

Dietary Patterns and Breast Cancer Recurrence and Survival Among Women With Early-Stage Breast Cancer

Marilyn L. Kwan, Erin Weltzien, Lawrence H. Kushi, Adrienne Castillo, Martha L. Slattery, and Bette J. Caan

A B S T R A C T

From the Division of Research, Kaiser Permanente, Oakland, CA; and University of Utah, Salt Lake City, UT.

Submitted July 30, 2008; accepted October 20, 2008; published online ahead of print at www.jco.org on December 29, 2008.

Supported by National Cancer Institute Grant No. R01 CA80027 and by Utah Cancer Registry Grant No. N01 PC67000, with additional support from the State of Utah Department of Health.

Authors' disclosures of potential conflicts of interest and author contributions are found at the end of this article.

Corresponding author: Marilyn L. Kwan, PhD, 2000 Broadway, First Floor, Oakland, CA 94612; e-mail Marilyn.L.Kwan@kp.org.

© 2008 by American Society of Clinical Oncology

0732-183X/09/2706-919/\$20.00

DOI: 10.1200/JCO.2008.19.4035

Purpose

To determine the association of dietary patterns with cancer recurrence and mortality of early-stage breast cancer survivors.

Patients and Methods

Patients included 1,901 Life After Cancer Epidemiology Study participants diagnosed with early-stage breast cancer between 1997 and 2000 and recruited primarily from the Kaiser Permanente Northern California Cancer Registry. Diet was assessed at cohort entry using a food frequency questionnaire. Two dietary patterns were identified: prudent (high intakes of fruits, vegetables, whole grains, and poultry) and Western (high intakes of red and processed meats and refined grains). Two hundred sixty-eight breast cancer recurrences and 226 all-cause deaths (128 attributable to breast cancer) were ascertained. Cox proportional hazards models were used to estimate hazard ratios (HRs) and 95% CIs.

Results

Increasing adherence to a prudent dietary pattern was associated with a statistically significant decreasing risk of overall death (P trend = .02; HR for highest quartile = 0.57; 95% CI, 0.36 to 0.90) and death from non-breast cancer causes (P trend = .003; HR for highest quartile = 0.35; 95% CI, 0.17 to 0.73). In contrast, increasing consumption of a Western dietary pattern was related to an increasing risk of overall death (P trend = .05) and death from non-breast cancer causes (P = .02). Neither dietary pattern was associated with risk of breast cancer recurrence or death from breast cancer. These observations were generally not modified by physical activity, being overweight, or smoking.

Conclusion

Women diagnosed with early-stage breast cancer might improve overall prognosis and survival by adopting more healthful dietary patterns.

J Clin Oncol 27:919-926. © 2008 by American Society of Clinical Oncology

INTRODUCTION

The influence of diet on breast cancer prognosis has been explored in previous studies demonstrating inconsistent results with fat intake¹⁻⁶ and modest inverse associations^{4,5,7,8} with fruit and vegetable consumption.⁴⁻⁸ Notably, two randomized dietary intervention trials among women with breast cancer reported contrasting findings. The Women's Intervention Nutrition Study found that a low-fat diet reduced breast cancer recurrence,¹ whereas the Women's Health Eating and Lifestyle Study reported that a diet high in vegetables, fruits, and fiber and low in total fat did not reduce recurrence or mortality.⁶

Although focusing on specific nutrients or foods may be warranted based on interests in biologic mechanisms, foods are not consumed in isolation, but rather as part of an overall dietary

pattern.⁹⁻¹¹ Thus, in epidemiologic studies, there is growing interest in the exploration of dietary patterns and their associations with disease.¹²⁻¹⁸ For example, food intake patterns that have been characterized as Western (high intakes of meat, refined grains, and high-fat foods) tend to be associated with increased risk of coronary heart disease,^{12,15} stroke,^{14,19} diabetes,^{18,19} and colon cancer,^{11,13,20-22} whereas prudent dietary patterns (high intakes of fruits and vegetables and whole grains) tend to be associated with decreased risk of these diseases.

To our knowledge, only one study has examined the role of dietary patterns in breast cancer survival.²³ Using data from the Nurses' Health Study (NHS), Kroenke et al²³ reported that higher intake of the prudent pattern and lower intake of the Western pattern was associated with decreased mortality from causes other than breast cancer but not with death from breast cancer or all-cause death.

Therefore, we undertook an analysis of dietary patterns and breast cancer prognosis among 1,901 participants in the Life After Cancer Epidemiology (LACE) Study, a prospective cohort study of long-term survival after breast cancer diagnosis.

PATIENTS AND METHODS

Study Cohort

The LACE cohort consists of 2,280 women diagnosed with invasive breast cancer between 1997 and 2000 and recruited primarily from the Kaiser Permanente Northern California (KPNC) Cancer Registry (82%) and the Utah Cancer Registry (12%). Further details on the cohort are provided elsewhere.²⁴

In brief, eligibility criteria included age between 18 and 79 years old at enrollment; a diagnosis of early-stage primary breast cancer (stage I \geq 1 cm, stage II, or stage IIIA); enrollment between 11 and 39 months after diagnosis; completion of breast cancer treatment (except for adjuvant hormonal therapy); free of recurrence; and no history of other cancers in the 5 years before enrollment.

