



Breast Cancer Care and Prevention: Non-Pharmacological Interventions

What Is Breast Cancer?

Cancer is marked by the uncontrolled growth of abnormal cells in the body caused by an interplay of genetic and environmental factors including: genetic vulnerability, food choices, lifestyle, and estrogen exposures.¹ Breast cancer occurs in one of eight women and is the most common cancer in women. It occurs in one percent of men.^{2,3} Seventy percent of breast cancers are hormone receptor positive, and genetic mutations such as BRCA 1 and 2 mutations increase breast cancer development with 60-80% lifetime risk.⁴⁻⁶

What Is an Integrative Approach to Breast Cancer Care?

Integrative medicine encourages an empowered approach to care which emphasizes lifestyle choices which may help prevent breast cancer, slow its growth when it occurs, and prevent recurrence.¹ It combines conventional and complementary and alternative (CAM) approaches to care that address physical, emotional and spiritual aspects of the person. Evidence based therapies are used when available. The healing intention of all therapies is emphasized. Cancer may serve as an opportunity for growth and greater health. CAM therapies, which interfere with conventional therapies, are avoided during that portion of treatment. Each person has a unique path to healing. CAM therapies may also reduce cancer treatment side effects.

What Are the Risk Factors for Breast Cancer?

Risk factors are reviewed by Costanza and Chen in UpToDate.⁷

• Risk factors that increase risk of breast cancer include:

- Alcohol consumption of greater than 1 drink per day^{1,8,9}
- Increased lifetime exposure to estrogen: exogenous and endogenous¹
- Obesity^{1,10,11}
- Increasing age¹
- High fat, low fiber, processed food diet, low intake of fruits and vegetables¹
- Exposure to radiation¹
- Paternal or maternal family history of breast cancer^{12,13}
- BRCA 1 or 2, or P53 mutations^{12,13}
- Night shift work¹⁴⁻¹⁶





Factors that decrease risk:

- Regular exercise 30-60 minutes 3-5 times per week.¹⁷ Prolonged breastfeeding¹²⁻¹³ 0
- 0
- Fresh foods including 5-9 servings of fruits and vegetables 0 daily^{10, 17}
- Higher ratio of weak 2-hydroxyestrones versus stronger 16hydroxyestrones metabolites in body. Can be measured with urine testing.18-20



Healthy Breast





What are Some Integrative Non-pharmacological Therapies for the Prevention and Treatment of Breast Cancer?

Two important monographs on exercise and nutrition, one for cancer prevention and the other focused on the period during and after treatment, were created by the American Cancer Society (ACS). A panel of experts reviewed the scientific evidence and best practices guidelines. These guidelines were published in 2006 and updated in 2012.^{10,17} Access condensed versions here. See links on page 10 for the complete articles.

- Prevention: http://www.cancer.org/acs/groups/cid/documents/webcontent/002577-pdf.pdf
- **Treatment:**<u>http://www.cancer.org/Treatment/SurvivorshipDuringandAfterTreatment/Nutritio</u> <u>nforPeoplewithCancer/nutrition-and-physical-activity-during-and-after-cancer-treatment-</u> <u>answers-to-common-questions</u>

Nutrition

Diets high in fruits and vegetables, fish, fresh foods, low in animal fat, and high in olive oil (the Mediterranean diet) may reduce the risk of breast cancer and many other cancers, whereas, the western diet high in fats and low in fruits and vegetables may increase risk.²¹ The Mediterranean diet favors weak estrogenic metabolites, which stimulate vulnerable breast tissue less than stronger estrogen metabolites, which may lead to breast cancer development.^{19,22,23} For an easy to follow food pyramid that defines key ingredients of the Mediterranean diet, see the website at the University of Michigan Integrative Medicine Program at http://www.med.umich.edu/umim/food-pyramid/about.htm.

• Polyunsaturated Fatty Acids

Polyunsaturated fatty acids include omega 3 and 6 fatty acids. In large quantities and especially if hydrogenated for extended shelf life, oils such as sunflower, safflower, soy, sesame and corn oils can be pro-inflammatory in the body. Omega 3 fatty acids including EPA and DHA are anti-inflammatory, and include fish oil, flax seed oil and the oil in walnuts. Omega 3 fatty acids are present in fatty fish such as salmon, sardines and mackerel, walnuts, green leafy vegetables and flax seed meal. The VITamins and Lifestyle (VITAL) Study demonstrated that fish oil reduced the risk of ductal but not lobular breast cancers.²⁴ In another study, fish omega 3 intake was found to reduce risk of breast cancer in pre and postmenopausal women with the greatest reduction in postmenopausal women.²⁵

Dosing: High potency fish oil: about 1000 mg of combined DHA and EPA daily in less than 3 gms of total fish oil. Flax seed oil can be substituted on a vegan diet.

Contraindications: If any bleeding occurs, stop fish oil immediately. Stop one week prior to surgery. Stop if platelets are less than 20,000K.



