

Cancer Association of South Africa (CANSA)



Research • Educate • Support

Fact Sheet on Nutrition for Individuals Diagnosed with Breast Cancer

Introduction

Good nutrition is especially important for any person living with cancer. Eating a variety of foods and well-balanced meals can help one feel better and stay stronger. Eating well during treatment helps to maintain body weight, improve strength and energy, decrease the risk of infection and assist the body in healing and recovery from cancer treatments.

Picture Credit: Nutrition in Cancer

Nutrition In Cancer



Most cancer treatments work better when one is well nourished. People with cancer who are well nourished and able to maintain a healthy body weight often have a better prognosis.

A healthy diet includes eating and drinking foods and liquids with nutrients that the body needs – proteins, carbohydrates, fats, vitamins, minerals, antioxidants, flavonoids, carotenoids and potable water. One's healthcare team, should include a registered dietitian who can assist one maintain nutrition throughout the period of one's treatment, after completion of treatment, and during times of experiencing any side effects. A dietitian is a key member of the healthcare team who is qualified to provide counselling about proper nutrition.

Nutrition and Breast Cancer

While there is no one single food or diet that can prevent or cause breast cancer, diet is an area in which individual choices can make a real difference. Breast Cancer is a complex disease with many contributing factors. Some of these factors, such as age, family history, genetics, and gender, cannot be controlled. There are, however, factors that individuals can control, which include not smoking, avoiding alcohol, exercising, being overweight, and diet.

Breast Cancer is the second highest form of cancer among black South African women. In a study by **Jacobs, et al.**, (2019), the researchers found that the "Incidence rates of breast cancer (BC) among South African black women are increasing. The aim of the current study was to investigate the association between dietary intake and BC risk in black South African women. The study population included 396 BC cases and 396 population-based controls matched on age and residence, participating in the South African Breast Cancer study. Diet was assessed using a validated quantified FFQ from which twelve energy-adjusted food groups were formed and

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analysed. OR were estimated using conditional logistic regressions, adjusted for confounding factors, comparing highest v. lowest median intake. Fresh fruit consumption showed an inverse association with BC risk (OR=0.3, 95 % CI 0.12, 0.80) in premenopausal women, whilst red and organ meat consumption showed an overall inverse association with BC risk (OR=0.6, 95 % CI 0.49, 0.94 and OR=0.6, 95 % CI 0.47, 0.91). Savoury food consumption (sauces, soups and snacks) were positively associated with BC risk in postmenopausal women (OR=2.1, 95 % CI 1.15, 4.07). Oestrogen receptor-positive stratification showed an inverse association with BC risk and consumption of nuts and seeds (OR=0.2, 95 % CI 0.58, 0.86). Based on these results, it is recommended that black South African women follow a diet with more fruit and vegetables together with a decreased consumption of less energy-dense, micronutrient-poor foods such as savoury foods. More research is necessary to investigate the association between BC risk and red and organ meat consumption. Affordable and practical methods regarding these recommendations should be implemented within health intervention strategies.”

There are no food or dietary supplements that will act as “magic bullets” to reduce the risk of breast cancer or from breast cancer returning. The following broad dietary guidelines can, however, be used to decrease the risk of breast cancer. Apart from not smoking, and being as active as possible, the following nutritional guidelines can assist breast cancer survivors:

- Increase intake of fresh fruits (in season), vegetables and whole grains
- Limit fat intake to less than 30 percent of kilojoules – especially animal fats
- Reduce (minimise) intake of cured, pickled, smoked, and processed foods
- Achieve and maintain a healthy weight
- Avoid alcohol consumption

Sadeghi, M., Vahid, F., Rachmani, D., Akbari, M.E. & Davoodi, S.H. 2019.

BACKGROUND: Breast cancer (BrCa) is the most frequently diagnosed cancer among females and second cancer after lung cancer in many societies. Ignoring the phenotypes of the BrCa can affect the interpretation of the association between diet and BrCa. The aim of this study was to determine the association between dietary patterns and estrogen receptor (ER), and progesterone receptor (PR) status in women with BrCa.

METHODS: This study includes 150 cases of BrCa. Controls were 150 healthy adults, frequency matching based on age. The individual information, food frequency questionnaire, and physical activity were completed while interviews. Information about the pathologic factors obtained from patients' files. Factor analysis method used to determine the dietary patterns; logistic regression used to measure the odds ratios.

RESULTS: Getting upper median intake of unhealthy diet had a strong association with BrCa-positive ER and positive PR (OR: 4.98, 95% CI: 2.65-9.34 and OR: 4.99, 95% CI: 2.56-9.75, respectively) compared to under median intake of unhealthy diet. In addition, the protective effect of the healthy diet was stronger on BrCa-negative ER, negative PR (OR: 0.11, 95% CI: 0.04-0.34 and OR: 0.10, 95% CI: 0.03-0.25, respectively).

CONCLUSION: The protective effect of a healthy dietary pattern was stronger on BrCa negative ER and negative PR. The unhealthy dietary pattern had a strong association with BrCa positive ER and positive PR.

De Cicco, P., Catani, M.V., Gasperi, V., Sibilano, M., Quaglietta, M. & Savini, I. 2019.

