Bioidentical Hormone Replacement References plus Breast Cancer Prevention References:

Dessole S, Rubattu G, Ambrosini G, et al. Efficacy of low-dose intravaginal estriol on urogenital aging in postmenopausal women. *Menopause.* 2004;11(1):49-56. (Vaginal estriol use lowered UTIs from 5.9/year to 0.5/year in women of comparable age)

Fitzpatrick L, Good A. Micronized progesterone: clinical indications and comparison with current treatments. *Fertil Steril.* 1999;72(3):389-397.
(Oral micronized progesterone has widespread clinical potential, particularly for the treatment of secondary amenorrhea and dysfunctional premenopausal bleeding, and as a component of postmenopausal hormone replacement therapy.)

Holtorf K. The bioidentical hormone debate: are bioidentical hormones (estradiol, estriol, and progesterone) safer or more efficacious than commonly used synthetic versions in hormone replacement therapy? *PostGrad Med.* 2009;121(1):1-13. (Results showed that BHRT is safer and more efficacious than traditional HRT with CEE and MPA)

Murkes D, Conner P, Leifland K, Tani E, Beliard A, Lundström E: Effects of percutaneous estradiol-oral progesterone versus oral conjugated equine estrogens-medroxyprogesterone acetate on breast cell proliferation and bcl-2 protein in healthy women. PMID:21067727 DOI:10.1016/j.fertnstert.2010.09.062.
(In a prospective, randomized clinical study 77 women were assigned randomly to receive sequential hormone therapy with either conventional oral conjugated equine estrogens (0.625 mg) with the addition on 14 of the 28 days of oral medroxyprogesterone acetate (5 mg) or natural E(2) gel (1.5 mg) with oral micronized P (200 mg) on 14 of the 28 days of each cycle. Because oral conjugated equine estrogens-medroxyprogesterone acetate induced a highly significant increase in breast cell proliferation in contrast to percutaneous E(2)-oral P with a difference between therapies approaching significance, the former therapy has a marked impact on the breast whereas natural percutaneous E(2)-oral micronized P has not.)

Plu-Bureau G, Le M, Thalabard J, et al. Percutaneous progesterone use and the risk of breast cancer: results from a French cohort study of premenopausal women with benign breast disease. *Cancer Detect Prev.* 1999;23:290-296. (1150 post-menopausal women with benign breast disease showed no adverse effects or breast proliferation with trans-dermal progesterone from 1976-1979)

Prior, Jerilynn & L Hitchcock, Christine. (2012). Progesterone for hot flush and night sweat treatment – effectiveness for severe vasomotor symptoms and lack of withdrawal rebound. Gynecological endocrinology: the official journal of the International Society of Gynecological Endocrinology. 28 Suppl 2. 7-11. 10.3109/09513590.2012.705390. Fertil Steril. 2011 Mar 1;95(3):1188-91. doi: 10.1016/j.fertnstert.2010.09.062. Epub 2010 Nov 10.

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Stephenson, Kenna & Neuenschwander, Pierre & K Kurdowska, Anna. (2013). The effects of compounded bioidentical transdermal hormone therapy on hemostatic, inflammatory, immune factors; cardiovascular biomarkers; quality-of-life measures; and health outcomes in perimenopausal and postmenopausal women. International journal of pharmaceutical compounding. 17. 74-85.

Zahl PH, Gotzsche PC, Maehlen J, Natural history of breast cancers detected in the Swedish mammography screening programme: a cohort study.*Lancet Oncol. 2011 Nov ;12(12):1118-24.*
(Interpretation: Because the cumulative incidence among controls did not reach that of the screened group, we believe that many invasive breast cancers detected by repeated mammography screening do not persist to be detected by screening at the end of 6 years, suggesting that the natural course of many of the screen-detected invasive breast cancers is to spontaneously regress.)