• Monounsaturated Fatty Acids

Oleic acid (omega 9 fatty acid) found in olive oil, as well as avocados, hazelnuts, and cashew nuts, may help suppress HER 2/Neu tumor cell growth.

o Green Tea

Green tea is a polyphenol and natural aromatase inhibitor. Green tea ingestion of 3 cups or more per day in two studies reduced the risk of breast cancer.^{26,27} Dosing: Three or more cups a day.

o Soy

Soy has been controversial in the past in estrogen positive tumors because it is a phytoestrogen with weak estrogen receptor binding properties. In rat models, isolated isoflavones stimulated estrogen positive tumors, but soy foods have opposite protective effects.²⁸ The large Shanghai Breast Cancer Survival Study showed that soy food intake was associated with increased survival and less recurrence of tumors in estrogen positive and negative women, and in users and nonusers of tamoxifen.²⁹ In other studies, this finding has been replicated.³⁰⁻³² One to three servings of soy foods are recommended daily unless sensitive to soy.

o Flax

Flax as flax seed meal or oil, is a rich source of phytoestrogens containing alphalinoleic acid. As an omega 3 fatty acid containing food, it inhibits aromatase activity, binds weakly to estrogen receptors, and increases the weaker 2-OHE's. It reduces the risk of breast cancer and decreases breast cancer cell growth.^{18,19,33} Use 1-2 tablespoons a day added to food.

• Antioxidants

Diets high in antioxidants contained in fruits and vegetables may lower risk of breast cancer.²¹ Carotenoids in fruits and vegetables reduced the risk of invasive breast cancer in premenopausal women.³⁴ Antioxidants in foods are safer than high dose supplement forms given synergistic effects and better absorption. Scant evidence exists for antioxidant supplements during cancer treatment, and there are potential risks of them interfering with treatment.³⁵ Recommend 5-9 servings of fruits and vegetables daily.

• Whey protein

Whey protein powder is a by-product of cheese production. It is much less allergenic than casein protein. It is high in glutamine and helps prevent mouth sores (stomatitis) in patients receiving chemotherapy and may be useful in preventing the peripheral neuropathy of certain chemotherapy agents such as taxanes. 20-30 gms of whey protein powder twice daily in smoothies will provide enough glutamine to help prevent these complications of chemotherapy. If there exists sensitivity or allergy to whey, glutamine can be taken as a supplement, 3-5 gms one to three times daily.³⁶



• Brassica (Cruciferous) vegetables

Cruciferous vegetables include kale, broccoli, cauliflower, brussels sprouts and cabbage. Indole-3-carbinol contained in these vegetables helps decrease cancer cell proliferation, increase apoptosis, and increases the ratio of weak to strong estrogens (2-OHE/16-OHE) favorably. Breast cancer risk may be reduced by 20-40% with 1-2 servings of cruciferous vegetables daily.^{23,37-39} Indole-3-carbinol as a supplement can interfere with Tamoxifen and is safer to eat in vegetable form than in supplement form.¹ 1-2 servings per day.

Exercise

In the prevention of cancer, exercise may help control weight, improve immunity and mood control. In cancer treatment, it may benefit mood, energy levels, immunity, overall health, survival, prevention of recurrence, and quality of life. Exercise may also improve balance with decrease in falls and improves vasomotor instability in menopause.^{40,41} Exercising more than 3 hours a week lowered breast cancer mortality.⁴² It also improves fitness during conventional cancer therapies.⁴³

Supplements

One important resource for evaluating which supplements can improve the effectiveness of chemotherapy agents, and which interfere is *The Definitive Guide to Cancer, 3rd Edition: An Integrative Approach to Prevention, Treatment and Healing* by Lise Alschuler, ND and Karolyn Gazella, 2010.¹

• Vitamin D

Vitamin D deficiency is common in latitudes farther from the equator and can result in osteoporosis, weakness, low back pain, and sternal pain. Individuals at risk include those 65 years or older, little unprotected sun exposure, darker skin color, and medication use with glucocorticoids or anticonvulsants.^{44,45} Strong evidence exists that adequate vitamin D levels may reduce breast cancer risk especially in those with higher levels.^{46,47} Food sources except oily fish contain inadequate amounts of vitamin D, and their taking a daily supplement is advised unless adequate sun exposure is available. One study found that levels of vitamin D in the 60-80 ng/ml

lowered the risk of premenopausal breast cancer.⁴⁸ Recommend obtaining a 25 hydroxy-vitamin D level in winter for patients living at latitudes farther from the equator. Recommend vitamin D3: 1000-2000 IU daily.⁴⁹⁻⁵¹ During the summer months at latitudes greater than 35-40 degrees north of the equator, or daily at latitudes closer to the equator, moderate exposure to sun, at least 20 minutes midday without sunscreen for patients who are not at risk for sunburn or skin cancer, will help maintain normal vitamin D levels.⁵²





o Melatonin

Melatonin has antioxidant, immune enhancing, cytotoxic, and estrogen regulating properties. It can help in the treatment of insomnia. It is contraindicated in bipolar illness, and in some vulnerable individuals may worsen depression. Exercise caution with other sedative medication. Melatonin comes in two forms: an immediate release preparation for individuals having difficulty in falling asleep, and a sustained release preparation for those having difficulty staying asleep.^{53,54} Dosing ranges from 1 mg to 20 mg before bed, and a starting dose is 3 mg before bed. Titrate to desired effect, without causing a hangover the next day.

