



## Original Contribution

# Physical Activity's Impact on the Association of Fat and Fiber Intake With Survival After Breast Cancer

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This study examined whether, after a breast cancer diagnosis, high intake of animal fat was associated with increased breast cancer mortality and high intake of fiber was associated with decreased breast cancer mortality. Participants were 3,846 US female nurses diagnosed with stages I–III breast cancer between 1976 and 2001 and followed until death or May 2006. Breast cancer mortality was calculated according to dietary intake quintiles first assessed at least 12 months after diagnosis and was cumulatively averaged and updated. There were 446 breast cancer deaths. In simple models adjusted for time since diagnosis, age, and energy intake, animal fat intake was associated with increased breast cancer death, and cereal fiber intake was associated with reduced breast cancer death. However, no associations were found in fully adjusted models: for animal fat, the relative risks for increasing quintiles were 1.00, 0.89, 0.86, 0.85, and 0.89 (95% confidence interval: 0.61, 1.28),  $P = 0.68$ ; for cereal fiber, they were 1.00, 0.95, 0.76, 0.81, and 1.00 (95% confidence interval: 0.71, 1.40),  $P = 0.59$ . Results of simple models adjusted additionally for physical activity were similar to those for full multivariate models. Results show that physical activity strongly confounds the association between diet and survival.

breast neoplasms; dietary fats; dietary fiber; exercise; survival

Abbreviations: CI, confidence interval; ER, estrogen receptor; WHEL, Women's Healthy Eating and Living; WINS, Women's Intervention Nutrition Study.

In the United States, 2.5 million women are now living after a breast cancer diagnosis (1). Length of survival after diagnosis varies widely, even after accounting for stage and treatment, suggesting that other factors may also be important. Cancer survivors commonly report diet and lifestyle changes after their cancer diagnosis, hoping to increase well-being, maintain health, and prevent recurrence (2).

Evidence from international comparisons and preclinical studies stimulated the hypothesis that a diet low in fat and high in fiber might prevent the development of breast cancer (3–5). Similarly, a diet low in fat and high in fiber was hypothesized to prevent recurrence and promote survival among women with breast cancer.

Two randomized trials tested these hypotheses: the Women's Intervention Nutrition Study (WINS) and the Women's Healthy Eating and Living (WHEL) trial. Unfortunately, the trials did not provide the definitive answers hoped for.

WINS randomly assigned 2,437 women with breast cancer to a low-fat diet (goal: 15% of energy from fat). After a median follow-up of 5 years, study authors found only an 8% difference in energy from fat between the intervention and control groups, with only 39% reporting on their diet at 5 years, suggesting challenges regarding long-term compliance with dietary trials. In interim results, the authors reported a marginally statistically significant reduction in breast cancer relapses in the intervention arm, although no difference in overall survival. However, the intervention group experienced greater weight loss than the control group, so it was unclear whether the observed differences were due to diet composition or weight loss (6).

WHEL randomly assigned 3,088 women with breast cancer to a diet low in fat and high in fruits, vegetables, and fiber. After 4 years of follow-up, study authors found a 30% higher fiber and 13% lower fat intake when they compared the intervention with the control group. After a mean of 7.3

years of follow-up, there was no difference in breast cancer recurrence or death between the intervention and control groups (7).

The Nurses' Health Study has repeated measures of diet and a follow-up time of up to 30 years, which could provide insights into long-term exposure not feasible in trials. We hypothesized that a diet high in total and animal fat and low in fiber would be associated with an increased risk of breast cancer death and recurrence in our cohort study of Nurses' Health Study participants with breast cancer.

## MATERIALS AND METHODS

### Study subjects and identification of breast cancer

The Nurses' Health Study was established in 1976, when 121,700 female registered nurses from across the United States, aged 30–55 years, answered a mailed questionnaire on cancer and cardiovascular risk factors. They have received follow-up questionnaires every 2 years since then. Follow-up of the entire cohort's person-years is 95% complete.

For any report of breast cancer, participants' written permission was obtained for our study physicians to review their medical and pathology records, blinded to exposure information. Overall, 99% of self-reported breast cancers for which medical records were obtained have been confirmed.