Progesterone, Estrogens and Breast Cancer

Bergkvist L, Adami HO, Persson I, Hoover R, Schairer C. The risk of breast cancer after estrogen and estrogen-progestin replacement. *N Engl J Med. 1989 Aug 3;321(5):293-7*
(Study of breast cancer risks in over 23,000 women over age 35. Among users of long-term unopposed CEE or estradiol, use increased breast cancer risk slightly, RR 1.1, and endometrial cancer significantly, RR 1.8)

Chang KJ, de Lignieres B, et. al.; Influences of percutaneous administration of estradiol and progesterone on human breast epithelial cell cycle in vivo. *Fertil Steril 1995 Apr;63(4):785-91.*
(Double-blind, randomized study involving 40 premenopausal women about to undergo breast cancer surgery. For 10 to 13 days prior to breast cancer surgery, these women underwent daily topical gel application to the breast of either placebo, estradiol, progesterone, or a combination of estradiol and progesterone. Findings showed that topical gel exposure to progesterone for 10 to 13 days prior to surgery reduced estradiol-induced spread of normal breast epithelial cells in the body.)

Cowan LD, Gordis L, ET. al.; Breast cancer incidence in women with a history of progesterone deficiency. *Am J Epidemiol 1981; 114(2):209-17.*
(Landmark study involving 1083 white women treated for infertility from 1945 to 1965. Subjects were monitored for 13 to 33 years to determine links between breast cancer risk and progesterone deficiency. Results showed that women in the low progesterone group had a 5-fold greater risk of premenopausal breast cancer and a 10x greater risk of death from malignant tumors compared to women with a normal progesterone level.)

De Lignieres B; Effects of progestogens on the postmenopausal breast. *Climacteric 2002 Sep; 5(3):229-35.*
(Describes studies indicating that breast cancer risk is higher with non-bioidentical HRT use, (oral conjugated equine estrogens combined with synthetic progestin) than with BHRT use (transdermal, bioidentical estradiol combined with progesterone). The article goes on to say that just because studies show that synthetic progestins do not adequately decrease estradiol's proliferation of cancer cells in the postmenopausal breast does not mean that progesterone does not as well. Placing all progestogens in the same class, regardless of their chemical structure, is not based on scientific evidence.)

Dew JE, Wren BG, Eden JA. A cohort study of topical vaginal estrogen therapy in women previously treated for breast cancer. Climacteric. 2003 Mar;6(1):45-52. PMID: 12725664.
(Study concluded that topical (vaginal) estriol was safe for use in post-menopausal women previously treated for breast cancer.)

Foidart JM, Colin C, Denoo X, Desreux J, et. al.; Estradiol and progesterone regulate the proliferation of human breast epithelial cells. *Fertil Steril 1998 May; 69(5): 963-9.*
(This double-blind, randomized study involved 40 untreated premenopausal women about to undergo breast cancer surgery who had plasma FSH levels of >30 mIU/mL and estradiol levels of <20 pg/mL. For 14 days prior to breast surgery or removal of a benign lesion, these women underwent daily topical application to both breasts of a gel containing placebo, estradiol, progesterone, or a combination of estradiol and progesterone. Findings showed that topical gel exposure to progesterone for 14 days prior to surgery reduced estradiol-induced spread of normal breast epithelial cells in the body.)

Formby B, Wiley TS; Progesterone inhibits growth and induces apoptosis in breast cancer cells: inverse effects on Bcl-2 and p53.
Ann Clin Lab Sci 1998 Nov-Dec;28(6):360-9.
(Study explaining the biological reasons why progesterone inhibits spread of breast cancer cells. Results indicated that this inhibition is due to progesterone's ability to induce apoptosis (i.e., cell death) that is controlled by specialized genes known as p53 and bcl-2. Analysis performed following progesterone exposure to cancer cells showed up to a 90 percent decrease in cancer cell growth, with p53 up-regulated and bcl-2 down regulated during apoptosis.)

Formby B, Wiley TS. Bcl-2, survivin and variant CD44 v7-v10 are downregulated and P53 is upregulated in breast cancer cells by progesterone; inhibition of cell growth and apoptosis.
Mol Cell Biochem; 1999 Dec;202(1-2):53-61

Fournier A, Berrino F, Riboli E, et. al.; Breast cancer risk in relation to different types of hormone replacement therapy in the E3N-EPIC cohort study. *Int J Cancer 2005 Apr 10;114(3):448-54.*
(French E3N cohort study analyzed breast cancer risk among 54,548 – 98,997 postmenopausal women on different HRT combinations. Estrogens used in conjunction with synthetic progestins increase breast cancer, RR=1.69 compared with estrogen use with bioidentical progesterone which did not increase risk of breast cancer, RR=1.0. Estrogen alone increased risk, RR=1.29. Weak estrogens such as estriol did not increase breast cancer risks.)

