Shore RE, Riboli E.</p> <p>Am J Epidemiol. 2001 Jun 15;153(12):1142-7.</p> | 2001 | <p>The consumption of vegetables and fruit may protect against many types of cancer, but research evidence is not compelling for breast cancer. Carotenoids are pigments that are present in most plants and have known antioxidant properties. Blood concentrations of carotenoids have been proposed as integrated biochemical markers of vegetable, fruit, and synthetic supplements consumed. In a case-control study (270 cases, 270 controls) nested within a cohort in New York during 1985-1994, the carotenoids lutein, zeaxanthin, beta-cryptoxanthin, lycopene, alpha-carotene, and beta-carotene were measured in archived serum samples using liquid chromatography. There was an evident increase in the risk of breast cancer for decreasing beta-carotene, lutein, alpha-carotene, and beta-cryptoxanthin. The risk of breast cancer approximately doubled among subjects with blood levels of beta-carotene at the lowest quartile, as compared with those at the highest quartile (odds ratio = 2.21; 95% confidence interval (CI): 1.29, 3.79). The risk associated with the other carotenoids was similar, varying between 2.08 (95% CI: 1.11, 3.90) for lutein and 1.68 (95% CI: 0.99, 2.86) for beta-cryptoxanthin. The odds ratio for the lower quartile of total carotenoids was 2.31 (95% CI: 1.35, 3.96). These observations offer evidence that a low intake of carotenoids, through poor diet and/or lack of vitamin supplementation, may be associated with increased risk of breast cancer and may have public health relevance for people with markedly low intakes.</p> | CC nested |  |  |  | N? |  |

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| Cancer:<br>breast | Ching S | <p>Serum levels of micronutrients, antioxidants and total antioxidant status predict risk of breast cancer in a case control study.</p> <p>Ching S, Ingram D, Hahnel R, Beilby J, Rossi E.</p> <p>J Nutr. 2002 Feb;132(2):303-6.</p>                         | 2002 | <p>We performed a case control study to assess the association between serum micronutrient and antioxidant levels and the risk of breast cancer. Newly diagnosed breast cancer cases were recruited before any treatment and matched with controls randomly selected from the electoral roll. Blood samples were collected from 153 breast cancer cases and 151 controls. Serum samples were analyzed for retinol, alpha-tocopherol, lycopene, alpha- and beta-carotene by HPLC, and total antioxidant status by the Trolox-equivalent antioxidant assay. Serum albumin, bilirubin and uric acid levels were also determined. After adjustment for age at menarche, parity, dietary fat and alcohol intake, we observed the following reductions in odds ratios for breast cancer risk comparing the highest with the lowest quartiles: 0.47 [95% confidence interval (CI) 0.24, 0.91] for beta-carotene; 0.53 (CI 0.28, 1.01) for retinol; 0.50 (CI 0.26, 0.97) for bilirubin and 0.47 (CI 0.24, 0.94) for total antioxidant status. We conclude that increased serum levels of beta-carotene, retinol, bilirubin and total antioxidant status are associated with reductions in breast cancer risk.</p>   | CC           |  |  |  | N?  |  |
| Cancer:<br>breast | Sato R  | <p>Prospective study of carotenoids, tocopherols, and retinoid concentrations and the risk of breast cancer.</p> <p>Sato R, Helzlsouer KJ, Alberg AJ, Hoffman SC, Norkus EP, Comstock GW.</p> <p>Cancer Epidemiol Biomarkers Prev. 2002 May;11(5):451-7.</p> | 2002 | <p>Previous prospective studies have raised the possibility that the antioxidant properties of carotenoids and vitamin E (alpha-tocopherol) and the role of vitamin A (retinol) in cellular differentiation may be associated with a reduced risk of subsequent breast cancer. To investigate the association between serum and plasma concentrations of retinol, retinyl palmitate, alpha-carotene, beta-carotene, beta-cryptoxanthin, lutein, lycopene, total-carotenoids, alpha-tocopherol, and gamma-tocopherol with subsequent development of breast cancer, a nested case control study was conducted among female residents of Washington County, Maryland, who had donated blood for a serum bank in 1974 or 1989. Cases (n = 295) and controls (n = 295) were matched on age, race, menopausal status, and date of blood donation, and the analyses were stratified by cohort participation. Median concentrations of beta-carotene, lycopene, and total carotene were significantly lower in cases compared with controls in the 1974 cohort (13.1, 12.5, and 7.9% difference; P = 0.01, 0.04, and 0.04, respectively) and for lutein in the 1989 cohort (6.7% difference; P = 0.02). The risk of developing breast cancer in the highest fifth was approximately half of that of women in the lowest fifth for beta-carotene [odds ratio (OR) = 0.41; 95% confidence interval (CI) 0.22-0.79; P trend = 0.007], lycopene (OR = 0.55; 95% CI 0.29-1.06; P trend = 0.04), and total carotene</p> | CC<br>nested |  |  |  | (-) |  |

