Nutrition & Breast Cancer

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Good nutrition may reduce the incidence of breast cancer and the risk of breast cancer progression or recurrence. There are many studies in progress to help further understand how diet and cancer are related. We do know, however, that improved nutrition reduces risk of chronic diseases, such as diabetes, obesity, hypertension and heart disease, and also enhances overall quality of life. It is estimated that one third of cancer deaths in the U.S. can be attributed to diet in adulthood [1].

Guidelines for a Healthy Diet

- Plant-based diet

    o Plenty of fruits and vegetables

    o High fiber – beans/legumes, seeds, whole grains

- Include protein with every meal - aim to include plant protein daily

- Low/moderate fat diet with emphasis on healthy fats

- Limit processed and refined grains/flours/sugars

- Drink plenty of fluids

- Be physically active to help achieve and/or maintain a healthy weight
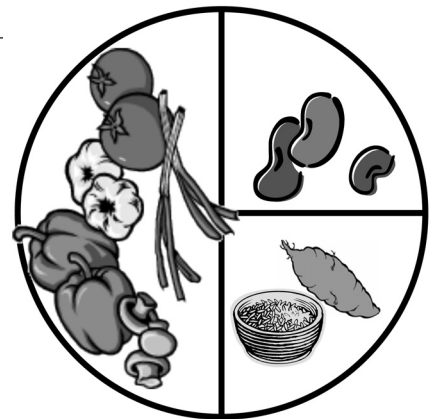
Healthy Plate Diagram
Fill your plate with approximately 50% (or more) vegetables, 25% (or more) protein, and up to 25% starchy vegetable or whole grain.

Plant based diet

A lifelong commitment to a plant based diet may lower a woman's risk of developing breast cancer and may also reduce the risk of recurrent breast cancer. A plant based diet consists primarily of fruits, vegetables, beans/legumes, nuts/seeds and whole grains. A large cohort* study with over 91,000 women showed a plant-based diet was associated with a 15% reduction in breast cancer risk; this effect was even more significant for those with estrogen-receptor negative and progesterone-receptor negative (ER-/PR-) tumors [2]. Similarly, following a Mediterranean dietary pattern of vegetables, fish and olive oil, legumes, and fruit was independently associated with a decreased risk of breast cancer [3].

* All words noted with an asterisk (*) are defined in the glossary on page 54.

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SUMMARY - HEALTHY BREAST CANCER DIET

- Eat 8 to 10 <u>colorful</u> fruit and vegetable servings daily

  o Two to three pieces of fruit

  o One cup or more of vegetables with lunch and dinner

  o 8 fl oz vegetable juice

- Consume 30 to 45 grams of fiber daily

  o You will likely meet your fiber goal if you eat 8 to 10 servings of fruits and vegetables plus one serving of beans/legumes, one serving of chia and/or flax seed, or at least two servings of whole grains daily.

- Avoid processed and refined grains/flours/sugar

  o Keep WHITE off your plate: bread, pasta, rice, cream sauces, cakes, and more.

- Lean protein with every meal; plant protein daily

- Limit fatty & processed meats, and dairy

- Include healthy fats like cold-water fish, chia seeds, flaxseeds, walnuts, soybeans, olive oil, avocados

- Eat chia seeds and ground flax daily   — 1-2 Tbsp daily

- Consume herbs and spices daily

- Limit alcohol consumption

- Drink 1 to 4 cups of green tea daily

- Ask your doctor about having a vitamin D blood test (serum 25 (OH)-vitamin D level). Maintain your level above 40 ng/ml through diet and, if needed, supplements

- Drink plenty of fluids, water or non-caffeinated beverages, daily to help meet fluid needs

- Engage in daily physical activity to help achieve and/or maintain a healthy weight

FRUITS AND VEGETABLES

- Contain vitamins, minerals, fiber, and various cancer-fighting phytonutrients* (for example: carotenoids, lycopene, indoles, isoflavones, flavonols).

- Vibrant, intense COLOR is one indicator of phytonutrient* content.

- There is extensive and consistent evidence that diets high in fruits and vegetables are associated with decreased risks of many cancers, and while results for breast cancer risk are not yet conclusive, they are promising [2-26].

- In a study of about 3,000 postmenopausal women, a protective effect for vegetables was observed [4].

  o Women who consumed 25 or more servings of vegetables weekly had a 37% lower risk of breast cancer compared with women who consumed fewer than 9 vegetable servings weekly.

- An epidemiological* study reported a significant protective effect of vegetables against breast cancer when case-control* and cohort* studies were considered together [6].

- A meta-analysis* – looking at the data from 17 studies [27] revealed that high vs. low vegetable consumption was associated with a 25% reduction in breast cancer risk, but these findings were not confirmed by data collected from 8 studies [28].

- A study of over 31,000 women showed an inverse association between vegetable consumption and breast cancer risk [23]. Vegetables of note were leafy vegetables, fruiting vegetables (peppers, tomatoes, eggplant), and raw tomatoes.

- In a cohort* study of nearly 21,000 participants, high consumption of fruit and salad was associated with a reduced risk of breast cancer, particularly in ER-/PR- tumors [15].

- A recent case-control* study reported women who consumed more than 3.8 servings of fruits and vegetables daily had a lower risk of breast cancer when compared with women who consumed fewer than 2.3 daily servings [29].

- Japanese women following a prudent dietary pattern (high in fruits and vegetables, low in fat) had a 27% decreased risk of breast cancer [7].

- A diet characterized by vegetables, fruit, and soy lowered risk of breast cancer among postmenopausal women by 30%; this effect was even stronger (43% risk reduction) for those following this diet pattern for 5 or more years [17].

- A Korean case-control* study reported that a high intake of certain fruits and vegetables resulted in a significantly lower risk of breast cancer in premenopausal (tomatoes) and postmenopausal women (grapes and green peppers) [8].

  o Pickled vegetables, however, may increase breast cancer risk [24].

- A meta-analysis of 12 studies concluded that the risk of breast cancer decreased significantly in women with a high flavonol and flavone intake [22]. Flavonol-rich foods include onions, kale, leeks, and broccoli and flavone-rich foods include parsley, thyme, celery, oregano, and chili peppers.

- A prospective analysis that included more than 75,000 women over a period of 24 years, reported the following:

  o 18% reduced risk of ER- breast cancer in women who consumed 2 servings of berries weekly

  o 31% reduced risk of ER- breast cancer in women who consumed 1 or more servings of blueberries weekly

  o 41% risk reduction of ER- breast cancer in women who consumed 2 servings of peaches/ nectarines weekly [19]

- Limonene, a bioactive food component from citrus peel oil may lead to cell-cycle arrest and reduced cell proliferation in breast tissue [30].

- While no effect was observed for vegetables, increasing total fruit intake significantly lowered the risk of breast cancer when comparing those in the highest to lowest tertile [31].

  o This effect was greater for those with ER+ tumors.

- Eating a salad vegetable dietary pattern (high consumption of raw vegetables and olive oil) exerted a significant protective effect against HER-2-positive cancers [12].

- This study found that while specific vegetables (carrots and cruciferous vegetables) may be protective for all breast cancer types, total vegetable consumption was associated with a decreased risk of ER-/PR- breast cancer types only [32].

- In a case-control* study of 6,917 Chinese women, total vegetable intake was inversely related to breast cancer risk, as were high intake of citrus and rosaceae fruits (apples, pears, quinces, apricots, plums, cherries, peaches, raspberries, loquats, and strawberries); no difference was observed between different tumor types [16].

- The Dietary Approaches to Stop Hypertension (DASH) diet was associated with a significantly lower risk of ER- breast cancer; this effect was largely explained by higher intakes of fruits and vegetables [33]. A vegetable-based, low-carbohydrate-diet was also associated with a significantly lower risk of ER- breast cancer. No association was found between ER+ tumors and fruit and vegetable intakes.

- A study assessing plasma or blood carotenoids as a marker for fruit and vegetable intake reported that individuals in the top 1/4 had a 43% lower risk of breast cancer recurrence when compared to those in the lowest 1/4 [34].

- However, no association was observed between fruit and vegetable consumption and breast cancer recurrence when women consumed five servings daily vs. eight servings daily [35].

- Breast cancer survivors significantly reduced mortality by following a diet low in fat, high in vegetables, high in fiber, and high in fruit [36].

- The combination of consuming five or more daily servings of vegetables and fruits, and accumulating 540+ metabolic equivalent tasks-min/wk (equivalent to walking 30 minutes 6 d/wk) decreased mortality by nearly 50% [13].

    o The effect was stronger in women who had ER+ or PR+ cancers.

- Vegetable intake has been inversely associated with serum insulin-like growth factor-I (IGF-I) levels [37]. IGF-I levels have been directly associated with breast cancer.

Beta-Carotene

- Beta-carotene is one of the 600 carotenoids that can be partially converted into vitamin A in the body.

- Carotenoids have a protective role for certain sites, including breast cancer [9, 38-41].

- Carotenoid intake was significantly associated with reduced mortality in breast cancer survivors [36].

- In various studies, serum beta-carotene levels were lower among breast cancer patients compared to women without cancer [38, 42-49].

    o One of these studies reported the risk of breast cancer to be 221% greater for women in the lowest quartile of serum beta-carotene compared to women in the highest quartile [29].

    o This inverse association was stronger for ER- tumors than ER+ tumors [48].

- A case-control* study reported that increased plasma levels of beta-carotene, retinol, and total antioxidant* status were associated with about a 50% reduced risk of breast cancer [45].

- Cell studies indicate that carotenoids may inhibit the production of breast cancer cells [50-51].

    o Beta-carotene may inhibit ER+ and ER- breast tumor development [39].

- Beta-carotene may hinder the development of breast cancer cells by inhibiting cell proliferation [52], arresting cell cycle [52], and inducing apoptosis* [52-53].

- Research indicates that dietary sources of beta-carotene are likely much more protective than supplemental sources against the risk of cancer [54-56].

  o Consuming higher amounts of dietary beta-carotene, lycopene, and beta-cryptoxanthin was associated with a lower risk of breast cancer among Chinese women [40].

  o Carrot intake was inversely associated with risk of breast cancer in the Black Women's Health Study [32].

  o Dietary consumption of alpha-carotene, beta-carotene, beta-cryptoxanthin, and lutein/zeaxanthin were all associated with a lower risk of breast cancer [57] in ER- breast cancer only [58].

    • Lycopene, however, did not result in a reduction of breast cancer risk.

  o Dietary alpha-carotene, beta-carotene, and lycopene were inversely associated with risk of ER+/ PR+ breast cancer [41].

  o Dietary beta-carotene intake was inversely associated with IGF-I levels in a large case-control study [37].

Cruciferous Vegetables

- Some evidence suggests that the cruciferous vegetables, in particular, are associated with a reduced risk of breast cancer [32, 59-65].

- A recent meta-analysis* of 13 epidemiologic studies indicated that high cruciferous vegetable intake was significantly associated with a reduced risk of breast cancer [66].

- A Swedish study of postmenopausal women reported one to two daily servings of cruciferous vegetables reduced the risk of breast cancer, possibly by as much as 20-40% [62].

- Cruciferous vegetable intake was associated with a significant decrease in risk of breast cancer in Japanese premenopausal women [60]. No significant association was observed for postmenopausal women and breast cancer.

- Women who ate more turnips and Chinese Cabbage (both in the cruciferous vegetable family) significantly reduced the risk of postmenopausal breast cancer [65].

- Consumption of cruciferous vegetables, particularly broccoli, was inversely associated, though not statistically significant, with breast cancer risk in women [61].

- The U.S. component of the Polish Women's Health Study found that women who consumed raw- or short-cooked cabbage and sauerkraut 3 or more times weekly had a significantly reduced risk of breast cancer [64].

  o Cabbage that was cooked for a long time had no effect on breast cancer risk.

  o Researchers suggested that glucosinolates, compounds in cabbage, may affect both the initiation phase of carcinogenesis*, cell mutation*, and inhibit apoptosis*.

- Cruciferous vegetables appear to shift estrogen metabolism in a favorable manner; increasing 2-hydroxyestrone:16-a-hydroxyestrone [67-68]. Fowke and colleagues [68] concluded that consuming more cruciferous vegetables across the population may have an impact on the incidence of breast cancer .

- Several studies suggest that compounds found in these foods, isothiocyanates (sulforaphane), have inhibitory effects on breast cancer cells in both cell studies and animal studies [59, 63, 69-71].

  o One mechanism appears to be through potent inhibition of phase I and induction of phase II detoxifying enzymes, such as glutathione-s-peroxidase [61, 65, 70].

  o Furthermore, these compounds reduced cell proliferation and inhibited cyclooxygenase-2 (COX-2) expression in breast cancer cells [72].

  o Inhibited cell growth and induced apoptosis has also been observed [73].

  o Human breast cancer stem cells decreased significantly when benzyl isothiocyanate was introduced into the diet [69].

- Indole-3-carbinol (I3C) is a compound found in cruciferous vegetables that has anticancer properties and anti-proliferative effects on breast cancer cells [74].

  o I3C may inhibit the growth of blood vessels that the tumor needs to grow (anti-angiogenesis) [75].

- I3C and diindolylmethane (DIM) induce apoptosis*, or cell death, in breast cancer cells [67,76] for both ER+ and ER- tumor cells [77].

- Furthermore, I3C and tamoxifen have been shown to act separately and/or cooperatively to inhibit the growth of ER+ breast cancer cells [78].

- Dietary I3C may have effects that bolster immune function [79].

- Another compound in cruciferous vegetables, calcium-D-glucarate, has been shown to inhibit beta-glucuronidase, an enzyme involved in phase II liver detoxification. Elevated beta-glucuronidase activity is associated with an increased risk for various cancers, particularly hormone-dependent cancers such as breast cancer [80].

Pomegranate (Punica granatum; Punicaceae)

- Various parts of the pomegranate fruit (for example: seed oil, juice, fermented juice and peel extract) have expressed suppressive effects on human breast cancer cells in laboratory research [81].

- Pomegranate seed oil and fermented juice block the cancer cells' oxygen supply, slow cell growth, and promote cell death [82].

- Fermented pomegranate juice polyphenols* appear to have twice the anti-proliferative effect as fresh pomegranate juice polyphenols* [83].

  o Pomegranate husk, rich in ellagitannins (polyphenols*), exhibited strong anti-proliferative activity against breast cancer cell lines and inhibits oxidative DNA damage [84].

- Pomegranate juice, or a combination of its components (luteolin, ellagic acid, punicic acid) increase cancer cell adhesion and decrease migration, while leaving normal cells unaffected [85].

- Furthermore, one study suggests that pomegranate seed oil may have the greatest preventive activity (87% reduction in lesions) compared to fermented pomegranate juice (42% reduction) [86].

- Pomegranate peel extract has important antioxidant effects, and has been shown to inhibit human breast cancer cells and holds promise as a possible treatment against breast cancer [87-89].

Nutrient	Dietary Sources	Recommendation
Beta-carotene	Carrots, sweet potatoes, winter squash, cantaloupe, and mango	Include these fruits and vegetables daily.
Cruciferous vegetables	Arugula, broccoli, Brussels sprouts, cabbage, cauliflower, collard greens, horseradish, kale, kohlrabi, mustard greens, radishes, rutabaga, turnips and turnip greens, and watercress	Include these vegetables daily.
Pomegranate	Pomegranate	Consider including pomegranate or pomegranate concentrate on a regular basis.