Holtorf K., The bioidentical hormone debate: are bioidentical hormones (estradiol, estriol, and progesterone) safer or more efficacious than commonly used synthetic versions in hormone replacement therapy? *Postgrad Med 2009 Jan;121(1):73-85.*
(This literature review provides evidence supporting the efficacy of bioidentical hormone therapy, as well as evidence that bioidentical hormones present lower risk for breast cancer and cardiovascular disease than synthetic or animal-derived hormones. The article sites numerous studies linking progestin use to cardiovascular system and breast cancer risks that can be avoided by using bioidentical progesterone.)

Lemon HM. Estriol prevention of mammary carcinoma induced by 7, 12-Dimethylbenzanthracene and procarbazine. *Cancer Res. 35 (1975):1341-53.*
(In a clinical trial of 29 pre- or postmenopausal women with breast cancer, treatment with physiologic doses of estriol arrested tumor growth or induced remission in 37 percent (6) of patients.)

Lemon HM. Estriol and prevention of breast cancer. *The Lancet. 1973;March 10:546-47.*
(Findings of estriol protective action against chemical carcinogens used to induce breast cancer in laboratory animals.)

Lemon HM, et al. Pathophysiologic considerations in the treatment of menopausal patients with estrogens; the role of estriol in patients in the prevention of mammary carcinoma. *Acta Endocrino Suppl. 1980;233:17-27*
(Findings that estriol, unlike estradiol or estrone, has protective action against chemical carcinogens used to induce breast cancer in laboratory animals.)

Lemon HM, et al. Reduced estriol excretion in patients with breast cancer prior to endocrine therapy. *JAMA. 1966;196:112-20*
(Findings that women with breast cancer produce less estriol than those without the disease)

Lyytinen H, Pukkala E, Ylikorkala O. Breast Cancer Risk in Postmenopausal Women Using Estrogen-Only Therapy. *Obst & Gyn 2006 Dec;108(6):1354-60*
(Study of nearly 8000 Finnish women over 50 who took estriol for as little as 6 months to over 5 years, found no increased risk of breast cancer.)

Mauvais-Jarvis P, Kuttenn F, Gompel A; Antiestrogen action of progesterone in breast tissue. *Horm Res 1987; 28(2-4):212-8.*
(This literature review explores international literature concerning the strong antiestrogen effect of progesterone and progestins on breast cells.)

Mohr PE, Wang DY, et.al.; Serum progesterone and prognosis in operable breast cancer. *Br J Cancer 1996 Jun;73(12):1552-5.*
(Study conducted between 1975 and 1992 involving 280 postmenopausal women whose blood serum was tested three days following breast cancer surgery. Results indicated that women with raised progesterone levels had an improved survival rate.)

Plu-Bureau G, Le MG, Thalabard JC, et. al.; Percutaneous progesterone use and risk of breast cancer: results from a French cohort study of premenopausal women with benign breast disease. *Cancer Detect Prev 1999; 23(4): 290-6.*(these results suggest an absence of deleterious effects caused by percutaneous progesterone use in women with benign breast disease.)

Siiteri PK. Pregnancy hormone estriol may reduce risk for breast cancer. *Doctor's Guide 2002 Sept 30; www.pslgroup.com/*
(Hormonal findings (serum samples) on 15,000 women followed up to 40 years at the California Kaiser Foundations Health Plan. A subset had become pregnant between 1959 and 1967. Of these women, 204 eventually developed breast cancer and had lower estriol levels during pregnancy than the 434 women who did not develop breast cancer. Data analysis found that the highest estriol levels had 58% less risk of breast cancer than the lowest estriol group.)

