Chapter 53
Lifestyle Issues in Breast Cancer Survivors

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Observational studies suggest that lifestyle factors, including obesity, low physical activity, and differences in dietary intake may influence breast cancer prognosis (1–3). Recently, two full-scale, randomized clinical trials have evaluated lifestyle interventions in women with early-stage, resected breast cancer (4,5). This chapter outlines the observational study evidence regarding lifestyle and breast cancer outcomes, with emphasis on recent reports, and presents and contrasts the design and findings from the two randomized trials.

BODY WEIGHT AND BREAST CANCER OUTCOME

Observational studies of the influence of obesity on clinical outcome in breast cancer patients have provided mixed results (1,6,7). In 36 of 51 studies, a significant adverse effect of higher body weight on breast cancer prognosis was seen, but few studies have adequately controlled for systemic adjuvant therapy use (6).

Several recent reports may be of more relevance. The influence of excess weight on breast cancer outcomes was recently examined in a cohort of 14,709 patients with localized disease. A consistent negative effect of obesity on clinical outcomes was seen: metastatic recurrence (hazard ratio [HR] 1.32, 95% confidence interval [CI] 1.19–1.48); overall survival (HR 1.43, 95% CI 1.28–1.60) and second primary cancer (HR 1.57, 95% CI 1.19–2.07) (8). In the Nurse's Health Study (NHS) cohort, higher body weight at diagnosis was associated with decreased survival in 5,204 women with localized breast cancer, but the relationship was statistically significant only in those who never smoked (9). Holick et al. (10) reported on a cohort of 3,924 women with localized breast cancer where obese women with a body mass index (BMI) 30 kg/m^2 or greater were more likely then lean women (BMI <23 kg/m^2) to die of breast cancer (HR 1.34, 95% CI 1.09–1.65). In a population-based cohort of 1,360 Australian women with early-stage breast cancer, a BMI 30 kg/m^2 or greater was associated with increased breast cancer recurrence (HR 1.57, 95% CI 1.11–2.22) and all cause mortality (HR 1.56, 95% CI 1.01–2.40) (11). Finally, in a similarly sized population of 1,376 breast cancer patients with stage I to II disease, significantly increased mortality was seen in the highest weight category, with greatest effects on hormone receptor-negative subgroups (12).

Potential Confounding Factors

To account for factors potentially confounding lifestyle and breast cancer associations, further study in populations receiving contemporary systemic treatment is needed. Estrogen modulation has been proposed as a potential mediator of the influence of obesity on prognosis (13,14). Current pharmacologic strategies effectively reduce estrogen levels, however, and no studies have reported on the influence of obesity on breast cancer outcome in postmenopausal women treated with aromatase inhibitors in the adjuvant setting. Race or ethnicity differences also can influence findings in this area. Black women are commonly heavier than white women and their breast cancers carry a worse prognosis (15,16). However, the prognosis has been more strongly associated with genetic factors rather than body weight or lifestyle differences (15). Another potential confounder is differential chemotherapy use. In population studies, obese women often received less than full dose chemotherapy, with consequent adverse impact on recurrence rates (17–19). Evidence from multicenter breast cancer adjuvant trials that control systemic therapy dose and schedule address, to some degree, these issues.

Body Weight and Breast Cancer Outcome (in Cooperative Group Trials)

The National Surgical Breast and Bowel Project (NSABP) examined associations among obesity, tamoxifen use, and clinical outcome in receptor-positive, early-stage breast cancer in 3,385 participants in a randomized trial comparing tamoxifen with placebo. With more than 166 months of follow-up, tamoxifen efficacy was not influenced by obesity, and both contralateral breast cancer risk and all cause mortality were significantly greater in obese women (HR 1.59, 95% CI 1.10–2.25 and HR 1.31, 95% CI 1.12–1.5, respectively) (20).