Organic Produce

- Organic fruits and vegetables have fewer pesticides, lower levels of total pesticides, and less overall pesticide toxicity than fruits and vegetables grown with chemicals. Although more research is needed, recent evidence indicates a significant increase in antioxidants* in organic and sustainably grown foods versus conventionally grown foods [90-95].

  o Organic vegetables contained a greater concentration of phytonutrients* (phenolic acids) when compared to conventionally grown vegetables [92, 93].

  o Organic fermented beetroot juices offered stronger anticancer activity than the conventional juice [95]. Additionally, organic fresh beets contained more vitamin C than the conventional beets.

  o The extracts from organically grown strawberries had a higher content of antiproliferative activity for breast cancer cells, and displayed a 43% inhibition [96].

- Consuming organic foods appears to increase salicylic acid, which may contribute to a lower risk of cancer [92].

- Pesticides such as organochlorine compounds (OCC), known as environmental pollutants, have been implicated in the etiology of estrogen-related disorders due to their potential estrogenic and anti-estrogenic properties [94].

- Results of some studies [94, 97-98], but not all [99] suggest that environmental exposure to organochlorine pesticide residues or PCBs may contribute to multifactorial pathogenesis of breast cancer.

  o In a study of women living on Long Island, New York, breast cancer risk was associated with lifetime residential pesticide use [100].

  o Organochlorine pesticide residues, including DDTs and HCHs, may increase women's risk of breast cancer, particularly in premenopausal women in China [97].

  o In mice, exposure to beta-HCH, an organochlorine pesticide residue, both accelerated the appearance and incidence of breast cancer tumors when compared to controls mice [98].

- The level of exposure may be integral in determining the effects of these OCC.

  o One study found that when breast adipose tissue reached levels higher than 2600 ppb, women with postmenopausal ER+ breast cancer exhibited high proliferation [101].

- Choosing organic produce will help you reduce your levels of pesticide exposure and will most likely increase your phytonutrient* consumption.

  o Although washing and peeling your non-organic fruits or vegetables may help to reduce pesticide residues, it will not eliminate them.

- Listed below are produce with the most and least pesticide contamination, both in terms of number of pesticides used and the level of pesticide concentration on an average sampling. Thus, for the fruits and vegetables shown on the most contaminated list, it is wise to buy organic. Alternatively, if organic choices are not available, you may want to consider substituting with produce that tends to contain the least amount of pesticides.

Produce most contaminated by pesticides:	Produce least contaminated by pesticides:
Apples	Avocados
Peaches	Sweet corn
Nectarines	Pineapple
Strawberries	Cabbage
Grapes	Sweet peas
Celery	Onions
Spinach	Asparagus
Sweet bell peppers	Mangos
Cucumbers	Papayas
Cherry tomatoes	Kiwi
Snap peas - imported	Eggplant
Potatoes	Grapefruit

**Adapted from Environmental Working Group – A Shopper's Guide to Pesticides in Produce

- **It is most important,** however, to eat fruits and vegetables – organic or conventional. If the availability or cost of organic produce is a barrier, you may wish to avoid those fruits and vegetables that have the highest pesticide residue content.

FIBER – A PLANT-BASED DIET IS NATURALLY HIGH IN FIBER

- A diet rich in natural fiber obtained from fruits, vegetables, legumes (for example: lentils, split peas, black beans, pinto beans), and whole-grains may reduce cancer risk and/or reduce risk of cancer progression.

- Fiber binds to toxic compounds and carcinogens, which are then later eliminated from the body [102].

- Various mechanisms have been proposed for the protective effects of dietary fiber against cancer. These include:

  o Increased fecal bulk and decreased intestinal transit time, which allow less opportunity for fecal mutagens to interact with the intestinal epithelium [103].

  o Binding to bile acids, which are thought to promote cell proliferation [104].

- o Fermentation in the gut, producing short-chain fatty acids (SCFA). SCFA improve the gut environment and may provide immune protection beyond the gut [103, 104].

- o Additionally, whole grains are rich in antioxidants*, including trace minerals and phenolic compounds, which have been linked to disease prevention [104].

- Furthermore, a high fiber diet works to reduce hormone levels that may be involved in the progression of breast cancer [103, 105-108].

  - o A high-fiber, low-fat diet intervention found that fiber reduced serum estradiol* (estrogen breaks down into estradiol* in the body) concentration in women diagnosed with breast cancer, the majority of whom did not exhibit weight loss. Thus, increased fiber intake was independently related to the reduction in serum estradiol* concentration [107].

  - o This decrease in estrogen levels in the blood thereby may potentially reduce the risk of hormone-related cancers, such as breast cancer.

  - o Reduced levels of serum estrone* and estradiol* were observed in premenopausal women with a greater intake of dietary fiber [106].

  - o Similarly, a high intake of dietary fiber was significantly associated with low serum levels of estradiol in postmenopausal breast cancer survivors [108].

  - o Dietary fiber intake increases the amount of estrogen excreted in the stool [109].

- A high fiber diet is also associated with less obesity [105] - a risk factor for postmenopausal breast cancer.

- A high fiber diet may also lower cancer risk via reduced inflammation. Breast cancer survivors who consumed >15.5 g/day of insoluble dietary fiber had a 49% reduction in the likelihood of having an elevated C-reactive protein (CRP) concentration, a biomarker that assesses inflammation [110].

- A meta-analysis* of 10 prospective cohort studies and 16,848 cases showed that for every 10 g fiber/day increase, there was an associated 7% reduction in breast cancer risk [111].

- In a study of 11,576 breast cancer cases, risk was inversely linked to total dietary fiber intake and fiber from vegetables [112]. The risk reduction was even more pronounced in ER-/PR- women.

- Similarly, soluble fiber intake was associated with a significantly reduced risk of breast cancer in pre-menopausal women; this effect was greatest in women with ER- tumors [113].

- A high fiber diet was associated with a lower risk of breast cancer in both pre- and post-menopausal women [114].

- In a study of women with primary breast cancer, a significant inverse association (69% reduced risk) was found between dietary fiber and breast cancer risk in ER+, ER-, PR+, ER+PR+, and ER-PR+ tumors [115].

- Total dietary fiber intake, particularly from cereals and fruit, was found to significantly reduce the risk of breast cancer in pre-menopausal, but not post-menopausal women [116].

- A recent cohort* study reported that high fiber intake was associated with a 42% lower risk of postmenopausal breast cancer, when comparing women in the highest quintile of fiber intake compared to the lowest quintile [117].

- An earlier prospective cohort* study, however, reported no protective effect of fiber against breast cancer when comparing women who consumed fewer than 26 grams dietary fiber compared to those who consumed even less [118]. This finding is not surprising given that the total grams of fiber consumption was less than 30 grams.

    o Similarly, another study that reported no significant findings compared women consuming less than 25 g fiber daily [119].

- Overall, case-control* studies have reported the greater the fiber intake, the lower the incidence of breast cancer [10, 114, 120-123]. Data from prospective studies is mixed, reporting protective effects [117, 124-125] or no effect observed [118, 119].

- Women who ate beans and lentils at least twice a week had a 24% lower risk of developing breast cancer than women who ate them less than once a month [126]. More recently, consumption of legumes was found to be inversely associated with breast cancer [16].

High-Fiber Sources

FRUITS:

Food	Serving Size	Fiber Grams/ Serving
Apple	1 medium	3.7
Banana	1 medium	2.8
Blackberries	1/2 cup	1.9
Blueberries	1 cup	1.3
Cantaloupe	1/2 cup	6.0
Figs (dried)	1/4 cup	6.0
Grapefruit	1 medium	3.4
Grapes	1 cup	1.6
Guava	1 medium	4.9
Kiwi	1 medium	2.6
Orange	1 medium	3.1
Pear	1 medium	4.0
Persimmon	1 medium	6.0
Prunes	1/4 cup	3.1

GRAINS & OTHER PRODUCTS:

Food	Serving Size	Fiber Grams/ Serving
Amaranth	1/4 cup dry	7.4
Barley	1/2 cup cooked	3.0
Beans, black	1/2 cup cooked	8.3
Beans, red kidney	1/2 cup cooked	8.2
Beans, garbanzo	1/2 cup cooked	5.0
Bran cereals	3/4 cup	Check labels (5.0-22.0)
Brown rice	1/2 cup cooked	1.4
Bulgur	1/2 cup cooked	4.0
Oatmeal	1/2 cup cooked	2.0
Peanuts	1/4 cup	2.9
Quinoa	1/4 cup dry	2.5

VEGETABLES:

| Food	Serving Size	Fiber Grams/ Serving
Artichokes	1 medium	6.9
Beets	1/2 cup cooked	1.7
Broccoli	1/2 cup cooked	2.3
Brussel sprouts	1/2 cup cooked	2.0
Carrots	1/2 cup cooked	2.6
Kale	1/2 cup cooked	1.3
Lima beans	1/2 cup cooked	4.5
Peas, green	1/2 cup cooked	4.4
Spinach	1/2 cup cooked	2.2
Squash, winter-type	1/2 cup cooked	3.4
Sweet potatoes (yams)	1/2 cup cooked	2.7

SUGARS AND THE ROLE OF INSULIN*

- High sugar foods are usually highly processed and refined, low in nutrient value, and also low in dietary fiber. In addition, these foods appear to increase serum insulin* and serum insulin-like growth factor (IGF-I) levels [127], which stimulate cancer cell growth.

    o Overexpression, or high amounts, of IGF increases mammary tumors in mice [128].

    o IGF's may work by stimulating cell cycle progression and prevent cells from premature death [129-132].

    o IGF-I may promote tumor growth via upregulation of ovarian steroid secretion [132-133].

    o Research indicates a synergistic effect between IGF-I and estrogen [134] as well as IGF-I and insulin* resistance [135] in breast cancer.

- Women in the highest quintile of IGF-I level had a 310% increased risk of all-cause mortality [136].

- A prospective cohort* study observed a significant 310% increased risk of breast cancer in premenopausal women who had the highest quartile of IGF-I compared to women with the lowest quartile [132].

  o A weaker association was found with fasting insulin* levels where premenopausal women in the two highest quartiles had a 70% greater risk for breast cancer.

  o In premenopausal women, women in the highest quartile of serum glucose had a 280% increased risk of breast cancer compared with women in the lowest quartile.

  o In postmenopausal women, the associations of glucose, insulin*, and IGF-I were associated with breast cancer risk in heavier subjects (BMI>26[1]).

  o Overall, these findings indicate that chronic change of glucose/sugar metabolism is related to breast cancer development.

- Other studies support a stronger link between IGF-I and breast cancer in premenopausal women [131, 137].

- Additionally, a case-control* study in China found that IGF-I significantly increased the risk of breast cancer [135].

- IGF-I levels were positively associated with the risk of ER+ breast tumors (pre- and postmenopausal women combined) and among women who were diagnosed with breast cancer at 50 years or older [138].

- Nonetheless, a meta-analysis* review of 18 studies reported no overall statistically significant association between circulating IGF-I levels and risk of breast cancer although the levels were greater in breast cancer patients than controls [130].

  o However, IGF-I levels did appear to increase breast cancer risk in premenopausal women by almost 40%.

- Similarly, a large prospective trial reported IGF-I significantly increased risk of breast cancer in premenopausal women under the age of 50; no significant relationship was noted for postmenopausal women [139].

- It has been suggested that decreasing IGF-I levels may be one factor that contributes to tamoxifen's anti-tumor activity in breast cancer therapy [140].

- While not all studies [141] agree, a cohort* study reported that higher insulin* levels significantly increased risk of breast cancer for both pre- and post-menopausal women [142].

- Recent studies indicate that high insulin* levels, increased concentration of IGF-I, and greater abdominal fat are associated with increased risk for breast cancer [143].

- One study noted a direct association, though not statistically significant, between non-fasting serum insulin* levels and 10-year mortality in postmenopausal breast cancer women [144].

- Among other factors, a diet low in fiber may favor the development of insulin* resistance and hyperinsulinemia [127].

- Hyperinsulinemia may contribute to the development of breast cancer in overweight or obese women [145].

[1]BMI refers to body mass index, which is calculated by body weight (kg)/height2(m2).

- Additionally, obesity and fasting hyperinsulinemia have been associated with a poorer prognosis in women with established breast cancer [146].

- A case-control* study reported that carbohydrate intake significantly increased risk of breast cancer; sucrose (table sugar) imparted the greatest risk [147]. This risk was lessened considerably with a higher fiber intake.

- A significant two fold increased risk of breast cancer was associated with women consuming the highest amount of sugar in the diet [114].

- Sugar and dessert intake was associated with an increased risk of breast cancer [18].

- Furthermore, an Italian case-control* study found that women who consumed the highest tertile of desserts and sugars had a 19% increased risk of breast cancer compared with women in the lowest tertile [148].

- A cross-sectional study of women showed that for increasing amounts of sugar-sweetened beverages, higher mammographic density occurs--a strong breast cancer risk factor [149].

- A case-control* study of 1,434 cases showed that consumption of sweet beverages, added sugars, and desserts was positively associated with breast cancer risk [150].

- The risks of distant metastasis and breast cancer deaths were significantly higher in women with higher fasting glucose levels compared to women in the lowest glucose quintile (reference <87 mg/dL) [152].

- Breast cancer mortality was significantly greater in ER+/PR+ women with a higher blood glucose (> 94 mg/dL) compared with those with normal glucose levels [153].

- The consumption of sweet foods with a high glycemic index* (GI) and glycemic load* (GL) have been implicated as a risk factor for breast cancer due to their effects on insulin and IGF-I [153-156].

    o Women who consumed the greatest intake of desserts (including biscuits, brioches, cakes, puffs and ice-cream) and sugars (including sugar, honey, jam, marmalade and chocolate) had a 19% increased risk of breast cancer compared with women who consumed the least desserts and sugars [153].

- Adding credence to the idea that blood sugar levels may affect disease progression, women who consumed a high GI and GL diet had a 57% and 253% increased risk of breast cancer, respectively [154].

    o This effect was most pronounced in premenopausal women and those women at a healthy body weight.

- GI and GL were both associated with an increased risk of breast cancer among postmenopausal overweight women; this effect was most pronounced for women with ER- breast cancer [155].

- GL was positively associated with overall breast cancer risk in two cohort* studies [157-158].

- This evidence was further supported by a meta-analysis* that reported GI to modestly increase the risk of breast cancer [156].
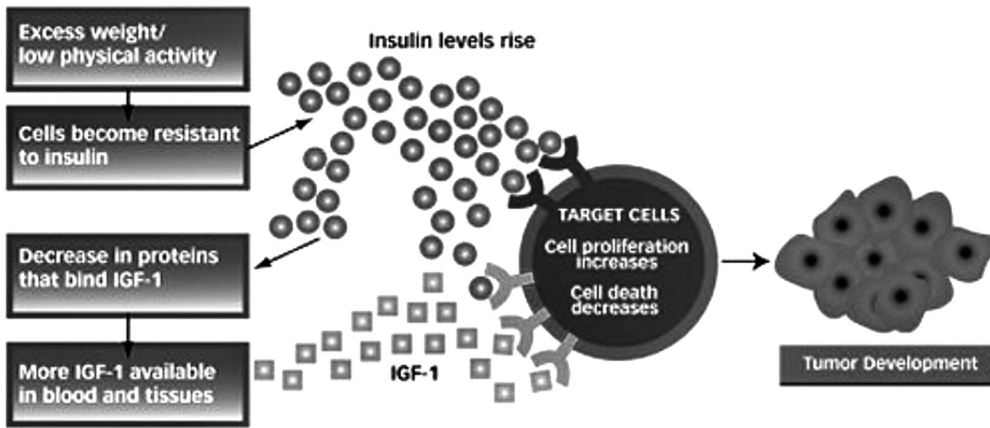
INSULIN HIGH TIDE. The observed link between obesity and cancer may be explained by the growth-promoting activities of insulin and IGF-1. One theory posits that excess weight sets off a biochemical cascade that increases insulin and, in turn, IGF-1 levels. Both hormones may activate IGF-1 receptors on cells, which can spur cell growth and inhibit cell death pathways that usually protect against tumor development.