Between January 2000 and April 2002, 5,656 women who initially met the LACE eligibility criteria were sent a recruitment package. Of these, 2,614 women (46%) agreed to participate and completed the questionnaires. Subsequent medical record review to confirm eligibility resulted in 334 exclusions. Reasons for exclusion were breast cancer recurrence, new primary breast cancer, or death between diagnosis and 3 months after study enrollment (37%); incorrect stage (34%); other cancer within 5 years before enrollment (10%); prior breast cancer (6%); more than 39 months since diagnosis (6%); incomplete demographic and medical data (3%); receiving treatment (2%); and language difficulty (2%). The remaining 2,280 women constitute the LACE cohort. Differences between KPNC participants and nonparticipants were compared,²⁴ and both groups were similar in terms of cancer severity (stage and number of positive nodes) and treatment (chemotherapy and type of surgery). The only significant differences were that women approached within 15 months of diagnosis were more likely to enroll than those approached later, and women less than 50 years old were less likely to enroll than older women. This analysis was restricted to 1,901 women (83%) who completed a dietary questionnaire at baseline, as described in the following section. The study was approved by the institutional review boards of KPNC and the University of Utah (Salt Lake City, UT).

Dietary Assessment

Diet was assessed at cohort entry using the Fred Hutchinson Cancer Research Center Food Questionnaire (FHCRC-FQ), a self-administered, semiquantitative food frequency questionnaire with 122 food and beverage items.^{25,26} For each food or beverage, participants marked frequency of consumption over the last 12 months and indicated the associated serving size as small, medium, or large.

A total of 1,962 women completed the FHCRC-FQ at baseline. Participants with questionnaires indicating extremes of total energy intake (< 500 or > 4,000 kcal; $n = 54$) or an excessive number of skipped items ($n = 7$) were considered unreliable and were excluded, leaving 1,901 women for the current analyses. Servings per day were calculated by multiplying portion size by frequency of consumption of each food and beverage item, standardized to daily consumption. Food items were classified into 38 food groups based on nutrient profiles and/or culinary usage, which was similar to previous studies.^{16,21,23} Foods with unique nutrient profiles and/or culinary usage were maintained as individual categories (eg, fried chicken, fried potatoes, mayonnaise).

Covariates

Information on clinical factors was obtained through electronic data sources available from KPNC or from medical chart review for the non-KPNC participants. Data included tumor size, number of positive lymph nodes, hormone receptor status, and treatments. Treatment data included surgical procedures and associated dates, as well as types and dates of chemotherapy,

radiation therapy, and hormone therapy. Tumor stage was calculated according to criteria of the American Joint Committee on Cancer (third edition). Data on race, family history of breast cancer, menopausal status, and weight gain were obtained from the mailed baseline questionnaire at cohort entry. Physical activity was assessed (metabolic equivalent [MET] hours per week) from a mailed questionnaire modeled loosely on the Arizona Activity Frequency Questionnaire.²⁷

Outcome Assessment

Four prognostic outcomes were considered: new breast cancer event (hereafter referred to as recurrence), all-cause death, death from breast cancer, and death from causes other than breast cancer. Recurrence includes a local or regional cancer recurrence, distant recurrence or metastasis, and development of a contralateral breast primary. All-cause death includes death from any cause including breast cancer; death from breast cancer includes death attributable to breast cancer as a primary or underlying cause on the death certificate; and death from causes other than breast cancer includes all other deaths. A physician reviewer was consulted in the event a cause of death was unclear. Recurrences were ascertained by a mailed semi-annual (until April 2005) or annual (after April 2005) health status update questionnaire that asked participants to report any events occurring in the preceding 6 or 12 months, respectively. All nonrespondents to the health status questionnaire were called to complete the questionnaire by telephone. Participants receiving care outside of KPNC who reported any event were contacted to obtain permission to view their protected health information. Medical records were reviewed to verify reported outcomes.

Participant deaths were determined through KPNC electronic data sources, a family member responding to a mailed questionnaire, or a phone call. In the event of a long-term nonresponse, death certificates were requested from the county or state of last known residence. For all study participants who were known to have died, copies of death certificates were obtained from the same sources to confirm cause of death.

For these analyses, 268 breast cancer recurrences (of which 84.3% were distant metastases) and 226 deaths were ascertained through May 29, 2008. Among the 226 deaths, 128 (56.6%) were attributable to breast cancer, 17 (7.5%) were attributable to other cancers, 29 (12.9%) were attributable to cardiovascular causes, and 52 (23.0%) were attributable to other causes not related to cancer or cardiovascular disease (CVD; International Classification of Diseases, 9th revision).

Statistical Analysis

To identify major dietary patterns, principal components analysis was used on the basis of the 38 predetermined food groups to identify factors that account for much of the variance in the variables.^{28,29} The food groups (factors) were rotated using an orthogonal transformation, resulting in uncorrelated, independent factors. Major factors were retained based on eigenvalue (> 1), Scree test, and factor interpretability. The factor score for each factor (pattern) was calculated by summing intakes of food groups weighted by factor loading, and each individual was assigned a score for each identified pattern. Individuals with a high score for a pattern compared with individuals with lower scores have a stronger tendency to follow that pattern. The scores were then categorized by quartiles. Comparisons of baseline cohort characteristics by category of dietary pattern were conducted using Pearson χ^2 , analysis of variance, and Kruskal-Wallis tests.