The International Breast Cancer Study Group combined several randomized adjuvant trials into a cohort of 6,792 early-stage breast cancer patients and related clinical outcomes to BMI in analyses incorporating conventional prognostic factors (21). Higher BMI at diagnosis was associated with decreased overall survival, with a suggestion of greater effect in pre- and perimenopausal women (comparing obese with not obese women, HR 1.22, 95% CI 1.05–1.42 and HR 1.11, 95% CI 0.97–1.24, respectively) (Table 53.1). More recently, a report from M.D. Anderson described negative effects of obesity on outcome of 606 women with advanced but not metastatic breast cancer. All received similar anthracycline chemotherapy and doses were not adjusted for weight. Obesity was associated with significantly lower 10-year survival for both locally advanced disease (57.3% vs. 42.4%, for obese women versus not, respectively $p < .05$) and inflammatory breast cancer (50.9% vs. 43.7, respectively, $p < .05$) (22). These reports provide provocative information regarding the potential role of obesity in altering breast cancer clinical outcome even in patients receiving contemporary anticancer adjuvant treatment.

Weight Gain after Diagnosis and Breast Cancer Outcome

The association between obesity and poor prognosis in early-stage breast cancer is especially worrisome given the weight gain seen in many women following diagnosis (23) where, even with anthracycline-based adjuvant regimens, weight gain of 2 to 6 kg is commonly reported (24,25). Four of five studies which looked at the impact of weight gain after diagnosis on recurrence reported an increased risk associated with weight gain (26–29). In a NHS report in 2,206 nonsmoking women with early-stage breast cancer, women who gained 2.0 kg/m^2 or more (median weight gain of 17 pounds) had higher risk of breast cancer recurrence, breast cancer death, and all-cause mortality than did women who did not gain weight (30).

Obesity and Breast Cancer Outcome: Summary

Obesity has been associated with increased dietary fat intake and decreased physical activity, and all these factors have all been related to adverse breast cancer outcome in at least some reports (3,31,32). Given the common association of these factors, it is unlikely that retrospective analyses of existing patient

Table 53.1 CLINICAL OUTCOMES COMPARING OBESE WITH NONOBESE WOMEN IN ADJUVANT BREAST CANCER MULTICENTER CLINICAL TRIAL GROUPS

	Obese (BMI >30) versus not		
Outcome	NSABP HR (95% CI)	IBCSG HR (95% CI)	
	Premenopausal and Postmenopausal	Premenopausal and Perimenopausal	Postmenopausal
Breast Cancer Recurrence[a]	0.98 (0.80, 1.18)	1.16 (1.02, 1.33)	1.06 (0.96–1.17)
Overall survival	1.31 (1.12, 1.54)	1.22 (1.05, 1.42)	1.11 (0.97–1.24)

BMI, body mass index; CI, confidence interval; HR, hazard ratio; IBCSG, International Breast Cancer Study Group; NSABP, National Surgical Adjuvant Breast Cancer Project.
[a]As disease-free survival, which includes recurrence rates, second nonbreast invasive cancer or death from any cause.

populations will provide definitive information regarding a role for weight loss or weight maintenance as a breast cancer management strategy. A few small pilot studies have looked at weight loss and weight maintenance interventions in breast cancer survivors and have demonstrated that increased physical activity and mild calorie restriction can help prevent weight gain during and after breast cancer treatment (6,33). An ongoing randomized trial (described below) will help determine whether losing weight after breast cancer diagnosis will help prevent recurrence and improve overall survival.

PHYSICAL ACTIVITY AND BREAST CANCER OUTCOME

Although the preponderance of observational studies suggest increased physical activity may modulate breast cancer incidence, until recently the effects of physical activity on breast cancer prognosis was largely unexamined. Three observational studies now suggest that women who engage in modest amounts of physical activity after breast cancer diagnosis have a better prognosis than more sedentary women, and another study demonstrates improved prognosis in premenopausal women who were physically active in the year before breast cancer diagnosis (Table 53.2).