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|                |           |  |      | (OR = 0.55; 95% CI 0.29-1.03; P trend = 0.02) in the 1974 cohort. There was generally a protective association for other micronutrients in both cohorts, although none reached statistical significance. The results suggest that carotenoids may protect against the development of breast cancer.   |                              |  |   |  |                     |   |
| Cancer: breast | Sesso HD  | Dietary and plasma lycopene and the risk of breast cancer.<br><br>Sesso HD, Buring JE, Zhang SM, Norkus EP, Gaziano JM.<br><br>Cancer Epidemiol Biomarkers Prev. 2005 May;14(5):1074-81. | 2005 | Lycopene is potentially effective in the prevention of breast cancer from laboratory and observational studies. Among 39,876 women initially free of cardiovascular disease and cancer, we first conducted a prospective cohort study of dietary lycopene and its food sources. Participants completed a baseline food frequency questionnaire and provided self-reports of breast cancer risk factors. Dietary lycopene levels were divided into quintiles, and lycopene food sources were categorized. During 9.9 years of follow-up, 1,076 breast cancer cases were confirmed by medical record review. In a nested case-control study, we then identified 508 breast cancer cases and 508 controls matched by age, smoking, and follow-up time. Plasma lycopene and other carotenoids were measured. In the prospective cohort study, women with increasing quintiles of dietary lycopene had multivariate relative risks (RR) of breast cancer of 1.00 (ref), 0.95, 1.00, 1.10, and 1.00 (P, linear trend = 0.71). Women consuming <1.5, 1.5 to <4, 4 to <7, 7 to <10, and > or =10 servings/week of tomato-based products had RRs of 1.00 (ref), 1.00, 1.20, 1.18, and 1.16 (P, linear trend = 0.11). No individual lycopene food sources were associated with breast cancer. In the nested case-control study, women in increasing quartiles of plasma lycopene had multivariate RRs of breast cancer of 1.00 (ref), 0.95, 1.15, and 0.93 (P, linear trend = 0.86). The stepwise addition of individual plasma carotenoids did not impact the RRs for plasma lycopene, nor were other carotenoids associated with breast cancer. In conclusion, neither higher dietary nor plasma lycopene levels were associated with a reduced risk of breast cancer in middle-aged and older women. | PC<br><br>~~~~~<br>CC nested |  | N |  | N<br><br>~~~~~<br>N | Diet lyco + food sources<br><br>~~~~~<br>Plasma |
| Cancer: breast | Tamimi RM | Plasma carotenoids, retinol, and tocopherols and risk of breast cancer.<br><br>Tamimi RM,  | 2005 | The roles of carotenoids, retinol, and tocopherols in breast cancer etiology have been inconclusive. The authors prospectively assessed the relations between plasma alpha-carotene, beta-carotene, beta-cryptoxanthin, lycopene, lutein/zeaxanthin, retinol, alpha-tocopherol, and gamma-tocopherol and breast cancer risk by conducting a nested case-control study using plasma collected from women enrolled in the Nurses' Health  | CC nested                    |  |   |  | N                   |   |

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|                |            | <p>Hankinson SE, Campos H, Spiegelman D, Zhang S, Colditz GA, Willett WC, Hunter DJ.</p> <p>Am J Epidemiol. 2005 Jan 15;161(2):153-60.</p>   |      | <p>Study. A total of 969 cases of breast cancer diagnosed after blood draw and prior to June 1, 1998, were individually matched to controls. The multivariate risk of breast cancer was 25-35% less for women with the highest quintile compared with that for women with the lowest quintile of alpha-carotene (odds ratio (OR) = 0.64, 95% confidence interval (CI): 0.47, 0.88; p(trend) = 0.01), beta-carotene (OR = 0.73, 95% CI: 0.53, 1.02; p(trend) = 0.01), lutein/zeaxanthin (OR = 0.74, 95% CI: 0.55, 1.01; p(trend) = 0.04), and total carotenoids (OR = 0.76, 95% CI: 0.55, 1.05; p(trend) = 0.05). The inverse association observed with alpha-carotene and breast cancer was greater for invasive cancers with nodal metastasis. The authors conclude that some carotenoids are inversely associated with breast cancer. Although the association was strongest for alpha-carotene, the high degree of collinearity among plasma carotenoids limits our ability to conclude that this association is specific to any individual carotenoid.</p>   |    |  |  |  |  |  |