Follow-up began at date of study entry and ended at date of first confirmed cancer recurrence or date of death, depending on the specific analysis. Individuals who did not have an event were censored at date of last contact. Hazard ratios (HRs) and 95% CIs representing the association between a defined event and quartiles of a dietary pattern were computed adjusting for covariates using the delayed entry Cox proportional hazards model.^{30,31} Because women entered the cohort over an approximately 3-year period since diagnosis, the delayed entry model ensures that a woman who enrolled onto the study t years after her initial breast cancer diagnosis was not considered at risk for a possible outcome before t years. A linear test for trend was estimated by modeling the median value of each category on an ordinal scale. All models were adjusted for age at diagnosis (years) and total energy intake (kcal).

A priori confounders included race, body mass index (BMI) at enrollment, family history of breast cancer, menopausal status, total physical activity at baseline, weight change from before diagnosis to study entry, smoking status, stage of disease, hormone receptor status, surgery, tamoxifen use, treatment, positive lymph nodes, and tumor size ≥ 2 cm, as specified in Tables 2 and 3.

Covariates were retained in the final multivariable model if they were statistically significant ($P < .05$) when added individually to the model adjusted for age at diagnosis and total energy intake. We also examined whether the associations between dietary patterns and prognosis varied by total physical activity at baseline ($> v <$ median MET-h/wk), BMI at enrollment ($< 25 v \geq 25$ kg/m²), and smoking status (ever v never smoker) by first generating strata-specific estimates and then including interaction terms in the models to test for statistical significance. A sensitivity analysis was conducted by excluding women who experienced recurrence or died within the first year of entering the cohort to address the possibility that sick patients with underlying cancer recurrences and limited survival may have altered their diet.

RESULTS

Dietary Pattern Characteristics

The following two distinct dietary patterns were identified at baseline: prudent and Western. Table 1 lists the factor-loading matrix between the individual food groups and the two major dietary patterns such that a higher factor loading value is indicative of a stronger correlation between the specific food group and relevant dietary pattern.

Higher prudent pattern scores at baseline were observed for women who were more physically active ($P < .0001$) and gained less weight from 1 year before diagnosis to enrollment ($P = .04$; Table 2). Higher Western pattern scores at baseline were observed for women who were younger ($P = .008$), had higher BMI at enrollment ($P < .0001$), had ever smoked ($P = .04$), and gained more weight from 1 year before diagnosis to enrollment onto the study ($P = .0002$; Table 3). In addition, Asian women were less likely to follow the Western dietary pattern, whereas Hispanic women were more likely to follow the Western dietary pattern ($P = .005$).

Baseline Dietary Patterns and Study Outcomes

Mean follow-up times from cohort entry until the end points of recurrence and death were 3.17 years (range, 0.27 to 8.20 years) and 4.20 years (range, 0.34 to 7.75 years), respectively. Overall, cohort members were observed 5.93 years from entry (range, 0.00 to 8.36 years). In both the age- and energy-adjusted only and full multivariable models adjusted for additional prognostic factors, increasing tendency to follow the prudent diet was associated with a lower risk of overall death and death from other causes aside from breast cancer (Table 4). The highest quartile of the prudent pattern was associated with a decreased risk of overall death (HR = 0.57; 95% CI, 0.36 to 0.90; P trend = .02) and death from non-breast cancer causes (HR = 0.35; 95% CI, 0.17 to 0.73; P trend = .003). Furthermore, in both the age- and energy-adjusted only and full multivariable models, increasing tendency to follow the Western pattern was associated with increased risk of overall death (HR for highest quartile = 1.53; 95% CI, 0.93 to 2.54; P trend = .05) and death from non-breast cancer causes (HR for highest quartile = 2.15; 95% CI, 0.97 to 4.77; P trend = .02; Table 4). No associations were observed between these dietary patterns and breast cancer recurrence or death from breast cancer. These results did not change after excluding the 35 women who experienced recurrence or died within 1 year of study enrollment.

Table 1. Food Groups Representing the Major Dietary Patterns Identified by Food Frequency Questionnaire at Baseline (N = 1,901) Using Principal Components Analysis in the LACE Study

Food Groups in the Prudent Diet*	Food Groups in the Western Diet*
Cruciferous vegetables	
Other vegetables	
Tomatoes	
Dark yellow vegetables	
Fruits	
Legumes	
Onions	
Leafy vegetables	
Fish	
Soups	
Whole grains	
Poultry, not fried	
Salad dressings (all types)	
Rice, grains, plain pasta	
Fruit juice	
Low-fat dairy	
Nuts	
Potatoes, not fried	
Cold cereals	
	Red meat
	Processed meats
	Creamy soups/sauces
	Butter
	Mayonnaise
	Italian foods
	Fried potatoes
	High-fat dairy
	Fried chicken
	Snacks
	Refined grains
	Pasta or potato salads
	Mexican foods
	Sweets
	High-energy drinks
	Eggs
	Organ meats

Abbreviation: LACE, Life After Cancer Epidemiology.
*Food groups are presented in descending order based on factor loadings with absolute values ≥ 0.15 .

In analyses of overall death stratified by total physical activity, BMI at enrollment, and smoking status, no significant interactions were observed (Table 5). For breast cancer recurrence, death from breast cancer, and death from other causes, the stratified analyses did not yield any significant differential effect of dietary patterns by these factors (data not shown).