The NHS investigators prospectively examined relationships among physical activity and clinical outcomes in a cohort of 2,987 women diagnosed with stage I-IIIA breast cancer. Questionnaire information on physical activity was collected 2 or more years after initial cancer diagnosis to generate a metabolic equivalent (MET) hr/wk score for duration and intensity of physical activity. Compared with women with less than 3 MET hr/wk of physical activity (equivalent to walking at a moderate pace for less than 1 hr/wk), the adjusted relative risk (RR) of breast cancer mortality was 0.80 95% CI, 0.60–1.06 for 3–8.9 MET hr/wk of activity and 0.50 (95% CI 0.31–0.82) for 9–14.9 MET hr/wk. Breast cancer recurrence and all-cause mortality demonstrated similar favorable associations with

Table 53.2 OBSERVATIONAL STUDIES EVALUATING PHYSICAL ACTIVITY ASSOCIATION WITH CLINICAL OUTCOME IN EARLY STAGE, RESECTED BREAST CANCER

					Clinical Outcome			
Author	Study Population	Age (y)	Total	Follow-up	Follow-up	Breast T Cancer Death	otal Death	Results
Holick et al. *Cancer Epidemiol Biomarkers Prev* 2008;17:379–386	Breast cancer patients in Collaborative Women's Longevity Study (CWLS) identified <2 yr after diagnosis	20–79 yr	4,482	5.6 yr (median)	—	109	412	Versus <2.8 MET-h/wk for breast cancer death: for 2.8–7.9, HR 0.58 (0.45–0.75); for 8.0–20.9, HR 0.52 (0.40–0.68)
Abrahamson et al. *Cancer* 2006;107: 1777–1785	Population-based cohort with diagnosed breast cancer	20–54 yr	1,264	8–10 yr	—	—	290	Total mortality lowest in highest quartile of physical activity (for obese/overweight) HR 0.70 (0.49–0.99)
Holmes et al. *JAMA* 2005;293:2479–2486	Participants in Nurse's Health Study (NHS) who developed breast cancer	30–55 yr at entry in NHS	2,987		370	280	463	Versus <3 MET-h/wk for total mortality: for 3.0–8.9, HR 0.71 for (0.56–0.80); for 9.0–14.9, HR 0.57 (0.38–0.85)
Pierce et al. *J Clin Oncol* 2007;25: 2345–2351	Breast cancer patients participating as controls in randomized trial, entered <2 yr after diagnosis	<70 yr	1,490	6.7 yr (mean)	236	135	118	Combination of ≥5 vegetable/fruit servings/day plus physical activity equivalent to walking 30 min, 6 days/wk, for total mortality vs. not: HR 0.56 (0.31–0.98)

HR, hazard ratio; MET, metabolic equivalent.

physical activity and benefit, seen in both pre- and postmenopausal women, was independent of BMI (3).

Holick et al. (10) prospectively studied associations between postdiagnosis physical activity and breast cancer mortality in 4,482 women with localized disease. Questionnaires on physical activity were used to calculate MET hr/wk and patients were subsequently followed for recurrence. Women expending more than 2.8 MET hr/wk had lower breast cancer mortality when compared with women with lower levels of activity (HR 0.65, 95% CI 0.39–1.08 for 2.8–7.9 MET hr/wk; and HR 0.59, 95% CI 0.35–1.01 for 8.0–20.9 MET hr/wk). A 15% decrease in breast cancer mortality for each additional 5 MET hr/wk was calculated (p for trend = 0.03) with associations independent of age, BMI, or disease stage.

Using a somewhat different study design, Abrahamson et al. (34) examined the association of prediagnosis physical activity and survival in 1,264 premenopausal women with early-stage breast cancer. A nonsignificant trend for reduced mortality (HR 0.78, 95% CI 0.56–1.08) was seen in favor of the quartile reporting more physical activity. Finally, the Women's Healthy Eating and Living Study (WHEL) examined the association between survival and physical activity, body weight, and dietary pattern in early-stage breast cancer patients randomized to the control group in a clinical trial evaluating a dietary lifestyle change (35). After 8.7 years median follow-up, a linear trend between mortality and physical activity was seen. Compared with inactive participants, those who performed 636 to 1,320 MET-minutes of activity per week and those who performed more than 1,320 MET-minutes of activity per week had 24% and 42% lower mortality, respectively (p for trend = 0.02). However, composite measures suggested the association was also dependent on dietary fruit and vegetable intake.

