

BHRT References:

Plu-Bureau G, Le M, Thalabard J, 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;23:290-296.

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.

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.

Fitzpatrick L, Good A. Micronized progesterone: clinical indications and comparison with current treatments. *Fertil Steril.* 1999;72(3):389-397

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.

Murkes D¹, 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

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. Breast Cancer Prevention in Research and Resources
Our belief that breast cancer is preventable is supported by key clinical studies and literature reviews. Here you'll find links to important international studies on breast cancer research, the role of hormones and hormone replacement therapy in breast cancer, breast cancer risk, and much more to empower you.

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

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 cites numerous studies linking progestin use to cardiovascular system and breast cancer risks that can be avoided by using bioidentical progesterone.

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.

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. Weak estrogens such as estriol did not increase breast cancer risks.

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.

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 synthetic 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.

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.

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.

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.

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.
French cohort study involving 1150 postmenopausal French women diagnosed with benign breast disease between 1976 and 1979 and followed up for an accumulative 12,462 person-years. Topically applied progesterone was prescribed to 58 percent of these women. Results showed no association between increased breast cancer risk and use of topical progesterone.

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

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.

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.

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.

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.

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 HRT, long-term or unopposed estradiol use increased breast cancer risk. Estriol did not increase breast cancer risk.

Mauvais-Jarvis P, Kuttann 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.

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.

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 Endocrinol 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. 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. 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.

Testosterone and Breast Cancer

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.*

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.

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.

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.

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 postmenopausal women on the island of Guernsey.

Br J Cancer 1997;76(3):401-5.

Synthetic Hormone Replacement Therapy (HRT) and Breast Cancer Risk

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.

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) health plan participants. In particular, between 2000 and 2004, a drop in breast cancer incidence was noted in this and other population-based studies.

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.

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.

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.

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 synthetic estrogen-progestin is risky to breast tissue.

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.

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

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 combinations are used.

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Researchers concluded that continued use of HRT containing progestins rendered the highest risks for breast carcinoma.

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.

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 synthetic HRT. These risks outweighed the benefits associated with the therapy including incidence of osteoporotic fractures and colorectal cancer.

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, synthetic 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.

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.

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.

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.

Obesity, Insulin Resistance, Diabetes and Breast Cancer

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 study found that women with abnormal levels of both had a three-fold rise in the incidence 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*

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.

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.

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.

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

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.

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

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.

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.

Longcope C et al. The effect of a low fat diet on estrogen metabolism.

J Clin Endocrinol Metab. 1987 Jun;64(6):1246-50

Nutrition, Alcohol, Lifestyle, Xenohormones and Breast Cancer

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.

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.

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.

Rock CI, 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.

Poschl G, Seitz HK. Alcohol and Cancer.

Alcohol. 2004 May-June;39(3):155-65

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.

Starek A. Estrogens and organochlorine xenoestrogens and breast cancer risk.

Int J Occup Med Environ Health. 2003; 16(2):113-24

The role of xenoestrogens in the initiation and promotion of breast cancer.

McTiernan A. Behavioural risk factors in breast cancer: Can risk be modified?

The Oncologist. 2003;8:326-334

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).

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

Laboratory experiments with breast cancer cells show omega-3 fats inhibit the growth of cancer cells.

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.

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.

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.

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.

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

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

Purohit V. Can alcohol promote aromatization of androgens to estrogens? A review.

Alcohol. 2000 Nov;22(3):123-7

Study of alcohol impact on estradiol levels measured in serum.

Trichopoulou A, et al. Cancer and Mediterranean dietary traditions.

Cancer Epidemiol Biomarkers Prev. 2000 Sep;9(9):869-73

Study looks at how dietary patterns of fat intake in different countries may protect against breast cancer.

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.

Weisburger JH. Antimutagens, anticarcinogens and effective world-wide cancer prevention.

J Environ Pathol Toxicol Oncol. 1999;18(2):85-93 Garland CF, et al.

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.

World Cancer Research fund panel. Food, nutrition and the prevention of cancer: a global

perspective. Washington, DC: *American Institute for Cancer Research*, 1997

Ginsburg ES, et al. Effects of alcohol ingestion on estrogens in post-menopausal women.

JAMA. 1996 Dec 4;276(21):1747-51

Impact of alcohol on serum estradiol levels.

Exercise and Breast Cancer

Bruce Cr, Hawley JA. Improvement in insulin resistance with aerobic exercise training: a

lipocentric approach. *Med Sci Sports Exer.* 2004 Jul;36(7):1196-201

Ross R. et al. Exercise-induced reduction in obesity and insulin resistance in women: a

randomized controlled trial. *Obes Res.* 2004 May;12(5):789-98

McTiernan A, et al; Effect of exercise on serum estrogens in postmenopausal women: a 12

month randomized clinical trial. *Cancer Res.* 2004 Apr 15;64(8):2923-8

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

A review of scientific studies published between 2000 and 2003 confirms physical exercise health and disease prevention benefits.

Lagerros YT, et al. Physical activity in adolescence and young adulthood and breast cancer risk: a quantitative review. *Eur J Cancer Prev.* 2004 Feb;13(1):5-12

Thune I, Furberg AS. Physical activity and cancer risk, all sites and site specific. *Med Sci Sports Exerc.* 2001 Jun;33(6 suppl):S530-50

Raastad T, et al. Hormonal responses to high and moderate intensity strength exercise. *Eur J Appl Physiol.* 2000 May;82(1-2):121-8

Tymchuk CN, et al. Changes in sex hormone binding globulin, insulin and serum lipids in post menopausal women on a low fat high fiber diet combined with exercise. *Nutr Cancer.* 2000;38(2):158-62

Kraemer WJ, et al. The effects of short-term resistance training on endocrine function in men and women. *Eur J Appl Physiol Occup Physiol.* 1998 Jun; 78(1):69-76

Thune I., et al. Physical activity and the risk of breast cancer. *N Eng J Med.* 1997 May1;336(18):1269–75

Stress and Breast Cancer

Reiche EM, et al. Stress, depression, immune system, and cancer. *Lancet Oncol.* 2004 Oct;5(10):617-25

Findings that stress and depression suppress T cells and natural killer cells with negative effect upon the immune system and defense against cancer.

Montazeri A, et al. The role of depression in the development of breast cancer: analysis of registry data from a single institute. *Asian Pac Cancer Prev.* 2004 Jul-Sep;5(3)316-9
Findings of relationship between depression and feelings of hopelessness with subsequent development of breast cancer.

Dalton SO, et al. Mind and cancer. Do psychological factors cause cancer?
Eur J Cancer. 2002 Jul;38(10):1313-23
Studies association between stress and breast cancers.

Jacobs Jr, Bovasso GB. Early and chronic stress and their relation to breast cancer. *Psychol Med.* 2000 May;30(3):669-78
Survey of 1213 women found that severe episodes of stress or depression up to 20 years before onset of cancer increased risk of developing the disease.