“Breast cancer (BC) is the second most common cancer worldwide and the most commonly occurring malignancy in women. There is growing evidence that lifestyle factors, including diet, body weight and physical activity, may be associated with higher BC risk. However, the effect of dietary factors on BC recurrence and mortality is not clearly understood. Here, we provide an overview of the current evidence obtained from the

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PubMed databases in the last decade, assessing dietary patterns, as well as the consumption of specific food-stuffs/food-nutrients, in relation to BC incidence, recurrence and survival. Data from the published literature suggest that a healthy dietary pattern characterized by high intake of unrefined cereals, vegetables, fruit, nuts and olive oil, and a moderate/low consumption of saturated fatty acids and red meat, might improve overall survival after diagnosis of BC. BC patients undergoing chemotherapy and/or radiotherapy experience a variety of symptoms that worsen patient quality of life.

“Studies investigating nutritional interventions during BC treatment have shown that nutritional counselling and supplementation with some dietary constituents, such as EPA and/or DHA, might be useful in limiting drug-induced side effects, as well as in enhancing therapeutic efficacy. Therefore, nutritional intervention in BC patients may be considered an integral part of the multimodal therapeutic approach. However, further research utilizing dietary interventions in large clinical trials is required to definitively establish effective interventions in these patients, to improve long-term survival and quality of life.”

Xu, L. & Peterson, L.L. 2019.

PURPOSE OF REVIEW: Breast cancer is the most common cancer in women, yet conclusive evidence of the effects of dietary modification in breast cancer survivors is lacking. Here, we summarize the literature and highlight important data regarding the association between dietary interventions and breast cancer outcomes.

RECENT FINDINGS: Long-term follow-up and secondary analysis of the Women's Health Initiative study demonstrated a significant improvement in overall survival for women who were randomized to the low-fat diet pattern compared with those in the usual-diet group. Dietary quality as measured by Healthy Eating Index score was also associated with both a decrease in cancer-specific mortality and overall mortality. Despite current evidence on the role of diet and nutrition in breast cancer outcomes, conclusive data to translate current findings to clinical practice is lacking and requires multidisciplinary prospective research to advance the field.

Hou, R., Wei, J., Hu, Y., Zhang, X., Sun, X., Chandrasekar, E.K. & Voruganti, V.S. 2019.

PURPOSES: Dietary patterns have been found to be associated with the overall cancer risk and survival. However, the associations of healthy dietary patterns and breast cancer remain unclear. We aimed to conduct a meta-analysis of prospective cohort studies to estimate the pooled results of the association of healthy dietary patterns with breast cancer risk and survival.

METHODS: PubMed, EMBASE, and Web of Science were searched for literature published until June 24th, 2018 that examined the associations between healthy dietary patterns and breast cancer risk and survival. Risk ratios (RRs) and 95% confidence intervals (CIs) were calculated by using a random-effects model for meta-analysis.

RESULTS: There were 32 articles retrieved for the meta-analysis, with 27 for breast cancer risk and five for breast cancer survival. There was a statistically significant lower risk of breast cancer associated with healthy dietary patterns (RR = 0.93, 95% CI: 0.88, 0.98). Subgroup analysis results suggested that there was an inverse association between breast cancer risk and posteriori-derived healthy patterns, but no statistically significant associations were found in other stratified subgroups (a priori-derived diet, study region, menopausal status, or breast cancer subtypes). Healthy dietary patterns were associated inversely with all-cause mortality (RR = 0.76, 95% CI: 0.63, 0.92); however, no association was found for breast cancer-specific mortality.

CONCLUSIONS: The results suggested that healthy dietary patterns might be associated with a reduced risk of breast cancer and all-cause mortality among breast cancer patients. It could be clinically relevant to

promote healthy dietary patterns for breast cancer prevention and improve survival among breast cancer patients.



Caution Expressed Around Consumption of Foods High in Phytoestrogens by Individuals Diagnosed with a Hormone-Sensitive Cancer

The Cancer Association of South Africa (CANSA) has noted:

- A statement by Memorial Sloan Kettering Cancer Center saying that “... because compounds isolated from rooibos leaves demonstrated estrogenic activity, patients with hormone-sensitive cancers should use caution before taking rooibos.” (Memorial Sloan Kettering Cancer Center).
- That phytoestrogens were successfully isolated from rooibos leaves by scientists from the School of Pharmaceutical Sciences, University of Shizuoka, Japan (Shimamura, *et al.*, 2006).
- That according to Deng, *et al.*, (2010), “... there are important safety concerns associated with dietary supplements and foods rich in phytoestrogens, especially for breast cancer patients with hormone-sensitive disease. Based on current evidence, we propose recommendations for advising breast cancer patients, ...”
- That, according to Nelles, Hu & Prins (2011), “Early work on the hormonal basis of prostate cancer focused on the role of androgens, but more recently estrogens have been implicated as potential agents in the development and progression of prostate cancer.”
- That, according to Reger, *et al.*, (2016), “Experimental studies suggest that phytoestrogen intake alters cancer and cardiovascular risk. Some urinary phytoestrogens were associated with cardiovascular and all-cause mortality in a representative sample of 5 179 participants. This is one of the first studies that used urinary phytoestrogens as biomarkers of their dietary intake to evaluate the effect of these bioactive compounds on the risk of death from cancer and cardiovascular disease.”