E. Roell/Source: Nature Reviews Cancer, 2004

Sugars & Insulin* – Bottom Line

- To help control your insulin* level:

  o Eat a high-fiber diet with limited refined/processed foods

  o Follow a low/moderate fat diet rich in omega-3 fatty acids

  o When you eat foods rich in carbohydrates, include protein at same meal/snack

  o Limit or avoid alcohol

  o Exercise

  o Maintain a healthy body weight

LOW FAT DIET

Many studies have investigated the relationship of fat and the risk of breast cancer, but the results remain inconsistent. However, several trials showed some promise in the area. The Women's Intervention Nutrition Study (WINS) found that a reduced fat intake improves relapse-free survival by 24% in postmenopausal women with breast cancer compared with women following a standard diet [159]. The risk of recurrence for women with ER- breast cancer decreased by 42%. Later, the European Prospective Investigation into Nutrition and Cancer (EPIC) Study reported that eating a higher fat diet significantly increased the risk of breast cancer; women who had a 35% and 39% fat diet were at a greater risk than those eating a 31% fat diet [160]. While this diet would not be considered low fat, a significant effect was still observed.

While the Nurses' Health Study found that total fat intake was not associated with breast cancer risk [161], a systematic review and meta-analysis* reported that increased fat in the diet was associated with an increased risk of breast cancer [21]. Furthermore, a prospective trial suggested that a high fat diet was associated with increased risk in ER+/PR+ disease, but not ER-/PR- tumors [162].

The potential elevated cancer risk may be, in part, due to the fact that a high fat diet stimulates increased estrogen levels, which is associated with breast cancer growth. A study of adolescent females found that modest reductions in fat intake during puberty resulted in significantly lower concentrations of sex hormones (estradiol*, estrone*, progesterone) [163]. Further research is needed to determine if in fact these lower levels lead to a reduced risk of breast cancer.

Aim for close to 20-30% of your total calories from fat, with less than 8% of total calories from saturated fat. Likely more important, research indicates that the type of fat may be of paramount significance.

Saturated Fats

- Several studies indicate a positive association between saturated fat intake from meat and dairy products (animal sources) and cancer [164-167]. While breast cancer research is inconclusive, it is growing [161, 168-170].

- A systematic literature review concluded that higher saturated fat intake prediagnosis was associated with an increased risk of breast cancer-specific mortality [170].

- Total saturated fatty acid intake was significantly associated with breast cancer risk in cohort* studies in postmenopausal women, but not premenopausal women [171].

- Based on a seven-day diary for evaluating saturated fat intake, a high intake of saturated fat was reported to increase the risk of breast cancer [166].

- A meta-analysis* observed a 19% increased risk of breast cancer with greater intake of saturated fats [172].

- A prospective evaluation concluded that high total and saturated fat intake was associated with a greater risk of ER+PR+ disease, but not ER-PR- disease. High saturated fat was significantly associated with greater risk of HER2- disease [162].

- High-fat dairy intake, a significant source of saturated fats, was positively associated with breast cancer recurrence, breast cancer mortality, and overall mortality [169]. No association was observed between low-fat dairy and breast cancer.

  o 0.5 to <1.0 dairy servings/day increased breast cancer mortality by 20%.

  o ≥1.0 dairy servings/day increased breast cancer mortality by 49%.

- Other studies, however, have not found a significant association between saturated fats and breast cancer [173-175].

Trans-Fatty Acids

- Preliminary research indicates that these fatty acids may be associated with an increased risk of cancer [170, 176-179].

- Minimal research exists on the relationship between trans-fatty acids and risk of breast cancer, thus, more research is needed for conclusive evidence. However, evidence points to a positive association between these fats and breast cancer risk [178, 180].

- These fats may disrupt hormonal systems that regulate healing, lead to the destruction of defective membranes, and encourage the development of cancer.

- One study reported a 40% increased risk of breast cancer in postmenopausal women who had higher tissue levels of trans-fatty acids [181].

- Women who consumed greater amounts of trans-fatty acids significantly increased their risk of breast cancer [179].

  o Women in the highest quintile of trans-fatty acid consumption had a 75% increased risk compared with women in the lowest quintile.

- Postdiagnostic trans fat intake was associated with 45% and 78% increased risk of all-cause mortality [170].

Omega-9 Fatty Acids (Monounsaturated Fats)

- Most research at this time indicates a neutral relationship [173, 179] or a slightly protective effect [175, 182-184] between these fats and risk of breast cancer.

- Several case-control* studies reported that olive oil consumption, rich in omega-9 fats, resulted in a 13-34% reduction in breast cancer risk [185-188].

  o One study found that women who consumed ≥8.8 g/day of olive oil had a 73% lower risk of breast cancer [184].

- Oleic acid, an omega-9 fatty acid found in olive oil, has been observed to synergistically enhance the efficacy of trastuzumab (Herceptin) [189, 190].

- A meta-analysis*, however, that included three cohort* studies reported total monounsaturated fatty acids and oleic acid, to significantly increase breast cancer risk [171].

- That said, in a meta-analysis of 13,800 patients, it was found that the highest category of olive oil consumption was associated with lower odds of having any type of cancer [191].

  o These results were further supported by this meta-analysis showing those with the greatest consumption of olive oil having a 48% lower risk of breast cancer compared with the lowest intake [192].

- A prospective study, however, found no relationship between olive oil and breast cancer risk [193].

- Polyunsaturated fats have a clear stimulating influence on mammary carcinogenesis, whereas extra-virgin olive oil diets mainly have a negative modulatory effect on breast cancer development [194].

- Oleuropein, the main olive oil polyphenol, has anti-proliferative effects. It was found that treatment of breast cancer cells with oleuropein could help in prevention of breast cancer metastasis [195].

- Olive oil induces apoptosis in some cancer cells due to phenolic compounds like oleuropein [196].

Essential Fatty Acids (EFA)

Essential fatty acids are necessary for the formation of healthy cell membranes, the proper development and functioning of the brain and nervous system, and for the production of hormone-like substances called eicosanoids* (thromboxanes, leukotrienes, prostaglandins). Among other body functions, these chemicals regulate immune and inflammatory responses.

Eicosanoids* formed from the omega-6 fatty acids have the potential to increase blood pressure, inflammation, platelet aggregation, allergic reactions and cell proliferation. Those formed from the omega-3 fatty acids have opposing affects. Current research suggests that the levels of essential fatty acids and the balance between them may play a critical role in the prevention and treatment of cancer.

Omega-3 Fatty Acids

- Research is growing supporting a protective relationship between omega-3 fatty acids [alpha linolenic acid (ALA), eicosapentanoic acid (EPA), and docosahexanoic acid (DHA)] against the risk of breast cancer [170-171, 173, 188-190, 197-202].

- Studies show that omega-3 fatty acids inhibit breast cancer tumor growth and metastasis. Additionally, these fats are immune enhancing.

- Mechanisms proposed for their protective effects include:

  o Suppression of eicosanoid synthesis from arachidonic acid (omega-6 fatty acid), which impedes immune function [198, 203-204].

  o Inhibit cell growth and differentiation via effects on gene expression and signal transduction pathways [198, 203].

  o Alter estrogen metabolism, which reduces estrogen-stimulated cell growth [198, 203, 205].

  o Effects on insulin* sensitivity and membrane fluidity [203].

  o Anti-proliferative effects in breast cancer cells [206].

  o Inhibit proliferation and induce apoptosis [201].

- A prospective study reported that women who consumed 44 g or more of dietary marine sources of omega-3 fatty acids over a 12 month period reduced their risk of breast cancer by 26% when compared with women who consumed 25 g or less [173].

- Women with the greatest EPA, DHA, and total omega-3 fatty acids in their red blood cell membranes from fish had a 73%, 94%, and 89% lower risk of breast cancer, respectively [199].

- In a prospective cohort* study, women with a lower intake of marine-derived omega-3 fatty acids and a higher intake of omega-6 fatty acids had a significantly higher risk for breast cancer; the researchers suggested that the balance between omega-6 and omega-3 fats may be of greater importance than the amounts of specific fatty acids [207].

- High intake of fatty fish (more than 0.101 g of EPA and 0.213 g of DHA) was associated with a significantly reduced risk for breast cancer in both pre- and postmenopausal women [208].

- An inverse relationship was found between omega-3 fatty acids in breast tissue and the risk of breast cancer [190].

  o When comparing women in the highest tertile of ALA and DHA to the lowest tertile, cancer risk was reduced by 61% and 69%, respectively.

- While no overall effect was observed between omega-3 fatty acids and risk of breast cancer, omega-3 fatty acid intake significantly decreased the risk of breast cancer in obese women [209].

- In a multivariate analysis of Greek women, elevated total polyunsaturated fatty acids in breast adipose tissue and omega-3 in buttock adipose tissue were associated with reduced risk of breast cancer [210].

- Moderate intake of fats (saturated fatty acids, omega-3 fatty acids, and omega-6 fatty acids) from freshwater fish may decrease the risk of breast cancer among premenopausal women [211]. Interestingly, the type of fish had varying effects with black carp (>500 g/mo) and silver carp (>1000 g/mo) significantly reducing risk while crutian carp (>1000 g/mo) increased breast cancer risk.

- Preliminary research indicates that DHA may synergistically enhance taxane cytotoxicity [212]. More research is needed, but these findings would indicate that DHA during taxane administration may improve the effects of chemotherapy for breast cancer patients.

- Fish and plant-based foods, however, contain different types of omega-3 fatty acids.

  o Fish contains EPA and DHA, two specific fatty acids that have shown promising results in the research literature [188, 199, 208, 213-214].

  o Fish consumption in general has been associated with a protective effect against breast cancer [189, 197, 199, 208, 213, 215].

  o The plant-based omega-3 fatty acid sources, such as flaxseed and others listed in the table below, contain ALA. In an ideal environment, ALA is converted to EPA and DHA, however, this process is inefficient [102, 203, 216]. On the positive side, the conversion process is enhanced by following a diet that is low in saturated fats and low in omega-6 fatty acids [203, 217].

- Research suggests that higher intake of omega-3 fatty acid is related to decreased inflammation and decreased physical aspects of fatigue among breast cancer survivors [218].

  o Survivors with a high CRP, a marker of systemic inflammation, had 1.8 times greater odds of fatigue.

- Omega-3 fat intake suggested an inverse association with all-cause mortality [170].

- Fish oil may offset negative effects of aromatase inhibitors (AI) to bone; 4 g EPA and DHA daily for 3 months reduced bone resorption in breast cancer survivors [219].

- In a randomized double blind placebo controlled trial, 70% of patients who took an omega-3 supplement during chemotherapy did not develop peripheral neuropathy compared with 40.7% in the placebo group [220].

Omega-6 Fatty Acids

- Recent studies indicate that a high intake of omega-6 fatty acids (linoleic acid, which can be converted to arachidonic acid) promote breast tumor development and metastasis [167, 190, 197, 220-221].

- A meta-analysis* of 3 cohort* studies found palmitic acid, a type of omega-6 fatty acid, to be significantly associated with an increased risk of breast cancer [171].

- Additionally, researchers reported that arachidonic acid, an omega-6 fatty acid almost exclusively from meat, significantly increased oxidative damage as measured by urinary biomarkers [222].

- It is known that cyclooxygenase is the rate-limiting enzyme that catalyzes the conversion of arachidonic acid to prostaglandins. Furthermore, COX-2 is known to be overexpressed in various human cancers. In this breast cancer study, COX-2 overexpression was significantly correlated with larger tumor size and advanced clinical stage, which indicates a poorer prognosis [221].

- A very interesting finding was reported in a prospective study that found no overall association between omega-6 fatty acids and risk of breast cancer [173]. However, omega-6 fat consumption increased risk by 87% in women who consumed 25 g or less of marine omega-3 fatty acids. This effect was even greater for advanced breast cancer.

  o Thus, the balance between omega-6 and omega-3 fatty acids may be of paramount importance. This was further supported by other studies [190, 197, 223-224].

- In this study, higher intake of omega-6 fatty acids to omega-3 fatty acids was associated with significantly higher CRP values and these patients were significantly more likely to experience fatigue [218].

Fat – Bottom Line

- Aim for low to moderate fat; focus on type and quality. Note that all fats are equally high in calories.

- Limit animal fats.

- Avoid hydrogenated fats.

- Focus on extra-virgin olive oil, avocados, and nuts/seeds as healthy fat sources.

- Increase omega-3 fatty acids.

Fatty Acid	Dietary Sources	Recommendation
Saturated fatty acids	Meats, poultry skin, baked goods, coconut oil, and whole milk dairy products, including butter, cheese, and ice cream	Reduce or eliminate meat and whole milk dairy products.
Trans fatty acids	Margarine, fried foods, commercial peanut butter, salad dressings and various processed foods including breads, crackers, cereals, and cookies	Avoid trans or hydrogenated fats. Products may be labeled "trans fat free" if they contain less than 0.5 mg per serving.
Omega-9 fatty acids	Extra-virgin olive oil, almond oil, canola oil, macadamia nut oil, almonds, and avocados	Include these healthy fats daily. Limit consumption of nuts to no more than ¼ cup with meal or snack to limit total fat and calories.
Omega-3 fatty acids: EPA and DHA ALA	Cold-water fish (for example: salmon, sardines, black cod, trout, herring), and DHA-enriched eggs Flaxseeds, chia seeds, walnuts, hempseeds, and pumpkin seeds	Include these healthy fats daily through diet and/or supplements. It may be wise to consume cold water fish or fish oil supplements at least twice weekly to obtain an adequate amount of EPA and DHA. If you choose to use a supplement, opt for one that is highest in EPA and DHA concentration.
Omega-6 fatty acids: Arachidonic acid Linoleic acid	Meats, butter, egg yolks, whole milk, and whole milk dairy products Common vegetable oils, such as corn oil, safflower oil, sunflower oil, and cottonseed oil, and processed foods made with these oils	Reduce or eliminate meat and whole milk dairy products. Limit consumption of linoleic acid-rich oils. Substitute an omega-9 fatty acid-rich oil for your current cooking oil or fat.

Meta

- Animal fat [26, 161, 225] and meat appear to increase the risk of breast cancer in recent studies [16, 168]. Conversely, plant fat has been negatively associated with breast cancer [225].

- In a study of over 35,000 women, meat consumption significantly increased the risk of breast cancer in both premenopausal and postmenopausal women [226].

   o Women eating 1.75 oz of processed meat daily increased the risk of breast cancer by 64% in postmenopausal women compared to women who did not eat meat.

- Consumption of red and fried meat quadrupled the risk of breast cancer in a case-control study in Brazil [14].

- Meat consumption increased the risk of breast cancer risk by 56% for each additional 100 g (3.5 oz) daily of meat consumption in a French case-control study [190].

- Regular consumption of fatty red meat and pork fat increased the risk of breast cancer by 348% and 632%, respectively in a small Brazilian study [227].

- A large case-control* study found that women who consumed very well-done meat for hamburger, bacon, or steak had a 54%, 64%, and 221% increased risk for breast cancer, respectively [228].

   o Frequent consumers of these well-done meats had a 462% greater risk of breast cancer.

- High intake of red meat is associated with a significantly higher breast cancer risk, especially for well-done red meat [229]. This is slightly stronger for postmenopausal women than premenopausal women.