Takahashi K, Manbe A, Okada M, Kurioka H, Kanasaki H, Myazaki K. Efficacy, and safety of oral estriol for managing postmenopausal symptoms. *Maturitas. 2000 Feb 15;34(2):169-77*
(Study found treatment with estriol to be safe and effective in relieving symptoms in post-menopausal women.)

Valdivia I, Ortega D. Mammographic density in postmenopausal women treated with tibolone, estriol or conventional hormone replacement therapy. *Clin Drug Invest. 2000 Aug;20(2):101-7*
(Estriol does not increase breast density in post-menopausal women treated with estriol or conventional hormone replacement therapy.)

Testosterone and Breast Cancer

Dimitrakakis C, Jones RA, Liu A, Bondy CA. Breast cancer incidence in postmenopausal women using testosterone in addition to usual hormone therapy.
Menopause 2004;11(5):531-5

Dimitrakakis C, Zhou J, Wang J, Belanger A, LaBrie F, Cheng C, Powell D, Bondy C. A physiologic role for testosterone in limiting estrogenic stimulation of the breast.
Menopause 2003;10(4):292-8.

Hofling M, Hirschberg AL, Skoog L, Tani E, Hägerström T, von Schoultz B. Testosterone inhibits estrogen/progestogen-induced breast cell proliferation in postmenopausal women. *Menopause 2007;14(2):183-90.*

Key TJ, Appleby PN, Reeves GK, et al. and the Endogenous Hormones Breast Cancer Collaborative Group. Body mass index, serum sex hormones, and breast cancer risk in postmenopausal women.*J Natl Cancer Inst 2003;95(16):1218-26.*

Ortmann J, Prifti S, Bohlmann MK, Rehberger-Schneider S, Strowitzki T, Rabe T. Testosterone and 5 alpha-dihydrotestosterone inhibit in vitro growth of human breast cancer cell lines.
Gynecol Endocrinol 2002;16(2):113-20.

Tamimi RM, Hankinson SE, Chen WY, Rosner B, Colditz GA. Combined estrogen and testosterone use and risk of breast cancer in postmenopausal women.
Arch Intern Med 2006;166(14):1483-9.

Thomas HV, Key TJ, Allen DS, Moore JW, Dowsett M, Fentiman IS, Wang DY. A prospective study of endogenous serum hormone concentrations and breast cancer risk in post-menopausal women on the island of Guernsey.
Br J Cancer 1997;76(3):401-5.

Non-bioidentical Hormone Replacement Therapy (HRT) and Breast Cancer Risk

Beral V; Million Women Study Collaborators; Breast cancer and hormone-replacement therapy in the Million Women Study. *Lancet. 2003 Aug 9;362(9382):419-27.*
(In the Million Women Study, 1,084,100 UK women, ages 50-64, provided information about their use of HRT and were followed up for cancer incidence and death. Findings indicated that current use of HRT is associated with a 66 percent greater risk of incident breast cancer and a 22 percent greater chance of dying from breast cancer, particularly when estrogen-progestagen, non-bioidentical combinations are used.)

Berry DA, Ravdin PM; Breast cancer trends: a marriage between clinical trial evidence and epidemiology. *J Natl Cancer Inst 2007;99: 1139-41.*
(Study examining how changes in screening mammography and use of HRT affected decreases in breast cancer incidence between 1980 and 2006 in Kaiser Permanente Northwest (KPNW)

Campagnoli C, Clavel-Chapelon F, Kaaks R, et. al.; Progestins and progesterone in hormone replacement therapy and the risk of breast cancer. *J Steroid Biochem Mol Biol 2005 Jul;96(2):95-108.*
(This literature review indicates that combining natural progesterone with estrogen does not increase breast cancer risk, but that, continued use of combined non-bioidentical estrogen-progestin is risky to breast tissue.)

CANCER March 15, 2003/Volume 97/Number 6
(Researchers concluded that continued use of HRT containing progestins rendered the highest risks for breast carcinoma.)

Chelbowski RT et. Al. Influence of estrogen plus progestin on breast cancer and mammography in healthy post-menopausal women. The women's health initiative randomized trial.
JAMA. 2002 Jun 25.289(24):3243-53
(Study revealed that menopausal women receiving Premarin and Provera (artificial, non-bioidentical hormones) have a higher occurrence of breast cancer.)