The study was approved by the Institutional Review Board of Brigham and Women's Hospital, Boston, Massachusetts. It included women diagnosed with stages I–III breast cancer between 1976 and 2001, with data on diet beginning in 1980, when it was first assessed. Women with 4 or more positive nodes but lacking a metastatic workup were excluded. A metastatic workup consisted of a negative chest radiograph (or chest computed tomography), bone scan, and liver function tests (or liver scan) or documentation from a physician that the patient did not have detectable metastatic disease. A total of 6,319 women were diagnosed with breast cancer within the study time range. Women were excluded for the following reasons: stage IV at diagnosis or information on stage missing ( $n = 363$ ), stage III but lacking a complete metastatic workup ( $n = 557$ ), and missing diet information ( $n = 1,553$ ). Thus, 3,846 women were available for the analysis.

### Exposure assessment

Dietary assessments were administered in 1980, 1984, 1986, 1990, 1994, 1998, and 2002 by using validated semi-quantitative food frequency questionnaires (8). For each food or beverage, participants were asked how often, on average, they had consumed a specified amount over the past year. Participants could choose from 9 prespecified frequency categories (never, 1–3 per month, 1 per week, 2–4 per week, 5–6 per week, 1 per day, 2–3 per day, 4–5 per day, and 6 or more per day). Mean daily intakes of dietary factors were calculated by using US Department of Agriculture food composition sources supplemented with data from manufacturers and other sources. The baseline

diet was the one that most closely followed the diagnosis, with a minimum lag of at least 12 months.

### Endpoints: breast cancer death and recurrence

Women were followed until death or May 2006, whichever occurred first. Deaths were reported by the family or post office. In addition, questionnaire nonresponders were searched for in the National Death Index (9). More than 98% of deaths in the Nurses' Health Study have been identified by these methods. Physicians ascertained cause of death from death certificates, supplemented as needed by medical records. The primary endpoint was death from breast cancer.

A secondary endpoint was distant breast cancer recurrence, ascertained as described previously (10). Numbers of cases of recurrent breast cancer calculated in this manner are similar to those expected given the recurrence rates found in a large ( $N = 5,569$ ) trial of radiation treatment in early-stage breast cancer (11).

### Covariates

Covariates included factors previously associated with breast cancer survival in this cohort, including dietary factors, physical activity, body mass index, weight change, and reproductive factors (12–14). Additional adjustment was performed for treatment (chemotherapy, radiation, and hormonal therapy) and for smoking, because it is associated with total mortality (10).

Breast cancer characteristics, including year of diagnosis, stage, and estrogen receptor (ER) status, were extracted from the medical record by physician review. Treatment was by self-report. Leisure-time physical activity was assessed in total metabolic equivalent task-hours per week beginning in 1986 and was updated in 1988, 1992, 1996, 1998, 2000, and 2004, with physical activity measured at least 2 years after diagnosis to avoid assessment of physical activity during active treatment. All other covariates were taken from the questionnaire immediately preceding the breast cancer diagnosis. Categories were created for missing data. Simple models were adjusted for time since diagnosis, age at diagnosis, and energy intake.

### Statistical analysis

Cox proportional hazards models, with time since diagnosis as the underlying time variable, were used to calculate relative risks and 95% confidence intervals. In the main analysis, death from breast cancer was the endpoint, and deaths from other causes were censored. In secondary analyses, breast cancer recurrence and death from any cause were considered separately as endpoints.

To reduce within-subject variation and best represent long-term effects of diet, the cumulative average of intakes from all available dietary questionnaires was calculated beginning with the baseline dietary assessment after diagnosis and up to the start of each 2-year follow-up interval (15). For example, for a subject diagnosed with breast cancer in 1978, fiber intake from the 1980 questionnaire was used for the

**Table 1.** Age-standardized Levels of Covariates, According to Quintiles of Baseline Energy-adjusted Dietary Intake, Among US Female Nurses Diagnosed With Breast Cancer in 1976–2001 (N = 3,846)

	Animal Fat			Cereal Fiber		
	Q1	Q3	Q5	Q1	Q3	Q5
Mean						
Age at diagnosis, years	58.2	58.4	58.2	58.2	58.4	58.5
Age at first birth (parous women), years	24.7	25.0	25.1	25.1	25.0	24.9
Parity (parous women), no.	2.9	3.1	3.2	3.2	3.0	3.0
Energy intake after diagnosis, kilocalories/day	1,729	1,733	1,644	1,632	1,762	1,647
Body mass index at diagnosis, kg/m <sup>2</sup>	23.8	25.4	25.5	25.0	25.1	25.1
Physical activity after diagnosis, MET-hours/week	18	15	12	14	15	17
Percentage						
Ever used oral contraceptives	47	43	27	31	39	49
Postmenopausal at diagnosis	89	85	86	85	84	86
Estrogen receptor positive	73	81	83	77	81	80
Current smoking at diagnosis	7	12	21	22	9	8
Stage I disease	63	62	58	56	62	63
Stage II disease	30	30	34	35	30	29
Stage III disease	5	8	8	9	8	8
Radiation treatment	45	42	33	34	44	44
Chemotherapy	34	28	25	23	30	32
Hormonal treatment	58	54	46	45	57	59