Food Category	Summary	Recommendation
Fruits and vegetables	One serving = ½ cup fruit or vegetable 1 cup raw leafy greens ¼ cup dried fruit or vegetable 6 oz fruit or vegetable juice Eat 1 cup or more vegetables with lunch and dinner.	At least 5, preferably 8-10 total servings daily [230] 5 or more vegetable servings 3 fruit servings
Fiber	Choose breads with 3 or more grams of fiber per slice. First ingredient on the label should be whole or sprouted grain flour, not white flour, unbleached white flour, or enriched wheat flour. Whole grains include oats, barley, brown rice, quinoa, amaranth, bulgur, millet, buckwheat, spelt, wild rice, whole wheat, and teff.	30-45 grams daily This goal can be achieved by meeting your fruit and vegetable goal plus one serving of chia/ flax seeds or one serving of legumes or at least two servings of whole grains.

Refined carbohydrates and sugars	Dietary sources include products made with refined flours (for example: white bread, white rice, white pasta) or refined grains, alcohol, sodas, drinks containing added sugars, and desserts, such as candy, cookies, cakes, and pastries.	Limit or avoid consumption.
Meat	Dietary sources include beef, pork, and lamb. Processed meats include deli meats, bacon, sausages, and hot dogs.	Reduce or eliminate meat consumption. Avoid processed, grilled or fried meats.

GENOTOXINS: Heterocyclic Amines (HCAs) & Polycyclic Aromatic Hydrocarbons (PAHs)

- Natural components in meat, such as amino acids, creatine*, and polysaccharide precursors, are converted to HCAs during high-temperature cooking. HCAs are known to cause cancer in laboratory animals [231-233].

- While human research is forthcoming, the majority of studies [228, 231-236], although not all [237-238] have observed a significant association between HCAs and breast cancer.

  o PhIP, one of the most abundant HCAs from cooked meat has potent estrogenic effects [233]. Researchers have theorized that the estrogenic properties of PhIP influence metastatic potential.

- Daily intake of smoked meats more than doubled the risk for breast cancer in both pre- and postmenopausal women; this risk more than tripled in women who carried the SULTA1A1 genotype [236].

- Carcinogenic activity of HCA's is affected by various dietary factors [239]:

  o Factors that enhance carcinogenesis* when combined with HCAs include:

    - High-fat diet

    - Caffeine

  o Factors that inhibit carcinogenesis* when combined with HCAs include:

    - DHA

    - Conjugated linoleic acid (CLA)

    - Isoflavones

    - Diallyl Sulfides (found in the allium family, such as garlic, onions, leaks, and shallots)

    - Green tea catechins* [240]

    - Indole-3 carbinol

    - Probiotics

- Gamma-tocopherol
- The most important variables contributing to the formation of HCAs are:
  o Cooking temperature (greater than 300°F)
  o Cooking time (greater than 2 minutes)
  o Cooking method (frying, oven grilling/broiling, barbecuing)
- Charring of food (charcoal-broiled or smoked foods) contribute to PAHs [241].
- Meat can potentially be made "safer" to eat by being cooked in a way that does not lead to HCA formation.
  o Choose lean, well-trimmed meats to grill.
  o Using marinades significantly reduces the amount of HCAs.
  o Brief microwave preheating substantially reduces HCA content of cooked meat.
  o Small portions require less time on the grill.
- Additionally, the type of protein cooked can also affect the concentration of HCAs. It has been reported, for example, that chicken has more than 100 times the number of HCAs than salmon [239]. London broiled steak had more than 600 times the amount of HCAs when compared to salmon.
- Grill vegetables or meat alternatives that do not lead to the formation of HCAs or PAHs.
- Research suggests that our genetics may also influence risk.
  o Consumption of well-done meat increased breast cancer risk 8-fold for postmenopausal women who carried the NAT2 genotype, compared to those who consume medium-done or rare meats [242].
  o Daily intake of smoked meat was significantly associated with a greater overall breast cancer risk for those with the SULT1A1 genotype, in both pre- and post-menopausal women [236, 243].

ALCOHOL

- Regular consumption of alcohol may increase the risk for breast cancer [244-254].
  o A recent review study reported that data from many well-designed studies consistently shows a small rise in breast cancer risk with increasing consumption of alcohol [249].
- A recent study found that as little as a half a glass of wine a day raised a woman's risk of developing breast cancer by 6% (increased risk by 18% in postmenopausal women) [244].
  o Furthermore, 1-2 drinks a day increased risk by 21% and 2 or more drinks a day increased risk by 37%.
  o The heightened risk was more pronounced for women with ER+ and PR+ tumor types.
- Consuming as little as 3-6 drinks/week was associated with increased breast cancer risk, and women who had at least 2 drinks daily on average had a 51% greater risk of breast cancer compared to those who never consumed alcohol [255].

- Women who drank two or more alcoholic drinks daily in the five years prior to diagnosis had an 82% increased risk of breast cancer compared to non drinkers [250].

- A pooled analysis of six prospective studies suggests that the risk of breast cancer increases linearly by 9% with each 10 g/day (~1 drink) alcohol [256]. The risk increased to 41% when comparing women who consumed 30-60 g/day (~2-5 drinks) to nondrinkers.

- A large meta-analysis* revealed that one drink daily increased breast cancer risk by 11% [257]. A later meta-analysis* found similar findings [258].

- Since then, another meta-analysis* reported that breast cancer risk increased by 32% and 46% in women who consumed 35-44 g alcohol (~3-4 drinks) daily and 45 g or more (~4.5 drinks or more) daily, respectively [247].

  o For each additional 10 g of alcohol (~1 drink) daily, risk increased by 7%.

- Other studies claim that one glass of alcohol daily does not increase risk, but consuming 2-5 drinks daily increases the risk of breast cancer by 40% compared to non-drinkers [245].

  o Greatest risk was among heavy drinkers who were also postmenopausal and had a history of benign breast disease or who used hormone replacement therapy (HRT).

- Similarly, a French study found that drinking 10-12 g wine (~ 1-1.5 drinks) daily lowered the risk of breast cancer, but when intake increased above 12 g daily, the risk of breast cancer increased [259].

- Alcohol consumption between menarche and first pregnancy was associated with a greater risk of breast cancer; this risk increased with longer menarche to pregnancy intervals [260].

- Among ER+ postmenopausal women, those who consumed approximately 3 drinks or more daily had a 76% increased risk of breast cancer when compared with women who did not consume alcohol [261].

  o The association between alcohol and ER- tumors was less clearly associated.

  o Additionally, there was no clear association between alcohol and premenopausal risk of breast cancer.

- A recent cohort* study of postmenopausal women reported that alcohol consumption was associated with an increased risk of breast cancer in ER+, but not ER- tumors [262].

- On a similar note, a recent meta-analysis* reported that an increase in 10 g (~1 drink) alcohol daily increased the risk of breast cancer, especially for women with ER+ breast cancers – ER+ (12% ↑ risk), all ER- (7% ↑ risk), ER+PR+ (11% ↑ risk) ER+PR- (15% ↑ risk), ER-PR- (no effect) [251].

- Petri and colleagues [248] observed a stronger relationship between alcohol and breast cancer in postmenopausal women compared to premenopausal women.

  o Premenopausal women drinking more than 27 drinks per week had a 3.5% higher risk than women who had one drink per week.

  o Postmenopausal women drinking six or more alcoholic beverages per week had a 2.4% higher risk than women who had one drink per week.

- On the contrary, women who drank about 1.5 drinks per week had a 40% greater likelihood of developing breast cancer compared to non drinkers and this was most pronounced in women who were premenopausal at diagnosis [252].

- Alcohol consumption (1 drink/day) during a woman's fifties increased risk for postmenopausal breast cancer by 12% in a large cohort* study, but statistical significance was not reached for women in their twenties, thirties, or forties [246].

- These differing findings between pre- and postmenopausal women are likely related to the effect of alcohol on estrogen levels. Alcohol appears to increase endogenous* estrogen levels [263-267].

- Another theory is that alcohol consumption could metabolically convert "low-risk" breast cancer patients to "high-risk" status via oxidative mitochondrial metabolism by fueling tumor cell growth [268]. Antioxidants such as N-acetyl cysteine (NAC) can effectively reverse or prevent ethanol-induced oxidative stress in cancer-associated fibroblasts.

- Folate, a B vitamin, may be of even greater significance with alcohol consumption. It has been observed that women with low folate and high alcohol consumption had a 43% greater risk of breast cancer when compared with nondrinkers with adequate folate intake [269].

Alcohol – Bottom Line

• It is best to limit or avoid alcohol.

ADEQUATE FLUIDS

The functions of water in the body include the following:

- o Carries nutrients and waste products.

- o Participates in chemical reactions.

- o Acts as a lubricant and cushion around joints.

- o Acts as a shock absorber in the eyes and spinal cord.

- o Aids in the body's temperature regulation.

- o Maintains blood volume.

- Increased fluid intake is needed for a high fiber diet.

- Drink plenty of water daily to help meet fluid needs.

CALORIC INTAKE

- The risk of breast cancer is much higher in industrial countries than in developing countries where women are characterized by lower energy intake and higher energy expenditure.

- Modest caloric restriction has been shown to inhibit tumor growth in animal models decrease oxidative DNA damage [270].

- Modest caloric restriction has been shown to decrease oxidative DNA damage.

- The mechanism involved may be related to the decrease in IGF-I observed when caloric intake is restricted [271-272].

- Furthermore, evidence suggests that a high calorie diet may increase IGF-I levels [273].

BODY MASS

- Women with a BMI of ≥25 kg/m^2 had a 58% increased risk of breast cancer [7].

- Epidemiologic evidence suggests a positive association between body mass and postmenopausal breast cancer in many [273-281], but not all studies [282-284].

o Increasing BMI was associated with a 40% increased incidence and mortality of breast cancer in postmenopausal women [285]. Similarly, a high BMI (>27 kg/m^2) increased breast cancer mortality in ER+PR+ women [224].

  o Women with a BMI of ≥25 kg/m^2 had a 58% increased risk of breast cancer [7].

  o Obese postmenopausal women had 3.26-fold increased risk for breast cancer compared to healthy weight women [286].

  o In women with breast cancer, height and BMI were associated with postmenopausal breast cancer [287].

- This effect was most pronounced in women with ER+ tumors.

  o Obese postmenopausal women had a 50% increased risk for breast cancer [277].

  o BMI was positively associated with risks of ER+ and triple-negative breast cancer in women ages 50 to 84 who were not users of hormone therapy [279].

  o Increasing BMI was associated with a 40% greater incidence and mortality of breast cancer in postmenopausal women [285].

- A case-control* study of 2,000 women found that women who gain weight, particularly after age 50, significantly increase their risk of breast cancer [288]. Conversely, women (young and middle-aged) who lose weight may decrease the risk of breast cancer.

  o This study suggests excess body fat increases estrogen levels, which may in turn increase the risk for breast cancer.

  o An earlier study reported similar findings with total weight gain serving as a strong predictor of breast cancer risk, specifically among former and never HRT users [274].

  o Weight gain throughout adulthood is associated with an increased risk of breast cancer in Chinese women [289].

  o High recent BMI was associated with increased risk of ER- and PR+ tumors among postmenopausal African-American women [282].

- Results from a systematic review showed that, when adjusted for BMI, a larger waist size increased risk of breast cancer among premenopausal women [290]. This study supports the idea that central obesity is of greater concern than general obesity in regards to breast cancer risk.

  o However, for postmenopausal women, a large trial found that, while general obesity was a significant predictor of breast cancer risk, central obesity did not appear to be associated with increased risk [291].

- Total body weight, BMI, and hip circumference were significantly associated with breast cancer risk among HRT nonusers; obese women (BMI >30 kg/m²) had a 31% greater risk compared to women with BMI <25 kg/m² [291].

- Premenopausal women with a BMI of ≥25.0 kg/m² showed a tendency towards ER- tumors when compared to premenopausal women with a BMI of <25.0 kg/m² [292].

- Data from two large prevention trials suggests that higher levels of BMI were significantly associated with increased breast cancer risk in premenopausal women older than 35 years, but not postmenopausal women [284].

- However, results of a meta-analysis* using 50 studies found no significant correlation between BMI and premenopausal breast cancer risk [280].

- Two studies reported that BMI was significantly associated with a larger-tumor size at diagnosis and a higher probability of having positive axillary lymph nodes [283, 293].

- Overweight or obesity is associated with poorer prognosis in the majority of the studies that have examined body mass and breast cancer [151, 294-300].

- Many studies [151, 294-305], though not all [306], report increased BMI or body weight to be a significant risk factor for recurrent disease, survival, or both. It has been suggested that the association of obesity with poorer outcomes after breast cancer observed in previous studies may be driven predominantly by the relationship between morbid obesity (≥40 kg/m²) and mortality. However in one study, women with a ≤24.0 kg/m² BMI had increased risk of locoregional recurrence [307].

  o High BMI and breast cancer may be related due to increased estrogen [277, 308-310] and elevated insulin* [310] and IGF, which can stimulate cell proliferation [140, 308].

  o Obese postmenopausal women (BMI >30 kg/m²) had 35% higher concentrations of estrone* and 130% higher concentrations of estradiol* compared with lighter-weight women (BMI <22.0 kg/m²) [294]. Additionally, free estradiol* and free testosterone were two to three times greater in overweight and obese women compared with lighter-weight women.

  o Aromatase inhibitors may be less effective at lowering estradiol values in obese women [311].

  o Similarly, while normal weight patients who used anastrozole for an additional 3 years halved their risk of disease recurrence and death and had only a fifth of the risk of distant metastases, overweight and obese patients derived no benefit from an additional 3 years of anastrozole [302]. On the other hand, another study found that BMI may not influence outcomes for women with hormone receptor-positive breast cancer using aromatase inhibitors [312].

  o Recent findings indicated that oxidative damage, measured by urinary biomarkers, was significantly greater in women with a higher BMI [222].

  o Obesity among premenopausal women, however, may not be associated with increased risk of breast cancer. Nonetheless, obesity during menstruating years is associated with obesity throughout life and therefore to an eventual increased risk of breast cancer [185]. However, other research suggests a stronger relationship between body weight and breast cancer in premenopausal women [298, 300].

  o A cohort* study of 1,300 women reported that breast cancer recurrence and death increased with body weight in both premenopausal and postmenopausal women [232].

  o In a cohort* study with more than 1,100 women, a BMI (≥23.0 kg/m²) was independently associated with poor prognosis in hormone receptor-positive breast cancer [305].

  o BMI ≥25.8 kg/m² was associated with breast cancer-specific death and BMI <21.2 kg/m² was associated with all-cause and breast cancer-specific death among patients with ER + or PR + tumors [281].

- o Obesity was associated with poorer survival in women with node-positive breast cancer [301, 304] and in younger women [304].

- o However, no significant relationship was observed between obesity and recurrence-free survival or overall survival in patients with triple negative breast cancer [313-314].

- o BMI may not influence survival for women with metastatic breast cancer [315].

- Body weight prior to breast cancer diagnosis significantly increased risk of recurrence and death in nonsmokers [298].

  - o Additionally, nonsmokers who gained weight after diagnosis had an elevated risk of breast cancer death during follow-up (median, 9 years), compared with women who maintained their weight.

- Research suggests a potential link between obesity, diabetes mellitus and breast cancer [316].

- Eating foods high in vitamin C, such as fruits and vegetables, may provide a protective effect from breast cancer for overweight women (BMI>25 kg/m²) [317].

