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Research Article

Better Postdiagnosis Diet Quality Is Associated with Reduced Risk of Death among Postmenopausal Women with Invasive Breast Cancer in the Women's Health Initiative

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Abstract

Background: Few studies have evaluated whether adherence to dietary recommendations is associated with mortality among cancer survivors. In breast cancer survivors, we examined how postdiagnosis Healthy Eating Index (HEI)-2005 scores were associated with all-cause and cause-specific mortality.

Methods: Our prospective cohort study included 2,317 postmenopausal women, ages 50 to 79 years, in the Women's Health Initiative's Dietary Modification Trial ($n = 1{,}205$) and Observational Study ($n = 1{,}112$), who were diagnosed with invasive breast cancer and completed a food frequency questionnaire after being diagnosed. We followed women from this assessment forward. We used Cox proportional hazards models to estimate multivariate-adjusted HRs and 95% confidence intervals (CI) for death from any cause, breast cancer, and causes other than breast cancer, according to HEI-2005 quintiles.

Results: Over 9.6 years, 415 deaths occurred. After adjustment for key covariates, women consuming better quality diets had a 26% lower risk of death from any cause ($HR_{Q4:Q1}$, 0.74; 95% CI, 0.55–0.99; $P_{trend} = 0.043$) and a 42% lower risk of death from non–breast cancer causes ($HR_{Q4:Q1}$, 0.58; 95% CI, 0.38–0.87; $P_{trend} = 0.011$). HEI-2005 score was not associated with breast cancer death ($HR_{Q4:Q1}$, 0.91; 95% CI, 0.60–1.40; $P_{trend} = 0.627$). In analyses stratified by tumor estrogen receptor (ER) status, better diet quality was associated with a reduced risk of all-cause mortality among women with ER^+ tumors ($n = 1{,}758$; $HR_{Q4:Q1}$, 0.55; 95% CI, 0.38–0.79; $P_{trend} = 0.0009$).

Conclusion: Better postdiagnosis diet quality was associated with reduced risk of death, particularly from non–breast cancer causes.

Impact: Breast cancer survivors may experience improved survival by adhering to U.S. dietary guidelines. *Cancer Epidemiol Biomarkers Prev; 23(4); 575–83. ©2014 AACR.*

Introduction

By 2022, it is estimated that the population of women living with a history of cancer will increase to 9.2 million. Among U.S. women, breast cancer is the most commonly diagnosed cancer (40% of all cancers) and the second leading cause of death. The overall relative 5-year survival rate for women diagnosed with breast cancer is around 90% (1), but long-term survival varies widely for women with invasive breast cancer (2). Cancer diagnosis is a teachable moment in which many survivors think about making lifestyle changes (3). Guidelines for promoting health after cancer diagnosis have been published (4), and evidence-based messages are available promoting these general tenets and their application (5). An important next step is to implement lifestyle changes on an individual basis as part of breast cancer care to improve longevity (6). To accomplish this, more population-level research is needed to determine how specific lifestyle prescriptions relate to health after cancer for the large and growing population of breast cancer survivors.

The effect of diet after breast cancer has been a growing area of research interest during the past decade and has evolved from a focus on single macro- and micronutrients to the study of the overall diet quality. The latter approach takes in account the complexity of the diet and the potentially synergistic or antagonistic effects of all individual dietary components (7). Nonetheless, few studies have examined survival benefits associated with overall dietary patterns (8–11), and new research in this area in

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studies with the ability to control for many factors important for survival after breast cancer and longevity could be valuable for informing postdiagnosis recommendations for breast cancer survivors.

Among a large cohort of postmenopausal breast cancer survivors in the Women's Health Initiative (WHI; ref. 12–14), we examined survival after breast cancer associated with a measure of diet quality, the Healthy Eating Index (HEI)-2005, which was created by the U.S. Department of Agriculture and the National Cancer Institute and assesses conformance to U.S. Federal dietary guidance, the Dietary Guidelines for Americans (15–18). The HEI-2005 is a measure for which implementable and user-friendly plans and tools are available for population- and individual-level guidance (15–18), making it ideal for investigation in the context of survivorship and care planning.