Abbreviations: MET, metabolic equivalent task; Q, quintile.

follow-up between 1980 and 1984, mean fiber intakes from the 1980 and 1984 questionnaires were used for the follow-up between 1984 and 1986, and so on. To better differentiate the long-term and short-term effects of diet on breast cancer survival, we performed analyses using diet assessments at different time points: baseline diet and simple updating; that is, we applied each dietary assessment to the subsequent time period, without averaging.

Each participant accumulated person-time beginning with her date of breast cancer diagnosis until the analysis endpoint or May 2006, whichever occurred first. In this paper, relative risks and 95% confidence intervals are shown for quintiles of dietary intake, with the lowest intake being the reference. The 2-tailed *P* value for the linear trend test across quintiles of intake was calculated by assigning the median value to each category. Interaction terms were calculated by multiplying the 2 risk factors and entering them into the relevant models, and likelihood ratio tests were used to assess their statistical significance. Relative risks and 95% confidence intervals for quintiles of simple updated physical activity were determined similarly.

Assessment of diet during the first 12 months after diagnosis was avoided to minimize effects on diet due to treatment or its side effects, which may include nausea. In addition, women who develop recurrent disease may also change their diet, which may bias results. This potential bias

was coped with in several different ways. As described previously, analyses were performed with baseline, simple updated, and cumulatively averaged and updated diet information to better understand the effects of diet over time. Analyses were also performed with recurrence as the endpoint.

## RESULTS

Among 3,846 participants, there were 446 breast cancer deaths and 91 additional breast cancer recurrences in women who did not die during follow-up. Median length of follow-up was 83 months, and maximum length of follow-up was 321 months. Age-standardized characteristics according to quintiles of animal fat and cereal fiber intake in the baseline diet are shown in Table 1. Lower intake of animal fat and higher intake of cereal fiber appear to be indicators of a healthy lifestyle; they were associated with higher levels of physical activity, more oral contraceptive use, more breast cancer treatment, and less smoking.

We calculated the relative risks and 95% confidence intervals of breast cancer death for intake of cumulatively averaged and updated dietary factors, including total fat, animal fat, vegetable fat, total fiber, and cereal fiber. Model 1 is the simple model, adjusted for time since diagnosis, age at

**Table 2.** Relative Risks of Breast Cancer Deaths of US Female Nurses Diagnosed in 1976–2001 by Quintiles of Cumulatively Averaged and Updated Quintiles<sup>a</sup> of Animal Fat and Cereal Fiber Intake, According to Simple Models, Model 1 Plus Other Covariates One at a Time, and Full Models

Model	Animal Fat							Cereal Fiber					
	RR			Q5		P Trend	RR			Q5		P Trend	
	Q2	Q3	Q4	RR	95% CI		Q2	Q3	Q4	RR	95% CI		
Model 1 <sup>b</sup>	1.19	1.15	1.15	1.60	1.14, 2.24	0.004	0.87	0.62	0.62	0.63	0.46, 0.87	0.0004	
Model 1 + body mass index	1.27	1.24	1.21	1.67	1.19, 2.35	0.003	0.92	0.64	0.67	0.64	0.47, 0.89	0.0008	
Model 1 + weight change	1.19	1.15	1.15	1.61	1.14, 2.25	0.003	0.87	0.62	0.62	0.63	0.46, 0.87	0.0004	
Model 1 + age at first birth and parity	1.16	1.12	1.13	1.57	1.12, 2.20	0.004	0.88	0.62	0.63	0.64	0.47, 0.89	0.0006	
Model 1 + oral contraceptive use	1.19	1.14	1.14	1.55	1.10, 2.18	0.008	0.88	0.63	0.64	0.64	0.47, 0.89	0.0008	
Model 1 + menopause and HRT	1.13	1.11	1.07	1.49	1.06, 2.09	0.01	0.92	0.65	0.70	0.73	0.53, 1.01	0.01	
Model 1 + smoking	1.20	1.16	1.17	1.62	1.15, 2.28	0.003	0.86	0.61	0.61	0.62	0.45, 0.85	0.0003	
Model 1 + stage of disease	1.03	1.02	1.05	1.42	1.02, 2.00	0.01	0.83	0.64	0.62	0.68	0.49, 0.93	0.003	
Model 1 + treatment	1.18	1.09	1.09	1.43	1.02, 2.01	0.03	0.92	0.66	0.68	0.69	0.50, 0.95	0.004	
Model 1 + physical activity	1.13	1.04	0.95	1.07	0.76, 1.50	0.97	1.04	0.80	0.86	0.92	0.66, 1.28	0.33	
Model 2 <sup>c</sup>	0.89	0.86	0.85	0.89	0.61, 1.28	0.68	0.95	0.76	0.81	1.00	0.71, 1.40	0.59	