• Botanicals

Botanicals may be helpful in the treatment of cancer but must be used carefully during chemotherapy, since many botanicals can interfere with the metabolism of the chemotherapy agent by increasing or decreasing its metabolism in the body. Certain botanicals interfere with the metabolism of taxanes, platinum based drugs, cyclophosphamide, doxyrubicin, etoposide, and irinotecan.¹ Generally, botanicals do not interfere with radiotherapy. Botanicals such as St John's Wort can interact with other drugs the patient may be taking via the cytochrome P450 metabolic pathway.

For specific information on botanical and supplement interactions with chemotherapy drugs, refer to the text *The Definitive Guide to Cancer, 3rd Edition: An Integrative Approach to Prevention, Treatment and Healing* by Lise Alschuler and Karolyn Gazella, Celestial Arts, 2010.

• Spiritual and Emotional Care

Small group psychological interventions for breast cancer patients led by a psychologist and concentrating on stress management and strategies to optimize conventional treatment and improve mood helped decrease recurrence and mortality.⁵⁵

Integrative Management of Side Effects from Breast Cancer Treatment

• Fatigue

Fatigue is a common symptom of cancer and treatment. Daily gentle exercise and acupuncture may help.^{40,56-58}

• Vasomotor Instability

Exercise, acupuncture, and a number of pharmacological medications may help with vasomotor instability from menopause.⁵⁹⁻⁶³ Black cohosh is not estrogenic; in one study it decreased risk of breast cancer, but generally it is not helpful in controlling hot flashes.^{35,64,65} Black cohosh can cause liver toxicity and must be used cautiously.

Breast cancer survivors tend to have 10% more sleep disturbances even long term than age matched women without cancer. These sleep disturbances in both groups are associated with hot flashes, depression, more distress, and worse physical conditioning.⁶⁶ In one study, breast cancer survivors had less physical activity and more hot flashes than women without breast cancer.⁶⁷



Nausea and Vomiting

Acupuncture with and without moxibustion helped alleviate nausea and vomiting in cancer treatment.⁶⁸⁻⁷¹ Nausea intensity decreased in one study with exercise.⁷² Ginger may also help alleviate nausea. Its mechanism for this is unknown. Take 500 to 1000 mg ginger root extract every 4 to 6 hours as needed, or eat 1 tsp or 5 gm crystallized ginger every 2 to 3 hours as needed. Too much ginger may cause heartburn.⁷³ A systematic review to evaluate the use of cannabis as a therapeutic agent for treating chemotherapy-induced nausea and vomiting in cancer patients concluded that dronabinol was statistically and clinically more effective as an anti-emetic than neuroleptics. Caution is suggested related to the small sample size and number of studies.⁷⁴

Anxiety/ Stress/ Depression

Anxiety and depression may be improved with a number of studied interventions including acupuncture, an 8-week Mindfulness-based Stress Reduction Program, art therapy, and exercise.^{57,75-79} Massage therapy, yoga, and support groups have also proved beneficial to cancer patients.^{68,78-86} Aromatherapy, dance, journaling, guided imagery, biofeedback, cognitive behavioral therapy, meditation, relaxation, and hypnosis also were helpful during treatment.^{35,87}

Insomnia and Other Sleep Disturbances

Good sleep hygiene helps induce sleep at night when production of melatonin is optimal. Minimizing sleep during the day, exercising regularly, sleeping in a quiet dark room, and going to sleep at a similar time each night promotes sleep. Relaxation, meditation and yoga can increase melatonin and optimize sleep.⁸⁸ Cognitive behavioral therapy also has positive effects on sleep.⁸⁹

Regular exercise can help to reinforce normal circadian rhythm and endogenous melatonin production by increasing wakefulness during the day and sleep at night.⁴⁰ Melatonin in supplemental form can be used.