- Additionally, breast cancer survivors whose BMI was ≥30 kg/m² at the time of breast cancer treatment were approximately 3.6 times more likely to develop lymphedema at 6 months after diagnosis than those with a BMI<30 kg/m² at the time of cancer treatment [318].

PHYSICAL ACTIVITY

- Low levels of physical exercise appear to be associated with the risk of breast cancer [249, 276, 319-322]. Similarly, physical activity seems to reduce the risk of breast cancer [323-331].

  - o In a cohort* study of over 50,000 women, the effect was strongest in postmenopausal women ER+, PR+ disease [331].

  - o A large review of 73 studies found that breast cancer risk was reduced by 25% amongst physically active women as compared to the least active women [327].

  - o The EPIC study reported that among women diagnosed with breast cancer after age 50, the largest risk reduction was found with highest activity, whereas for cancers diagnosed before age 50 strongest associations were found for moderate total physical activity [329].

  - o African American women who engaged in vigorous physical activity (≥ 2 hours/week in the past year) had a 64% reduced risk of breast cancer compared to those who did not participate in any vigorous activity [330]. However, in one study, greater physical activity was associated with reduced breast cancer risk among White women only; this study only assessed total activity not intensity [322].

- Lifetime total physical activity has been associated with a decreased risk of breast cancer [332-335] and breast cancer-specific mortality [336-337].

  - o Some studies indicate that physical activity has a more significant effect in reducing risk of breast cancer in postmenopausal women [338].

  - o Exercise between the years of 14-20 appears to be the most beneficial in reducing risk of breast cancer [332].

  - o While physical activity did not decrease breast cancer risk for women who were long-term users of HRT, risk did decline for women who did not use HRT, who used HRT for <5 years, or who were currently using estrogen alone [335].

- A case-control* study reported significantly reduced breast cancer risk among women who maintained, on average, 17.6 MET-h/week[2] from menarche onward [276]. This decreased risk with physical activity was limited to women without a family history of breast cancer when adjusted for BMI.

- Post-menopausal women who exercised the equivalent to running for 3 hours weekly and those that were active to the equivalent of 24 hours weekly of moderate household work reduced breast cancer risk by 40% [339].

- A cohort* study of over 73,000 women reported that the most active women (those reporting >42 MET-h/week)[3] experienced a 25% lower risk of breast cancer than the least active women [325].

  o 47% of women reported walking as their only recreational activity; among these women, a 14% lower risk was observed for ≥7 hours/week relative to ≤3 hours/week of walking.

- A cohort* study reported that postmenopausal women who were most physically active (>42.0 MET-h/week)3   at baseline had a 29% lower incidence of breast cancer than active women with the least activity (>0-7.0 MET-h/week)[4] [321]. This difference was greatest for women who did not use HRT at enrollment.

- Women who engaged in regular strenuous physical activity at age 35 had a 14% reduced risk of breast cancer compared with less active women [320]. A similar trend was observed for regular strenuous activity at age 18 and at age 50. These findings were consistent with women who did and did not use HRT.

- Furthermore, a prospective observational study reported that physical activity after a breast cancer diagnosis may reduce the risk of death from this disease [319]. The greatest benefit occurred in women who performed the equivalent of walking 3 to 5 hours per week at an average pace. The benefit of physical activity was particularly apparent among women with hormone-responsive tumors.

- As noted earlier, the combination of consuming five or more daily servings of vegetables and fruits, and accumulating 540+ metabolic equivalent tasks-min/wk (equivalent to walking 30 minutes 6 d/wk) decreased mortality by nearly 50% [13].

  o The effect was stronger in women who had ER+ cancers.

- While total physical activity had a stronger inverse relationship for ER+/PR+ breast tumors, household physical activity was inversely associated with ER-/PR- tumors [329].

- Increased physical activity following breast cancer diagnosis significantly decreased the risk of dying from breast cancer and improved overall survival when compared with women who exercised <2.8 MET-h/wk [340].

- A lower risk of all-cause death was observed for women who engaged in an average of ≥9 MET-h/wk (~3 h/wk of fast walking) of recreational physical activity from menarche to diagnosis compared with women who did not exercise [337].

- A meta-analysis* of cohort* studies reported that both prediagnosis and postdiagnosis physical activity were associated with reduced breast cancer-specific mortality and all-cause mortality [341].

- Findings from a randomized controlled trial suggested that those who were most active at baseline had a 53% lower mortality risk compared to the least active women [342].

[2] This is equivalent to a 150 lb individual burning 1257 kcals/week through physical activity.
[3] This is equivalent to a 150 lb individual burning about 3000 kcals/week through physical activity.
[4] This is equivalent to a 150 lb individual burning 500 kcals/week or less through physical activity.

- Post-diagnosis running, a more vigorous exercise, is associated with significantly lower breast cancer mortality than post-diagnosis walking [343].

- Women participating in 9 MET-h/wk or more (~3 h/wk of fast walking) of physical activity before diagnosis had a lower all-cause mortality compared with inactive women [344].

  o Women participating in ≥ 9 or more MET-h/wk of physical activity after diagnosis had lower breast cancer mortality and lower all-cause mortality.

- Survival may be enhanced by physical activity in those women who exercised the year prior to diagnosis, especially women who were overweight or obese [345].

- Physical activity can help ease cancer-related fatigue during and following cancer treatment [228, 229, 348] and improve quality of life among survivors [346-348].

  o Survivors that reported greater weekly moderate vigorous physical activity also reported less depressed mood and lower clinician-rated depression [348].

- A review of survivorship studies found that most reports demonstrated that physical activity led to an improved overall and breast cancer-specific survival [349]. This effect may even be greatest in older women.

- Physical activity may reduce the risk of breast cancer through an influence on ovarian function and a decrease in progesterone and estrogen concentrations via reduced body fat [320]. Furthermore, exercise may increase sex hormone-binding globulin* (SHBG) levels and thereby reduce estradiol*.

- An increase in lean body mass (often achieved through physical activity) was associated with a favorable change in 2-hydroxyestrone: 16-a-hydroxyestrone, a proposed biomarker of breast cancer risk [350].

- Additionally, exercise reduces CRP levels [352], serum insulin* levels [351-352], serum IGF-I levels [217,232], and improves insulin* sensitivity [320, 352].

  o Moderate- to vigorous-intensity activity also associated with a lower fasting plasma glucose [352].

- Greater physical activity in obese women was associated with significantly less mammographic density, possibly suggesting another mechanism for the protective effect of physical activity [353].

- Moderate-intensity exercise lowers the increased risk of breast cancer in diabetic women [354].

- Healthy weight control is encouraged with an emphasis on exercise to preserve or increase lean muscle mass.

Additional Nutritional and Lifestyle Factors for Breast Cancer Survivors

ANTIOXIDANTS* – Found in abundance in fruits and vegetables!

- Prevent oxidative damage in body cells.

  o Research indicates a link between oxidant damage and breast carcinogenesis*.

- Examples of antioxidant* nutrients and non-nutrients include vitamins A, C, and E, selenium, lycopene, and beta-carotene.

- While research generally supports dietary antioxidants more so than supplemental antioxidants*, a Canadian case-control* study reported that compared to no supplementation, women who took vitamin C, E, beta-carotene, and zinc supplements for 10 or more years may be protected from developing breast cancer [355].

- Note that patients may be advised to NOT consume high-dose antioxidant* supplements during chemotherapy or radiation therapy. Antioxidant* consumption via food sources and a basic multivitamin supplement are considered safe.

Selenium

- Antioxidant* that scavenges free radicals and suppresses damage due to oxidation. Also is essential for the immune system.

- Promising evidence indicates that selenium may decrease the risk of breast cancer [356-363].

  o Selenium inhibits cell proliferation and induces apoptosis* [360-361, 364].

  o Selenium may interfere and alter estrogen receptors decreasing mammary tumor incidence [358].

- In a Swedish cohort* study of over 3,000 women diagnosed with breast cancer, dietary selenium intake was inversely associated with breast cancer mortality and overall mortality [362].

- Research shows that selenium reduces the incidence of malignant cells in animal models [359], and enhances the effects of chemotherapeutic drugs, such as [357] taxol and adriamycin [357, 361].

- Toenail selenium concentrations tended to be lower in postmenopausal breast cancer patients when compared with healthy non-cancer patients, but the differences did not reach statistical significance [365].

  o Interestingly, this study also found that plasma triiodothyronine (T3) (a thyroid hormone) concentration was positively associated with toenail selenium in breast cancer patients and controls. T3 concentration was significantly lower in breast cancer patients compared to healthy non-cancer patients.

- One study suggested the combination of selenium and iodine, typical of a Japanese diet, act synergistically in decreasing breast cancer risk [366]. It is known that iodine plays an important role in thyroid function. Thus, selenium status may affect both thyroid hormone status and iodine availability.

- Selenium is a precursor to the glutathione* (GSH) antioxidant* system. GSH is the principal protective mechanism of the cell and is a crucial factor in the development of the immune response by the immune cells [367].

  o Studies suggest the ratio of selenium to glutathione* is lower in breast cancer patients [356]. Research indicates that dietary selenium supplements correct abnormal glutathione* turnover.

- Additionally, the type of selenium may have influential effects. Selenium in the form of selenomethionine or methylseleninic acid may reduce/delay breast cancer metastasis whereas sodium selenite appears to exacerbate cancer growth [368].

Turmeric (Curcumin)

- Curcumin, the yellow pigment and active component of turmeric and many curries, is a potent antioxidant*, that exhibits chemopreventive and growth inhibitory activity in several tumor cell lines [369-375].

  o Tetrahydrocurcumin, one of the major metabolites of curcumin, exhibits significant inhibition of breast cancer cell growth [376].

  o Curcumin and tamoxifen synergistically inhibited cancer cells [373].

  o Note that curcumin has been shown to inhibit cyclophosphamide-induced apoptosis*, thus it's advisable to not use curcumin supplements when taking cyclophosphamide [377].

- Evidence suggests that curcumin may suppress tumor initiation, promotion and metastasis [371, 378].

  o This may occur through enhanced apoptosis* [369, 371].

- Additionally, curcumin promotes detoxification in the liver and possesses anti-inflammatory activity, possibly by inhibiting COX-2 activity [379-380].

- Curcumin prolonged tumor-free survival in mice [375].

Vitamin C

- Studies assessing vitamin C and the risk of breast cancer are mixed – about half of the studies support vitamin C to be protective [9, 36, 381-383] while the other half suggest no association [384-390].

  o Vitamin C induces apoptotic effects on breast cancer cells [382].

- Low plasma levels of vitamin C have been associated with a greater risk of breast cancer [391].

- Dietary vitamin C has been significantly associated with reduced mortality in breast cancer survivors [36].

- Furthermore, risk of recurrence and mortality was reduced in women who consumed vitamin C supplements for more than three years [392].

- Women in the highest quartile of pre-diagnosis vitamin C intake had a 25% lower risk of breast cancer mortality compared with those in the lowest quartile yet no association was found between post-diagnosis vitamin C supplement use and mortality from breast cancer [393].

- A meta-analysis* examining vitamin C intake and breast-cancer specific mortality concluded that post-diagnosis vitamin C supplementation may be associated with a reduced risk of mortality [383].

- In a study of 45 patients with various cancers, 7.5-50 g of vitamin C were administered after standard chemotherapy treatments; high dose intravenous vitamin C lead to lower CRP values, a biomarker for inflammation [394].

- A randomized 5-month study of breast cancer patients undergoing chemotherapy showed that co-administration of vitamins C (500 mg daily) and E (400 IU daily) restored their antioxidant* status, reduced DNA damage, and may be useful in protecting against chemotherapy related side-effects [395].

Vitamin E

- Vitamin E acts as a cellular antioxidant* and an anti-proliferating agent. It consists of both tocopherols and tocotrienols.

    o Some research indicates that tocotrienols are the components of vitamin E responsible for growth inhibition in human breast cancer cells [396].

- Research is inconsistent on the protective effects of vitamin E and breast cancer. Data from most prospective studies have not revealed a protective relationship between vitamin E and risk of breast cancer [384].

- While supplemental vitamin E does not consistently appear to offer protection against breast cancer [222], taking vitamin E for more than three years has been associated with a modest protective effect [392]. Additionally, these researchers reported a decreased risk of recurrence and mortality associated with long-term use of vitamin E supplements.

- The Shanghai Breast Cancer study was a population based case-control* study that found a 20% reduction in breast cancer risk with vitamin E supplementation [397].

- Additionally, low plasma levels of vitamin E have been associated with a greater risk of breast cancer [391].

- It was demonstrated recently that dietary vitamin E, unlike supplemental sources of vitamin E, significantly reduced oxidative damage as measured by urinary biomarkers [222].

- Note that findings suggest that vitamin E supplements (400 mg) may interfere with the therapeutic effects of tamoxifen [398].

Resveratrol

- Resveratrol is a polyphenol* found primarily in red grape skins with known antioxidant and anti-inflammatory properties, and is emerging as a potent chemopreventive and anticancer drug [399].

- Resveratrol has exhibited potential anticarcinogenic activities in several studies.

    o Reduced tumor growth, decreased angiogenesis, and induced apoptosis in mice [400].

    o Less tumors and longer tumor latency in a rat study [401].

    o May inhibit IGF-I mediated cell migration in breast cancer cells [402].

    o Induces apoptosis in breast cancer cells [399-400, 403].

    o Decreased levels of vascular endothelial growth factor (VEGF) in breast cancer cells [400].

    o Inhibited cell growth and regulates IGF-II in breast cancer cells [404].

    o Lessened DNA damage [403].

- Recent evidence indicates that resveratrol and glucans have significant synergistic effects on immune function [405].

- Even at low concentrations, phytoestrogens such as resveratrol have anti-proliferative effects on breast cancer cells in an ER-dependent manner. At the same time, they also have the capability of maintaining normal breast cell survival via an ER-independent mechanism [406].

Nutrient/Phytonutrient	Summary	Recommendation
Selenium	Dietary sources include Brazil nuts, seafood, enriched brewer's yeast, and grains. Selenium content depends somewhat on the amount of selenium in the soil in which the products are grown.	200 mcg selenium daily through diet and/or supplements Two Brazil nuts provide 200 mcg selenium.
Turmeric (curcumin)	A deep orange-yellow spice commonly used in curries and Indian cuisine.	Eat liberally.
Vitamin C	Dietary sources include various fruits and vegetables, including papaya, citrus fruits, kiwi, cantaloupe, mango, strawberries, bell peppers, broccoli, and tomatoes.	Include these fruits and vegetables daily.
Vitamin E	Dietary sources include vegetable oils, wheat germ, sweet potatoes, nuts, seeds, and avocados.	Eat vitamin E-rich foods regularly. More research is needed to assess whether or not supplements would be beneficial.
Resveratrol	Dietary sources include grapes, grape products, peanuts, soy, mulberries, and cranberries.	Eat resveratrol-rich foods regularly. More research is needed to assess whether or not supplements would be beneficial.

Flax

- Flax may work to block tumor growth, inhibit angiogenesis*, and enhance the immune system [407].

- Consumption of 5 or 10 g flax for 7 weeks significantly decreased blood levels of estrone* and estradiol* [408].

- Flax has been shown to enhance the effects of tamoxifen [409].

- Flaxseed is the greatest source of mammalian lignans* [410-411], phytoestrogens found in flax, which appear to bind with estrogen and lower circulating levels of estrogen. This action may act as one of the protective mechanisms of flax against breast cancer.

   o Lignans* facilitate the removal of estrogens via increased retention within the gut, which are later eliminated in the feces [412-413].

- Furthermore, lignans* positively influence estrogen metabolism by improving the ratio of 2:16a hydroxyestrone [412-413].

