Can Alterations in Diet and Exercise Reduce the Risk of Relapse and Death from Early Breast Cancer?

Evidence from a number of recent studies suggests that lifestyle factors, such as diet and physical activity, may reduce the risk of recurrence in patients with early breast cancer. At the 2005 ASCO meeting, Rowan Chlebowski reported the initial results of the Women's Intervention Nutrition Study (WINS), a randomized trial conducted at 37 centers in the United States, which demonstrated a reduction in relapse rate as a result of a modest decrease in dietary fat intake. Surprisingly, this benefit was confined to patients with estrogen receptor-negative breast cancer. Another recent report by Holmes and colleagues demonstrated a reduction in recurrence rate and mortality in breast cancer patients who engaged in regular physical activity, particularly in patients with estrogen receptor-positive tumors. The clinical and research implications of these and other related clinical research findings on complementary oncologic interventions are uncertain but are likely to be of great interest to patients with breast cancer.

RECENT STUDIES EVALUATING THE ASSOCIATION BETWEEN DIETARY FACTORS AND BREAST CANCER RECURRENCE

Study	N	Status	Intervention
Life Without Cancer Epidemiology (LACE)	2,400	Ongoing	Detailed data on dietary intake, physical activity, weight change and recurrence collected at regular intervals
Women's Healthy Eating and Living (WHEL)	3,088	Ongoing	Comprehensive dietary intervention to increase vegetable intake versus control with biological samples collected at baseline and regular intervals to establish the biological link between dietary intake, nutritional factors and the progression of breast cancer
Women's Intervention Nutrition Study (WINS)	2,437	Reported, ASCO 2005	Dietary intervention to reduce fat intake as an adjuvant to standard breast cancer therapy versus control with disease recurrence and survival as trial endpoints

SOURCES: Rock CL. *J Mammary Gland Biol Neoplasia* 2003;8(1):119-32; Chlebowski RT et al. Presentation. ASCO 2005;Abstract 10.

WINS TRIAL DESIGN — RECRUITMENT 1994-2001, MEDIAN FOLLOW-UP: 60 MONTHS

Eligibility	**Women 48-79 years; early breast cancer; primary surgery +/- XRT; systemic therapy*; dietary fat intake ≥20% of calories**
ARM 1	**Dietary intervention (n = 975) to reduce fat intake while maintaining nutritional adequacy**
ARM 2	**Control (n = 1,462)**

* Tamoxifen required, chemo Rx optional for ER+; chemo Rx required for ER-; strata = nodal status; systemic Rx; sentinel node

SOURCE: Chlebowski RT et al. Presentation. ASCO 2005;Abstract 10.

WINS RELAPSE-FREE SURVIVAL BY TREATMENT GROUP

Groups	Diet (events/n)	Control (events/n)	HR (95% CI)	*p*-value*
All patients	96/975	181/1,462	0.76 (0.60-0.98)	0.034
ER-positive	68/770	122/1,189	0.85 (0.63-1.14)	0.277
ER-negative	28/205	59/273	0.58 (0.37-0.91)	0.018

* All *p*-values from adjusted Cox proportional hazards model. The disease-free survival outcome (adding other cancers and all deaths including 389 events) was similar (adjusted Cox HR 0.81, 95% CI 0.65-0.99, $p = 0.042$), favoring dietary intervention.

SOURCE: Chlebowski RT et al. Presentation. ASCO 2005;Abstract 10.

PHYSICAL ACTIVITY AND SURVIVAL AFTER BREAST CANCER DIAGNOSIS

Objective: Determine effect of exercise on breast cancer recurrence and survival

Design, setting and participants: Prospective observational study of 2,987 women from the Nurses' Health Study who were diagnosed with Stage I-III breast cancer between 1984-1998 and followed until death or 2002

Assessment of physical activity: Assessment of eight activities, including duration and intensity, two years after breast cancer diagnosis

Outcome: Breast cancer mortality according to metabolic equivalent task hours per week (MET-h/wk) of physical activities

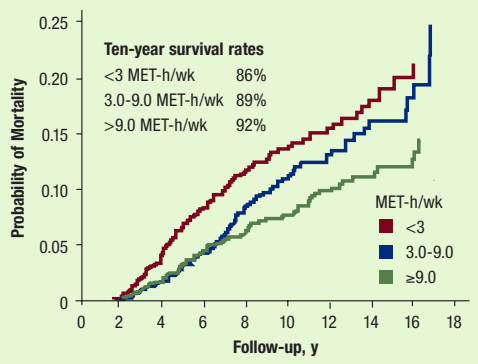
EXAMPLES OF MET SCORES

Activity	MET score
Sitting quietly	1.0
Walking at average pace	3.0
Jogging	7.0
Running	12.0

MET = metabolic equivalent task

SOURCE: Holmes MD et al. *JAMA* 2005;293(20):2479-86.