• Pain and Peripheral Neuropathy

Acupuncture may be helpful with pain relief. One study showed improved pain scores and psychological functioning with an 8-week course of acupuncture.⁵⁷ The Society for Integrative Oncology upon review of the literature strongly endorses acupuncture for this indication.⁶⁸ Massage may also be very helpful in relieving pain.⁶⁸ Exercise maintains fitness during treatment.⁴³ Cannabinoids may also help neuropathic pain.⁹⁰ Mind-body therapies may also be efficacious for pain.⁹¹

Lymphedema and Musculoskeletal Issues

Lymphatic massage and exercise may prevent some degree of lymphedema and prevent or relieve shoulder dysfunction.^{68,92} One study showed that gentle weight lifting twice weekly did not worsen lymphedema, but improved it and increased strength.⁹³ Acupuncture increased shoulder range of motion and decreased lymphedema and its symptoms of heaviness and tightening in a small study by Alem and Gurgel.⁹⁴

• Dermatitis from Radiation Therapy

Calendula cream applied multiple times daily to the skin being irradiated may reduce the severity of dermatitis from therapy.⁹⁵



SYMPTOM	TREATMENT
Fatience	Exercise
ratigue	Acupuncture
Post menopausal hot flashes	 Medications such as SSRI's, SNRI's, and gabapentin Acupuncture
Nausea and vomiting due to chemotherapy	 Exercise Acupuncture Ginger Cannabis
Anxiety, stress, depression	 Acupuncture Mindfulness Based Stress Reduction Art Therapy Exercise Yoga Massage Support groups
Insomnia	 Exercise Melatonin Relaxation techniques Sleep hygiene
Pain and peripheral neuropathy	 Acupuncture Exercise Cannabinoids Massage Mind-body therapies
Lymphedema	AcupunctureExerciseLymphatic massage
Radiation dermatitis	Calendula cream

Therapeutic Review: Treatment of Symptoms in Cancer Treatment

Patient Education

Three patient handouts related to breast cancer care and prevention are also available.

- Breast Cancer Care and Prevention: Guidelines for a Healthy Lifestyle
- Breast Cancer Care and Prevention: Non-Drug Approaches
- Integrative Ways to Reduce Side Effects of Breast Cancer Treatment

PEARLS FOR CLINICIANS



WEB RESOURCES⁹⁶

	Summary of important	To subscribe to newsletters, email:
InspireHealth	research studies that	mwiebe@inspirehealth.ca
Integrated Cancer Care	inform integrative cancer	Hard copy or electronic copy.
Research Updates	care. International	Phone: 604-734-7125 1330 West 8 th
·	studies reviewed.	Avenue, Vancouver, BC V6H 4A6
	Monographs sited in	Brovention
	references on the	Prevention:
	research of exercise and	http://onlinelibrary.wiley.com/doi/10.3322/
American Cancer	nutrition in the	Caac.20140/pui
Society	prevention, and during	bttp://enlinelibrory.wiley.com/doi/10.2222/
-	and after cancer	http://onlinelibrary.wiley.com/doi/10.3322/
	treatment.	caac.21142/pui
Susan G. Komon	Dedicated to education	
Broast Cancor	and research about	
Eoundation	causes, treatment, and	www.komen.org
Foundation	the search for a cure.	
Society for Integrative		www.integrativeonc.org
Oncology	International	
	organization of clinicians,	Deng GE, Frenkel M, Cohen L et al.
Monograph available	researchers and others	Evidence-based clinical practice
for integrative	interested in evidence	guidelines for integrative oncology:
oncology practice	based integrative	complementary therapies and botanicals.
guidelines.	oncology	J Soc Integrative Oncology 2009;7(3):
		85-120.
	Breast Cancer	
	Recovery's mission is to	
	help women heal in	
Broast Cancor	mind, body and spirit	www.bcrecovery.org
Breast Cancer Recovery	after breast cancer. All	www.bcrecovery.org
Recovery	programs are designed	
	and conducted by	
	survivors for survivors.	
National Institutes of		
Health, National Cancer	Evidence based	
Institute (NCI) Office of	information on CAM and	http://www.cancer.gov/cancertopics/cam
Cancer Complementary	its applications in	
and Alternative	oncology	
Medicine (OCCAM)		



WEB RESOURCES (con't.)

National Institutes of Health, Office of Dietary Supplements	Provides information on dietary supplements. The PubMed Dietary Supplement Subset succeeds the International Bibliographic Information on Dietary Supplements (IBIDS) database active from 1999-2010.	<u>http://www.dietary-</u> <u>supplements.info.nih.gov</u> <u>http://ods.od.nih.gov/Research/PubMed</u> <u>Dietary_Supplement_Subset.aspx</u>
Memorial Sloan- Kettering Cancer Center	Maintains a searchable database that provides evidence-based information on herbs, botanicals, vitamins, and other supplements. It includes evaluations of alternative or unproven cancer therapies.	<u>http://www.mskcc.org/mskcc/html/1157</u> <u>0.cfm</u>
Natural Standard	Evidence based review of CAM therapies. Founded by clinicians and researchers.	www.naturalstandard.com
The University of Texas MD Anderson Cancer Center	Evidence based review of CAM and integrative medicine therapies.	www.mdanderson.org/CIMER
Natural Medicines Comprehensive Database	Subscription service for evidence based reviews of supplements and botanicals. Excellent patient version handouts.	www.naturaldatabase.com

