# Fat, Fruits, Vegetables, and Breast Cancer Survivorship

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BREAST CANCER IS THE MOST COMMONLY DIAGNOSED CANcer and the second most common cause of cancer mortality among women in the United States.[1] Advances in early detection, surgical treatment, and chemotherapy have led to significant improvements in breast cancer survival, particularly among women with early stage disease. Current estimates indicate that there are at least 2.4 million women who are breast cancer survivors in the United States.[1] Among these women, there is particular concern about the long-term risk of recurrence. Whether that risk might be modified through changes in lifestyle habits such as diet has been an important question for investigation. Results of observational epidemiologic studies on associations of dietary patterns high in fruits and vegetables, low in fat, or both with risk of recurrence or survival are inconsistent.[2-5] Although it is not possible to draw firm conclusions about the potential benefits of such dietary patterns from the results of those studies, a growing body of evidence is emerging from randomized clinical trials designed specifically to examine the effects of dietary interventions on breast cancer prognosis.

In this issue of *JAMA*, Pierce and colleagues[6] report the results of the Women's Healthy Eating and Living (WHEL) Study. The WHEL Study was a randomized controlled trial designed to assess whether an intensive dietary intervention aimed at increasing fruits to 3 servings/d, vegetables to 5 servings/d, and fiber to 30 g/d and decreasing fat intake to 15% to 20% of total calories would reduce the risk of recurrence, new primary invasive breast cancer, or mortality among survivors of early stage (stages I-IIIA) breast cancer. In this multicenter study, 3088 women who had diagnosis and treatment within the past 4 years were randomly assigned to either the intensive intervention group or a less-intensive comparison group that was advised to follow the 5-A-Day program.[7] After an average follow-up period of 7.3 years, there were no differences in the risk of recurrence or incidence of a new primary breast cancer ($P=.63$) or in the risk of overall mortality ($P=.43$) between the 2 groups. Similarly, there were no between-group prognostic differences according to baseline demographic characteristics, including body mass index, or clinical characteristics, including tumor stage and hormone receptor status. Furthermore, the intervention showed no benefit for women whose diet at baseline was low in fruits, vegetables, or fiber or high in fat.

The Women's Intervention Nutrition Study (WINS)[8] is another randomized clinical trial designed specifically to assess whether a low-fat diet (15% of total calories) affects breast cancer recurrence or survival. In that study, which enrolled 2437 women within 1 year of diagnosis of early stage breast cancer (stages I-IIIA), interim results showed a significant benefit ($P=.03$) on the hazard ratio for relapse-free survival after a median of 5 years of follow-up among women randomized to the low-fat dietary intervention group compared with the control group, which received minimal dietary guideline information.[8] Results of an exploratory analysis suggested that the beneficial effect of the low-fat intervention might be isolated to women with estrogen and progesterone receptor–negative breast cancers. While there is debate regarding the differential effects of the low-fat intervention according to hormone receptor status and whether this difference could be explained by variation in the hazard rates for recurrences of hormone receptor–positive vs –negative breast cancers according to length of follow-up,[9] a recent update and analysis of WINS data based on 8 years of follow-up demonstrated similar benefits in the low-fat diet group.[10]

These conflicting results from the WHEL Study and WINS regarding the potential benefits of a dietary modification on long-term breast cancer prognosis require careful consideration. In particular, a key issue is the difference in energy balance that was achieved between WINS and WHEL Study participants. In WINS, over the 5-year follow-up, there was a continuous increase in the difference in self-reported total energy intake between the intervention and comparison groups. Consequently, women randomized to the low-fat intervention experienced significant weight loss, with a 6-lb (2.7 kg) weight difference between intervention and control women at 5 years.[8] Conversely, in the WHEL Study, self-reported total energy intake decreased to a comparable extent in both the intervention and comparison groups through 6 years of follow-up, and both groups experienced small weight gains (ie, 0.6 and 0.4 kg, respectively).[4] It is unclear whether the difference in energy balance, as reflected by weight change, partly accounts

**See also p 289.**

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for the beneficial effects of the intervention on survival observed in WINS and no intervention effect as observed in the WHEL Study. Taken together, these data support findings from observational studies suggesting that a high level of obesity, weight gain, or both after diagnosis is adversely associated with breast cancer disease-free survival and overall survival.[11]

Other related considerations raised by the results of the WHEL Study include adherence to the intended dietary modification and validity of the dietary data collected. As expected, based on the 24-hour dietary recalls there were clear differences between the intervention and comparison groups in fruit and vegetable intake through 4 years and, to a lesser extent, at 6 years of follow-up.[4] These self-reported differences were validated by higher levels of plasma carotenoids in the intervention group vs the control group. However, the intervention goal to reduce fat intake to 15% to 20% of total calories was not achieved. Indeed, at no time during follow-up was average self-reported fat intake less than 21% of total calories, and by year 4, fat intake was more than 27% of total caloric intake in both groups. Moreover, at the 6-year follow-up, the average percentage of calories from fat reported by both intervention group and control group participants was higher than reported at baseline. Whether this lack of adherence to the intervention goal for fat reduction explains any of the null findings in this study is unclear.

Of further concern is that baseline mean total daily caloric intakes were 1719 kcal in the intervention group and 1717 kcal in the comparison group, but by year 6, the respective mean total daily caloric intakes were 1538 kcal and 1559 kcal, respectively. In the absence of changes in physical activity, it would be expected that an average decrease of nearly 180 kcal per day would result in a decrease in body weight during the study period. However, these women experienced small increases in body weight during the study period. These results call into question the validity of some components of the self-reported dietary data.

Several issues remain to be addressed regarding the effects of dietary interventions on breast cancer prognosis. It is becoming increasingly clear that evaluating dietary effects is complex and requires careful monitoring to ensure adherence to the intervention goals so that any hypothesized effect can be detected. In addition, studies assessing whether breast cancer prognosis would be improved with interventions that focus on the complex components of energy balance (ie, physical activity and energy intake) appear warranted. Unfortunately, available data do not support best practice dietary recommendations to improve long-term prognosis for early stage breast cancer survivors.

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# Triglycerides and Risk for Coronary Heart Disease

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EVIDENCE THAT ELEVATED SERUM TRIGLYCERIDE LEVels are associated with increased risk for atherosclerotic events is increasing. In this issue of *JAMA*, 2 large, long-term prospective cohort studies conducted in different populations by Bansal and colleagues[1] and by Nordestgaard and colleagues[2] support the role of nonfasting triglyceride levels as a significant risk factor for coronary heart disease (CHD) events. However, a high serum triglyceride level is associated with abnormal lipoprotein metabolism, as well as with other CHD risk factors including obesity, insulin resistance, diabetes mellitus, and lowered levels of high-density lipoprotein cholesterol (HDL-C).[3]

**See also pp 299 and 309.**

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