Materials and Methods

Study population

The WHI has been previously described in depth (12–14). Briefly, between 1993 and 1998 through 40 clinical centers, postmenopausal women who were 50 to 79 years at study entry were recruited into either a Clinical Trials (CT) component (n = 68,132) or an Observational Study (OS) component (n = 93,676 women). The CT and OS were closed in 2004–2005 and the participants were invited to continue being followed in the WHI Extension Study, which currently has follow-up events through 2010. For the present analysis, we focused on women in the intervention and comparison arms of Dietary Modification Trial (WHI-DM) of the WHI CT and women in the OS who were diagnosed with invasive breast cancer during the course of follow-up and completed a food frequency questionnaire (FFQ) after being diagnosed with invasive breast cancer (overall = 2,412; OS = 1,156; WHI-DM = 1,256). In the WHI, only the WHI-DM and OS had multiple FFQs which enabled us to look at postdiagnosis diet quality, so we focused on these groups. Of these, 2,319 women [OS = 1,114 (96%); WHI-DM = 1,205 (96%)] were considered to have valid data for the FFQ, which we defined as reporting energy in the range of 600–5,000 kcals/day. Two women from the OS were missing data on postmenopausal hormone therapy use and were excluded from this analysis. Our final sample included 2,317 women.

Dietary assessment

A standardized written protocol, centralized training of staff, and quality assurance visits by the Clinical Coordinating Center (CCC) were used to ensure uniform administration of data collection. Diet was measured in WHI using a self-administered FFQ developed and validated for the study (19), adapted from the Health Habits and Lifestyle Questionnaire (20). The three sections of the WHI FFQ included 122 composite and single food line items asking about frequency of consumption and portion size, 19 adjustment questions related to type of fat intake, and 4 summary questions asking about the usual intake of fruits and vegetables and added fats for comparison with information gathered from the line items. In the WHI-DM, all participants completed an FFQ at baseline and year 1 of follow-up, and a one-third subset completed an FFQ each year on a rotating basis thereafter from years 2–9. In the OS, participants completed an FFQ at baseline and during year 3 of follow-up. For this analysis, we identified the FFQ closest to but after participants' diagnoses of invasive breast cancer. The postdiagnosis FFQ occurred, on average, 1.5 years after diagnosis for both WHI-DM and OS participants and the range was 0–6 years for WHI-DM participants and 0–4 years for OS participants.

The WHI-FFQ was designed to capture foods relevant for multiethnic and geographically diverse population groups, and has been shown to produce reliable ($r_{\text{all nutrients}} = 0.76$) and comparable estimates to 8 days of dietary intake from 4 24-hour dietary recalls and 4-day food records (r = 0.37, 0.62, 0.41, 0.36, with energy, percent energy from fat, carbohydrate, and protein; ref. 19).

The nutrient database used to analyze the WHI-FFQ is derived from the Nutrition Data Systems for Research (NDS-R, version 2005, University of Minnesota, Minneapolis, Minnesota; refs. 21, 22). NDS-R provides nutrient information for >140 nutrients and compounds, including energy, saturated fat, and sodium. We measured diet quality with the HEI-2005 (15–18), created by the U.S. Department of Agriculture and the National Cancer Institute. This index aligns with the U.S. Dietary Guidelines for Americans (23). HEI-2005 score is calculated using diet data in units of MyPyramid equivalents, so we established a customized link (8) between NDS-R and the MyPyramid Equivalents Database (24).

The HEI-2005 scores 12 components, using an energy-adjusted density approach to set standards (e.g., per 1,000 calories or as a percent of calories; refs. 16, 17, 25). Six components (total fruit; whole fruit; total vegetables; dark-green vegetables, orange vegetables, and legumes; total grains; whole grains) are worth 0–5 points; five components (milk; meats and beans; oils; saturated fat; and sodium) are worth 0–10 points; and one component (calories from solid fat, alcohol, and added sugar) is worth 0–20 points. The latter three components are reverse-scored. For each participant, we scored each component and calculated a total score (100 possible points). We classified HEI-2005 scores into quartiles to best separate those with "better quality" diets (Q4) and "poor quality" diets (Q1).

Other covariate assessments

At baseline, participants completed self-administered health history questionnaires. Weight and height were measured during clinic visits using standard methods at baseline and annually at years 1–9 in the WHI-DM and at baseline and year 3 in the OS. We calculated body mass index (BMI) as weight (kg)/height (m)^2. For height and weight, we chose the assessment closest to the postdiagnosis FFQ but no more than 30 days after the FFQ completion. Recreational moderate-vigorous intensity physical activity, including walking, was assessed by questionnaire at baseline in the WHI-DM and OS and we calculated metabolic equivalent task hours (MET-h)/week of physical activity for each participant, as described in detail in Irwin and colleagues (26) and defined physical activity level (0 MET-h/wk; 0.1–3 MET-h/wk; 3.1–8.9 MET-h/wk; 9 or more MET-h/wk; ref. 15).