References:

- 1. Alschuler LN, Gazella KA. The definitive guide to cancer: an integrative approach to prevention, treatment, and healing. Berkeley: Celestial Arts; 2010.
- 2. Jemal A, Siegel R, Xu J, Ward E. Cancer statistics 2010. CA Cancer J Clin 2010;60:277-300.
- 3. Jemal A, Murray T, Ward E, et al. Cancer Statistics 2005. CA Cancer J Clin 2005;55:10-30.
- 4. Pasqualini JR, Schatz B, Varin C, et al. Recent data on estrogen sulfatases and sulfotransferases activities in human breast cancer. J Steroid Biochem Mol Biol 1992; 41:323-329.
- 5. Dumestrescu RG, Cotarla I. Understanding breast cancer risk where do we stand in 2005? J Cell Mol Med 2005;9:208-221.
- 6. Collaborative Group on Hormonal Factors in Breast Cancer: Familial breast cancer: collaborative reanalysis of individual data from 52 epidemiological studies including 58,209 women with breast cancer and 101,986 women without the disease. Lancet 2001;358:1389-1399.



- 7. Costanza ME and Chen WY. Epidemiology and risk factors for breast cancer. UpToDate <u>www.uptodate.com</u> Updated October 5, 2010.
- Li CI, Chlebowski RT, Freiberg M, et al. Alcohol consumption and risk of postmenopausal breast cancer by subtype: the Women's Health Initiative Observational Study. J Natl Cancer Inst 2010;10218:1422-1431.
- 9. Deandra S, Talamini R, Foschi R, et al. Alcohol and breast cancer risk defined by estrogen and progesterone receptor status: a case control study. Cancer Epidemiology Biomarkers and Research 2008;178:2025-2028.
- Rock, C. L., Doyle, C., Demark-Wahnefried, W., Meyerhardt, J., Courneya, K. S., Schwartz, A. L., Bandera, E. V., Hamilton, K. K., Grant, B., McCullough, M., Byers, T. and Gansler, T. (2012), Nutrition and physical activity guidelines for cancer survivors. CA: A Cancer Journal for Clinicians, 62: 242–274. doi: 10.3322/caac.21142
- 11. Rolls BJ, Drewnowski A, Ledikwe JH. Changing the energy density of the diet as a strategy for weight management. J Am Diet Assoc 2005:105(suppl):s98-s103.
- 12. DeSilva M, Senarath U, Gunatilake M, et al. Prolonged breastfeeding reduces risk of breast cancer in Sri Lankan women: a case-control study. Cancer Epidemiology 2010;343:267-273.
- 13. Awatef M, Olfa G, Imed H, et al. Breastfeeding reduces breast cancer risk: a case-controlled study in Tunisia. Cancer Causes and Control 2010;213:393-397.
- 14. Megdal SP, Kroenke CH, Laden F et al. Night work and breast cancer risk: a systematic review and meta-analysis. Eur J Cancer 2005;41:2023-2032.
- 15. Hanson J. Increased breast cancer risk among women who work predominantly at night. Epidemiology 2001;12:74-77.
- Schernhammer ES, Rosner B, Willett W, et al. Epidemiology of urinary melatonin in women and its relation to other hormones and night work. Cancer Epidemiology Biomarkers Prev 2004:13:936-943.
- Kushi, L. H., Doyle, C., McCullough, M., Rock, C. L., Demark-Wahnefried, W., Bandera, E. V., Gapstur, S., Patel, A. V., Andrews, K., Gansler, T. and The American Cancer Society 2010 Nutrition and Physical Activity Guidelines Advisory Committee (2012), American Cancer Society guidelines on nutrition and physical activity for cancer prevention. CA: A Cancer Journal for Clinicians, 62: 30–67. doi: 10.3322/caac.20140
- 18. Clemons M, Goss P. Estrogen and the risk of breast cancer. N Engl J Med 2001;344:276-285.
- 19. Lord RS, Bongiovanni B, Bralley JA. Estrogen metabolism and the diet-cancer connection: rationale for assessing the ratio of urinary hydroxylated estrogen metabolites. Altern Med Rev 2002;7:112-129.
- 20. Kabat GC, O'Leary ES, Gammon MD, et al. Estrogen metabolism and breast cancer. Epidemiology 2006;17:80-88.
- 21. Cottet V, Touvier M, Fournier A, et al. Postmenopausal breast cancer risk and dietary patterns in the E3N-EPIC prospective cohort study. J Epidemiol 2009;17010:1257-1267.
- 22. Bentz AT, Schneider CM, Westerlind KC. The relationship between physical activity and 2hydroxyestrone, 16 alpha-hydroxyestrone, and the 2/16 ratio in premenopausal women. Cancer Causes Control 2005;16:455-461.
- 23. Terry P, Wolk A, Persson I, et al. Brassica vegetables and breast cancer risk. JAMA 2001;285:2975-2977.
- Brasky TM, Lampe JW, Potter JD, et al. Specialty supplements and breast cancer risk in the vitamins and lifestyle (VITAL) cohort. Cancer Epidemiol Biomarkers Prev 2010;197:1696-708. BMC Cancer 2009:9216.
- 25. Kim J, Lim SY, Shin A, et al. Fatty fish and fish omega-3 fatty acid intakes decrease the breast cancer risk: a case-control study. BMC Cancer 2009;9:216.
- 26. Ogunleye AA, Xue F, Michels KB. Green tea consumption and breast cancer risk or recurrence: a meta-analysis. Breast Cancer Research and Treatment 2010;1192:477-484.
- 27. Huang X, Holman CD. Dietary intakes of mushrooms and green tea combine to reduce the risk of breast cancer in Chinese women. International Journal of Cancer 2009;1246:1404-1408.