Chen, CL, Weiss, NS, et. al.; Hormone replacement therapy in relation to breast cancer.
JAMA 2002 Feb 13;287(6):734-41.
(This case-control study examined causal relationships between breast cancer incidence and long-term use of HRT. The study involved 705 postmenopausal women, ages 50 to 74, diagnosed with breast cancer between 7/1/90 and 12/31/95 and 692 control subjects. Data indicated that recent long-term use of HRT (whether estrogen alone or estrogen in combination with progestin) increases breast cancer incidence.)

Chen WY, Mason JE, Hankinson SE, et. al.; Unopposed estrogen therapy and the risk of invasive breast cancer. *Arch Intern Med. 2006 May 8;166(9):1027-32.*
(Long-term study, involving large numbers of postmenopausal women with hysterectomy, that explored the relationship between long-term use of unopposed estrogen and breast cancer incidence. Beginning in 1980, 11,508 women completed biennial questionnaires pertaining to their estrogen use. Every 2 years, subjects were expanded. By the final follow-up period from 2000 to 2002, 28,835 women were included in the study. Results indicated that long-term use of unopposed estrogen resulted in greatest breast cancer incidence.)

Colditz GA; Relationship between estrogen levels, use of hormone replacement therapy, and breast cancer. *J Natl Cancer Inst 1998 Jun 3;90(11):814-23.*
(This literature review draws strong causal relationships between use of estrogens and progestins, estrogen levels detected in the body, and breast cancer risk in postmenopausal women. The literature further indicates that HRT may act to promote the late stages of cancer among postmenopausal women and to encourage growth of malignant cells.)

Fournier A, Berrino F, Riboli E, et. al.; Breast cancer risk in relation to different types of hormone replacement therapy in the E3N-EPIC cohort study. *Int J Cancer 2005 Apr 10;114(3):448-54.*
(French E3N cohort study analyzed breast cancer risk among 54,548 postmenopausal women on different combinations of HRT. Subjects on estrogen and a synthetic progestin showed a 40% increased risk breast cancer compared to non-users. Findings in women on estrogen plus a bioidentical progesterone showed a 10% decrease in breast cancer risk. Results indicated that even short-term use of synthetic progestins combined with oral or transdermal estrogens increases breast cancer risk.)

JAMA 2002 Jul 17;288(3):321-33.
This well-publicized, randomized, controlled study involved 16,608 postmenopausal women, ages 50-79, having intact uterus. Subjects were recruited between 1993 and 1998 and were prescribed conjugated equine estrogens plus medroxyprogesterone acetate (progestin) or placebo. (The study, originally planned for 8.5 years, was stopped after an average of 5.6 years due to severe health risks, including increased incidence of breast cancer and stroke, associated with non-bioidentical HRT. These risks outweighed the benefits associated with the therapy including incidence of osteoporotic fractures and colorectal cancer.)

Jernstrom H, et al . A prospective study of different types of hormone replacement therapy use and the risk of breast cancer: the women's health in the Lund area (WHILA) study (Sweden).
Cancer Causes Control. 2003 Sep; 14(7):673080

Ravdin PM, Cronin KA, Howlader N, et al.; The decrease in breast-cancer incidence in 2003 in the United States. *New Engl J Med 2007;356:1670-4.*
Rossouw JE, Anderson GL, Prentice RL, et. al.; Writing Group for the Women's Health Initiative Investigators (2002). Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial.
(This data analysis from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) registries links the 2003 decrease (6.7 percent) in breast cancer incidence in postmenopausal women > 50 with sharp drop in HRT use in response to initial Women's Health Initiative findings.)

Schairer C, et al. Cause-specific mortality in women receiving hormone replacement therapy.
Epidemiology 1997 Jan;8(1):59-65
(One of the largest HRT studies of 23,000 Swiss women, most of whom took estradiol or estriol showed that there was a 28% decrease in death from breast cancer. Compared with the general population, the standardized mortality ratio for all-cause mortality in this cohort was 0.77 (95% confidence limits = 0.73, 0.81). Deaths in each of the 12 major categories of causes of death except for injuries occurred 12% to 86% less frequently than expected.)