| Cancer: breast | Thomson CA | <p>Plasma and dietary carotenoids are associated with reduced oxidative stress in women previously treated for breast cancer.</p> <p>Thomson CA, Stendell-Hollis NR, Rock CL, Cussler EC, Flatt SW, Pierce JP.</p> <p>Cancer Epidemiol Biomarkers Prev. 2007 Oct;16(10):2008-15.</p> | 2007 | <p>Dietary carotenoids show numerous biological activities, including antioxidant activity, induction of apoptosis, and inhibition of mammary cell proliferation. Studies examining the role of carotenoid consumption in relation to breast cancer recurrence are limited and report mixed results. We tested the hypothesis that breast cancer survivors with high dietary and plasma carotenoids would show significantly lower levels of oxidative stress than breast cancer survivors with low dietary and plasma carotenoid levels. Two hundred seven postmenopausal breast cancer survivors from the Women's Healthy Eating and Living Study volunteered for this ancillary study. Dietary data were analyzed by the Arizona Food Frequency Questionnaire and plasma carotenoids alpha-carotene, beta-carotene, lutein plus zeaxanthin, lycopene, and beta-cryptoxanthin and quantified with high-performance liquid chromatography, and immunoaffinity chromatography-monoclonal antibody-based ELISAs were used to analyze the urine samples for 8-hydroxy-2'-deoxyguanosine (8-OHdG) and 8-iso-prostaglandin-F2alpha (8-iso-PGF2alpha). The correlations between dietary and plasma carotenoids were 0.34 for beta-carotene, 0.46 for alpha-carotene, 0.39 for beta-cryptoxanthin, 0.27 for lycopene, 0.30 for lutein plus zeaxanthin, and 0.30 for total carotenoids. The 8-OHdG oxidative stress biomarker was significantly reduced at the highest quartile of total plasma carotenoid concentrations (P = 0.001) and 8-iso-PGF2alpha was</p> | CS |  |  |  | <p>(-)</p> <p>↓ 8-OHdG (ox stress marker) with plasma [lyco]</p> |  |



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|                |              |   |      | <p>moderately reduced (P = 0.088). Dietary carotenoid levels were not significantly associated with oxidative, stress indicators, although dietary lycopene and lutein/zeaxanthin were modestly associated with 8-OHdG levels (P = 0.054 and 0.088, respectively). Key findings include a significant inverse association between total plasma carotenoid concentrations and oxidative stress as measured by urinary 8-OHdG and a moderately significant inverse association with 8-iso-PGF2alpha, a protective association that was not shown for dietary carotenoid intake.</p>  |           |  |  |  |               |  |
| Cancer: breast | Dorjgochoo T | <p>Plasma carotenoids, tocopherols, retinol and breast cancer risk: results from the Shanghai Women Health Study (SWHS).</p> <p>Dorjgochoo T, Gao YT, Chow WH, Shu XO, Li H, Yang G, Cai Q, Rothman N, Cai H, Franke AA, Zheng W, Dai Q.</p> <p>Breast Cancer Res Treat. 2009 Sep;117(2):381-9. Epub 2008 Dec 20.</p> | 2009 | <p>Evidence from some previous studies suggests that lipophilic antioxidants, particularly carotenoids, may reduce the risk of breast cancer. We prospectively investigated the associations of plasma levels of tocopherols, retinol, carotenoids with the risk of developing breast cancer among Chinese women. We conducted a study of 365 incident breast cancer cases and 726 individually matched controls nested within a large cohort study of women aged 40-70 years at baseline. We observed no associations between breast cancer risk and any of the tocopherols, retinol, and most carotenoids. However, high levels of plasma lycopene other than trans, 5- and 7-cis or trans alpha-cryptoxanthin were inversely associated with the risk of developing breast cancer. Our results do not support an overall protective effect of lipophilic antioxidants on breast cancer risk. The few inverse associations observed for subtype of carotenoids may need to be confirmed in future studies.</p> | CC nested |  |  |  | (-)           |  |