PEARLS FOR CLINICIANS



- 28. Messina M, Wu AH. Perspectives on the soy-breast cancer relation. Am J Clin Nutr 2009;895:1673s-1679s.
- 29. Chen XO, Zheng Y, Cai H, et al. Soy food intake and breast cancer survival. JAMA 2009;302(22):2437-2443.
- 30. Kang X, Zhang Q, Wang S, et al. Effect of soy isoflavones on breast cancer recurrence and death for patients receiving adjuvant endocrine therapy. CMAJ 2010;182(17):1857.
- 31. Iwasaki M, Hamada GS, Nishimoto IN, et al. Dietary isoflavone intake and breast cancer risk in case controlled studies in Japanese, Japanese Brazilians, and non-Japanese Brazilians. Breast Cancer Res Treat 2009;1162:401-411.
- 32. Cho YA, Kim K, Park S, et al. Effect of dietary soy intake non breast cancer risk according to menopause and hormone receptor status. Eur J Clin Nutr 2010;649:924-932.
- 33. Thompson LU, Chen JM, Li T, et al. Dietary flaxseed alters tumor biological markers in postmenopausal breast cancer. Clin Cancer Res 2005;11:3828-3835.
- 34. Mignone LI, Giovannucci E, Newcomb PA, et al. Dietary carotenoids and the risk of invasive breast cancer. International Journal of Cancer 2009;12412:2929-2937.
- 35. Tripathy D. Integrative Medicine and Breast Cancer. In Integrative Oncology. Eds. Abrams D and Weil A. Oxford: Oxford Press, 2009:396-412.
- 36. Murray M, Pizzorno J, Pizzorno L. The encyclopedia of healing foods. New York: Atria Books, 2005.
- 37. Brew CT, Aronchik I, Hsu JC, et al. Indole 3 carbinol activates the ATM signaling pathway independent of DNA damage to stabilize p53 and induce G1 arrest of human mammary epithelial cells. Int J Cancer 2006;118:857-868.
- 38. Ambrosone CB, McCann SE, Freudenheim JL, et al. Breast cancer risk in premenopausal women is inversely associated with consumption of broccoli, a source of isothiocyanates, but is not modified by GST genotype. J Nutr 2004;134:1134-1138.
- 39. Fowke JH, Chung FL, Jin G, et al. Urinary isothiocyanate levels, brassica and human breast cancer. Cancer Res 2003;63:3980-3986.
- 40. Schwartz AL. Cancer Fitness: exercise programs for patients and survivors. New York: Simon and Schuster, 2004.
- 41. Saeed SA, Antonacci DJ, Bloch RM. Exercise, yoga and meditation for depressive and anxiety disorders. Am Fam Physician 2010;81(8):981-986.
- 42. West-Wright CN, Henderson KD, Sullivan-Halley J, et al. Long-term and recent recreational physical activity and survival after breast cancer: the California teacher's study. Cancer Epidemiology Biomarkers and Prevention 2009;1811:2851-2859.
- 43. Griffith K, Wenzel J, Shang J, et al. Impact of a walking intervention on cardio-respiratory fitness, self-reported physical function, and pain in patients undergoing treatment for solid tumors. Cancer 2009;11520:4874-4884.
- 44. Meyer C. Scientists probe role of vitamin D. JAMA 2004;292(12):1416-1418.
- 45. Bordelon P, Ghetu MV, Langan R. Recognition and management of vitamin D deficiency. Am Fam Physician 2009;80(8):841-846.
- 46. Edlich R, Mason SS, Chase ME, et al. Scientific documentation of the relationship of vitamin D deficiency and the development of cancer. Journal of Environmental Pathology, Toxicology and Oncology 2009;282:133-141.
- 47. Blackmore KM, Lesosky M, Barnett H, et al. Vitamin D from dietary intake and sunlight exposure and the risk of hormone-receptor-defined breast cancer. Am J Epidemiol 2008;1688:915-924.
- 48. Garland CF, Gorham ED, Mohr SB, Garland FC. Vitamin D for cancer prevention: global perspective. Ann Epidemiol 2009;197:468-483.
- 49. Bischoff-Ferrari HA. Optimal serum 25 hydroxyvitamin D levels for multiple health outcomes. Adv Exp Med Biol 2008;624:55-71.
- 50. Ingraham BA, Bragdon B, Nohe A. Molecular basis of the potential of vitamin D to prevent cancer. Curr Med Res Opinion 2008;241:139-149.