Smigel K; Swedish studies link hormone use to higher breast cancer risk.
J Natl Cancer Inst. 1989 Aug 16;81(16):1210-1.
(Swedish study involving 23,244 women treated for menopause symptoms with a combination of estrogen and progestin. Results showed a 10 percent greater risk of breast cancer for those taking estrogen-progestin briefly, and a 70 % greater risk for those taking estrogen-progestin for 9 years or more.)

Vankrunkelsven P, Kellen E, et. al.; Reduction in hormone replacement therapy use and declining breast cancer incidence in the Belgian province of Limburg.
Breast Cancer Res Treat. 2009 Nov;118(2):425-32.
(Study exploring whether reduction in HRT use was linked to breast cancer incidence in Belgium's Limburg province. Subjects included Belgian women previously diagnosed with invasive breast cancer between 1/1/96 and 12/31/05. Results indicated decreased breast cancer incidence following early termination of the Women's Health Initiative trial in 2002 after which HRT use dropped significantly worldwide.)

Obesity, Insulin Resistance, Diabetes and Breast Cancer

Friedenreich CM. Review of anthropometric factors and breast cancer risk.
Eur J Cancer Prev 2001; 10:15-32
(Findings on the link between obesity and increased risk of breast cancer.)

Goodwin PJ, et al. Fasting insulin and outcome in early-stage breast cancer: results of a prospective cohort study. *Journal of Clinical Oncology 2002 Jan;20(1):42-51*

Huang Z, Willett WC, et. al.; Waist circumference, waist:hip ratio, and risk of breast cancer in the Nurses Health Study.
Am J Epidemiol 1999 Dec 15;150(12):1316-24.
(Study conducted from 1986 to 1994, involving 47,382 US registered nurses, examining associations between breast cancer risk and waist circumference and waist:hip circumference ratio. Results showed that greater waist circumference increases risk of breast cancer, particularly for postmenopausal women at lower risk because of never having used estrogen replacement hormones. Slightly weaker associations were found between waist:hip ratio and breast cancer risk.)

Lawlor, DA, Davey Smith, G, Ebrahim S; Hyperinsulinaemia and increased risk of breast cancer: findings from the British women's heart and health study. *Cancer Causes and Control. 2004; 15: 267–275.*
(This study of 3,868 British women, ages 60-79 years, indicated that higher fasting insulin levels are associated with increased breast cancer risk)

Malin A, et al. Evaluation of the synergistic effect of insulin resistance and the insulin-like growth factors on the risk of breast carcinoma. *Cancer. 2004 Feb 15; 100(4):694-700*
(The results of the current study suggest that insulin resistance and IGFs may synergistically increase the risk of breast carcinoma.)

Michels KB, et al. Type 2 diabetes and subsequent incidence of breast cancer in the nurses' health study.
Diabetes Care. 2003 26:1752-58
(Findings bear out the links between Type 2 Diabetes and increased risk of breast cancer.)

Renehan AG, et al. Insulin like growth factor (IGF-1), IGF binding protein-3 and cancer risk; systematic review and meta-regression analysis. *Lancet. 2004 April:363(9418):1346-53*

Rose DP, et al. Adverse effects of obesity on breast cancer prognosis, and the biological actions of leptin (review). *Int J Oncol.2002 Dec;21(6):1285-92*
(Studies the impact of leptin upon growth of cancer cells.)

Stoll B.A. Adiposity as a risk determinant for postmenopausal breast cancer.
Int J Obes Relat Metab Disord 24(5) (2000):527-33

Stoll, B.A. Western Nutrition and the Insulin Resistance Syndrome: a link to breast cancer.
Eur J Clin Nutr 53(2) (1999)10:83-87

Zumoff B. Hormonal abnormalities in obesity.
Acta Med Scand Suppl. 1988;723:153-60
(The study shows activity of free, unbound estrogen levels stimulates breast cancer cells.)