DISCUSSION

In this prospective cohort study of early-stage breast cancer survivors, increasing adherence to a prudent dietary pattern, characterized by high intakes of fruits, vegetables, legumes, whole grains, low-fat dairy products, poultry, and fish, was associated with a decreasing risk of overall death and death from causes other than breast cancer. In a complementary trend, increasing consumption of a Western dietary pattern consisting of high intakes of red and

Table 2. Baseline Characteristics of LACE Study Participants (N = 1,901) by Quartiles of the Prudent Dietary Pattern

Characteristic	Quartiles of Prudent Dietary Pattern								P*
	Q1 (n = 476)		Q2 (n = 474)		Q3 (n = 475)		Q4 (n = 476)		
	No. of Participants	%	No. of Participants	%	No. of Participants	%	No. of Participants	%	
Age at diagnosis, years†									.94
Mean	58.6		58.4		58.8		58.4		
Standard deviation	11.5		10.8		10.4		10.5		
Race									.50
White	381	80	389	82	402	85	387	81	
Black	26	5	17	4	16	3	16	3	
Hispanic	30	6	24	5	21	4	26	5	
Asian/Pacific Islander	23	5	31	7	25	5	27	6	
Other	16	3	11	2	11	2	20	4	
BMI at enrollment, kg/m ² †									.08
Mean	27.9		27.6		27.2		27.0		
Standard deviation	5.6		5.8		5.7		5.8		
Positive family history of breast cancer	96	20	80	17	105	22	102	21	.20
Menopausal status at diagnosis									.45
Postmenopausal	308	65	308	65	324	68	295	62	
Premenopausal	106	22	97	21	97	20	106	22	
Unknown	62	13	67	14	54	11	75	16	
Physical activity, MET-h/wk of total activity‡									< .0001
Median	37.8		45.8		49.7		58.4		
Range	0-171		0-259		1-237		1-307		
Weight change from before diagnosis to enrollment, lb†									.04
Mean	5.0		4.4		3.1		2.1		
Standard deviation	16.8		17.1		14.6		16.9		
Ever smoker	227	47.7	225	47.8	217	45.7	223	46.9	.91
Stage									.44
I ≥ 1 cm	234	49	230	49	229	48	217	46	
IIA	156	33	158	33	143	30	163	34	
IIB	75	16	70	15	80	17	85	18	
IIIA	10	2	15	3	21	4	11	2	
Hormone receptor status									.44
ER negative/PR negative	82	17	69	15	80	17	60	13	
ER negative/PR positive	7	1	6	1	13	3	9	2	
ER positive/PR negative	66	14	71	15	63	13	74	16	
ER positive/PR positive	316	67	323	69	314	67	325	69	
Surgery type									.99
Breast-conserving surgery	242	51	240	51	237	50	242	51	
Mastectomy	234	49	234	49	238	50	234	49	
Tamoxifen use	373	78	376	79	356	75	374	79	.38
Treatment									.67
None	92	19	80	17	83	17	80	17	
Chemotherapy only	92	19	94	20	83	18	96	20	
Radiation only	130	27	114	24	121	26	131	27	
Both	160	34	185	39	187	39	169	36	
Positive nodes	158	34	165	37	166	37	146	33	.52
Tumor size ≥ 2 cm	216	46	205	44	206	44	230	49	.42

Abbreviations: LACE, Life After Cancer Epidemiology; BMI, body mass index; MET, metabolic equivalent; ER, estrogen receptor; PR, progesterone receptor.

*Pearson χ^2 test, unless otherwise specified.

†Analysis of variance.

‡Kruskal-Wallis test.

processed meats, refined grains, sweets, high-fat dairy products, snacks, and butter was related to an increasing risk of overall death and death from causes other than breast cancer. In contrast, neither dietary pattern was associated with risk of breast cancer recurrence or death from breast cancer. Women who tended to follow the prudent dietary pattern were more physically active, whereas

women who had greater adherence to the Western dietary pattern were more likely to be overweight or obese and gained more weight (on average, 6 lb) after diagnosis. The corresponding protective and deleterious effects of a prudent diet and Western diet, respectively, on survival did not vary markedly by these or other modifiable lifestyle factors.

Dietary Patterns and Breast Cancer Prognosis

Table 3. Baseline Characteristics of LACE Study Participants (N = 1,901) by Quartiles of the Western Dietary Pattern

Characteristic	Quartiles of Western Dietary Pattern								P*
	Q1 (n = 475)		Q2 (n = 475)		Q3 (n = 475)		Q4 (n = 476)		
	No. of Participants	%	No. of Participants	%	No. of Participants	%	No. of Participants	%	
Age at diagnosis, years†									.008
Mean	59.3		58.9		58.9		57.1		
Standard deviation	10.3		10.6		11.1		11.1		
Race									.005
White	378	80	392	82	397	84	392	83	
Black	20	4	17	4	18	4	20	4	
Hispanic	15	3	24	5	31	6	31	6	
Asian/Pacific Islander	45	9	27	6	17	4	17	4	
Other	17	4	15	3	12	2	14	3	
BMI at enrollment, kg/m ² †									< .0001
Mean	25.6		27.2		27.7		29.1		
Standard deviation	4.7		5.5		5.8		6.4		
Positive family history of breast cancer	95	20	94	20	102	21	92	19	.87
Menopausal status at diagnosis									.04
Postmenopausal	319	67	325	68	309	65	282	59	
Premenopausal	88	18	100	21	99	21	119	25	
Unknown	68	14	50	11	67	14	73	15	
Physical activity, MET-h/wk of total activity‡									.52
Median	47.4		48.3		44.4		46.8		
Range	0-307		1-192		0-237		0-259		
Weight change from before diagnosis to enrollment, lb†									.0002
Mean	1.2		3.6		3.6		6.1		
Standard deviation	14.7		15.7		15.7		18.9		
Ever smoker	197	41.5	226	47.7	232	48.8	237	50.0	.04
Stage									.45
I ≥ 1 cm	233	49	216	45	240	50	221	47	
IIA	156	33	167	35	134	28	163	34	
IIB	68	14	80	17	87	18	75	16	
IIIA	16	3	12	3	14	3	15	3	
Hormone receptor status									.14
ER negative/PR negative	70	15	72	15	70	15	79	17	
ER negative/PR positive	6	1	11	2	12	2	6	1	
ER positive/PR negative	78	17	50	11	69	15	77	17	
ER positive/PR positive	315	67	339	72	320	68	305	65	
Surgery type									.97
Breast-conserving surgery	237	50	238	50	244	51	242	51	
Mastectomy	238	50	237	50	231	49	234	49	
Tamoxifen use	373	78	359	76	381	80	366	77	.35
Treatment									.83
None	89	19	75	16	83	17	88	18	
Chemotherapy only	85	18	103	22	84	18	93	20	
Radiation only	123	26	124	26	132	28	117	25	
Both	176	37	173	36	174	37	178	37	
Positive nodes	147	33	169	38	157	35	162	37	.51
Tumor size ≥ 2 cm	215	46	222	47	217	46	203	44	.80