- Lignans appear to modulate the development of breast cancer cells and significantly inhibit cell growth [414].

- In one study, flaxseed (25 g daily) and its metabolites, such as lignans*, reduced tumor growth in patients with breast cancer [410].

- Additionally, a recent pilot study observed lower breast density with a greater intake of dietary lignans* [415]. Dense breasts are a risk factor for breast cancer.

- Flax has been shown in vitro and in human trials to decrease tumor proliferation of breast cancer cells [410, 416].

- An animal study reported that flaxseed inhibited established human breast cancer growth and reduced incidence of metastasis by 45% [409].

- Tumor growth was reduced by 26% and 38%, respectively, when mice consumed a 5% flaxseed diet and 10% flaxseed diet compared with those who ate no flaxseed [411].

  o This effect may be partially due to its downregulation of IGF-I [409, 411, 417], decreased cell proliferation [409, 416, 418], and increased apoptosis* [409, 416, 418].

- Consumption of flaxseed or flax bread, at least weekly, was associated with ~20% reduction in the risk of breast cancer [419].

- Flaxseed oil enhanced the effectiveness of Herceptin in mice [420].

  o Flaxseed oil with low dose Herceptin was as effective as high dose Herceptin.

GREEN TEA

- Tea contains phytonutrients* known as polyphenols* (flavonoids) that provide antioxidant* and anticancer properties [421].

  o May block the formation of cancer-causing nitrosamines* [422].

  o Prevents DNA damage [423].

  o May inhibit tumor growth and induce apoptosis* [424-426].

  o Increase immune response [425].

  o Epigallocatechin gallate (EGCG) alters gene expression to lower the risk of breast cancer [427].

- There is a significant amount of in vitro and in vivo evidence suggesting tea polyphenols* have chemopreventive actions against various cancers [424, 428-429]. More human data is needed.

  o Green tea and its catechin* components inhibit breast cancer growth and angiogenesis* in both cell and animal studies.

  o Studies suggest green tea extract has been successful inhibiting cell proliferation and breast cancer [421].

- Many studies indicate a lower risk of breast cancer with green tea consumption, but more research is needed for conclusive evidence [430-434].

- EGCG has been shown in human studies to inhibit human breast cancer cell proliferation, reduce tumor invasion and metastasis and prevent recurrence of breast cancer in early stage cases (stage I & II) [435-437].

- A meta-analysis* reported that drinking green tea decreased the risk of breast cancer by 22% when comparing women with the highest vs lowest intake [430].

- A case-control study* found that green tea consumption was associated with a significant reduction in risk of breast cancer [433].

  o Risk ↓ by 13% for women consuming 1-249 g of dried green tea leaves annually.

  o Risk ↓ by 32% for women consuming 250-499 g of dried green tea leaves annually.

  o Risk ↓ by 41% for women consuming 500-749 g of dried green tea leaves annually.

  o Risk ↓ by 39% for women consuming ≥750 g of dried green tea leaves annually.

  o Moreover, protection was greater with a longer duration of drinking green tea, a greater number of cups consumed and the more new batches prepared daily.

- However, combined studies of 35,000 Japanese women found that green tea did not affect risk of breast cancer [438].

- Research suggests that while green tea did significantly decrease tumor mass, when green tea was combined with soy phytonutrients*, the tumor mass decreased even further [439]. Further evidence indicates a possible synergistic relationship between soy and green tea consumption [432].

- Similarly, a synergistic effect of green tea and Ganoderma lucidum mushroom extracts on the suppression of growth and invasiveness of metastatic breast cancers was observed [440].

- Additionally, green tea increased the inhibitory effect of tamoxifen on the proliferation of ER + breast cancer cells [441-442].

- Furthermore, some evidence suggests that the association of tea catechins* and breast cancer may depend on specific genotypes [432].

SOY

- Associated with reduced rates of heart disease [443-445], protection against osteoporosis [446-447], and certain types of cancer, including breast cancer [448-450].

- While there has been contention regarding soy and breast cancer, research findings are predominantly neutral [451-453], if not protective [8, 450, 454-461].

  o The majority of short-term soy intervention studies conducted in premenopausal women show a reduction in endogenous* estrogen levels in association with soy intake, and thus, possibly protecting from breast cancer.

  o The conflicting data on the effects of soy isoflavones and breast tumor growth are based on cell studies.

- Recent human research has been more promising.

  o A study of 3,088 breast cancer survivors over 7.3 years showed that women with the highest isoflavone intake of >16.3 mg/day had a 54% reduction in risk of death [452].

  o Similarly, a prospective study concluded that the highest soy isoflavone intake was associated with decreased breast cancer mortality in the Chinese population [457].

- A case-control* study in China showed that the highest relative soy isoflavone intake was associated with a 58% decrease risk of breast cancer, and the highest intake of soy protein decreased breast cancer risk by 54% [450]. Interestingly, these results were strongest in postmenopausal women and ER+/PR+ women.

- A statistically significant inverse association between plasma genistein and breast cancer was reported among Japanese women [454].

- A recent meta-analysis of well-controlled studies that included high-soy-consuming Asians reported a significant trend of decreasing risk with increasing soy food intake. Risk was lowest among those who consumed ≥20 mg isoflavones daily [455].

- High soybean intake in Korean women resulted in a significantly lower risk of breast cancer in postmenopausal women [8].

- Postdiagnosis soy consumption of greater than 10 mg soy isoflavones daily significantly reduced the risk of recurrence among both US and Chinese women [459]. Additionally, breast cancer mortality and overall mortality were nonsignificantly reduced.

- In a large population based cohort study of over 5000 breast cancer survivors in China, soy food intake was inversely associated with mortality and recurrence [460]. This association was evident among women with either ER+ or ER- breast cancer and was present in both users and nonusers of tamoxifen.

- It's becoming more apparent that the timing of soy exposure is critical. Consumption of soy foods or an exposure to a soy isoflavone genistein during childhood and adolescence in women, and before puberty onset in animals, appears to reduce the risk of breast cancer later in life [462].

- The type of soy consumed may provide some insight to the inconsistent findings. It has been demonstrated that soy processing increases tumor growth in mice for postmenopausal ER+ breast cancer [463].

  - The difference in tumor growth observed may be related to isoflavone metabolism and bioavailability, but more research is needed [464].

  - Nonetheless, these studies suggest that WHOLE SOY FOODS appear to not have a negative effect on postmenopausal ER+ breast cancer.

  - A recent cohort* study of breast cancer patients found that soy foods had no negative impact on breast cancer survival [465-466].

- An Asian-American study on soy found that women, pre- and postmenopausal, who consumed tofu, had a 15% reduced risk of breast cancer with each additional serving per week [448].

- Moreover, a recent trial reported that women in the highest tertile intake of tofu had a 51% decrease risk of premenopausal breast cancer when compared with women in the lowest tertile [449]. No statistical significant association was observed between soy intake and breast cancer risk among postmenopausal women.

- A prospective trial reported breast cancer mortality reduced 36-38% with an average intake of soy isoflavone above 17.3 mg/day [467]. Furthermore, prognosis was better for women with ER+ tumors with a high intake of soy isoflavones.

- A meta-analysis* of 35 studies analyzing the association between soy intake and breast cancer risk discovered that soy isoflavone intake lowered the risk of breast cancer for both pre- and post-menopausal women in Asian countries, but the evidence was nonsignificant for women in Western countries [453]. Thus, region could also be significantly influencing results.

- Soy consumption has been suggested to exert potential cancer-preventive effects in premenopausal women, such as increased menstrual cycle length and SHBG* levels and reduced estrogen levels.

    o 40 mg/day soy isoflavones increased menstrual cycle length in Western women [468].

    o Research also suggests that soy isoflavones may significantly improve the 2-hydroxyestrone:16-a-hydroxyestrone ratio [469].

    o Additionally, soy intake increases time spent in the follicular cycles, when proliferation is at its lowest [468].

- Furthermore, vegan protein sources, such as soy, appear to decrease circulating IGF-I activity, which may impede cancer induction [444, 470-471].

- Recent literature assessing the effects of soy and tamoxifen have yielded neutral [472] or beneficial findings [473].

    o In a study of Asian American breast cancer survivors on tamoxifen, soy intake had no effect on levels of tamoxifen or its metabolites [472].

    o The combination of tamoxifen and genistein inhibited the growth of ER+/HER2- human breast cancer cells in a synergistic manner in vitro [473].

- In a randomized placebo-controlled study, it was found that gene expression associated with soy protein intake and high plasma genistein is due to an overexpression of FGFR2 and cell cycle proliferation genes, leading to the conclusion that soy can adversely affect women with this type of gene expression [474].

Source	Amount of Soy Protein (gm)	Amount of Soy Isoflavones (mg)
Miso (1 tbsp)	2	7-10*
Soybeans, edamame (1/2 cup)	11	35*
Soy milk (8 fl oz)	10	23*
Soy nuts (1/4 cup)	19	40-50*
Tempeh (1/2 cup)	19.5	36*
Tofu (4 oz)	13	39*

* Isoflavone content varies by brand

Vitamin D

- Epidemiological studies suggest an inverse relationship between sun exposure, serum levels of 25(OH)-vitamin D, and vitamin D intake and the risk of developing and/or surviving cancer [475-476].

    o Possible mechanisms to explain the protective effects of vitamin D may be its role as a nuclear transcription factor that regulates cell growth, differentiation, apoptosis and a wide range of cellular mechanisms central to the development of cancer.

    o Furthermore, breast density, a factor that may increase the risk of breast cancer, was inversely associated with vitamin D intake [477].

- The women in the Nurses' Health Study observed a 30% reduction in risk of breast cancer comparing the highest with lowest quintiles of 25(OH)-vitamin D levels [478].

- Post-menopausal breast cancer risk was significantly inversely associated with serum 25(OH)-vitamin D levels [479].

  o Risk decreased as women's levels increased from 30 nM (12 ng/ml) to ≥ 75 nM (30 ng/ml).

- A meta-analysis* of prospective studies reported that with a 5 ng/mL increase in 25(OH)-vitamin D levels, vitamin D was associated with a 12% lower risk of breast cancer, with suggestive flattening at higher doses (>35 ng/mL) [480].

- A case-control* study in China found that women with the highest quartile 25(OH)D level showed a significant decreased breast cancer risk and every 1 ng/ml increment of plasma 25(OH)D level led to a 16% lower odds of breast cancer [481].

- In a population-based case-control* study, dietary vitamin D intake was positively associated with breast cancer, whereas vitamin D supplement use was inversely associated with breast cancer [482].

  o These associations were observed for ER+/PR+ and ER-/PR- breast cancers, but not for ER+/PR- disease.

- Larger tumor size at diagnosis significantly correlated with lower 25(OH)-vitamin D serum levels [483]. Additionally, postmenopausal women with higher 25(OH)-vitamin D levels had an improved breast cancer-specific outcome.

- Three meta-analyses* showed that high blood 25(OH)-vitamin D levels in breast cancer patients were significantly associated with lower breast cancer mortality [484-486].

  o 25(OH)-vitamin D levels >30 ng/ml in breast cancer patients were associated with significantly lower mortality [487].

- It is now believed that the recommended vitamin D dose should be between 1,000 and 5,000 IU per day, and in some cases, even higher.

  o Research indicates that vitamin D3 (cholecaciferol) is better absorbed than vitamin D2 (ergocalciferol) [488].

- Due to the likelihood of a biochemical deficiency without clinical symptoms or signs, a serum 25(OH)-vitamin D level is recommended.

  o Optimal serum 25-hydroxy vitamin D levels have not been established though research suggests that restoring levels to 30-80 ng/ml may be ideal [485]. Earlier research had suggested 36-40 ng/ml [489].

  o While supplementation may be recommended, more appropriate dosing of vitamin D supplementation can be made once a serum 25(OH)-vitamin D level has been established.

Food or Beverage	Summary	Recommendation
Flaxseed	Good source of omega-3 fatty acids and fiber, contains protein, calcium, potassium, B vitamins, iron, and boron. Opt for ground flax seeds rather than whole flax seeds, flax seed oil, flax supplements to increase bioavailability. Flax seeds may be ground in a coffee grinder, blender, or food processor.	2 Tbsp ground flaxseed daily Flax can have a laxative- like effect, thus, it is wise to gradually increase consumption. Sprinkle into various foods and beverages, including hot cereals, tomato sauces, fruit smoothies, brown rice or other grains. Store flax in the refrigerator or freezer.
Green tea	Green tea contains does contain caffeine though much less than coffee or black tea. If opting for decaffeinated green tea, opt for those naturally decaffeinated with water as typical caffeine extraction results in a significant loss of phytonutrients.	1-4 cups daily
Soy	Contains various nutrients, including protein, fiber, calcium, and B vitamins. Rich in antioxidants*, known as isoflavones, namely genistein and daidzein. Among others, dietary sources include soybeans, edamame, tofu, soymilk, tempeh, miso, and soy nuts.	Unless soy has been a part of your diet for years, postmenopausal individuals with ER+ breast cancer may be advised to limit soy consumption to 1-3 daily servings. Soy supplements or isoflavone extracts are not recommended.
Vitamin D	A fat-soluble vitamin that we generate through skin synthesis of sunlight (ultraviolet rays). Dietary sources include cold-water fish, eggs, and fortified products, such as milk, soy milk, and cereals.	1,000-4,000 IU daily Maintain serum 25 (OH)-vitamin D >40 ng/mL.

MELATONIN

- Melatonin is a hormone produced by the pineal gland. Its primary function involves the regulation of the body's circadian rhythm, endocrine secretions, and sleep patterns.

- Some research indicates that individuals with low levels of melatonin are at greater risk for breast cancer.

- The risk of breast cancer was reduced by 33% in postmenopausal women who slept 9+ hours compared to those who slept ≤6 hours daily [500].

- o Melatonin levels were 42% higher in those who slept 9+ hours vs ≤6 hours daily.

- o Previous studies have reported an increased risk of breast cancer in night-shift workers who are exposed to light at night [501-503].

- It may be that the length of time working night shifts makes a difference as evidenced by this study where women who reported more than 20 years of rotating night shift work faced an increased risk of breast cancer compared with women who did not report any rotating night shift work [502].

  - o In vitro and animal research has supported the protective effect of melatonin against breast cancer [504-505].

  - o A recent study found that women with higher urinary melatonin levels had a 30-41% reduced risk of breast cancer [506].

- Melatonin may act by:

  - o Inhibiting cell proliferation [505, 507-508].

  - o Inducing apoptosis* [509].

  - o Inhibiting angiogenesis* [505].

  - o Enhancing the immune system [507, 510-511].

- May improve survival in cancer patients by protecting the immune system from damage caused by chemotherapy [509].

  - o Reducing IGF-I [512-513].

  - o Decreasing the number and activity of estrogen receptors, thus reducing ways that the cancer cell connects to estrogen [514-515]. Specifically, recent studies show that melatonin suppresses estrogen production in breast adipose fibroblasts, and lower levels of melatonin in aging women may increase ER+ breast cancer [516].

- Various studies indicate that melatonin may inhibit breast cancer by interfering with estrogen pathways, thus acting in an anti-estrogenic manner [508, 510, 516-518].

  - o Melatonin decreases the formation of estrogen from androgens by inhibiting aromatase activity [508].

- Furthermore, the combination of melatonin and retinoids* [519], the combination of all-trans retinoic acid, somatostatin, and melatonin [520], and the combination of melatonin and vitamin D3 [521] appear to work synergistically to inhibit the growth of breast cancer cells.

- Melatonin does have blood thinning properties, thus it is recommended to not use supplemental melatonin 7-10 days prior to surgery.