<u>Nutrition, Alcohol, Lifestyle, Xenohormones and Breast Cancer</u>

Abbas S, Linseisen J, Slanger T, et. al.; Serum 25-hydroxyvitamin D and risk of post-menopausal breast cancer—results of a large case-control study.
Carcinogenesis. 2008 Jan;29(1):93-9.
(German study exploring the associations between blood serum levels of 25-hydroxyvitamin D and post-menopausal breast cancer risk. Subjects included 1394 German breast cancer patients and 1365 controls, between the ages of 50 and 74, studied between 2002 and 2005. Results indicated a strong relationship between low 25-hydroxyvitamin D blood serum levels and breast cancer risk.)

Damianaki, A., et al. Potent inhibitory action of red wine polyphenols on human breast cancer cells. *J Cell Biochem 78(3) (2000): 429-441*

Eng ET, et al. Anti-aromatase chemicals in red wine. *Ann NY Acad Sci. 2002 Jun;963:239-46*
(Chemicals found in red wine inhibit aromatization of estrogen in fat cells.)

Etique N, et al. Ethanol stimulates proliferation, ER-alpha and aromatase expression in human breast cancer cells. *Int J Mol Med. 2004 Jan;13(1):149-55* (Study demonstrating effects of ethanol content in alcohol and promotion of breast cell growth.)

Fowke JH, et al. Brassica vegetable consumption shifts estrogen metabolism in healthy postmenopausal women. *Cancer Epidemiol Biomarkers Prev. 2000 Aug;9(8):773-9*
(Findings that cruciferous vegetables promote favorable "2-hydroxy" estrogen metabolism pathways that protect against breast cancer.)

Gunzerath L, et al. National Institute on Alcohol Abuse and Alcoholism report on moderate drinking. *Alcohol Clin Exp Res. 2004 Jun;28(6):829-47*
(Paper weighs the risks/benefits of moderate drinking.)

Hamajima, N, et al. Alcohol, tobacco and breast cancer-collaborative reanalysis of individual data from 53 epidemiological studies, including 58, 515 women with breast cancer and 95,063 women without the disease. *Br J Cancer 2002;87:1234-45*
(Combined analysis of 53 worldwide studies documenting raised risks of breast cancer with alcohol usage.)

La Vecchia c, et al. Vegetables, fruits, anti-oxidants and breast cancer; a review of Italian studies. *Eur J Nutr. 2001 Dec;40(6):261-7*
(Data from multiple case control studies conducted in Italy from 1983-1999 show significant breast cancer protection with use of anti-oxidants, vitamin C, and E and beta carotene.)

La Vecchia, C. Proceedings of European Breast Cancer Conference, Barcelona, Spain. March 25, 2010.
(Presentation of International Agency for Research on Cancer figures estimating that 25 to 30 percent (one-third) of breast cancer cases could be avoided if women maintain ideal weight and exercise.)

McTiernan A. Behavioural risk factors in breast cancer: Can risk be modified?
The Oncologist. 2003;8:326-334

Owen, R.W., et al. The Antioxidant/Anticancer potential of phenolic compounds isolated from olive oil. *Eur J Cancer 36(10) (2000):1235-1247*

Poschl G, Seitz HK. Alcohol and Cancer.
Alcohol.2004 May-June;39(3):155-65 (Epidemiological data have identified chronic alcohol consumption as a significant risk factor for upper alimentary tract cancer, including cancer of the oropharynx, larynx and the oesophagus and of the liver. The increased risk attributable to alcohol consumption of cancer in the large intestine and in the breast is much smaller. However, although the risk is lower, carcinogenesis can be enhanced with relatively low daily doses of ethanol. Considering the high prevalence of these tumours, even a small increase in cancer risk is of great importance, especially in those individuals who exhibit a higher risk for other reasons.)

Purohit V. Can alcohol promote aromatization of androgens to estrogens? A review.
Alcohol. 2000 Nov;22(3):123-7
(Rat study of alcohol impact on estradiol levels measured in serum. In male rats, heavy chronic alcohol administration (36% of total calories=12–18 g/kg/day) can promote aromatization of androgens to estrogens in liver, but the data are equivocal for the hypothalamus. Alcohol-induced hepatic aromatization may be responsible for the feminization of some male alcoholics.)

