

Multivitamin Supplement May Reduce Breast Cancer Recurrence: *Enhancing positive health effects of diet and exercise*

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Introduction

There is a great deal of controversy regarding the value of multiple vitamin supplements in cancer prevention. With respect to preventing breast cancer recurrence a very important study was published in the Journal of Breast Cancer Research and Treatment in 2011, by Kwan ML et al. The LACE Study, as it is known (Life After Cancer Epidemiology study), involved 2,236 women diagnosed from 1997 to 2000 with early-stage breast cancer (Stage I $\geq$ 1 cm, II, or IIIA). Participants were enrolled about two years post-diagnosis. Multivitamin use pre-diagnosis and post-diagnosis was assessed via mailed questionnaire

In this study the researchers found that for those women who were in the top 25% of the cohort adhering to a healthy lifestyle, defined as a healthy diet (consuming at least 5.5 servings of fruits and vegetables per day) and physical activity (engaging in non-sedentary activity of at least 16 hours/week), persistent multivitamin use was associated with a 60–70% reduction in risk of dying from any cause during the two-year follow-up period. No associations were observed among women who were leading less healthy lifestyles. Furthermore, among women who only had radiation therapy and no chemotherapy as part of their adjuvant treatment, multivitamin use was associated with a consistent reduction in risk of recurrence, breast cancer death, and overall death.

The researchers conclude that these results add to the evidence that multivitamin use after a breast cancer diagnosis may be safe, and suggest that consistent use of multivitamins may add a further survival benefit to subgroups of breast cancer survivors who already follow a healthy lifestyle, and those who were treated by radiotherapy (but not chemotherapy).

The evidence showed that women who strongly adhered to a healthy lifestyle achieved further benefit from taking multivitamins, specifically lowering their risk of dying from any cause. However, using multivitamins as the only preventive action did not seem to be beneficial, as results showed that among the non-healthy lifestyle followers, multivitamin use did not appear to influence prognosis. As such, this suggests that other lifestyle factors play a larger role in influencing breast cancer outcomes (diet, exercise) and that use of a multivitamin enhances the efficacy of these proactive lifestyle strategies, hence the term, “supplement”.

In previous LACE analyses it has been shown that consuming a more healthful diet of fruits and vegetables, whole grains, and poultry, and engaging in at least moderate physical activity, were each associated with decreased overall mortality but not breast cancer-related outcomes.(1)

Previous Studies and Anti-Cancer Mechanisms

Many experimental studies have shown that various vitamins and minerals exhibit a variety of anti-cancer properties including, anti-angiogenesis, immune modulation, enhancing cell differentiation, inhibiting tumor cell proliferation, and inducing apoptosis (2, 3). A human intervention trial assessing the effects of antioxidant supplements on breast cancer survival showed promising results in preventing cancer recurrence. This prospective study of 4,877

breast cancer survivors in Shanghai, China examined antioxidant use (vitamin C, vitamin E, and/or multivitamins) during the first six months post-diagnosis and showed it was associated with decreased risk of cancer recurrence by 22% and overall mortality by 18%. (4)

In another LACE analysis assessing the influence of individual supplements the researchers noted that post-diagnosis use of Vitamin C was associated with a 27% reduced risk of breast cancer recurrence and Vitamin E was associated with a 24% reduced risk of breast cancer recurrence and overall mortality. (1)

A study published in March 2014 in the *Journal Anticancer Research* also showed that breast cancer survivors who had more optimal blood levels of Vitamin D had twice the survival rate compared to those with lower Vitamin D blood levels.

These researchers analyzed data from five large breast cancer studies, involving a total of 4,443 breast cancer patients, with an average follow-up period of nine years. The data showed that women who had an average Vitamin D blood level of 30ng/ml (75nmol/L) experienced survival rates double that of women who had an average blood Vitamin D blood level of 17ng/ml (42nmol/L).