Taken together, the results are consistent with a modest increase in physical activity being associated with substantial improvement in clinical outcome for patients with early-stage breast cancer. No randomized trial has reported on an intervention designed to increase physical activity in breast cancer patients in this setting.

Observational studies have demonstrated that a breast cancer diagnosis often is associated with a substantial decrease in physical activity (36). Intervention trials of physical activity in women with localized breast cancer have been largely limited to relatively short duration trials with end points including quality of life (37), fitness, weight change (38–40), and potential biomarkers of breast cancer risk and prognosis, such as estrogen (41) and insulin (42). These trials have demonstrated that physical activity is both feasible during and after breast cancer therapy, and is associated with improved quality of life and decreased fatigue (43,44), and fewer treatment-related side effects. Large-scale, randomized clinical trials are needed to determine whether increasing physical activity after breast cancer diagnosis will not only help women feel better, but also lead to improvements in prognosis.

DIETARY INTAKES AND BREAST CANCER OUTCOME

Studying the relationship between postdiagnosis dietary intakes and breast cancer prognosis represents an especially challenging area for observational studies, with methodologic issues related to the optimal timing of data collection, difficulty in accurately measuring the dietary exposure, and the modest range of intake for nutrients of interest in a general population (2).

The relationship between dietary fat intake and breast cancer outcome has been examined in 14 observational studies. Although recent analyses suggest that commonly used instruments may have difficulty in accurately measuring this parameter (44,45), 7 reports demonstrated a significant association between lower fat intakes and lower recurrence risk (1,4). These reports did not adjust for BMI or total energy intake, however, making interpretation problematic. Reports relating vegetable and related nutrient intake to breast cancer prognosis presents a similarly mixed picture with three of eight reports describing significant associations between higher intake and lower recurrence risk (5,46). Recently, two randomized clinical trials have provided a higher level of evidence on the question of the influence of nutrient intake on breast cancer outcomes.

POTENTIAL MEDIATORS OF LIFESTYLE CHANGE

At present, while estrogen, leptin, and inflammatory factors are of interest, no mediator of lifestyle influence on breast cancer outcome has been definitively identified. However, an emerging body of preclinical and observational study evidence suggests that insulin may play a substantial role in the process (47). Higher fasting insulin levels have been associated with obesity and also with increased recurrence risk and death in early-stage breast cancer patients, with greatest influence seen on hormone receptor-negative cancers (48). In a similar study, women with either high insulin levels or the insulin resistance syndrome had significantly more beast cancer mortality. In this cohort of 603 early-stage breast cancer patients, high insulin levels were significantly associated with mortality risk as well (RR 1.9 95% CI 0.7–6.6) (49). Finally, in an adjuvant study in hormone receptor-positive postmenopausal women receiving tamoxifen, high levels of c-peptide (a break down product of proinsulin cleavage) were significantly associated with worse breast cancer outcomes (50).

Cross sectional analyses in postmenopausal women without cancer suggest both low physical activity and high caloric intake are related to higher fasting insulin levels (51). Ligibel et al. (42) has examined the impact of increasing physical activity on insulin levels, in a randomized trial evaluating a mixed strength and endurance exercise intervention in 82 overweight, sedentary women with early-stage breast cancer. The 16-week intervention reduced circulating insulin levels by 28% (p = .03) with a trend toward improvement in insulin sensitivity. Although further study is needed, insulin remains a potential mediator of lifestyle influence on breast cancer outcome (42).

ADJUVANT BREAST CANCER RANDOMIZED TRIALS EVALUATING LIFESTYLE CHANGE

Two recently reported full-scale, randomized clinical trials have evaluated lifestyle interventions targeting dietary change in the adjuvant breast cancer setting. The Women's Intervention Nutrition Study (WINS) and WHEL study enrolled different populations and studied different dietary patterns, but both aimed to reduce dietary fat intake. These trials are compared and contrasted below (Table 53.2).