FOOD SAFETY

- Especially important for those with weakened or impaired immune systems and while on chemotherapy.

- The following recommendations have been adapted from guidelines provided by the American Cancer Society.

  - o Wash foods thoroughly before eating.

- o Keep all aspects of food preparation meticulously clean.

- o Use special care in handling raw meats, poultry, and eggs.

- Thoroughly clean all utensils, countertops, cutting boards, and sponges that contacted raw meat.

- Thaw meats and fish in the refrigerator.

  - o Transfer large volumes of leftovers, such as soup, rice, or casseroles, to shallow containers and place in refrigerator. This process ensures proper cooling.

  - o Do not eat perishable foods that have been left out of the refrigerator for more than two hours.

  - o Store foods at low temperatures (less than 40°F) to minimize bacterial growth.

  - o When eating in restaurants, avoid foods that may have bacterial contamination, including sushi, salad bars, buffets, unpasteurized beverages or food products, and raw or undercooked meat, poultry, fish, and eggs.

BONE HEALTH

- Pre- and postmenopausal survivors of breast cancer are at great risk for development of osteoporosis.

  - o Thus, screening and preventive strategies for osteoporosis are imperative.

- Even small amounts of increased bone mass provide great risk reduction for fractures.

- Generally, humans reach peak bone mass around 30 years. After the age of 30, the goal is to maintain or prevent loss of bone mass.

  - o On average, humans lose 0.3 – 0.5% bone mass yearly after 30 years.

- First signs of osteoporosis are seen in spine, hip, and wrist.

  - o Symptoms include back pain or tenderness, loss of height, and slight curving of upper back.

- Risks for osteoporosis include: female, Asian or white ethnicity, age, menopause, amenorrhea, low testosterone levels in men, sedentary lifestyle, family history, diet low in calcium, diet low in vitamin D, excessive alcohol and tobacco use, excessive caffeine use, diet high in sodium, diet excessive in protein or very low in protein, certain medications (diuretics, steroids, thyroid meds), celiac disease

- Many nutrients have bone-building effects, including calcium, vitamin D, phosphorus, magnesium, vitamin K, potassium, and boron (see table below).

- Exercise increases bone mass before menopause and slows bone loss after menopause.

  - o Include weight-bearing exercise, such as walking, jogging, skiing, stair climbing, aerobics, and others.

  - o Resistance training exercises are useful to strengthen muscles and bones.

- Recent research indicates diets high in fruits and vegetables have a positive effect on bone health.

  - o Good source of minerals (potassium, magnesium) that may have direct effects on bone cells.

  - o Counteract acid environment.

  - o Lower urinary calcium loss.

- o   Enhanced calcium bioavailability of most vegetables.

- Soy protein and/or soy isoflavones have been proposed to delay bone loss.

  - o   May help to prevent urinary calcium loss.

  - o   Soy contains phytosterols that mimic the actions of estrogen.

  - o   May help to prevent rapid bone loss of menopause years.

  - o   Studies report that soy may increase BMD.

- Calcium supplements

  - o   Take 500 mg or less per meal to maximize absorption.

  - o   Calcium citrate, lactate, or gluconate are recommended if you have iron deficiency.

- These do not decrease iron absorption like calcium carbonate.

  - o   Calcium carbonate is least expensive, but may increase gas and bloating in some individuals.

- What about antacids with calcium?

  - o   Trace minerals like zinc or iron may be less well-dissolved and absorbed with a lower stomach acidity.

  - o   If you're only taking enough antacid for the purpose of calcium needs, should not present a major problem, but not ideal.

  - o   May interact with thyroid medication.

- DEXA (dual-energy X-ray absorptiometry) instruments allow rapid, painless, noninvasive, and highly reproducible measurements of bone density to be made [522].

  - o   These measurements are used to diagnose osteoporosis, low bone density, and risk of fracture and to determine rates of bone loss or the effectiveness of treatment over time [523-524].

Bone Health – Bottom Line

- Balanced diet – high in fruits and vegetables

- Calcium

  - o   Aim for 3 rich sources daily.

  - o   Include a supplement if necessary.

- Vitamin D

  - o   Meet needs from sun, multivitamin, or other supplement.

  - o   Consider serum vitamin D test.

- Exercise

  - o   Weight-bearing exercise for at least 30 minutes on most days.

- Good posture

- Request to have a full body DEXA scan.

Bone Building Nutrients

Nutrient*	Dietary Sources	Function	Recommendation
Calcium	Dairy products, canned fish with soft bones, beans, leafy greens (especially collard greens, bok choy, and kale), tofu, almonds, fortified products, such as soy milk, cereal, and orange juice	↑ calcium absorption and bioavailability from foods, especially plant sources Vitamin D is essential for calcium absorption.	1000-1200 mg daily
Vitamin K	Dark leafy greens, liver, tomatoes, soybeans, and garbanzo beans Also produced by intestinal bacteria	Associated with ↓ bone turnover and ↓ urinary calcium excretion.	90 mcg daily
Phosphorus	Meat, poultry, fish, eggs, milk, products, legumes, and nuts	Combines with calcium to strengthen bones.	700 mg daily
Magnesium	Whole grains, nuts, seeds, spinach, and most fruits and vegetables	Important in calcium and potassium uptake.	320 mg daily
Potassium	Bananas, strawberries, tomatoes, prunes, potatoes, spinach, and beans	Associated with ↓ urinary calcium and phosphorus excretion.	4700 mg daily
Boron	Apples, avocados, beans, milk, peanuts, peanut butter, pecans, raisins, prunes, and potatoes	Improves calcium absorption. ↓ effects of vitamin D and magnesium deficiency.	2 mg daily
Zinc	Seafood, meats, tofu, whole grains, black-eyed peas, wheat bran and germ	Important in calcium uptake and immune function.	8-15 mg daily

* Vitamin D is listed in the previous table

Hot Flashes

- Hot flashes are a major cause of morbidity among postmenopausal women, including many survivors of breast cancer.

- Approximately 75% of postmenopausal women who had breast cancer report experiencing hot flashes [525].

  o More than 90% of young survivors also experience hot flashes, which can be more severe and long lasting, with iatrogenic ovarian ablation or antiestrogen therapy.

- A cross-sectional study of 300 breast cancer survivors showed that women who gained at least 10 lbs since breast cancer diagnosis were twice as likely to have hot flashes than those who maintained or lost weight [526].

- Various non-hormonal therapies have been studied for improving hot flashes, including soy, black cohosh, red clover, and vitamin E – the clinical value has been limited.

- Supplemental vitamin E at 400 IU/day [527] and 800 IU/day [528] has shown some limited efficacy in improving hot flashes.

- Systematic reviews of randomized controlled trials have observed contradictory results, and meta-analyses* demonstrate no statistically significant reduction of vasomotor symptoms for phytoestrogens [529].

  o Individual trials report significant reductions in vasomotor symptoms for red clover and soy phytoestrogens.

  o The placebo effect in many of these studies was quite strong [530].

  o Studies assessing black cohosh and red clover have had inconsistent results, with some trials showing benefit and some no difference compared with placebo [531].

  o In one study, women receiving black cohosh reported a mean decrease in hot flash score of 20% compared with a 27% decrease for patients on placebo [532].

    - Mean hot flash frequency was reduced 17% on black cohosh and 26% on placebo.

  o A previous study reported reduced hot flashes with soy isoflavones by 9 to 40% in some trials, but most trials observed no effect when compared with placebo [531].

- Black cohosh extract had no effect on serum estrogenic markers [533].

- The use of black cohosh appears to be safe in breast cancer patients [534].

- Psychoeducational interventions, including relaxation, seem to alleviate hot flashes in menopausal women and breast cancer survivors; however, the methodological quality of published research has been considered to be fair or poor [535].

- A summarization of six prospective studies showed a 43.2% reduction of hot flashes from baseline to the end of acupuncture treatment; effects continued on for at least 3 months after the end of acupuncture treatment [536].

- A preliminary study of 25 breast cancer patients reported that 400 mg-800 mg magnesium oxide for 4 weeks resulted in a hot flash score reduction of 50.4% and frequency reduction by 41.4% [537]. Note that magnesium glycinate would be the preferred magnesium source given its increased bioavailability.

WORDS OF WISDOM

"Let food be your medicine and medicine be your food."
- Hippocrates

For additional information or resources, please visit the Ida and Joseph Friend Cancer Resource Center at 1600 Divisadero St. on the first floor , or call at (415) 885-3693. The information in this publication is designed for educational purposes only and is not intended to replace the advice of your physician or health care provider, as each patient's circumstances are individual. We encourage you to discuss with your physician any questions and concerns that you may have.

Three Day Menu Plan: 3 Meals + Snack

This menu is based on 1600 calories, calories can be adjusted by altering portion sizes. The menu has been designed to merely serve as a guide in making healthy food choices. Experiment with substitutions as desired.

Day 1	Day 2	Day 3

Oatmeal, cooked (1cup)
   Non-dairy milk (1 cup)
Flaxseed, ground (1 tbsp)
Chia seeds (1 tbsp)
Blueberries (1/2 cup)
 	
Egg, hard boiled (1 lg)
 	
Green tea (2 cups)
	Green Smoothie
	   Greens (3 cups)
	   Berries, frozen (1/2 cup)
	   Protein powder (1 svg)
	   Ground flax (1-2 tbsp)
	   Chia seed (1 tbsp)
	   Almond milk, unsweetened
	(3/4 cup)
		Egg scramble
		   Eggs (2 lg)
		   Onions (1/4 cup)
		   Spinach (1 cup)
		   Mushrooms (1/2 cup)
		
		Apple (1 med)
		   Almond butter (1 tbsp)
		
		Green tea (2 cups)

Salad
   Spinach (3 cups)
   Broccoli (1/2 cup)
   Carrots (1/2 cup)
   Tomato (1/2 cup)
   Chicken breast (4 oz)
   Barley, cooked (1/2 cup)
Avocado (4 slices)
   Olive oil (1/2 tbsp)
   Vinegar, balsamic (1 1/2 tbsp)
 	
Orange (1 med)
	Vegetable Bean Soup (2 cups)
	
	Corn tortilla (1 med)
	
	Green salad (2 cups)
	   Oil/vinegar dressing (1 tbsp)
		Black bean corn salad (2 cups) over steamed kale (1 cup)

Vegetable juice (12 oz)
 	
Popcorn, air-popped (2 cups)
	Fruit salad (1 cup)
	
	Almonds (1/4 cup)
		Fruit smoothie
		   Banana (1/2 med)
		   Berries (1/2 cup)
		   Flaxseed, ground (2 tbsp)
		   Chia seeds (1 tbsp)
		   Yogurt, Greek plain (1/2 cup)
		   Non-dairy milk (1 cup)

Tempeh fajitas (4 oz)
   Onions & peppers (1.5 cups)
   Salsa (1/4 cup)
   Avocado (1/4 ea)
   Corn tortillas (2 each)
	Chicken & vegetable stir-fry
	   Chicken breast (4 oz)
	   Mixed vegetables (2 cups)
	Walnuts (2 tbsp) OR
	   Olive oil (1/2 tbsp)
	
	Brown rice, cooked (1 cup)
		Salmon (4 oz)
		
		Quinoa, cooked (1 cup)
		
		Asparagus (2 cups)

Recipes

Green Smoothie

Ingredients:

- 3-5 cups greens (spinach, kale, collards, or other)
- 1 tbsp chia seeds
- 1-2 tbsp ground flax seeds
- 3/4 cup unsweetened almond milk
- 1/2 cup frozen blueberries (or other fruit)
- 1 serving unsweetened protein powder

Place liquid in blender followed by the remaining ingredients. Blend and enjoy!

Makes 16 ounces.

Nutrition Information (per 16 oz):

Calories: 363	Dietary fiber: 15gm	Protein: 30 gm
Sodium: 300 mg	Fat: 14.6 gm	Calcium: 633 mg
Saturated fat: 1.6 gm	Iron: 5 mg	Carbohydrates: 34 gm

Recipe developed by Natalie Ledesma, MS, RD, CSO

Baked Tofu

Ingredients:

- 1pound tofu,firm, drained
- 3 tablespoons low sodium tamari or other soy sauce
- 1 teaspoon toasted sesame oil
- 2 cloves garlic, minced
- 1 teaspoon finely minced gingerroot
- 1/2 teaspoon red pepper flakes
- 1 teaspoon brown rice syrup or dark brown sugar

Chop drained firm tofu into 1" cubes. Place tofu cubes in glass dish for baking. Pour marinade or sauce over tofu, stir well. Place tofu in oven at 350 F for 1 hour. Stir every 15-20 minutes.

Makes four 4-ounce servings.

Nutrition Information (per 4 oz serving):

Calories:120	Dietaryfiber: <1gm	Protein:8 gm
Sodium:575 mg	Fat:5 gm	Calcium: 155mg
Saturated fat:<1 gm	Iron:1.4 mg	

Recipe from the Hippy Gourmet's Quick and Simple Cookbook for Healthy Eating

Washington Insider Salad

Ingredients:

- 1 can (15 oz) kidney beans, drained
- 1 can (15 oz) black eyed peas, drained
- 1 1/2 cups cooked barley (substitute quinoa, wild rice, or brown rice to make gluten free)
- 6 tbsp cilantro, chopped finely
- 1 can (11 oz) corn
- 1 1/2 cups tomatoes, diced
- 3 tbsp balsamic vinegar
- 2 tbsp olive oil

Prepare vegetables. Mix all ingredients together, and serve on a bed of dark green leafy lettuce. Add salt and pepper to taste.

Makes 8 servings (1 cup each).

Nutrition Information (per serving):

Calories: 215	Protein: 10 gm	Fat: 4 gm
Dietary fiber: 9 gm		

Recipe developed by Sous Chef Chris at the Occidental Grill, Washington D.C.

Spinach Spread

Ingredients:

- 1 package (10.5 ounces) silken tofu
- 1 tbsp lemon juice
- 1/4 tsp garlic powder
- 3/4 tsp onion powder
- 1/2 tsp dried tarragon
- 1/4 tsp salt
- 1 box (10 ounce) frozen chopped spinach, thawed
- 1 cup coarsely shredded carrots
- 1/4 cup chopped green onion

Puree the tofu and lemon juice in blender until smooth. Whirl in the garlic and onion powders, tarragon, and salt just to blend. Scrape into a mixing bowl. Squeeze the spinach as dry as possible. Stir it into the tofu, along with the carrots and green onion. Mix well. Serve with crackers, pita triangles, or vegetables.

Makes 8 servings (1/4 cup each).

Nutrition information (per serving):

Calories: 39	Sodium: 82 mg	Fat: 1 gm
Calcium: 51 mg	Saturated fat: 0 gm	Carbohydrate: 5 gm
Protein: 4 gm	Dietary Fiber: 2 gm	

Recipe from the U.S. Soyfoods Directory.

Curried Hummus

Ingredients:

- 1/4 cup currants
- 2 cups cooked chickpeas, or 1 15-ounce can, drained and rinsed
- 2 tbsp water
- 2 tbsp freshly squeezed lemon juice
- 1 tbsp tahini
- 1 tbsp extra-virgin olive oil
- 1 tsp curry powder
- 1 tsp ground ginger
- ½ tsp sea salt

Place the currants in a small bowl of hot water to soak and plump up. Combine the chickpeas, water, lemon juice, tahini, olive oil, curry powder, ginger, and salt in a food processor and process until smooth. Transfer to a mixing bowl and adjust the seasoning to taste. Add a spritz of lemon if it needs a little extra zing. Before serving drain the currants thoroughly and stir them into the hummus. Serve with chopped, raw vegetables or whole grain crackers.