Abbreviations: CI, confidence interval; HRT, hormone replacement therapy; RR, relative risk.

<sup>a</sup> Quintile (Q)1 = reference group.

<sup>b</sup> Model 1 was adjusted for time since diagnosis (months), age at diagnosis (years), and energy intake (quintiles).

<sup>c</sup> Model 2 was adjusted for time since diagnosis (months), age at diagnosis (years), energy intake (quintiles), body mass index (<21, 21–22.9, 23–24.9, 25–28.9, ≥29 kg/m<sup>2</sup>), body mass index change (<–0.5, –0.5 to 0.5, >0.5 kg/m<sup>2</sup>), age at first birth and parity (nulliparous, <25 years and 1–2 births, <25 years and >2 births, ≥25 years and 1–2 births, ≥25 years and >2 births), oral contraceptive use (never/ever), menopausal status and HRT use (premenopausal, postmenopausal and never, postmenopausal and past, postmenopausal and current, postmenopausal and unknown), smoking (never, past, current), stage of disease (I, II, III), radiation treatment (yes/no), chemotherapy and hormonal treatment (no and no, yes and no, no and yes, yes and yes), date of diagnosis (months), and physical activity (quintiles of MET-hours/week, missing).

diagnosis, and energy intake. Model 2 is the full multivariate model adjusted for all covariates.

In simple models, we found no association of cumulatively averaged and updated intake of total fat, vegetable fat, total fiber, or several fiber types (fruit fiber, crude fiber, soluble fiber, insoluble fiber, cellulose, hemicellulose, and lignin) with breast cancer death. Animal fat intake was associated with an increased risk of breast cancer death, and cereal fiber intake was associated with a decreased risk of breast cancer death (Table 2).

In multivariable-adjusted models, the positive association with animal fat and the inverse association with cereal fiber were greatly attenuated and no longer statistically significant. Refer to Table 2.

Additionally, in multivariable models using baseline or simple updated dietary assessments, no associations with breast cancer death were found for total, animal, or vegetable fat or for total or cereal fiber. Likewise, no associations with distant breast cancer recurrence were detected for cumulatively averaged and updated total, animal, or vegetable fat or for total or cereal fiber. However, in multivariable models using death from any cause as the outcome, cumulatively averaged and updated intake of vegetable fat and cereal fiber were associated with a decreased risk of death from any cause. For increasing quintiles of vegetable fat intake, the relative risks were 1.00 (referent), 0.70 (95% confidence interval (CI): 0.54, 0.91), 0.72 (95% CI: 0.56, 0.92), 0.58 (95% CI: 0.45, 0.76), and 0.63 (95% CI: 0.48, 0.84); *P* trend = 0.007. For increasing quintiles of cereal

fiber intake, the relative risks were 1.00 (referent), 0.93 (95% CI: 0.73, 1.18), 0.72 (95% CI: 0.56, 0.94), 0.64 (95% CI: 0.48, 0.86), and 0.71 (95% CI: 0.53, 0.96); *P* trend = 0.03.

To assess which covariate contributed most strongly to attenuating the associations found in simple models, covariates were added one at a time to the simple model (Table 2). Addition of body mass index, weight change, reproductive variables, smoking, stage of disease, and treatment did not appreciably change the relative risks for animal fat or cereal fiber intake compared with the relative risks for the simple models. Instead, physical activity appeared to have the greatest impact on the observed association.