The WINS is a randomized, prospective multicenter clinical trial evaluating the impact of a dietary intervention on disease-free survival (DFS) in women with resected, early-stage breast cancer receiving conventional cancer management (4). Participants were required to have histologically confirmed, resected early-stage, invasive breast cancer, be between 49 and 79 years of age, and receive acceptable adjuvant therapy. The dietary intervention was designed to reduce fat intake with

eight every-other-week visits during the intensive intervention period followed by every-3-month contacts during the maintenance period, implemented by centrally trained, registered dietitians using a previously developed low-fat eating plan (52). Nutrient intake information was collected annually using unannounced telephone recalls and patients were followed for recurrence and survival.

After 5.6 years median follow-up, a sustained statistically significant reduction in dietary fat intake, in terms of both fat grams and percent calories from fat, was seen reduced in intervention participants (Table 53.3). Although weight loss was not a specific intervention target, significantly lower body weight was also seen in the intervention group throughout. More relapse events occurred in the control (181 of 1,462, 12.4%) compared with the intervention group (96 of 975, 9.8%, HR 0.76, 95% CI 0.60–0.98, $p = .034$). Preliminary analyses from an additional 3 years of follow-up provide similar results (relapse-free survival HR 0.79, 95% CI 0.62–1.00), but the difference is no longer statistically significant (53). Continued nonintervention follow-up of these patients is ongoing. In exploratory subgroup analyses, substantially greater influence was seen in women with ER-negative, PR-negative breast cancer (overall survival HR 0.34, 95% CI 0.16–0.70) (53). The WINS results suggest a hypothesis that a lifestyle intervention reducing dietary fat intake and associated with modest weight loss may improve outcome of breast cancer patients receiving conventional cancer management.

Although a primary prevention trial, results from the Women's Health Initiative Dietary Modification trial (WHI DM) may inform the WINS results. In the WHI DM 48,832, postmenopausal women without a breast cancer history were randomized to a dietary intervention program largely targeting dietary fat intake reduction (54). Statistically significant dietary fat intake reduction was achieved and fewer breast cancer diagnoses were made in the dietary intervention group, but the differences did not achieve statistical significance (HR 0.91, 95% CI 0.83–1.01). However, as in WINS, greater evidence of dietary effect was seen in risk of hormone receptor-negative breast cancer (54).

The Women's Healthy Eating and Living Randomized Trial

The WHEL is a multicenter, randomized prospective trial of a dietary intervention program being evaluated in 3,088 women with early-stage, resected breast cancer with an objective to determine whether a dietary pattern, including an increase in vegetable, fruit, and fiber intake and a decrease in fat intake, would influence breast cancer recurrence risk and all-cause mor-

Table 53.3 RANDOMIZED CLINICAL TRIALS EVALUATING LIFESTYLE CHANGE IN EARLY STAGE, RESECTED BREAST CANCER: STUDY DESIGNS AND REPORTED OUTCOME