Position of the Cancer Association of South Africa (CANSA) Regarding Phytoestrogens and Individuals Diagnosed with a Hormone-Sensitive Cancer

CANSA, therefore, wishes to advise individuals diagnosed with the following hormone-sensitive cancers, namely: Breast Cancer, Ovarian Cancer, Endometrial Cancer, and Prostate Cancer, to:

- use caution before taking Rooibos tea and to discuss the issue around Rooibos tea consumption with their treating Oncologist prior to consuming Rooibos tea
- also use caution before taking the following high phytoestrogen-containing foods: all soy foods (including soybeans, tofu, miso, and tempeh); legumes (especially lentils, peanuts and chickpeas) and flaxseed-containing foods. Patients are advised to discuss consumption of the listed high phytoestrogen-containing foods with their treating Oncologist prior to consuming them.

Research on Foods High in Phytoestrogens and Breast Cancer

Deng, G., Davatgarzadeh, A., Yeung, S. & Cassileth, B. 2010. Phytoestrogens: science, evidence, and advice for breast cancer patients. *Soc Integr Oncol.* 2010 Winter;8(1):20-30.

“There are important safety concerns associated with dietary supplements and foods rich in phytoestrogens, especially for breast cancer patients with hormone-sensitive disease. However, no consensus has been reached concerning specific dietary items that should be avoided, and safe levels of potentially problematic foods have yet to be determined. Excellent qualitative reviews of phytoestrogens and breast cancer have been published. These list agents that contain phytoestrogens and offer general cautions. Quantitative reviews, however, are needed but not yet available. Here we review quantitative data on phytoestrogens, their interaction with estrogen receptors, their bioavailability and pharmacokinetics, and their effects on breast cancer cells and animal models. We also note foods and botanicals with substances that interact with estrogen receptors and discuss the phytoestrogens they contain. Based on current evidence, we propose recommendations for advising breast cancer patients, which may also serve as a basis for the development of clinical practice guidelines.”

Shimamura, N., Miyase, T., Umehara, K., Warashina, T. & Fuji, S. 2006. Phytoestrogens from *Aspalathus linearis*. *Biol Pharm Bull.* 2006 Jun;29(6):1271-4.

“From the leaves of *Aspalathus linearis*, 24 known compounds and a new one, aspalalinin (25), were isolated. The structures of the compounds were determined mainly based on spectral evidence. The absolute configuration of aspalalinin was presented on the basis of X-ray analysis. Each isolate was assessed for its estrogenic activity by an estrogen ELISA assay. Compounds 12, 15, and 24 showed the estrogenic activity.”

Patisaul, H. & Jefferson, W. 2010. The pros and cons of phytoestrogens. *Front Neuroendocrinol.* Author manuscript; available in PMC 2011 Apr 12.

Phytoestrogens are plant derived compounds found in a wide variety of foods, most notably soy. A litany of health benefits including a lowered risk of osteoporosis, heart disease, breast cancer, and menopausal symptoms, are frequently attributed to phytoestrogens but many are also considered endocrine disruptors, indicating that they have the potential to cause adverse health effects as well. Consequently, the question of whether or not phytoestrogens are beneficial or harmful to human health remains unresolved. The answer is likely complex and may depend on age, health status, and even the presence or absence of specific gut microflora. Clarity on this issue is needed because global consumption is rapidly increasing. Phytoestrogens are present in numerous dietary supplements and widely marketed as a natural alternative to estrogen replacement therapy. Soy infant formula now constitutes up to a third of the US market, and soy protein is now added to many processed foods. As weak estrogen agonists/antagonists with molecular and cellular properties similar to synthetic endocrine disruptors such as Bisphenol A (BPA), the phytoestrogens provide a useful model to comprehensively investigate the biological impact of endocrine disruptors in general. This review weighs the evidence for and against the purported health benefits and adverse effects of phytoestrogens.

Rodriguez-Garcia, C., Sánchez-Quesada, C., Toledo, E., Delgado-Rodriguez, M. & Gaforio, J.J. 2019.

“Dietary guidelines universally advise adherence to plant-based diets. Plant-based foods confer considerable health benefits, partly attributable to their abundant micronutrient (e.g., polyphenol) content. Interest in polyphenols is largely focused on the contribution of their antioxidant activity to the prevention of various disorders, including cardiovascular disease and cancer. Polyphenols are classified into groups, such as stilbenes, flavonoids, phenolic acids, lignans and others. Lignans, which possess a steroid-like chemical

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structure and are defined as phytoestrogens, are of particular interest to researchers. Traditionally, health benefits attributed to lignans have included a lowered risk of heart disease, menopausal symptoms, osteoporosis and breast cancer. However, the intake of naturally lignan-rich foods varies with the type of diet. Consequently, based on the latest humans' findings and gathered information on lignan-rich foods collected from Phenol Explorer database this review focuses on the potential health benefits attributable to the consumption of different diets containing naturally lignan-rich foods. Current evidence highlight the bioactive properties of lignans as human health-promoting molecules. Thus, dietary intake of lignan-rich foods could be a useful way to bolster the prevention of chronic illness, such as certain types of cancers and cardiovascular disease.”



Research Highlighting the Importance of Fruit and Vegetable Consumption by Breast Cancer Survivors

Women who eat a high amount of fruits and vegetables each day may have a lower risk of breast cancer, especially of aggressive tumours, than those who eat fewer fruits and vegetables, according to a new study led by researchers from Harvard T.H. Chan School of Public Health. In their findings, cruciferous vegetables such as broccoli, and yellow and orange vegetables, had a particularly significant association with lower breast cancer risk.