Makes 6 servings.

Nutrition Information (per serving):

| Calories: 180 | Carbohydrate: 27 gm | Protein: 7 gm | Dietary fiber: 7 gm |
| Fat: 5.7 gm | Sodium: 630 mg | | |

Recipe from The Cancer-Fighting Kitchen by Rebecca Katz.

Alaska Salmon Bake with Walnut Crunch Coating

Ingredients:

- 1 pound salmon fillets, thawed if necessary
- 2 tbsp Dijon-style mustard
- 1-2 tbsp olive oil
- 4 tsp honey
- 1/4 cup bread crumbs
- 1/4 cup walnuts, finely chopped
- 2 tsp parsley, chopped
- Salt and pepper to taste
- Lemon wedges

Mix together mustard, olive oil, and honey in a small bowl; set aside. Mix together bread crumbs, walnuts, and parsley in a small bowl; set aside. Season each salmon fillet with salt and pepper. Place on a lightly greased baking sheet or broiling pan. Brush each fillet with mustard-honey mixture. Pat top of each fillet with bread crumb mixture. Bake at 450 F for 10 minutes per inch of thickness or until salmon just flakes when tested with a fork. Serve with lemon wedges.

Makes 4 servings (4 oz each).

Nutrition Information (per serving)

    Calories: 228   Protein: 20 gm   Fat: 12 gm
    Omega-3 fatty acids: 1.7 gm

Adapted from Alaska Seafood Marketing Institute.

Pumpkin Oat Bars

Ingredients:

- 3 cups gluten free or regular old fashioned oats
- 2 tsp baking powder
- 1/2 tsp baking soda
- 1/4 tsp salt
- 1 1/4 tsp cinnamon
- 1/8 tsp nutmeg
- pinch of ground cloves
- 1 cup canned pumpkin
- 2 tsp pure vanilla extract
- 1/2 cup unsweetened applesauce
- 1/2 cup dark brown sugar
- 1 tbsp melted coconut oil
    optional: 1/3 cup regular chocolate chips, dried cranberries, raisins, walnuts

Preheat oven to 350 degrees F. Spray 8×11 or 9 inch baking pan with nonstick cooking spray. Make oat flour: Place oatmeal into blender or food processor and blend for 1-2 minutes until oatmeal resembles flour. You may need to stop blender and stir oats a couple of times to ensure that all oats have been blended.

Place oat flour in a medium bowl. Whisk in baking powder, baking soda, salt and spices; set aside. In a separate large bowl, whisk together pumpkin, brown sugar, vanilla extract, oil, and applesauce for 1-2 minutes until the consistency is smooth and creamy. Slowly add in oat flour mixture and mix until just combined.

If using, gently fold in 1/3 cup of chocolate chips, dried fruit, and/or nuts. Pour batter into prepared pan. Bake for 15-25 minutes or until knife inserted into center comes out clean or with just a few crumbs attached. Timing will depend on what size pan you use, but definitely check around 15 minutes. Once finished baking, cool 10 minutes on wire rack. Cut into 16 slices.

Note: Bars can be frozen.

Makes 16 servings.

Nutrition Information (per serving):

    Calories: 107   Carbohydrate: 20 gm   Protein: 3 gm
    Dietary fiber: 2.6 gm   Fat: 2 gm   Sodium: 146 mg

Adapted from the Ambitious Kitchen Blog.

Dilled Salmon Salad with Peas

Ingredients:

- 1 can (15 oz) salmon, drained
- 1 package (16 oz) frozen peas, thawed
- 1/4 cup lemon juice
- 1/4 cup fresh dill (or 1-2 tbsp dried dill)
- 2 tbsp Dijon-style mustard
- 2 shallots, sliced thinly (about 1/2 cup)
- 1 bunch radishes (about 11 medium), thinly sliced
- 6 cups red leaf lettuce
- Salt and pepper to taste

Drain salmon, place in a mixing bowl, and break into pieces. Prepare the lemon juice, shallots, radishes, and lettuce. Add to the salmon the peas, lemon juice, dill, mustard, shallots, and radishes. Mix together gently. Add salt and pepper to taste. Serve salmon mixture over lettuce.

Makes 6 servings (2 cups each).

Nutrition Information (per serving):

| Calories: 160 | Protein: 17 gm | Fat: 4 gm |
| Dietary fiber: 5 gm | | |

Adapted from the Women's Healthy Eating & Living Study (WHEL) at the University of California, San Diego. Developed by Vicky Newman, MS, RD, WHEL nutrition coordinator.

Neat Loaf

Ingredients:

- 2 cups cooked brown rice
- 1 cup walnuts, finely chopped
- 1 onion, finely chopped
- 1/2 medium bell pepper, finely chopped
- 2 medium carrots, shredded or finely chopped
- 1 cup wheat germ (could substitute flax seed or almond meal to be gluten-free)
- 1 cup quick-cooking rolled oats
- 1/2 tsp each: thyme, marjoram, sage
- 2 tbsp soy sauce (or gluten-free tamari)
- 2 tbsp stone ground or Dijon mustard
- Barbecue sauce or ketchup

Preheat the oven to 350 F. Combine all the ingredients except the barbecue sauce or ketchup. Mix for 2 minutes with a large spoon. This will help bind it together. Pat into an oil-sprayed 5x9" load pan and top with barbecue sauce or ketchup. Bake for 60 minutes. Let stand 10 minutes before serving.

Makes 8-10 servings.

Nutrition Information (per serving):

Calories: 204	Sodium: 248 mg	Protein: 9 gm
Cholesterol: 0 mg	Fat: 9 gm	Carbohydrates: 19 mg

Recipe from The Peaceful Palate written by Jennifer Raymond.

Raw Kale Salad with Aged Balsamic Vinaigrette

Ingredients:

• 1 large bunch (about 1 pound) lacinato kale (also called"dinosaur" or "Tuscan" kale)
• Kosher salt and freshly ground pepper
• 2 tsp Dijon mustard (optional)
• 2 tbsp good quality balsamic vinegar
• 1/4 cup extra-virgin olive oil
• Juice of 1/2 lemon (optional)
• 1 medium shallot, finely chopped (optional)
• A handful toasted nuts such as almonds or walnuts (about 1 ounce or 1/4 cup)
• 1 apple, chopped or a handful dried fruit such as currants, cranberries, raisins, dried cherries, etc (about 1 ounce or 1/4 cup)

Strip the leaves off the stems. (Save the stems for another use such as green smoothies.) Wash and pat dry the leaves. Stack the leaves and cut them crosswise into strips about 1/4 inch wide. Pile the kale in a salad bowl and sprinkle with 1/4 teaspoon salt. With clean hands, massage the salt into the leaves until the kale begins to feel moist and darken a bit, about 2 or 3 minutes. You can do this well ahead of time, cover the salad with plastic wrap, and leave at room temperature or refrigerate for several hours.

In a small bowl, whisk together the mustard and vinegar. Grind in some pepper and then whisk in the oil. Taste for balance and add as much lemon juice, salt, and pepper as needed to create a vibrant, fresh, sweet/tart balance. Go easy on the salt to account for the salt already on the kale. When ready to serve, toss the greens with the dressing, shallots, apple or dried fruit, and nuts. Serve immediately.

Serves 6 to 8

Nutrition Information (per serving - 1/6 recipe):

Calories: 180	Sodium: 382 mg	Protein: 4 gm
Cholesterol: 0 mg	Fat: 13 gm	Dietary fiber: 2 gm
Carbohydrate: 15 gm		

Recipe adapted from Living On, Living Well, UCSF Survivorship Retreat by Penni Wisner, The Kitchen Coach.

Quinoa/ Sweet Potato Patties

Ingredients:

• 1 1/2 cups sweet potato, peeled and chopped
• 1 cup quinoa
• 2 tbsp parsley, fresh
• 1/2 tsp sea salt
• 2 tsp extra-virgin olive oil

Steam or bake sweet potatoes until done. Drain and mash potatoes. Wash the quinoa well and drain. Dry toast the quinoa in a skillet until slightly browned. Meanwhile, bring a pot of water to a boil. Add the toasted quinoa to the boiling water and cook, with lid off, for ~15 minutes. Drain well. Mix the mashed potatoes and quinoa. Add the parsley and salt. Form 8 patties and place in a lightly oiled pan over medium-high heat. Cook for about 5 minutes on each side and serve warm.

Makes 8 servings.

Nutrition Information (per serving):

Calories: 125	Sodium: 165 mg	Protein: 4 gm
Cholesterol: 0 mg	Fat: 2 gm	Carbohydrate: 22 gm

Recipe adapted from the Vegetarian Resource Group.

Coconut Quinoa Chia Granola

Ingredients:

• 1 cup rolled oats (or steel cut oats)
• 1/2 cup quinoa, uncooked
• 1/2 cup almonds, coarsely chopped/slivered/sliced
• 1/4 cup chia seeds
• 1/8 tsp sea salt
• 3 tbsp coconut oil
• 3 tbsp maple syrup
• 1 tsp vanilla extract
• 1/4 cup coconut flakes, unsweetened

Preheat oven to 325 degrees F and line baking sheet with parchment paper. In a medium mixing bowl, add oats, quinoa, almonds, chia seeds, salt and mix. In a small bowl, melt coconut oil in a microwave and add maple syrup and vanilla extract. Stir to combine and pour into a bowl with dry ingredients. Mix thoroughly and spread in an even layer on prepared baking sheet. Bake on a third rack from the bottom for 30 minutes. Remove granola from the oven and sprinkle with coconut flakes. Let cool completely and do not touch.

Makes 24 servings.

Nutrition Information (per 2 tbsp serving):

Calories: 60	Cholesterol: 0 mg	Carbohydrate: 7.8 gm
Sodium: 15 mg	Fat: 2.8 gm	Sugars: 1.9 gm
Fiber: 1.1 gm		

Recipe adapted from the iFoodReal.com.

Nutrition Resources

Books

Anticancer: A New Way of Life - written by David Servan-Schreiber (2008)

Five to Thrive - written by Lise Alschuler & Karolyn Gazolla (2011)

How to Prevent & Treat Cancer with Natural Medicine – written by Michael Murray (2002)

Life Over Cancer - written by Keith Block (2009)

The Color Code – written by James Joseph, Daniel Nadeau, & Anne Underwood (2002)

The UltraMind Solution - written by Mark Hyman (2009)

Ultra Metabolism – written by Mark Hyman (2006)

Cookbooks

One Bite at a Time – written by Rebecca Katz, Marsha Tomassi, & Mat Edelson (2004)

The Cancer-Fighting Kitchen - written by Rebecca Katz with Mat Edelson (2009)

The Cancer Wellness Cookbook - written by Kimberly Mathai (2014)

The Healthy Mind Cookbook - written by Rebecca Katz with Mat Edelson (2015)

The UltraMetabolism Cookbook - written by Mark Hyman (2007)

Newsletters/Magazines

Cooking Light http://www.cookinglight.com Fax: (205) 445-6600

Environmental Nutrition http://www.environmentalnutrition.com (800) 829-5384

Nutrition Action Health Letter http://www.cspinet.org/nah/ Fax: (202) 265-4954

Websites

American Cancer Society http://www.cancer.org (415) 394-7100

American Institute for Cancer Research http://www.aicr.org (800) 843-8114

Caring4Cancer - Provides up-to-date & comprehensive information on the connection between nutrition & cancer – http://www.caring4cancer.com

Consumer Lab - Evaluates quality of over-the-counter supplements http://www.consumerlab.com

Diana Dyer, MS, RD – Breast cancer survivor & dietitian http://www.cancerrd.com

Eating Well - Offers recipes, cooking tips, articles regarding health, and more. http://www.eatingwell.com

Harvard Nutrition Source http://www.hsph.harvard.edu/nutritionsource/

Ida & Joseph Friend Cancer Resource Center – UCSF Mt.Zion http://cancer.ucsf.edu/crc

(415) 885-3693

National Cancer Institute http://www.nci.nih.gov/ (800) 4-CANCER (800-422-6237)

Oncolink – Provides information regarding clinical trials, newsgroups, psychosocial support, & more. http://oncolink.upenn.edu

Oncology Nutrition DPG - Provides articles, recipes, & resources. http://www.oncologynutrition.org

San Francisco Vegetarian Society – Monthly restaurant outings & pot-luck dinners; call 415-273-5481. http://www.sfvs.org

The Vegetarian Resource Group - Provides vegetarian nutrition information & vegetarian recipes http://www.vrg.org

The World's Healthiest Foods - Provides healthful recipes and basic nutrient information. http://www.whfoods.com

WebMD http://my.webmd.com

Glossary

Angiogenesis – The formation of new blood vessels.

Antioxidant – A substance that inhibits oxidation or inhibits reactions promoted by oxygen or peroxides.

Apoptosis – Programmed cell death.

Carcinogenesis – Beginning of cancer development.

Case-Control Studies – An epidemiological study in which a group of, say, cancer patients (cases) is compared to a similar but cancer-free population (controls) to help establish whether the past or recent history of a specific exposure such as smoking, alcohol consumption and dietary intake, etc. are causally related the risk of disease.

Catechin – One of the tannic acids; phytonutrient, specifically, one of the flavonoids found in green tea.

Creatine – An amino acid that is formed in the muscle tissue of vertebrates; supplies energy for muscle contraction.

Cohort Studies – Follow-up study of a (usually large) group of people, initially disease-free. Differences in disease incidence within the cohort are calculated in relation to different levels of exposure to specific factors, such as smoking, alcohol consumption, diet and exercise, that were measured at the start of the study and, sometimes, at later times during the study.

Eicosanoids – Biologically active compounds that regulate blood pressure, blood clotting, and other body functions. They include prostaglandins, thromboxanes, and leukotrienes.

Endogenous – Originating from within, as within the body.

Estradiol – A naturally occurring powerful estrogen secreted by the mammalian ovary.

Estrone – A naturally occurring weak estrogen secreted by the mammalian ovary.

Glutathione – A polypeptide produced primarily in the liver; involved in DNA synthesis and repair, protein and prostaglandin synthesis, amino acid transport, metabolism of toxins and carcinogens, immune system function, prevention of oxidative cell damage, and enzyme activation.

Glycemic Index - A numerical value given to a carbohydrate-rich food that is based on the average increase in blood glucose levels occurring after the food is eaten.

Glycemic Load - An index indicating the amount of carbohydrate contained in a specified serving of a particular food. It is calculated by multiplying the food's glycemic index by its carbohydrate content in grams and then dividing by 100.

Insulin - Insulin is a hormone produced by the pancreas in the body that regulates the metabolism of carbohydrates and fats, especially the conversion of glucose to glycogen, which lowers the body's blood sugar level.

Lignans - Phytoestrogens that have a similar chemical structure to estradiol and tamoxifen; appear to offer protection against breast cancer.

Meta-analysis – The process of using statistical methods to combine the results of different studies.

Mutation – Abnormal cell development.

Nitrosamines – Derivatives of nitrites that may be formed in the stomach when nitrites combine with amines; carcinogenic in animals.

Phytonutrients – Plant compounds that appear to have health-protecting properties.

Polyphenols – Phytonutrients that act as an antioxidant; compounds that protects the cells and body chemicals against damage caused by free radicals, reactive atoms that contribute to tissue damage in the body.

Retinoids – Chemically related compounds with biological activity similar to that of retinol; related to vitamin A.

Sex hormone-binding globulin (SHBG) – A protein in the blood that acts as a carrier for androgens and estradiol; inhibits the estradiol-induced proliferation of breast cancer cells.

References

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