	WINS	WHEL	LISA
Eligibility			
Stage	I–III A	I– II A	I–III A
Time from surgery	≤12 mo	≤48 mo	≤15 mo
Chemotherapy	AC, CMF, FAC, or AC → Paclitaxel	Any (before randomization)	Any (before randomization)
Hormonal therapy	Tamoxifen	Any	Letrozole
Receptor status	Any	Any	Receptor positive
Age	48–79 yr	18–70 yr	Any postmenopausal (life expectancy >5 yr)
Weight/BMI	Any	Any	BMI ≥21 <40 kg/m^2
Diet at baseline	≥20% caloric from fat	Any	Any
Dietary Intervention			
Intervention phase	Eight individual dietitian visit over 16 wk	Eighteen telephone calls over 12 mo, 4 cooking classes (average attended)	Telephone calls (19–22) over 6 mo
Maintenance phase	Individual dietitian visits every 3 mo	Telephone calls every 3 mo	Telephone calls (19) over 2 yr
Number of patients (randomization type)	2,437 (3:2 randomization)	3,088 (1:1 randomization)	2,150 (1:1 randomization)
Intervention target			
Fat	↓ to 15% calories from fat	↓ to <20% calories from fat	↓ to 20% calories from fat
Calories			Decrease 500–1000 calories/day
Vegetable	Increase (no target)	Increase to 5 serving/day and 16 oz vegetable juice/day	Increase (no target)
Fruit	Increase (no target)	Increase to 3 servings/day	Increase (no target)
Body weight	N/A	N/A	10% loss to BMI ≥21 kg/m^2
Physical activity	N/A	N/A	Increase to 150–200 min/wk walking plus resistance/flexibility
Follow-up Interval	5 yr	7.3 yr	0 (Entering patients)
End point	Relapse-free survival	Breast cancer event free-survival	Disease-free survival
Self-monitoring	Daily "keeping score" book	No	Daily log books for diet and physical activity
Dietary assessment	Two 24-hr unannounced telephone calls/yr	Four prescheduled 24-hr telephone calls at 1, 4, and 6 yr	N/A
Endpoint events (n)	277	518	N/A
Primary breast cancer outcome	HR 0.76 (95% CI 0.60–0.98, $p = .034$)[a]	0.96 (95% CI 0.80–1.14, $p = .63$)[b]	N/A

AC, doxorubicin (adriamycin) and cyclophosphamide (Cytoxan); BMI, body mass index; CMF, cyclophosphamide, methotrexate and 5-fluorouracil; FAC, Fluorouracil (5-FU), doxorubicin and cyclophosphamide; LISA, Lifestyle Intervention Study in Adjuvant Treatment of Early Breast Cancer; WHEL, Women's Healthy Eating and Living Study; WINS, Women's Intervention Nutrition Study.
[a]Chlebowski RT, Blackburn G, Thomson CA, et al. *J Natl Cancer Inst* 2006;98(24):1767–1776.
[b]Pierce JP, Natarajan L, Caan BJ, et al. *JAMA* 2007;298:289–298.

tality (5). Intervention participants received a telephone counseling program involving 18 calls during the first year with a subsequent decrease in intensity (55) (Table 53.3). Significant changes were achieved in the nutrition targets: vegetables plus 65%, fruit plus 25%, fiber plus 30%, and energy intake from fat minus 13%. Over the 7.3-year mean follow-up, no difference emerged in invasive breast cancer events (HR 0.96, 95% CI 0.80–1.14, $p = .63$) or overall (HR 0.91, 95% CI 0.72–1.15; $p = .43$) (5).

Although both WINS and WHEL included dietary fat intake reduction as an objective and entered early-stage breast cancer patients, substantial differences between these trials exist (Table 53.3) (56). The WHEL intervention resulted in a substantial and sustained increase in vegetable, fruit, and fiber intake and a relatively short duration, moderate reduction in fat intake. The WINS intervention did not report increased vegetable, fruit, or fiber intake, but resulted in a substantial, sustained reduction in fat intake, which was associated with significant weight loss (Table 53.4), which may account for the apparent differences in influence on clinical outcome seen.

The Lifestyle Intervention Study in Adjuvant Treatment of Early Breast Cancer

One adjuvant breast cancer trial is currently evaluating an intervention designed to reduce weight through increased physical activity and dietary modification. The Lifestyle Intervention Study in Adjuvant treatment of early breast cancer (LISA) of the Ontario Clinical Oncology Group is an ongoing trial that will evaluate the impact of an individualized weight loss intervention (telephone and mail-based) on DFS in postmenopausal women with recently diagnosed, hormone receptor-positive breast cancer (47). In this multicenter, randomized clinical trial involving 2,150 women, intervention group participants will receive a program targeting individual weight loss, dietary fat reduction, and increased physical activity. Participants will be postmenopausal women with stage I-II A, resected breast cancer who have a BMI between 24 and 40 kd/m^2, have completed chemotherapy, and are on letrozole adjuvant hormone therapy. The WINS, WHEL, and LISA trials are compared in Table 53.2.