Increasing levels of physical activity were associated with a decreased risk of death from breast cancer, even after adjustment for both animal fat and cereal fiber and for all other covariates. The relative risks for increasing quintiles of physical activity were 1.00 (referent), 0.53 (95% CI: 0.39, 0.71), 0.36 (95% CI: 0.26, 0.51), 0.28 (95% CI: 0.19, 0.41), and 0.17 (95% CI: 0.11, 0.27); *P* trend < 0.001.

Finally, analyses were stratified by ER status of the tumor (Table 3). In multivariable models, higher cumulatively averaged and updated intake of animal fat seemed associated with a higher risk, and higher intake of cereal fiber appeared associated with a lower risk of breast cancer death for women with ER– tumors. However, with the small numbers of deaths and wide confidence intervals, the linear associations did not reach statistical significance, indicating limited power to detect an association among women with ER– tumors.

**Table 3.** Analyses of Breast Cancer Deaths<sup>a</sup> of US Female Nurses Diagnosed in 1976–2001 by Quintiles of Cumulatively Averaged and Updated Quintiles<sup>b</sup> of Animal Fat and Cereal Fiber Intake, Stratified by Estrogen Receptor Status<sup>c</sup>

Stratification Factor	Q2		Q3		Q4		Q5			P Trend	P Interaction
	No. of Deaths	RR	No. of Deaths	RR	No. of Deaths	RR	No. of Deaths	RR	95% CI		
<i>Animal fat</i>											
ER+ <sup>d</sup>	49	0.91	54	0.69	63	0.80	69	0.87	0.55, 1.36	0.69	
ER- <sup>e</sup>	14	2.64	16	3.81	15	1.84	25	3.44	0.77, 15.31	0.32	0.13
<i>Cereal fiber</i>											
ER+ <sup>d</sup>	67	0.82	44	0.67	39	0.72	47	1.04	0.70, 1.55	0.98	
ER- <sup>e</sup>	21	1.12	12	1.06	13	0.80	4	0.59	0.17, 2.05	0.35	0.05

Abbreviations: CI, confidence interval; ER, estrogen receptor; RR, relative risk.

<sup>a</sup> Sum of total deaths across strata may not equal 678 because of missing values.

<sup>b</sup> Quintile (Q)1 = reference group.

<sup>c</sup> Analyses were adjusted for all covariates (similar to model 2 in Table 2).

<sup>d</sup> Total no. of deaths = 271.

<sup>e</sup> Total no. of deaths = 73.

For the interaction between cereal fiber and ER status, the *P* value for interaction reached borderline statistical significance.

## DISCUSSION

In 1999, the Nurses' Health Study reported on associations between dietary factors after breast cancer diagnosis and risk of death from any cause. A modestly, but not statistically significant increased risk of total mortality was found for women in the highest compared with the lowest quintile of total fat intake (relative risk = 1.34, 95% CI: 0.97, 1.85; *P* trend = 0.40). There was also decreased total mortality with a higher intake of fiber: the relative risk for extreme quintiles of intake was 0.69 (95% CI: 0.50, 0.97; *P* trend = 0.02) (16). The 1999 analysis had limited power and follow-up with 1,982 women and 378 total deaths, included a single dietary assessment after diagnosis, and did not adjust for physical activity.

The current analysis had several strengths over the previous one (16). It included more than twice as many women and many more deaths from breast cancer, enabling us to examine breast-cancer-specific mortality and providing more statistical power. Our study also used repeated measures of diet as well as baseline diet, and it additionally adjusted for weight change and physical activity because we have since learned that these factors are important predictors of breast cancer mortality in our cohort (13, 14). In addition, the Nurses' Health Study, after 1999, collected information on treatment, which was adjusted for in the current study. These differences allowed a more thorough examination of the associations between diet and survival after breast cancer.

Limitations of our study include that information on diet, physical activity, treatment, and recurrence was self-reported by the nurse participants. However, our frequent updating improves accuracy (17). The range of lifestyle factors in this population may be more limited than that

needed to find an effect. The type of dietary assessment (food frequency questionnaire compared with food records) used may affect the observed strength of an association (18). With the assessment methods we used, dietary factors were clearly associated with breast cancer mortality, supporting the ability of these methods to detect associations with outcomes, but these associations were confounded by physical activity. Confounding is always a limitation of observational studies, but we controlled for most known breast cancer risk factors. Finally, to be included in the analysis, these women with breast cancer needed to live long enough and be well enough to provide a dietary assessment at least 1 year after diagnosis. Therefore, the results may not be generalizable to a sicker population of women with breast cancer.