Research has found that women who ate more than 5.5 servings of fruits and vegetables each day had an 11% lower risk of breast cancer than those who ate 2.5 or fewer servings. (A serving is defined as one cup of raw leafy vegetables, half a cup of raw or cooked vegetables, or half a cup of chopped or cooked fruits.)

Amiot-Carlin, M.J. 2019.

“Epidemiological studies on the relationships between fruit and vegetable consumption and the risk of chronic non-communicable diseases indicate a convincing protective effect against cardiovascular diseases, and suggestive protective effect on weight gain, diabetes, colorectal cancer and ER-negative breast cancer. For cardiovascular diseases the risk reductions are observed up to 800 g/day and for cancer up to 600 g/day. Interestingly, each additional portion of fruit or vegetable reduces the risk of cardiovascular diseases. Fruits and vegetables are rich sources of protective constituents: fibres, vitamins -B9, C-, minerals, polyphenols, carotenoids and sulphur compounds -glucosinolates and allyl sulphides-. White fruits -apples, pears-, cruciferous vegetables, green leafy vegetables, fruits and vegetables rich in beta-carotene, and those rich in vitamin C were shown to protective against cardiovascular diseases and, cruciferous and green-yellow vegetables appeared protective against cancer incidence. Promoting the consumption of sufficient quantities of all types of fruits and vegetables, raw and cooked, is essential in a balanced diet in which ultra-processed and sweet products must be limited. An increase in fruit and vegetable consumption up to 800 g/day does not lead to exceeding the toxicological reference values of the contaminants.”

Nasir, A., Bullo, M.M.H., Ahmed, Z., Imtiaz, A., Yaqoob, E., Jadoon, M., Ahmed, H., Afreen, A. & Yaqoob, S. 2019.

“Due to change in lifestyle and food habits, people are more at risk of diet-related diseases and cancers. It is also established that dietary modifications significantly reduce the risk of diseases. Nutrigenomics is relatively fresh discipline, but possess an enormous potential that can apply for prevention and management of certain carcinomas and diseases. This review enables us to generate useful information for scientists and health professionals regarding the role of Nutrigenomics in the prevention of diet and lifestyle-related diseases like cancer. It influences health conditions of individuals and susceptibility of disease by defining the metabolic

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response and gene expression. Epigenetic modifications can perform a significant role in disease occurrence and pathogenesis. DNA methylation and chromatin remodeling are the most common epigenetic mechanisms. Omega 3 fatty acids are the best example of nutrients and gene interaction not involving DNA methylation while certain bioactive food compounds have a proven role in cancer prevention through an epigenetic mechanism. Dietary polyphenols substantially take part in prevention of oral, breast, skin, esophageal, colorectal, prostate, pancreatic and lung cancers. Moreover, minerals and vitamins involve regulatory processes. Zinc, Selenium and folate involve in DNA repairing process have anticancer properties. Consumption of multivitamins prevents methylation of cancer cells.”

Strober, J.W. & Brady, M.J. 2019.

“In the past century the western world has found a way to combat most communicative diseases; however, throughout that time the prevalence of obesity, hyperglycemia, and hyperlipidemia have drastically increased. These symptoms characterize metabolic syndrome—a non-communicable disease which has become one of the greatest health hazards of the world. During this same time period the western diet had dramatically changed. Homecooked meals have been replaced by highly-processed, calorically dense foods. This conversion to the current western diet was highlighted by the incorporation of high-fructose corn syrup (HFCS) into sweetened beverages and foods. The consumption of large amounts of dietary sugar, and fructose in particular, has been associated with an altered metabolic state, both systemically and in specific tissues. This altered metabolic state has many profound effects and is associated with many diseases, including diabetes, cardiovascular disease, and even cancer (1). Specific types of cancer, like triple-negative breast cancer (TNBC), are both responsive to dietary factors and exceptionally difficult to treat, illustrating the possibility for preventative care through dietary intervention in at risk populations. To treat these non-communicable diseases, including obesity, diabetes, and cancer, it is imperative to understand systemic and localized metabolic abnormalities that drive its progression. This review will specifically explore the links between increased dietary fructose consumption, development of metabolic disturbances and increased incidence of TNBC.”



Research on The Role of Vitamins in Breast Cancer

Vitamin and mineral supplement use after a breast cancer diagnosis is common and controversial. Dosages used and the timing of initiation and/or discontinuation of supplements have not been clearly described. The role of vitamin supplements in preventing breast cancer still remains unclear. Although biologic mechanisms exist to support the anticancer effects of vitamins, there is no clear evidence for an effect in cancer prevention for vitamin supplements.

Some research studies suggest a protective effect of B-vitamins on breast cancer risk. Research also suggests that women with low levels of vitamin D have a higher risk of breast cancer. Vitamin D may play a role in controlling normal breast cell growth and may be able to stop breast cancer cells from growing.

Hatami, M., Vahid, F., Esmaeil Akbari, M., Sadeghi, M., Ameri, F., Eini-Zeinab, H., Jamshidi-Naeini, Y. & Hossein Davoodi. S. 2019.

BACKGROUND: Some micronutrients like folate, vitamin B12, B6, and B2 are the source of coenzymes, which participate in one-carbon metabolism. Any disruption in this metabolism can interfere with DNA replication, repair and regulation of gene expression and ultimately promote the likelihood of carcinogenesis. This study

aimed at investigating the relationship between the intakes of micronutrients involved in one-carbon metabolism with breast cancer (BrCa) and its subtype's odds.