Table 53.4 DIETARY INTAKE AND BODY WEIGHT CHANGE DURING WINS AND WHEL INTERVENTION

	WHEL	WINS
%Energy from fat		
Baseline	28.5 ± 0.18	29.6 ± 7.1
1 yr	22.7 ± 0.20	20.3 ± 7.8
4 yr	27.1 ± 0.24	22.6 ± 8.5
6 yr	28.9 ± 0.25	23.0 ± 9.2
Body weight (kg)		
Baseline	73.5 ± 0.42	72.7 ± 15.9
1 yr	73.0 ± 0.45	70.6 ± 15.2
4 yr	74.2 ± 0.51	71.2 ± 14.9
6 yr	74.1 ± 0.54	69.4 ± 13.9
Fiber g/d		
Baseline	21.1 ± 0.21	18.4 ± 4.1
1 yr	29.0 ± 0.28	19.5 ± 4.7
Vegetable Servings/d		
Baseline	3.9 ± 0.06	Not reported
1 yr	7.8 ± 0.09	—
Fruit Servings/d		
Baseline	3.5 ± 0.05	Not reported
1 yr	4.2 ± 0.06	—

WHEL, Lifestyle Intervention Study in Adjuvant Treatment of Early Breast Cancer; WINS, Lifestyle Intervention Study in Adjuvant Treatment of Early Breast Cancer.
WINS values, all mean ± standard deviation (SD); WHEL values, all mean ± standard error (SE).
In WINS, dietary fat intake difference comparing both intervention with control groups and baseline with each time period value in the intervention group was substantially significant ($p < .0001$). In WHEL, dietary fat intake differences comparing intervention with control groups was statistically significant ($p < .001$). In WHEL, the baseline to each time period value in the intervention group was not tested for significance.
In WINS, body weight difference comparing intervention with control groups and baseline with each time period value in the intervention group were statistically significant ($p < .005$) at all intervals. In WHEL, no significant body weight differences were seen.
In WINS, fiber, vegetable, and fruit intake were either not reported or not significantly different. In WHEL, vegetables, fruit, and fiber intake comparing intervention with control groups were statistically significant ($p < .001$) for each dietary target across the control intervention period.

CONCLUSIONS

As the evidence linking lifestyle factors and breast cancer outcomes mounts, there is a growing desire on the part of many patients to make lifestyle changes after breast cancer diagnosis. However, given the relative paucity of available randomized data, and that most medical oncologists lack expertise in this area, many breast cancer patients do not receive any guidance to help make these changes.

Observational evidence suggests that women who are overweight or obese at the time of breast cancer diagnosis, and those who gain weight during and after cancer treatment, appear to have a worse prognosis as compared with leaner women. Similar evidence suggests that women who are inactive after breast cancer diagnosis also have a poor prognosis compared with women who engage in modest amounts of physical activity. Randomized data suggest that lowering fat intake, or modest weight loss, is associated with a modest decrease in breast cancer recurrence, whereas increasing fruit, vegetable, and fiber intake does not appear to have an impact on breast cancer outcomes. The LISA trial will help determine whether weight loss decreases the risk of cancer recurrence in breast cancer survivors, but it will be several years until the results of this study will be available and further work is clearly needed to help define the role of lifestyle change in breast cancer patients.

MANAGEMENT SUMMARY

- Advocating weight maintenance for women with a BMI less than 25, and moderate weight loss for overweight and obese women, are reasonable goals for most breast cancer patients.
- Reduction in caloric intake is essential for weight loss, whereas exercise has been demonstrated to be a key component of maintaining weight in a target range.
- Specific recommendations for individual patients will depend on the goals of the treatment plan (weight maintenance vs. weight loss), as well as the presence of comorbid conditions that could influence diet or activity level.
- For weigh loss, a diet emphasizing complex carbohydrates and limiting refined sugars and fats could be recommended for most breast cancer patients.
- The U.S. Surgeon General recommends 30 minutes of moderate exercise five times per week as a general health measure, and this level of physical activity may be associated with improved survival in breast cancer patients.

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