- 51. Garland CF, Gorham ED, Mohr SB et al. Vitamin D and prevention of breast cancer: pooled analysis. J Steroid Biochem Mol Biol 2007;1033(5):708-711.
- 52. Holick MF. Sunlight, uv-radiation, vitamin D and skin cancer: how much sunlight do we need? Adv Exp Med Biology 2008;6241:15.
- 53. Natural Standard Research Collaboration: an evidence based systematic review of melatonin. <u>www.naturalstandard.com</u>
- 54. Blask DE, Daughy RT, Sauer LA. Putting cancer to sleep at night: the neuroendocrine/ circadian melatonin signal. Endocrine 2005;27:179-188.
- 55. Andersen BL, Yang HC, Farrar WB, et al. Psychological intervention improves survival for breast cancer patients: a randomized controlled trial. Cancer 2008;11312:3450-3458.
- 56. Courneya KS. Exercise in cancer survivors: an overview of research. Med Sci Sports Exerc 2003;35:1846-1852.
- 57. Dean-Clower E, Doherty-Gilman AM, Keshaviah A, et al. Acupuncture as palliative therapy for physical symptoms and quality of life for advanced cancer patients. Integrative Cancer Therapies 2010;92:158-167.
- 58. Takahashi H. Effects of acupuncture on terminal cancer patients in home care setting. Medical Acupuncture 2009;212:123-129.
- 59. Rada G, Capurro D, Pantoja T, et al. Non-hormonal interventions for hot flushes in women with a history of breast cancer. Cochrane Database of Systematic Reviews 2010: 9004923.
- 60. Bayles B, Usatine R. Evening primrose oil. Am Fam Physician 2009;80(12):1405-1408.
- 61. Walker EM, Rodriguez AI, Kohn B, et al. Acupuncture versus venlafaxine for the management of vasomotor symptoms in patients with hormone-receptor-positive breast cancer: a randomized controlled trial. J Clin Oncology 2010;284:634-640.
- 62. DeValois BA, Young TE, Robinson N, et al. Using traditional acupuncture for breast cancer-related hot flashes and night sweats. J Alternative and Complementary Medicine 2010;1610:1047-1057.
- 63. Hervik J and Mjaland O. Acupuncture for the treatment of hot flashes in breast cancer patients: a randomized controlled trial. Breast Cancer Res Treat 2009;1162:311-316.
- 64. Obi N, Chang-Claude J, Berger J, et al. The use of herbal preparations to alleviate climacteric disorders and risk of postmenopausal breast cancer in a German case-control study. Cancer Epidemiology, Biomarkers, and Prevention 2009;188:2207-2213.
- 65. Ruhlen RL, Haubner J, Tracy JK, et al. Black cohosh does not exert an estrogenic effect on the breast. Nutr Cancer 2007;59(2):269-77.
- Otte JL, Carpenter JS, Russell KM, et al. Prevalence, severity, and correlates of sleep-wake disturbances in long-term breast cancer survivors. J Pain and Sympt Management 2010;39(3):535-547.
- 67. Berger AM, Farr L. The influence of daytime inactivity and nighttime restlessness on cancer-related fatigue. Oncol Nurs Forum 1999;26:1663-1671.
- 68. Deng GE, Frenkel M, Cohen L et al. Evidence-based clinical practice guidelines for integrative oncology: complementary therapies and botanicals. J Soc Integrative Oncology 2009;7(3):85-120.
- 69. Lee MS, Choi TY, Park JE, et al. Moxibustion for cancer care: a systematic review and metaanalysis. BMC Cancer 2010:10130.
- 70. NIH Consensus Statement on Acupuncture. (1997). http://consensus.nih.gov/1997/1997Acupuncture107html.htmInt.
- 71. Roscoe JA, Jean-Pierre P, Morrow GR, Hickok JT, Issell B, Wade JL, et al. Exploratory analysis of the usefulness of acupressure bands when severe chemotherapy-related nausea is expected. J Society for Integrative Oncology 2006;4:16–20.
- 72. Lee J, Dodd MJ, Dibble SL, et al. Nausea at the end of adjuvant cancer treatment in relation to exercise during treatment in patients with breast cancer. Oncol Nurs Forum 2008;9(355):830-835.
- 73. Pittler EE. Efficacy of ginger for nausea and vomiting: A systematic review of randomized clinical trials. Br J Anaesth 2000;84:367-371.