Abbreviations: LACE, Life After Cancer Epidemiology; BMI, body mass index; MET, metabolic equivalent; ER, estrogen receptor; PR, progesterone receptor.

*Pearson χ^2 test, unless otherwise specified.

†Analysis of variance.

‡Kruskal-Wallis test.

Although several studies have investigated the role of dietary patterns in relation to risk of primary breast cancer,^{17,32-38} to our knowledge, only the NHS²³ has examined the impact of this measure of diet on breast cancer survival in a cohort of 2,619 women over a median follow-up time of 9 years since diagnosis. Our results agree with the NHS findings in that women who followed a more prudent diet had a decreased risk of death from causes other than breast cancer, whereas those who followed a more Western diet had an increased risk

of death from causes other than breast cancer. Our death rates (56.6% as a result of breast cancer and 44.4% as a result of other causes after a median of 6.3 years of follow-up) were similar to those of the NHS (58.5% as a result of breast cancer and 41.5% as a result of other causes after a median of 9 years of follow-up). Among women who died of non-breast cancer causes in our study (n = 98), 29.6% died of CVD, 17.3% died of other cancers, and 53.1% died of causes aside from CVD and cancer, compared with rates of 22%, 45%, and 33%, respectively,

Table 4. Delayed Entry Cox Proportional Hazards Models of Quartiles of Dietary Patterns and Breast Cancer Recurrence and Survival in the LACE Study

Quartiles of Dietary Pattern	No. of Participants	Recurrence			Overall Death			Death From Breast Cancer			Death From Other Causes		
		No. of Events	HR	95% CI	No. of Events	HR	95% CI	No. of Events	HR	95% CI	No. of Events	HR	95% CI
Prudent pattern, quartiles													
Model 1*													
Q1	476	65	Referent		73	Referent		37	Referent		36	Referent	
Q2	474	63	0.98	0.69 to 1.40	54	0.74	0.52 to 1.06	29	0.80	0.49 to 1.31	25	0.69	0.41 to 1.16
Q3	475	73	1.15	0.82 to 1.63	56	0.75	0.52 to 1.07	34	0.95	0.58 to 1.54	22	0.56	0.32 to 0.97
Q4	476	67	1.03	0.70 to 1.51	43	0.53	0.34 to 0.81	28	0.78	0.45 to 1.36	15	0.31	0.16 to 0.62
<i>P</i> for trend				.76			.006			.50			< .001
Model 2†													
Q1	451	62	Referent		66	Referent		34	Referent		32	Referent	
Q2	449	60	0.95	0.66 to 1.37	51	0.78	0.53 to 1.14	27	0.78	0.46 to 1.32	24	0.78	0.45 to 1.35
Q3	456	71	1.09	0.76 to 1.56	55	0.79	0.54 to 1.15	34	0.94	0.57 to 1.57	21	0.61	0.34 to 1.10
Q4	454	63	0.95	0.63 to 1.43	41	0.57	0.36 to 0.90	26	0.79	0.43 to 1.43	15	0.35	0.17 to 0.73
<i>P</i> for trend				.94			.02			.57			.003
Western pattern, quartiles													
Model 1*													
Q1	475	73	Referent		57	Referent		39	Referent		18	Referent	
Q2	475	66	0.90	0.64 to 1.26	46	0.89	0.60 to 1.32	28	0.76	0.47 to 1.25	18	1.16	0.60 to 2.26
Q3	475	62	0.86	0.60 to 1.23	61	1.31	0.89 to 1.92	26	0.77	0.46 to 1.31	35	2.49	1.36 to 4.54
Q4	476	67	0.93	0.60 to 1.43	62	1.76	1.10 to 2.81	35	1.26	0.68 to 2.31	27	2.80	1.32 to 5.94
<i>P</i> for trend				.75			.007			.41			.002
Model 2†													
Q1	451	68	Referent		54	Referent		37	Referent		17	Referent	
Q2	460	65	0.90	0.63 to 1.28	46	0.88	0.59 to 1.33	28	0.80	0.48 to 1.33	18	1.05	0.53 to 2.08
Q3	449	58	0.83	0.57 to 1.21	55	1.13	0.75 to 1.69	23	0.68	0.39 to 1.19	32	2.01	1.07 to 3.79
Q4	450	65	0.98	0.62 to 1.54	58	1.53	0.93 to 2.54	33	1.20	0.62 to 2.32	25	2.15	0.97 to 4.77
<i>P</i> for trend				.94			.05			.60			.02

Abbreviations: LACE, Life After Cancer Epidemiology; HR, hazard ratio; Q, quartile.