| Cancer: breast | Kabat GC     | <p>Longitudinal study of serum carotenoid, retinol, and tocopherol concentrations in relation to breast cancer risk among postmenopausal women.</p> <p>Kabat GC, Kim M, Adams-Campbell LL, Caan BJ,</p>   | 2009 | <p>BACKGROUND: Prospective studies have examined the association of serum and plasma carotenoids and micronutrients and breast cancer; however, to date, studies have only assessed exposure at one point in time. OBJECTIVE: This study analyzed baseline and repeated serum measurements of carotenoids, retinol, and tocopherols to assess their associations with postmenopausal breast cancer risk. DESIGN: Serum concentrations of alpha-carotene, beta-carotene, beta-cryptoxanthin, lycopene, lutein + zeaxanthin, retinol, alpha-tocopherol, and gamma-tocopherol were measured in a 6% sample of women in</p>  | PC        |  |  |  | (+)<br>↑ risk |  |

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|                |           | <p>Chlebowski RT, Neuhouser ML, Shikany JM, Rohan TE; WHI Investigators.</p> <p>Am J Clin Nutr. 2009 Jul;90(1):162-9. Epub 2009 May 27.</p>  |      | <p>the Women's Health Initiative clinical trials at baseline and at years 1, 3, and 6 and in a 1% sample of women in the observational study at baseline and at year 3. The association of baseline compounds and breast cancer risk was estimated by Cox proportional hazards models. In addition, repeated measurements were analyzed as time-dependent covariates. Of 5450 women with baseline measurements, 190 incident cases of breast cancer were ascertained over a median of 8.0 y of follow-up.</p> <p>RESULTS: After multivariable adjustment, risk of invasive breast cancer was inversely associated with baseline serum alpha-carotene concentrations (hazard ratio for highest compared with the lowest tertile: 0.55; 95% CI: 0.34, 0.90; P = 0.02) and positively associated with baseline lycopene (hazard ratio: 1.47; 95% CI: 0.98, 2.22; P = 0.06). Analysis of repeated measurements indicated that alpha-carotene and beta-carotene were inversely associated with breast cancer and that gamma-tocopherol was associated with increased risk.</p> <p>CONCLUSIONS: The present study, which was the first to assess repeated measurements of serum carotenoids and micronutrients in relation to breast cancer, adds to the evidence of an inverse association of specific carotenoids with breast cancer. The positive associations observed for lycopene and gamma-tocopherol require confirmation. This trial was registered at ClinicalTrials.gov as NCT00000611.</p> |           |  |  |  |                              |  |
| Cancer: breast | Tamimi RM | <p>Circulating carotenoids, mammographic density, and subsequent risk of breast cancer.</p> <p>Tamimi RM, Colditz GA, Hankinson SE.</p> <p>Cancer Res. 2009 Dec 15;69(24):9323-9. Epub</p> | 2009 | <p>Mammographic density is one of the strongest predictors of breast cancer risk. Recently, it has been suggested that reactive oxygen species may influence breast cancer risk through its influence on mammographic density. In the current study, we addressed this hypothesis and also assessed if the association between carotenoids and breast cancer risk varies by mammographic density. We conducted a nested case-control study consisting of 604 breast cancer cases and 626 controls with prospectively measured circulating carotenoid levels and mammographic density in the Nurses' Health Study. Circulating levels of alpha-carotene, beta-carotene, beta-cryptoxanthin, lycopene, and lutein/zeaxanthin were measured. We used a computer-assisted thresholding method to measure percent mammographic density. We found no evidence that circulating carotenoids are inversely associated with mammographic density. However, mammographic density significantly modified the association between</p>  | CC nested |  |  |  | (-)<br>in high mammo density |  |

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|  |  |  | <p>total circulating carotenoids and breast cancer (P heterogeneity = 0.008). Overall, circulating total carotenoids were inversely associated with breast cancer risk (P trend = 0.01). Among women in the highest tertile of mammographic density, total carotenoids were associated with a 50% reduction in breast cancer risk (odds ratio, 0.5; 95% confidence interval, 0.3-0.8). In contrast, there was no inverse association between carotenoids and breast cancer risk among women with low mammographic density. Similarly, among women in the highest tertile of mammographic density, high levels of circulating alpha-carotene, beta-cryptoxanthin, lycopene, and lutein/zeaxanthin were associated with a significant 40% to 50% reduction in breast cancer risk (P trend &lt; 0.05). Our results suggest that plasma levels of carotenoids may play a role in reducing breast cancer risk, particularly among women with high mammographic density.</p> |  |  |  |  |  |  |
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