- 74. Machado Rocha FC, Stefano SC, Haiek RC, Oliveira LM, Da Silveira DX. Therapeutic use of Cannabis sativa on chemotherapy-induced nausea and vomiting among cancer patients: systematic review and meta-analysis. *European Journal of Cancer Care*.2008;**17**(5):431-443.
- 75. Matousek, RH, Dobkin PL. Weathering storms: a cohort study of how participants in a mindfulnessbased stress reduction program benefits women after breast cancer treatment. Current Oncology 2010;174:62-70.
- 76. Foley E, Baillie A, Price M et al. Mindfulness-based cognitive therapy for individuals whose lives have been affected by cancer:a randomized controlled trial.J Consult Clin Psychol 2010;781:72-79.
- 77. Svensk A, Oster I, Thyme E et al. Art therapy improves experienced quality of life among women undergoing treatment for breast cancer: a randomized controlled study. European Journal of Cancer Care 2009;181:69-77.
- 78. Rao MR, Raghuram N, Nagendra HR, et al. Anxiolytic effects of a yoga program in early breast cancer patients undergoing conventional treatment: a randomized controlled trial. Complement Ther Med 2009;171:1-8.
- 79. Danhauer SC, Tooze JA, Farmer DF et al. Restorative yoga for women with ovarian or breast cancer: findings from a pilot study. J Soc Integrative Oncology 2008;6(2):47-58.
- 80. Stringer J, Swindell R, Dennis M. Massage in patients undergoing intensive chemotherapy reduces serum cortisol and protein. Psychooncology 2008;1710:1024-1031.
- 81. Spiegel D, Bloom JR, Kraemer HC, & Gottheil E. Effect of psychosocial treatment on survival of patients with metastatic breast cancer. Lancet 1989;2(8668), 888–891.
- Edmonds CV, Lockwood GA, & Cunningham AJ. Psychological response to long-term group therapy: A randomized trial with metastatic breast cancer patients. Psycho-oncology 1999;8:74–91.
- 83. Edelman S, Bell DR, & Kidman AD. A group cognitive behaviour therapy programme with metastatic breast cancer patients. Psycho-oncology 1999;8:295–305.
- Goodwin PJ, Leszcz M, Ennis M, Koopmans J, Vincent L, Guther H, et al. The effect of group psychosocial support on survival in metastatic breast cancer. New Engl J Med 2001;345:1719– 1726.
- 85. Classen C, Butler LD, Koopman C, Miller E, DiMiceli S, Giese-Davis J, et al. Supportive-expressive group therapy and distress in patients with metastatic breast cancer: A randomized clinical intervention trial. Archives of General Psychiatry 2001;58:494–501.
- 86. Zimmerman T, Heinrichs N, Baucom DH. Does one size fit all? Moderators in psychosocial interventions for breast cancer patients: a meta-analysis. Ann Behavioral Med 2007;343:225-239.
- 87. Devine EC, Westlake SK. The effects of psycho-educational care provided to adults with cancer: meta-analysis of 116 studies. Oncol Nurs Forum 1995;22:1369-81.
- Carlson LÉ, Speca M, Patel KD, & Goodey E. Mindfulness-based stress reduction in relation to quality of life, mood, symptoms of stress and levels of cortisol, dehydroepiandrosterone sulphate (DHEAS) and melatonin in breast and prostate cancer outpatients. Psychoneuroendocrinology 2004;29:448–474.
- 89. Espie CA, Fleming L, Cassidy J, et al. Randomized Controlled clinical effectiveness trial of cognitive behavior therapy compared with treatment as usual for persistent insomnia in patients with cancer. J Clinical Oncology 2008;2628:4651-4658.
- 90. Abrams DI, Guzman M. Cannabinoids and Cancer. In Integrative Oncology eds. Abrams D and Weil A. Oxford: Oxford University Press, 2009:147-170.
- 91. Astin JA, Shapiro SL, Eisenberg DM, and Forys KL. Mind-Body Medicine: State of the Science, Implications for Practice. J Am Board Fam Pract 2003;16:131-147.
- 92. McNeely ML, Campbell K, Ospina M, et al. Exercise interventions for upper limb dysfunction due to breast cancer treatment. Cochrane Database of Systematic Reviews 2010:6005211.
- 93. Schmitz KH, Ahmed RL, Troxel A, et al. Weight lifting in women with breast-cancer-related lymphedema. N Engl J Med 2009;3617:664-673.
- 94. Alem M, and Gurgel MSC. Acupuncture in the rehabilitation of women after breast cancer surgerya case series. Acupuncture Med 2008;262:86-93.



- 95. Kassab S, Cummings M, Berkovitz S, et al. Homeopathic medicines for adverse effects of cancer treatments. Cochrane Database of Systematic Reviews 2009.
- 96. Marchand L. Breast Cancer. In Integrative Medicine, Third Edition. Ed. Rakel D. Philadelphia: Saunders Elsevier, 2012.

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