*Adjusted for age at diagnosis and total energy intake (kcal).

†Adjusted for age at diagnosis, total energy intake (kcal), race, body mass index at enrollment, total physical activity, smoking, menopausal status at diagnosis, weight change from before diagnosis to baseline, stage of cancer, hormone receptor status, and treatment as designated in Tables 2 and 3.

in the NHS. Also similar to the NHS, we found no association between either of the dietary patterns and risk of death from breast cancer. Although the NHS did not observe an association between dietary patterns and risk of overall death, our study noted an inverse relationship of increasing adherence to the prudent dietary pattern and decreasing risk of all-cause mortality and a direct relationship of increasing adherence to the Western dietary pattern and increasing risk of all-cause mortality.

Our results are consistent with the NHS²³ and studies of diet and cardiovascular disease^{12,15} and suggest that dietary patterns may represent a more important factor in the etiology of overall health and outcomes not related to breast cancer, as opposed to outcomes related to breast cancer. In fact, previous studies have reported somewhat modest and/or mixed associations of specific foods and/or food groups in relation to breast cancer prognosis.³⁹ Furthermore, in another analysis from the LACE Study, no association was observed between postdiagnosis weight gain (which is strongly correlated with increasing adherence to the Western dietary pattern and weaker adherence to the prudent dietary pattern in the present study) and breast cancer–related outcomes.⁴⁰

Strengths of the LACE study include being one of the few existing cohorts of early-stage breast cancer survivors and one of the first studies to comprehensively examine the association between dietary

patterns and breast cancer recurrence and survival. Although our analyses rely on self-report of diet on the FHCRC-FQ, this questionnaire has been validated in the Women's Health Initiative.^{26,41} Cause-specific mortality may have been misclassified on death certificates from which we extracted cause of death information. Although misclassification of cause of death has been an issue in most studies of cause-specific mortality, it is somewhat reassuring that our findings regarding deaths not associated with breast cancer are consistent with results from the NHS.²³ Because the LACE cohort consists of early-stage breast cancer survivors who were enrolled on average 2 years after diagnosis, we would not be able to detect associations with breast cancer death if the associations were only related to deaths that occurred in the immediate survivorship period (within 2 years) but not in the extended survivorship period (after 2 years). Finally, our results are not generalizable to women diagnosed with advanced-stage breast cancer and apply only to women who have survived, on average, 2 years since diagnosis.

In summary, we found that higher consumption of prudent and Western dietary patterns are associated with decreased and increased risks of overall death and death from causes other than breast cancer, respectively, but the patterns had no association with risk of breast cancer recurrence or breast cancer–related deaths. These results indicate that although dietary habits may not influence breast

Table 5. Delayed Entry Cox Proportional Hazards Models of Quartiles of Dietary Patterns and Risk of Overall Death by Selected Lifestyle Factors in the LACE Study

Factor	No. of Participants	No. of Events	Q1 HR	Quartile						P for Trend	P for Interaction
				Q2		Q3		Q4			
				HR	95% CI	HR	95% CI	HR	95% CI		
Prudent dietary pattern											
Total physical activity*											
< median (46.7 MET-h/wk)	948	122	Referent	0.61	0.37 to 1.00	0.83	0.52 to 1.34	0.38	0.19 to 0.77	.03	.12
≥ median (46.7 MET-hrs/wk)	949	91	Referent	1.24	0.65 to 2.35	0.74	0.38 to 1.45	0.88	0.45 to 1.75	.39	
BMI at enrollment†											
Not overweight/obese	852	84	Referent	0.97	0.53 to 1.76	0.73	0.38 to 1.40	0.58	0.28 to 1.24	.12	.75
Overweight/obese (≥ 25 kg/m ²)	999	133	Referent	0.70	0.43 to 1.13	0.81	0.50 to 1.31	0.58	0.32 to 1.03	.12	
Smoking status‡											
Never	1006	93	Referent	1.08	0.60 to 1.92	0.97	0.54 to 1.76	0.62	0.29 to 1.32	.27	.53
Ever	892	120	Referent	0.61	0.36 to 1.02	0.67	0.40 to 1.10	0.51	0.29 to 0.92	.04	
Western dietary pattern											
Total physical activity*											
< median (46.7 MET-h/wk)	948	122	Referent	0.99	0.56 to 1.73	1.29	0.74 to 2.25	2.07	1.03 to 4.16	.04	.91
≥ median (46.7 MET-hrs/wk)	949	91	Referent	0.84	0.46 to 1.56	1.16	0.63 to 2.13	1.23	0.59 to 2.56	.48	
BMI at enrollment†											
Not overweight/obese	852	84	Referent	0.76	0.40 to 1.44	1.28	0.70 to 2.36	1.36	0.58 to 3.20	.33	.69
Overweight/obese (≥ 25 kg/m ²)	999	133	Referent	0.98	0.57 to 1.67	1.14	0.66 to 1.97	1.64	0.86 to 3.11	.13	
Smoking status‡											
Never	1006	93	Referent	1.36	0.76 to 2.44	1.24	0.65 to 2.37	2.14	0.95 to 4.79	.13	.20
Ever	892	120	Referent	0.59	0.33 to 1.05	1.06	0.62 to 1.79	1.20	0.62 to 2.31	.29	

Abbreviations: LACE, Life After Cancer Epidemiology; HR, hazard ratio; MET, metabolic equivalent; BMI, body mass index.