Ascertainment of death

Vital status of participants was collected through clinical center follow-up of participants and surrogates. In addition, periodic searches of the National Death Index were conducted. Cause of death was determined by medical record and death certificate review at the CCC.

Statistical analysis

Participants were followed from postdiagnosis FFQ until death, loss to follow-up, or the end of the previously described WHI-Extension Study 1 on September 30, 2010. Participants who did not consent to the Extension Study and were alive at study closeout on September 12, 2005 were censored on that date.

Means, SDs, and frequencies of demographic, clinical, and lifestyle characteristics of the study sample were calculated by quartiles of HEI-2005 scores.

Cox proportional hazards models were fit to our data using person-years as the underlying time metric. We estimated multivariate HRs and 95% confidence intervals (CI) for death from any cause, death from breast cancer, and death from causes other than breast cancer associated with increasing quartiles of HEI-2005 scores. The test for linear trend across HEI-2005 quartiles was performed by assigning participants the median value of their categories and entering it as a continuous term in a regression model.

We considered covariates that have been shown to be important predictors of death among breast cancer survivors and death from any cause among general populations. These included age at study entry, race/ethnicity, education, income, breast cancer stage, estrogen receptor (ER) status, and progesterone receptor (PR) status, years from diagnosis to FFQ, number of alcohol servings per week, physical activity, and use of postmenopausal hormone therapy. We also adjusted all models for energy intake (27) and WHI study component/arm (WHI-DM-intervention, WHI-DM-comparison, OS). None of these covariates acted as significant confounders, changing the magnitude of HRs by at least 10%, but we retained them in models and presented unadjusted, age and energy-adjusted, and multivariate-adjusted models to illustrate this point. We did not have data on cancer treatment, but adjusted for stage and ER/PR status which influence types of treatment received, and treatment and stage have been shown to be correlated in other studies of early-stage breast cancer survivors (28). We also ran models with and without stage to examine any differences in results. We investigated confounding by BMI separately, given its potential role as a mediator of the diet-mortality and the disease specific-mortality relationships (29, 30). Then, we ran an additional sensitivity analysis excluding women whose postdiagnosis FFQs were completed within 6 months after their diagnoses ($n = 430$), during which time treatment may have affected dietary intake and reporting.

To test whether any one component was responsible for the overall association for diet quality and mortality, we ran models for each of the 12 HEI-2005 component scores, adjusting for the residual HEI-2005 score (HEI-2005 total score-HEI-2005 component score).

Given clinical trial evidence that the relationship with diet and breast cancer outcomes may vary by ER status (31), as an exploratory analysis, we planned *a priori* to conduct a stratified analysis by ER status. We investigated heterogeneity of the diet quality and all-cause mortality relationship by tumor ER status, by using likelihood ratio tests for both the interaction of diet quality with ER status ($\alpha = 0.1$) and by evaluating the difference in model fit of full and reduced models.

All statistical tests were based on *a priori* hypotheses, and therefore there was no adjustment for multiple testing. All statistical analyses were conducted using SAS (version 9.2). All tests were two-sided with statistical significance set at $P < 0.05$.

Results

After a median follow-up of 9.6 years, 415 deaths occurred, 188 from breast cancer and 227 from non–breast cancer causes. The main causes of non–breast cancer-related death were cardiovascular disease and other cancers. As shown in Table 1, compared to women with poor dietary quality, those with better dietary quality were more physically active, reported lower daily energy intake and weekly alcohol servings, had higher levels of education and income, had lower BMI, and were less likely to be in the WHI-DM control group.

Women consuming better quality diets, as defined by higher HEI-2005 scores, had a 26% lower risk of death from any cause ($HR_{Q4:Q1}$, 0.74; 95% CI, 0.55–0.99; $P_{trend} = 0.043$) and a 42% lower risk of death from causes other than cancer ($HR_{Q4:Q1}$, 0.58; 95% CI, 0.38–0.87; $P_{trend} = 0.011$) even after multivariate adjustment (Table 2). We did not observe an association between HEI-2005 score and risk of death from breast cancer ($HR_{Q4:Q1}$, 0.91; 95% CI, 0.60–1.40; $P_{trend} = 0.627$). Models without stage as a covariate yielded similar results (data not shown). Inclusion of BMI in the model as a categorical variable resulted in similar HRs and tightened CIs (data not shown). When we excluded women whose postdiagnosis FFQs were completed within 6 months after their diagnoses ($n = 430$), HRs were also similar (data not shown).