Indeed, the fact that dietary associations were confounded by physical activity was our most important finding. Physical activity has been associated with improved survival in women with breast cancer in the Nurses' Health Study (14) and in 3 other cohort studies (19–21). Two other cohort studies found no association, however (22, 23).

Physical activity was correlated with lower intake of animal fat and higher intake of cereal fiber. Intakes of dietary fat and cereal fiber were no longer associated with survival after adjustment for physical activity, yet higher physical activity was still associated with improved survival even after adjustment for diet. The WHEL trial found similar results. In an assessment conducted before random assignment of the 2,819 subjects, higher physical activity levels were strongly associated with adherence to National Cancer Institute dietary recommendations (*P* < 0.001) even after adjusting for demographic, cancer-related, and psychosocial factors (24).

The WINS trial reported a decreased risk of breast cancer recurrence at any site (local, regional, and distant) with a low-fat dietary intervention (relative risk = 0.76, 95% CI: 0.60, 0.98), but there was no difference in overall survival (relative risk = 0.89, 95% CI: 0.65, 1.21) (6). Although body weight was not an intervention target, the

intervention group weighed approximately 6 pounds (2.7 kg) less than the control group throughout the 5 years of the intervention, a statistically significant difference (6). The adverse influence of body weight and weight gain on survival after breast cancer is well known (13, 25–28), and the WINS investigators have proposed that their trial's low-fat diet caused modest weight loss, which led to improved insulin metabolism, reducing insulin's tumor-promoting effects and thus improving relapse-free survival (29). WINS has not reported on the physical activity levels of its participants.

In contrast to WINS, the WHEL intervention targeted not only lower dietary fat but also increased fruits, vegetables, and fiber. In WHEL, the trial intervention group did not lose weight, and no association with diet and survival was found (7).

Furthermore, in other intervention trials, weight loss has occurred with interventions regardless of fat intake (30), and reductions in percentage of energy from dietary fat do not appear to cause long-term weight loss (31, 32). Thus, a more likely explanation for the WINS findings is that the intensive intervention involving close monitoring of food intake and feedback resulted in weight loss, which in turn reduced recurrence of breast cancer.

The WINS trial found that the low-fat intervention was associated with a lower risk of relapse among women with ER– tumors (relative risk = 0.58, 95% CI: 0.37, 0.91) compared with women with ER+ tumors (relative risk = 0.85, 95% CI: 0.63, 1.14), although the *P* value for interaction did not reach statistical significance (*P* = 0.15) (6). Our results, also not statistically significant, are compatible. Larger studies will be needed to determine whether dietary changes may benefit women with ER– tumors, which would be welcome because of fewer therapeutic options for ER– tumors.

In trials of lifestyle factors, subjects cannot be blinded to the intervention that may lead to unforeseen effects, such as weight loss. Those randomly assigned to the control arm cannot be prevented from taking up the intervention on their own, and compliance can be difficult for those assigned to the intervention. Yet, causal effects of interventions can be inferred from randomized controlled trials. Despite the challenges involved, the impact of lifestyle factors on survival of women with breast cancer above and beyond medical treatment is a key research issue.

Current knowledge from trials seems to indicate that a particular kind of diet does not affect breast cancer outcomes on its own (7) but that weight loss might (6, 29). If weight loss is truly important for women with breast cancer, the optimal intervention for weight loss might be different from the interventions studied in the WHEL and WINS trials. The Dietary Intervention Randomized Controlled Trial conducted in moderately obese men and women without cancer recently reported that a low-fat diet was less effective in promoting weight loss than a Mediterranean diet or a low-carbohydrate diet, both of which had a higher fat content (32).

Several recent reviews of subjects without cancer have concluded that the addition of exercise to diet is important for long-term maintenance of weight loss and diabetes pre-

vention (33–35). It is unknown whether participants randomly assigned to a healthier diet in a trial might choose to exercise more, even if that was not an intervention goal.

This study reconfirmed our previous finding that physical activity was associated with decreased risk of breast cancer death among women with breast cancer (14), and this association was independent of dietary intake. Importantly, it found that physical activity confounded the association between diet and survival. Future analyses of the relation between lifestyle factors and survival after breast cancer should consider the possible effects of physical activity. Ongoing randomized trials may clarify the relation of physical activity and diet with survival after breast cancer.

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