METHODS: Nutrients' intake from diet and supplements were collected through interviewing 151 cases and 154 controls by a 168-item semiquantitative food frequency questionnaire. Logistic regression was used to determine the relationship between dietary and/or total intake of studied nutrients and odds of BrCa and its subtypes.

RESULTS: After adjusting the effects of confounding variables in the models, the odds of BrCa was significantly lower in the highest intake quartile compared with the lowest quartile for total intake of vitamin B2 (OR = 0.17, 95% CI, 0.07-0.39; $P_{\text{trend}} < 0.001$), vitamin B6 (OR = 0.11, 95% CI, 0.05-0.27; $P_{\text{trend}} < 0.001$), vitamin B12 (OR = 0.20, 95% CI, 0.09-0.43; $P_{\text{trend}} < 0.001$) and folate (OR = 0.09, 95% CI, 0.04-0.21; $P_{\text{trend}} < 0.001$). Also, those with the highest quartile of vitamin B6, B12, B2 and folate intake compared with the lowest quartile were less likely to develop estrogen receptor (ER)+ and progesterone receptor (PR)+ subtypes, ER- status, PR- and human epidermal growth factor receptor 2 (HER2)+ subtypes and HER2- status.

CONCLUSION: High intakes of vitamins B2, B6 and folate are associated with reduced odds of BrCa in overall and all ER, PR and HER2 subtypes. Also, high intakes of vitamin B12 reduced the odds of all subtypes of BrCa except ER- subtype.

Hossain, S., Beydoun, M.A., Beydoun, H.A., Chen, X., Zonderman, A.B. & Wood, R.J. 2019.

CONTEXT: Breast cancer (BC) is the most common malignancy among women in the US. Vitamin D status and intakes are thought to be inversely associated with BC occurrence.

OBJECTIVES: In our systematic review and meta-analysis, we evaluated evidence linking serum 25(OH)D (both in serum and diet) with breast cancer (BC) occurrence.

DATA SOURCES AND EXTRACTION: Only observational studies from databases such as PubMed and Cochrane (January 1st 2000 through March 15th, 2018) were included using PRISMA guidelines. Publication bias and consistency upon replication were assessed, while harmonizing risk ratios (RR, 95% CI) of BC, per fixed increment of 5 exposures [10 ng/mL of 25(OH)D; 100 IU/d for total/dietary vitamin D intakes; vitamin D deficiency; supplement use]. RRs were pooled using random effect models.

DATA ANALYSIS: Pooled findings from 22 studies suggested a net direct association between 25(OH)D deficiency and BC, with $RR_{\text{pooled}} = 1.91$, 95% CI: 1.51-2.41, $P < 0.001$). Total vitamin D intake ($RR_{\text{pooled}} = 0.99$, 95% CI: 0.97-1.00, $P = 0.022$, per 100 IU/d) and supplemental vitamin D ($RR_{\text{pooled}} = 0.97$, 95% CI: 0.95-1.00, $P = 0.026$) were inversely associated with BC. No evidence of publication bias was found; all 5 exposures of interest were consistent upon replication.

CONCLUSIONS: 25(OH)D deficiency was directly related to BC while total vitamin D and supplemental vitamin D intakes had an inverse relationship with this outcome. Randomized clinical trials are warranted pending further evidence from primary meta-analyses of observational studies.

Karkeni, E., Morin, S.O., Bou Tayeh, B., Goubard, A., Josslin, E., Castellano, R., Fauriat, C., Guittard, G., Olive D. & Nunès, J.A. 2019. *Front Immunol.* 2019 Jun 6;10:1307. doi: 10.3389/fimmu.2019.01307. eCollection 2019. "Women with low levels of vitamin D have a higher risk of developing breast cancer. Numerous studies associated the presence of a CD8+ T cell infiltration with a good prognosis. As vitamin D may play a key role in the modulation of the immune system, the objective of this work was to evaluate the impact of vitamin D on the breast cancer progression and mammary tumor microenvironment. We show that vitamin D decreases breast cancer tumor growth. Immunomonitoring of the different immune subsets in dissociated tumors revealed an increase in tumor infiltrating CD8+ T cells in the vitamin D-treated group. Interestingly, these CD8+ T cells exhibited a more active T cell ($T_{EM/CM}$) phenotype. However, in high-fat diet conditions, we observed an opposite effect of vitamin D on breast cancer tumor growth, associated with a reduction of CD8+ T cell infiltration. Our data show that vitamin D is able to modulate breast cancer tumor growth and

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inflammation in the tumor microenvironment *in vivo*. Unexpectedly, this effect is reversed in high-fat diet conditions, revealing the importance of diet on tumor growth. We believe that supplementation with vitamin D can in certain conditions represent a new adjuvant in the treatment of breast cancers.”

Mastroianni, A., Ciniselli, C.M., Panella, R., Macciotta, A., Cavalleri, A., Venturelli, E., Taverna, F., Mazzocchi, A., Bruno, E., Muti, P., Berrino, F., Verderio, P., Morelli, D. & Pasanisi, P. 2019.