PROBABILITY OF BREAST CANCER MORTALITY BASED UPON MET-HOURS PER WEEK OF PHYSICAL ACTIVITY



MET = metabolic equivalent task

SOURCE: Reproduced with permission. Holmes MD et al. *JAMA* 2005;293(20):2479-86. Copyright © 2005, American Medical Association. All rights reserved.

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Chlebowski RT et al. **Dietary fat reduction in postmenopausal women with primary breast cancer: Phase III Women's Intervention Nutrition Study (WINS).** *Proc ASCO* 2005;Abstract 10.

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Rock CL. **Diet and breast cancer: Can dietary factors influence survival?** *J Mammary Gland Biol Neoplasia* 2003;8(1):119-32.

Winters BL et al. **Dietary patterns in women treated for breast cancer who successfully reduce fat intake: The Women's Intervention Nutrition Study (WINS).** *J Am Diet Assoc* 2004;104(4):551-9.

WOMEN'S INTERVENTION NUTRITION STUDY (WINS): DIETARY FAT INTAKE AND RISK OF RECURRENCE

The issue of dietary fat intake has been around in breast cancer for about 25 years. To address this issue, we conducted a randomized clinical trial and entered 2,437 women about 220 days after initial surgery. Patients at 37 centers in the United States were entered after they completed their primary therapy.

The diet group was given a dietary fat gram goal by centrally trained registered dieticians, implementing a predefined, low-fat eating plan. Patients received eight biweekly individual counseling sessions, then one session every three months. Monthly group sessions were held, and patients self-monitored their fat intake.

The control group saw the dieticians every three months and talked about nutritional adequacy. Fat gram intake for the intervention group went from about 56 to 33 fat grams per day — about a 40 percent reduction in daily fat gram intake, which was sustained by most of the individuals.

Our primary study endpoint was relapse-free survival, which included all breast cancer recurrence sites, including contralateral breast cancers. We found that the dietary group had a longer relapse-free survival than the control population.

In the control group, 12.4 percent had a relapse compared to 9.8 in the diet group, which was a 2.6 percent absolute difference at five years, or a 24 percent reduction in risk of recurrence. We did subgroup analysis by receptor status.

The hazard ratio was 0.85 for relapse-free survival in patients with estrogen receptor-positive tumors and not significant. In the 478 patients with ER-negative disease, the hazard ratio was 0.58, with a 42 percent reduction in risk and eight percent absolute difference at five years. This is hypothesis generating but rather intriguing to us.

— Rowan T Chlebowski, MD, PhD.
Breast Cancer Update *2005 (7)*

PHYSICAL ACTIVITY AND SURVIVAL AFTER BREAST CANCER

Women who engaged in an amount of physical activity equivalent to walking one or more hours per week had better survival compared with those who exercised less than that or not at all. After adjusting for factors predictive of survival after breast cancer, the RRs of adverse outcomes including death, breast cancer death, and breast cancer recurrence were 26% to 40% lower comparing women with the highest to the lowest category of activity. The association was particularly apparent among women with hormone-responsive tumors. Our results suggest a possible hormonal mechanism for improved survival among women who are physically active.

— Michelle D Holmes, MD, DrPH et al.
JAMA *2005;293(20):2479-86.*

FRUIT AND VEGETABLE INTAKE, PLASMA CAROTENOIDS AND RISK OF RECURRENCE

Being in the highest versus the lowest quartile of plasma total carotenoid concentration was associated with an estimated 43% reduction in risk for a new breast cancer event. Plasma carotenoids are a biologic marker of vegetable and fruit intake, so these results support the suggestion from prior studies, based on self-reported dietary intakes, that increased consumption of those foods may reduce the risk of recurrence or increase the likelihood of survival after the initial diagnosis and treatment of breast cancer.

— Cheryl L Rock et al.
J Clin Oncol *2005;23(27):6631-8.*