*Adjusted for age at diagnosis, total energy intake (kcal), race, BMI at enrollment, weight change from before diagnosis to baseline, smoking, menopausal status at diagnosis, stage of cancer, hormone receptor status, and treatment as designated in Tables 2 and 3.

†Adjusted for age at diagnosis, total energy intake (kcal), race, total physical activity, smoking, menopausal status at diagnosis, stage of cancer, hormone receptor status, and treatment as designated in Tables 2 and 3.

‡Adjusted for age at diagnosis, total energy intake (kcal), race, total physical activity, BMI at enrollment, weight change from before diagnosis to baseline, menopausal status at diagnosis, stage of cancer, hormone receptor status, and treatment as designated in Tables 2 and 3.

cancer-related outcomes for women diagnosed with breast cancer, they are nonetheless strong predictors of overall prognosis after breast cancer diagnosis. Consistent with dietary guidelines directed towards the general population for overall chronic disease or cancer prevention,⁴²⁻⁴⁴ women diagnosed with early-stage breast cancer may benefit from dietary patterns that include healthier foods such as fruits, vegetables, whole grains, and poultry and less consumption of red meat and refined foods.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

REFERENCES

- Chlebowski RT, Blackburn GL, Thomson CA, et al: Dietary fat reduction and breast cancer outcome: Interim efficacy results from the Women's Intervention Nutrition Study. *J Natl Cancer Inst* 98:1767-1776, 2006
- Holm LE, Nordevang E, Hjalmar ML, et al: Treatment failure and dietary habits in women with breast cancer. *J Natl Cancer Inst* 85:32-36, 1993
- Holmes MD, Hunter DJ, Colditz GA, et al: Association of dietary intake of fat and fatty acids

- with risk of breast cancer. *JAMA* 281:914-920, 1999
- Holmes MD, Stampfer MJ, Colditz GA, et al: Dietary factors and the survival of women with breast carcinoma. *Cancer* 86:826-835, 1999
- Jain M, Miller AB, To T: Premorbid diet and the prognosis of women with breast cancer. *J Natl Cancer Inst* 86:1390-1397, 1994
- Pierce JP, Natarajan L, Caan BJ, et al: Influence of a diet very high in vegetables, fruit, and fiber and low in fat on prognosis following treatment for breast cancer: The Women's Healthy Eating and Living (WHEL) randomized trial. *JAMA* 298:289-298, 2007

AUTHOR CONTRIBUTIONS

Conception and design: Marilyn L. Kwan, Lawrence H. Kushi, Martha L. Slattery, Bette J. Caan
Financial support: Bette J. Caan
Administrative support: Marilyn L. Kwan, Adrienne Castillo
Provision of study materials or patients: Adrienne Castillo
Collection and assembly of data: Erin Weltzien, Adrienne Castillo, Martha L. Slattery, Bette J. Caan
Data analysis and interpretation: Marilyn L. Kwan, Erin Weltzien, Lawrence H. Kushi, Martha L. Slattery, Bette J. Caan
Manuscript writing: Marilyn L. Kwan, Bette J. Caan
Final approval of manuscript: Marilyn L. Kwan, Erin Weltzien, Lawrence H. Kushi, Adrienne Castillo, Martha L. Slattery, Bette J. Caan

- Fink BN, Gaudet MM, Britton JA, et al: Fruits, vegetables, and micronutrient intake in relation to breast cancer survival. *Breast Cancer Res Treat* 98:199-208, 2006
- Pierce JP, Stefanick ML, Flatt SW, et al: Greater survival after breast cancer in physically active women with high vegetable-fruit intake regardless of obesity. *J Clin Oncol* 25:2345-2351, 2007
- Kant AK, Schatzkin A, Block G, et al: Food group intake patterns and associated nutrient profiles of the US population. *J Am Diet Assoc* 91:1532-1537, 1991