“Metformin (MET) is currently being used in several trials for cancer prevention or treatment in non-diabetics. However, long-term MET use in diabetics is associated with lower serum levels of total vitamin B₁₂. In a pilot randomized controlled trial of the Mediterranean diet (MedDiet) and MET, whose participants were characterized by different components of metabolic syndrome, we tested the effect of MET on serum levels of B₁₂, holo transcobalamin II (holo-TC-II), and methylmalonic acid (MMA). The study was conducted on 165 women receiving MET or placebo for three years. Results of the study indicate a significant overall reduction in both serum total B₁₂ and holo-TC-II levels according with MET-treatment. In particular, in the MET group 26 of 81 patients and 10 of the 84 placebo-treated subjects had B₁₂ below the normal threshold (<221 pmol/L) at the end of the study. Considering jointly all B₁₂, Holo-TC-II, and MMA, 13 of the 165 subjects (10 MET and 3 placebo-treated) had at least two deficits in the biochemical parameters at the end of the study, without reporting clinical signs. Although our results do not affect whether women remain in the trial, B₁₂ monitoring for MET-treated individuals should be implemented.”



Research on the Implications for Breast Cancer Survivors Who fail to Adhere to Nutritional Guidelines

Diet is thought to be partly responsible for about 30% to 40% of all cancers. No food or diet can prevent one from getting breast cancer. But some foods can make one’s body the healthiest it can be, boost one’s immune system, and help keep one’s risk for breast cancer as low as possible. Research has shown that getting the nutrients one needs from a variety of foods, especially fruits, vegetables, legumes, and whole grains, can make one feel one’s best and give one’s body the energy it needs.

Eating food grown without pesticides may protect against unhealthy cell changes associated with pesticide use in animal studies. Breast cancer is less common in countries where the typical diet is plant-based and low in total fat (polyunsaturated fat and saturated fat).

Springfield, S., Odoms-Young, A., Tussing-Humphreys, L., Freels, S. & Stolley, M. 2019.

PURPOSE: The American Cancer Society (ACS) and the American Institute for Cancer Research (AICR) each created dietary and physical activity guidelines to improve cancer survivorship. Despite African American breast cancer survivors (AABCS) having the lowest survival rates of any racial or ethnic group, limited information exists on their adherence to cancer-specific lifestyle recommendations. The study's purpose was to measure adherence to ACS/AICR dietary recommendations in AABCS.

METHODS: Two hundred ten AABCS enrolled in the Moving Forward intervention trial, a randomized, community-based, 6-month weight loss study, were assessed for socio-demographics, dietary intake (via food frequency questionnaire), and related health factors at baseline. We operationalized the dietary recommendations put forth by ACS/AICR and created component and total adherence index scores. Descriptive statistics were used to calculate the proportion of women who met recommendations. Student's t test and χ^2 tests were used to compare participant characteristics by median adherence scores.

RESULTS: The mean total ACS/AICR score was 12.7 ± 2.5 out of 21 points (median, 13; range, 5 to 21). Over 90% were moderately or completely adherent to limiting alcohol and red & processed meat consumption,

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but the majority failed to meet the other recommendations to eat whole grains, legumes, fruits, vegetables, and avoid added sugars. Women with total scores below the median were younger, with higher BMI, had fewer years of education, and lower income levels.

IMPLICATIONS FOR CANCER SURVIVORS: The present study extends the literature on AABCS adherence to cancer survivor-specific dietary guidelines. Findings will inform future dietary lifestyle interventions in this population.



Research on Sugar Consumption and Breast Cancer

Scientific studies indicate that younger and older women (possibly pre- and post-menopausal women) differ with respect to correlation as far as sugar consumption is concerned. In older women a strong correlation was found between breast cancer mortality and sugar consumption (correlation coefficient = 0.9), and a weaker correlation, possibly of marginal interest, with fat consumption (correlation coefficient = 0.7). In younger women the correlation with diet seems weak. A possible connecting link between sugar consumption and breast cancer is insulin. This is an absolute requirement for the proliferation of normal mammary tissue and experimental mammary tumours may regress in its absence. Insulin secretion occurs in response to blood glucose level and could be excessive if the regulatory mechanism is overtaxed by large sugar intake. The same mechanism might account for the increased risk of mammary cancer in diabetics.

Chazelas, E., Srour, B., Desmetz, E., Kesse-Guyot, E., Julia, C., Deschamps, V., Druesne-Pecollo, N., Galan, P., Hercberg, S., Latino-Martel, P., Deschasaux, M. & Touvier, M. 2019.

OBJECTIVE: To assess the associations between the consumption of sugary drinks (such as sugar sweetened beverages and 100% fruit juices), artificially sweetened beverages, and the risk of cancer.

DESIGN: Population based prospective cohort study.

SETTING AND PARTICIPANTS: Overall, 101 257 participants aged 18 and over (mean age 42.2, SD 14.4; median follow-up time 5.1 years) from the French NutriNet-Santé cohort (2009-2017) were included. Consumptions of sugary drinks and artificially sweetened beverages were assessed by using repeated 24 hour dietary records, which were designed to register participants' usual consumption for 3300 different food and beverage items.

MAIN OUTCOME MEASURES: Prospective associations between beverage consumption and the risk of overall, breast, prostate, and colorectal cancer were assessed by multi-adjusted Fine and Gray hazard models, accounting for competing risks. Subdistribution hazard ratios were computed.