There were no significant associations with any of the mortality outcomes for any of the individual HEI-2005 component scores when the residual HEI-2005 score was taken into account (data not shown).

Table 1. Demographic, clinical, and lifestyle characteristics of 2,317 women with invasive breast cancer in the WHI by HEI-2005 quartiles

	Poor-quality diets		Mixed-quality diets				Better-quality diets		
	Healthy Eating Index-2005 Score Quartile 1 (34–63)		Healthy Eating Index-2005 Score Quartile 2 (63–71)		Healthy Eating Index-2005 Score Quartile 3 (71–77)		Healthy Eating Index-2005 Score Quartile 4 (77–91)		
	N	(%)	N	(%)	N	(%)	N	(%)	*P*[a]
Number of participants	579		579		580		579		
Age at screening for WHI									
Mean (SE)	63.6 (0.3)		63.6 (0.3)		63.4 (0.3)		63.9 (0.3)		0.639
Years since diagnosis									
Mean (SE)	1.6 (0.4)		1.5 (0.05)		1.4 (0.04)		1.6 (0.04)		0.366
Calories (kcals/day)									
Mean (SE)	1665 (27.1)		1558.7 (23.7)		1454.4 (21.0)		1470.2 (19.8)		<0.0001
Alcohol servings/wk									
Mean (SE)	3.3 (0.3)		2.6 (0.2)		1.7 (0.1)		1.0 (0.1)		<0.0001
MET-hours/week of MVPA[b]									
Mean (SE)	8.1 (0.5)		9.9 (0.5)		10.6 (0.5)		13.3 (0.7)		<0.0001
BMI[c]									
Mean (SE)	29.3 (0.3)		28.6 (0.2)		27.8 (0.2)		27.0 (0.2)		<0.0001
Race/ethnicity									0.773
White	510	88	505	87	516	89	522	90	
Black	41	7	38	7	28	5	24	4	
Hispanic	12	2	16	3	13	2	13	2	
Other	15	3	20	3	20	3	19	3	
Unknown	1	0	1	0	2	0	1	0	
Education									0.002
High school or less	121	21	94	16	86	15	86	15	
Some college	236	41	214	37	221	38	189	33	
College	65	11	75	13	79	14	77	13	
Postgraduate	152	26	190	33	189	33	225	39	
Missing	5	1	6	2	5	1	2	0	
Income									0.029
≥$50,000	199	34	228	39	250	43	249	43	
$20,000–49,999	259	45	257	44	237	41	238	41	
<$20,000	81	14	69	12	66	11	56	10	
Missing	40	7	25	4	27	5	36	6	
WHI component/arm									<0.0001
WHI Observational Study	264	46	247	43	278	48	323	56	
WHI-DM-control	253	44	222	38	151	26	114	20	
WHI-DM-intervention	62	11	111	19	150	26	142	25	
Stage									0.974
Localized	436	75	427	74	436	75	443	77	
Regional	132	23	142	25	136	23	128	22	
Distant	6	1	4	1	3	1	3	1	
Unknown	5	1	6	1	5	1	5	1	
Estrogen receptor status									0.197
Positive	429	74	455	79	451	78	423	73	
Negative	90	16	65	11	72	12	90	15	
Unknown	60	10	59	10	57	10	66	11	

(Continued on the following page)

Table 1. Demographic, clinical, and lifestyle characteristics of 2,317 women with invasive breast cancer in the WHI by HEI-2005 quartiles (Cont'd)

	Poor-quality diets		Mixed-quality diets				Better-quality diets		
	Healthy Eating Index-2005 Score Quartile 1 (34–63)		Healthy Eating Index-2005 Score Quartile 2 (63–71)		Healthy Eating Index-2005 Score Quartile 3 (71–77)		Healthy Eating Index-2005 Score Quartile 4 (77–91)		
	N	(%)	N	(%)	N	(%)	N	(%)	P^a
Progesterone receptor status									0.751
Positive	358	62	357	62	371	64	349	60	
Negative	153	26	153	26	135	23	150	26	
Unknown	68	12	69	12	74	13	80	14	
Postmenopausal hormone therapy									0.122
Never	213	37	195	37	192	33	189	33	
Past	86	15	91	17	71	12	69	12	
Current	280	48	293	51	317	55	321	55	

[a]*P* for χ^2 test for categorical variables or trend test for continuous variables.
[b]For 2,149 of 2,317 participants with known MVPA.
[c]For 2,297 of 2,317 participants with known measured BMI.