Vitamin D has been shown to reduce cancer development and progression in a number of ways:

- Vitamin D slows down the rate of cell division, which reduces the likelihood that cancerous mutations will emerge.
- Vitamin D promotes maturation (differentiation) of newly formed cells, which reduces transformation to a cancerous state.
- Vitamin D favourably modulates the function of immune cells, many of which are responsible for identifying and destroying emerging cancer cells
- Vitamin D is responsible for increasing the cell's production of a surface receptor (antennae) known as E-cadherin, which enables the cell to bind to and communicate with adjacent cells or supporting tissues. Very aggressive cancer cells tend to have low levels of E-cadherin, which enables them to replicate unchecked by adjacent cells, giving themselves the green light to invade adjacent tissues and spread into the blood and lymphatic system in their quest to metastasis throughout the body (5)

As well another study presented in 2011, at the *102nd American Association for Cancer Research 102nd Annual Meeting* (April 2-6), showed that the consumption of soy products by breast cancer survivors reduced risk of cancer recurrence and progression, compared to cancer survivors who ingested little or no soy foods. The report featured data that combined four National Cancer Institute-funded studies: the *Shanghai Breast Cancer Survival Study*; the *Life After Cancer Epidemiology Study*; the *Women's Healthy Eating and Living Study*; and the *Nurses' Health Study*. Together this included 18,312 women between the ages of 20 and 83 years, who had previously been diagnosed with invasive primary breast cancer.

Nine years after the initial breast cancer diagnosis, the combined data showed the following: Those who consumed the highest amounts of soy isoflavones (more than 23 mg per day) were compared with the outcomes of those whose intake was lowest (0.48 mg per day or lower). Women in the highest intake category of more than 23 mg per day

had a 9 percent reduced risk of mortality and a 15 percent reduced risk for recurrence, compared to those who had the lowest intake level. (6)

Studies show that the anti-breast cancer properties of soy foods and soy extract are likely due to their ability to:

- Lower endogenous estrogen levels by acting as an inhibitor of enzymes that produce more potent estrogens (aromatase and 17 β -hydroxysteroid dehydrogenase enzyme inhibition)
- Stimulate the production of sex hormone-binding globulin (SHBG) by the liver, which in turn leads to more estrogen bound to SHBG and less free estradiol. This reduces the amount of estrogen available to bind to estrogen receptors within breast cells.
- Inhibit the enzymes that promote cell proliferation (protein tyrosine kinase, DNA topoisomerase and ornithine decarboxylase)
- Inhibit angiogenesis (which prevents the building of life-supporting blood vessels in and around malignant tumors)
- Provide antioxidant defense
- Induce cell differentiation
- Further, the weak estrogenic potential (more than 1,000 times weaker than estradiol) of soy isoflavones do not elicit a strong estrogenic response and thus have an anti-estrogenic effect that tends to inhibit the growth and proliferation of estrogen-dependent cancer cells, as demonstrated by the research of A. Molteni et al. (7,8,9)

Conclusion

From a total perspective, evidence is emerging to show that female breast cancer survivors may be well advised to adopt pro-active lifestyle strategies to help reduce cancer recurrence and reduce overall mortality. Eating at least 5 fruit and vegetables per day, along with regular exercise is highly supported by the findings of the LACE study. Adding a multiple vitamin to this game plan appears to provide further benefit, with special emphasis on doses of Vitamin C and Vitamin E, according to the LACE and Shanghai, China study noted above.

Other recent studies encourage the attainment of a blood level of Vitamin D at or above 30ng/ml (75 nmol/L) and the frequent inclusion of soy foods (with high isoflavone content), as part of an anti-cancer diet program.

With respect to multivitamins, the researchers in the LACE study conclude, “in stratified analyses, women who consistently used multivitamins before and after diagnosis and ate more fruits/vegetables (p for trend = 0.008) and were more physically active (p for trend = 0.034) had better overall survival. Multivitamin use along with the practice of other health-promoting behaviors may be beneficial in improving breast cancer outcomes in select groups of survivors”. (1)

Although additional research is required before definitive statements can be made, health practitioners should alert breast cancer **patients** to these emerging findings as a means to help them make an informed decision about proactive lifestyle strategies they may wish to pursue regarding the prevention of cancer recurrence and improved survival.

***For more information on this or other related topics,
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