Rock Cl, et al. Effects of high-fiber, low-fat diet intervention on serum concentration of reproductive steroid hormones in women with a history of breast cancer.
J Clin Oncol. 2004 Jun 15;22(12)2379-87
(Findings that high fiber intake lowers insulin levels and serum estrogen levels—both risk factors for breast cancer.)

Sato R, et al. Prospective study of carotenoids, tocopherols, and retinoid concentrations and risk of breast cancer. *Cancer Epidemiol Biomarkers prev. 2002 May;11(5) 451-7*
(A study of serum concentrations of vitamin E, A and beta-carotene in women who donated blood found lower baseline antioxidant levels in those who later developed breast cancer vs. women who did not.)

Singletary KW, et al. Alcohol and breast cancer: review of epidemiologic and experimental evidence and potential mechanisms. *JAMA 2001;87:2143-51*
(Researches the link between alcohol and increased risk of breast cancer.)

Starek A. Estrogens and organochlorine xenoestrogens and breast cancer risk.
Int J Occup Med Environ Health. 2003; 16(2):113-24
(In the last decade, the organochlorine chemicals, which include pesticides, polychlorinated biphenyl congeners and other representatives of the dioxin family, have been regarded as xenoestrogens. These chemicals are capable of modulating hormonally regulated processes and inducing changes in growth factors that may be responsible for carcinogenic effect. Many case-control studies have shown the distinct association between breast adipose tissue concentrations of several organochlorine xenoestrogens and breast cancer risk. Also in some studies, the women with breast cancer had higher organochlorine levels in serum as compared with controls.)

Terry PD, et al. Intakes of fish and marine fatty acids and risks of cancers of the breast and prostate and other hormone related cancers: a review of the epidemiologic evidence.
Am J Clin Nutr. 2003 Mar;77(3):532-43
(Despite the many epidemiologic studies that have been published, the evidence from those studies remains unclear. Most of the studies did not show an association between fish consumption or marine fatty acid intake and the risk of hormone-related cancers.)

Trichopoulou A, et al. Cancer and Mediterranean dietary traditions.
Cancer Epidemiol Biomarkers Prev. 2000 Sep;9(9);869-73 (Although estimates can only be crude, it can be calculated that up to 25% of the incidence of colorectal cancer, approximately 15% of the incidence of breast cancer, and approximately 10% of the incidence of prostate, pancreas, and endometrial cancer could be prevented if the populations of highly developed Western countries could shift to the traditional healthy Mediterranean diet.)

Weisburger JH. Antimutagens, anticarcinogens and effective world-wide cancer prevention.
*J Environ Pathol Toxicol Onclo. 1999;18(2):85-93*Garland CF, et al.
(About 35% of known cancers are associated with tobacco use and about 55% with inappropriate nutritional habits. In the Western world, the type and amount of fat play a critical role that operates through specific promoting mechanisms to modify the action of genotoxic carcinogens. In most Western countries where mixed fats and oils are consumed, the total amount of fat at 35 to 40% of calories acts as a powerful promoter. On the other hand, in Italy and Greece, where the monounsaturated oil, olive oil, is used almost exclusively without promoting effect, little enhancement by fat is observed.)

Calcium and vitamin D; their potential roles in colon and breast cancer prevention.

Ann NY Acad Sci 1999:889:107-19
(Findings of Vitamin D deficiency in northern vs. southern populations have more MS, diabetes, arthritis, hypertension, and breast/prostate cancers.)

Welsh J, et al. Vitamin D-3 receptor as a target for breast cancer prevention.
J Nutr. 2003 Jul;133(7Suppl) 2425S-2433S
(Findings that Vitamin D arrests growth of cancer cells and encourages differentiation and natural cell death (apoptosis).)

World Cancer Research fund panel. Food, nutrition and the prevention of cancer: a global perspective. Washington, DC: *American Institute for Cancer Research, 1997*

Exercise and Breast Cancer

Bauman AE. Updating the evidence that physical activity is good for health: an epidemiological review 2000–2003. J Science Med Sport. 2004 Apr;7(1Suppl):6-19
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