RESULTS: The consumption of sugary drinks was significantly associated with the risk of overall cancer (n=2193 cases, subdistribution hazard ratio for a 100mL/d increase 1.18, 95% confidence interval 1.10 to 1.27, P<0.0001) and breast cancer (693, 1.22, 1.07 to 1.39, P=0.004). The consumption of artificially sweetened beverages was not associated with the risk of cancer. In specific subanalyses, the consumption of 100% fruit juice was significantly associated with the risk of overall cancer (2193, 1.12, 1.03 to 1.23, P=0.007).

CONCLUSIONS: In this large prospective study, the consumption of sugary drinks was positively associated with the risk of overall cancer and breast cancer. 100% fruit juices were also positively associated with the risk of overall cancer. These results need replication in other large scale prospective studies. They suggest that sugary drinks, which are widely consumed in Western countries, might represent a modifiable risk factor for cancer prevention.

STUDY REGISTRATION: ClinicalTrials.gov [NCT0333564](https://clinicaltrials.gov/ct2/show/study/NCT0333564)

Romanos-Nanclares, A., Toledo, E., Gardeazabal, I., Jiménez-Moleón, J.J., Martínez-González, M.A. & Gea, A. 2018.

PURPOSE: Breast cancer (BC) incidence is increasing worldwide. Higher insulin resistance may potentially lead to an increased risk of BC. Sugar-sweetened beverages (SSB) are an acknowledged dietary factor that increases insulin resistance. However, the association between SSB and BC has not been widely explored. We evaluated the association between baseline consumption of SSB and the incidence of BC among relatively young women in a cohort of Spanish university graduates.

METHODS: We evaluated 10,713 middle-aged, Spanish female university graduates (median age 33) from the Seguimiento Universidad de Navarra (SUN) cohort, initially free of BC. SSB consumption was collected at baseline using a validated 136-item semi-quantitative food-frequency questionnaire. Incidence of BC was confirmed by a trained oncologist using medical records. We fitted Cox regression models to assess the relationship between baseline categories of SSB consumption and the incidence of BC during follow-up. We stratified the analyses by menopausal status.

RESULTS: During 106,189 person-years follow-up, 100 incident cases of BC were confirmed. Among postmenopausal women, regular consumption of SSB was associated with a significantly higher incidence of BC (HR 2.12; 95% CI 1.02, 4.41) in the fully adjusted model, compared to women who never or seldom consumed SSB. No association was found among premenopausal women (HR 1.16; 95% CI 0.66, 2.07).

CONCLUSIONS: Even though the number of cases was small, in this Mediterranean cohort, we observed a direct association between SSB consumption and BC risk among postmenopausal women. Nonetheless further larger longitudinal studies are needed to support this association.



Research on Obesity and Breast Cancer Risk

One's risk of developing breast cancer increases if one is overweight or obese after the menopause. The menopause is when one stops having periods and are not able to get pregnant naturally. Putting on weight throughout adulthood also increases one's risk of developing breast cancer after the menopause. The more weight one gains over the course of adult life, the higher the risk. Being obese when diagnosed with breast cancer can increase the risk that the cancer will recur (come back after treatment). It can also reduce one's chances of surviving the disease.

Engin, A. 2017.

"Several studies show that a significantly stronger association is obvious between increased body mass index (BMI) and higher breast cancer incidence. Furthermore, obese women are at higher risk of all-cause and breast cancer specific mortality when compared to non-obese women with breast cancer. In this context, increased levels of estrogens due to excessive aromatization activity of the adipose tissue, overexpression of pro-inflammatory cytokines, insulin resistance, hyperactivation of insulin-like growth factors (IGFs) pathways, adipocyte-derived adipokines, hypercholesterolemia and excessive oxidative stress contribute to the development of breast cancer in obese women. While higher breast cancer risk with hormone replacement therapy is particularly evident among lean women, in postmenopausal women who are not taking exogenous hormones, general obesity is a significant predictor for breast cancer. Moreover, increased plasma cholesterol leads to accelerated tumor formation and exacerbates their aggressiveness. In contrast to postmenopausal women, premenopausal women with high BMI are inversely associated with breast cancer risk. Nevertheless, life-style of women for breast cancer risk is regulated by avoiding the overweight and a high-fat diet. Estrogen-plus-progestin hormone therapy users for more than 5 years have elevated risks of both invasive ductal and lobular breast cancer. Additionally, these cases are more commonly node-positive and have a higher cancer-related mortality. Collectively, in this chapter, the impacts of obesity-related estrogen, cholesterol, saturated

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fatty acid, leptin and adiponectin concentrations, aromatase activity, leptin and insulin resistance on breast cancer patients are evaluated. Obesity-related prognostic factors of breast cancer also are discussed at molecular basis.”

Seiler, A., Chen, M.A., Brown, R.L. & Fagundes, C.P. 2018.

“Obesity-associated inflammation is strongly linked to breast cancer risk and progression, largely via two processes: inflammatory pathways and dysregulated metabolism. Cytokine production in excess adipose tissues creates a chronic inflammatory microenvironment, which favors tumor development. Lifestyle factors, including diet, have long been recognized as important determinants of breast cancer risk and mortality.

“Obesity increases the risk of developing breast cancer in both pre- and postmenopausal women and also negatively affects breast cancer recurrence and survival. Poor dietary habits characterized by the high intake of refined starches, sugar, and both saturated and trans-saturated fats, as well as the low intake of omega-3 fatty acids, natural antioxidants, and fiber, modulate inflammation and, thereby, appear to be linked to increased risk of breast cancer and mortality.”