10. Randall E, Marshall JR, Graham S, et al: Patterns in food use and their associations with nutrient intakes. *Am J Clin Nutr* 52:739-745, 1990
11. Slattery ML, Boucher KM, Caan BJ, et al: Eating patterns and risk of colon cancer. *Am J Epidemiol* 148:4-16, 1998
12. Brunner EJ, Mosdol A, Witte DR, et al: Dietary patterns and 15-y risks of major coronary events, diabetes, and mortality. *Am J Clin Nutr* 87:1414-1421, 2008
13. Fung T, Hu FB, Fuchs C, et al: Major dietary patterns and the risk of colorectal cancer in women. *Arch Intern Med* 163:309-314, 2003
14. Fung TT, Stampfer MJ, Manson JE, et al: Prospective study of major dietary patterns and stroke risk in women. *Stroke* 35:2014-2019, 2004
15. Fung TT, Willett WC, Stampfer MJ, et al: Dietary patterns and the risk of coronary heart disease in women. *Arch Intern Med* 161:1857-1862, 2001
16. Hu FB, Rimm E, Smith-Warner SA, et al: Reproducibility and validity of dietary patterns assessed with a food-frequency questionnaire. *Am J Clin Nutr* 69:243-249, 1999
17. Mannistö S, Dixon LB, Balder HF, et al: Dietary patterns and breast cancer risk: Results from three cohort studies in the DIETSCAN project. *Cancer Causes Control* 16:725-733, 2005
18. Nettleton JA, Steffen LM, Ni H, et al: Dietary patterns and risk of incident type 2 diabetes in the multi-ethnic study of atherosclerosis. *Diabetes Care* 31:1777-1782, 2008
19. Cai H, Shu XO, Gao YT, et al: A prospective study of dietary patterns and mortality in Chinese women. *Epidemiology* 18:393-401, 2007
20. Kim MK, Sasaki S, Otani T, et al: Dietary patterns and subsequent colorectal cancer risk by subsite: A prospective cohort study. *Int J Cancer* 115:790-798, 2005
21. Meyerhardt JA, Niedzwiecki D, Hollis D, et al: Association of dietary patterns with cancer recurrence and survival in patients with stage III colon cancer. *JAMA* 298:754-764, 2007
22. Wu K, Hu FB, Fuchs C, et al: Dietary patterns and risk of colon cancer and adenoma in a cohort of men (United States). *Cancer Causes Control* 15:853-862, 2004
23. Kroenke CH, Fung TT, Hu FB, et al: Dietary patterns and survival after breast cancer diagnosis. *J Clin Oncol* 23:9295-9303, 2005
24. Caan B, Sternfeld B, Gunderson E, et al: Life After Cancer Epidemiology (LACE) Study: A cohort of early stage breast cancer survivors (United States). *Cancer Causes Control* 16:545-556, 2005
25. Block G, Hartman AM, Dresser CM, et al: A data-based approach to diet questionnaire design and testing. *Am J Epidemiol* 124:453-469, 1986
26. Patterson RE, Kristal AR, Tinker LF, et al: Measurement characteristics of the Women's Health Initiative food frequency questionnaire. *Ann Epidemiol* 9:178-187, 1999
27. Staten LK, Taren DL, Howell WH, et al: Validation of the Arizona Activity Frequency Questionnaire using doubly labeled water. *Med Sci Sports Exerc* 33:1959-1967, 2001
28. Cody RP, Smith JK: Factor analysis, in Yagan S (ed): *Applied Statistics and the SAS Programming Language*. Upper Saddle River, NJ, Pearson Prentice Hall, 2006, pp 320-335
29. Kleinbaum DG, Kupper LL, Muller KE: Variable reduction and factor analysis, in Payne M (ed): *Applied Regression Analysis and Other Multivariable Methods* (ed 2). Pacific Grove, CA, Duxbury Press, 1988, pp 595-642
30. Cox DR, Oakes D: *Analysis of Survival Data*. London, United Kingdom, Chapman & Hall, 1994
31. Therneau TM, Grambsch PM: *Modeling Survival Data: Extending the Cox Model*. New York, NY, Springer-Verlag, 2000
32. Adebamowo CA, Hu FB, Cho E, et al: Dietary patterns and the risk of breast cancer. *Ann Epidemiol* 15:789-795, 2005
33. Fung TT, Hu FB, Holmes MD, et al: Dietary patterns and the risk of postmenopausal breast cancer. *Int J Cancer* 116:116-121, 2005
34. McCann SE, McCann WE, Hong CC, et al: Dietary patterns related to glycemic index and load and risk of premenopausal and postmenopausal breast cancer in the Western New York Exposure and Breast Cancer Study. *Am J Clin Nutr* 86:465-471, 2007
35. Ronco AL, De Stefani E, Boffetta P, et al: Food patterns and risk of breast cancer: A factor analysis study in Uruguay. *Int J Cancer* 119:1672-1678, 2006
36. Hirose K, Matsuo K, Iwata H, et al: Dietary patterns and the risk of breast cancer in Japanese women. *Cancer Sci* 98:1431-1438, 2007
37. Cui X, Dai Q, Tseng M, et al: Dietary patterns and breast cancer risk in the Shanghai breast cancer study. *Cancer Epidemiol Biomarkers Prev* 16:1443-1448, 2007
38. Murtaugh MA, Sweeney C, Giuliano AR, et al: Diet patterns and breast cancer risk in Hispanic and non-Hispanic white women: The Four-Corners Breast Cancer Study. *Am J Clin Nutr* 87:978-984, 2008
39. Rock CL, Demark-Wahnefried W: Nutrition and survival after the diagnosis of breast cancer: A review of the evidence. *J Clin Oncol* 20:3302-3316, 2002
40. Caan BJ, Kwan ML, Hartzell G, et al: Pre-diagnosis body mass index, post-diagnosis weight change, and prognosis among women with early stage breast cancer. *Cancer Causes Control* 19:1319-1328, 2008
41. Neuhauser ML, Tinker L, Shaw PA, et al: Use of recovery biomarkers to calibrate nutrient consumption self-reports in the Women's Health Initiative. *Am J Epidemiol* 167:1247-1259, 2008
42. US Department of Health and Human Services and US Department of Agriculture: *Dietary Guidelines for Americans, 2005* (ed 6). Washington, DC: US Government Printing Office, 2005
43. World Cancer Research Fund/American Institute for Cancer Research: *Food, Nutrition, Physical Activity, and the Prevention of Cancer: A Global Perspective*. Washington, DC, American Institute for Cancer Research, 2007
44. Doyle C, Kushi LH, Byers T, et al: *Nutrition and physical activity during and after cancer treatment: An American Cancer Society guide for informed choices*. *CA Cancer J Clin* 56:323-353, 2006

Acknowledgment

We thank all Life After Cancer Epidemiology Study staff and participants.