Gérard, C. & Brown, K.A. 2018.

“One in eight women will develop breast cancer over their lifetime making it the most common female cancer. The cause of breast cancer is multifactorial and includes hormonal, genetic and environmental cues. Obesity is now an accepted risk factor for breast cancer in postmenopausal women, particularly for the hormone-dependent subtype of breast cancer. Obesity, which is characterized by an excess accumulation of body fat, is at the origin of chronic inflammation of white adipose tissue and is associated with dramatic changes in the biology of adipocytes leading to their dysfunction. Inflammatory factors found in the breast of obese women considerably impact estrogen signaling, mainly by driving changes in aromatase expression the enzyme responsible for estrogen production, and therefore promote tumor formation and progression. There is thus a strong link between adipose inflammation and estrogen biosynthesis and their signaling pathways converge in obese patients. This review describes how obesity-related factors can affect the risk of hormone-dependent breast cancer, highlighting the different molecular mechanisms and metabolic pathways involved in aromatase regulation, estrogen production and breast malignancy in the context of obesity.”

Kosalka, P., Johnson, C., Aturek, M., Sulpher, J., Law, A., Botros, J., Dent, S. & Aseyey, O. 2019. Effect of obesity, dyslipidemia, and diabetes on trastuzumab-related cardiotoxicity in breast cancer. *Curr Concol.* 2019 Jun;26(3):e314-e321. doi: 10.3747/co.26.4823. Epub 2019 Jun 1.

BACKGROUND: Clinical trials have demonstrated an increased risk of cardiotoxicity in patients with breast cancer (bca) receiving trastuzumab-based therapy. Diabetes, dyslipidemia, and obesity are known risk factors for cardiovascular disease. Studies have yielded conflicting results about whether those factors increase the risk of cardiotoxicity in patients with bca receiving trastuzumab.

METHODS: In this retrospective cohort study, data were collected for 243 patients with bca positive for her2 (the human epidermal growth factor receptor 2) who were receiving trastuzumab and who were referred to The Ottawa Hospital Cardio-oncology Referral Clinic between 2008 and 2013. The data collected included patient demographics, reason for referral, cardiac function, chemotherapy regimen (including anthracycline use), and 3 comorbidities (diabetes, dyslipidemia, obesity). Rates of symptomatic cancer treatment-related cardiac dysfunction (sctcd) and asymptomatic decline in left ventricular ejection fraction (adlvef) were calculated for patients with and without the comorbidities of interest.

RESULTS: Of the 243 identified patients, 104 had either diabetes, dyslipidemia, or obesity. In that population, the most likely reason for referral to the cardio-oncology clinic was adlvef. The combination of 2 or 3 comorbidities significantly increased the incidence of sctcd in our population, reaching a rate of 67% for

patients with obesity and dyslipidemia [relative risk (rr): 2.2; $p = 0.04$], 69% for patients with obesity and diabetes (rr: 2.3; $p = 0.02$), and 72% for patients with all 3 risk factors (rr: 2.4; $p = 0.08$).

CONCLUSIONS: The combination of 2 or 3 comorbidities significantly increases the incidence of symptomatic cancer treatment-related cardiotoxicity. Patients with bca experiencing cancer treatment-related cardiotoxicity who have a history of diabetes, dyslipidemia, and obesity might require more proactive strategies for prevention, detection, and treatment of cardiotoxicity while receiving trastuzumab-based treatment.

Inglis, J.E., Janelins, M.C., Culakova, E., Mustian, K.M., Lin, P.J., Kieckner, I.R. & Peppone, L.J. 2019.

PURPOSE: To assess the impact of obesity on cancer-related fatigue (CRF) in patients with breast cancer, through a secondary analysis of a large, longitudinal, nationwide study of breast cancer patients beginning chemotherapy.

METHODS: All patients (N = 565; aged 53 ± 10.6) with breast cancer completed the multidimensional fatigue symptom inventory and the symptom inventory to measure CRF symptoms at baseline, post-chemotherapy, and 6 months post-chemotherapy. Height and weight at baseline were used to categorize subjects based on body mass index (BMI): obese ($\geq 30.0 \text{ kg/m}^2$; n = 294), overweight (25.0-29.9 kg/m^2 ; n = 146), and normal weight (18.5-24.9 kg/m^2 ; n = 125). Multivariate regression models evaluated the relationship of obesity level to CRF over time, controlling for age, menopausal status, race, Karnofsky Performance Status, cancer stage, radiation, and exercise status.

RESULTS: At baseline, the obese had significantly higher CRF symptoms than the normal weight subjects for both the Multidimensional fatigue symptom inventory (MFSI) total (obese = 11.2 vs normal weight = 6.3; $p = 0.03$) and Symptom Inventory (SI) (obese = 3.5 vs normal weight = 2.9; $p = 0.03$). Significantly higher SI fatigue scores persisted at post-chemotherapy for the obese (obese = 5.0 vs normal weight = 4.4; $p = 0.02$). At 6 months post-chemotherapy, the obese patients still had significantly higher SI fatigue scores (obese = 3.5 vs normal weight = 3.0; $p = 0.05$).

CONCLUSION: Obese patients suffered greater CRF from pre-chemotherapy through 6 months post-chemotherapy. Recommendations for weight loss or weight maintenance may impact CRF levels in obese breast cancer patients before and after chemotherapy.



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