The inverse relationship between HEI-2005 score and all-cause mortality was stronger among women who were diagnosed with ER^+ tumors ($n = 1{,}758$; $HR_{Q4:Q1}$, 0.55; 95% CI, 0.38–0.79; $P_{trend} = 0.0009$) and was null among those with ER^- tumors ($n = 317$; $HR_{Q4:Q1}$, 1.14; 95% CI, 0.58–2.23; $P_{trend} = 0.811$), but there was no statistically significant interaction by ER status ($P = 0.449$; Table 3).

Discussion

To our knowledge, this is single largest prospective study to evaluate the association between adherence to the Dietary Guidelines for Americans, as represented by HEI-2005 score, and all-cause and cause-specific mortality after breast cancer. It is also is the first to address the potential heterogeneity of the HEI-2005-mortality relationship by ER status. In this large cohort of 2,317 postmenopausal women diagnosed with invasive breast cancer, we found that a higher versus lower (Q4 vs. Q1) HEI-2005 score was associated with reduced risk of dying from any cause and from causes other than breast cancer but not from breast cancer itself. Furthermore, we did not observe significant associations between individual HEI-2005 components and mortality, indicating that no one component was responsible for the overall diet quality and mortality association. The Dietary Guidelines for Americans aim to provide a dietary pattern that, if followed, could reduce the risk of major chronic disease. This study builds on results from large cohort studies of women without cancer demonstrating an association of HEI-2005 and risk of major chronic disease (32), cardiovascular disease (32), coronary heart disease (32), diabetes (32), stroke (32, 33), and cancer (32, 34, 35). Our study demonstrates how reported diets consistent with U.S. national dietary guidance are also related to improved survival among breast cancer survivors, regardless of stage of disease at diagnosis.

Our findings are consistent with results from our past work in the Health, Eating, Activity, and Lifestyle (HEAL) study, which also examined the associations of HEI-2005 and all-cause mortality among early-stage breast cancer survivors (8). In the HEAL study ($n = 670$), having a higher versus lower postdiagnosis HEI-2005 score was associated with a 60% reduced risk of death from any cause (8) and lower levels of chronic inflammation (36). These findings suggest that HEI-2005 reflects key U.S. dietary exposures well for breast cancer survivors.

Our results are also largely consistent with two large observational studies, the Nurses' Health Study (NHS) and the Life After Cancer Epidemiology (LACE) Study, that demonstrated associations between data-driven dietary patterns, a prudent dietary pattern and a Western dietary pattern, with all-cause mortality (LACE; ref. 9) and mortality from causes other than breast cancer (LACE, ref. 9; NHS, ref. 10). Results on *a priori* indices other than the HEI-2005 and mortality are mixed, and both studies were conducted in the NHS, one reporting significant associations of Alternative Healthy Eating Index (AHEI)-2010 scores and the Dietary Approaches to Stop Hypertension (DASH) scores with all-cause mortality and non–breast cancer mortality (37), the other reporting null associations between the AHEI-2005, Diet Quality Index-Revised, Recommended Food Score, and the alternate Mediterranean Diet Score and mortality after breast cancer (11). Future larger studies of patients with breast cancer with the ability to examine multiple common

Table 2. Postdiagnosis diet quality, risk of death from any cause, and risk of death from breast cancer among 2,317 postmenopausal women diagnosed with invasive breast cancer in the WHI

	Poor-quality diet	Mixed-quality diet		Better-quality diet	
	Healthy Eating Index-2005 Score Quartile 1 (34–63)	Healthy Eating Index-2005 Score Quartile 2 (63–71)	Healthy Eating Index-2005 Score Quartile 3 (71–77)	Healthy Eating Index-2005 Score Quartile 4 (77–91)	P_{trend}
N	579	579	580	579	
Death from any cause (*n*)	117	105	102	91	
Unadjusted HR (95% CI)	1.00	0.84 (0.65–1.09)	0.79 (0.61–1.03)	0.67 (0.51–0.88)	0.004
Age and energy-adjusted HR (95% CI)	1.00	0.83 (0.64–1.08)	0.77 (0.59–1.01)	0.63 (0.48–0.83)	0.0009
Multivariate-adjusted HR (95% CI)[a]	1.00	0.93 (0.71–1.22)	0.86 (0.65–1.14)	0.74 (0.55–0.99)	0.043
Death from breast cancer (*n*)	51	48	44	45	
Unadjusted HR (95% CI)	1.00	0.89 (0.60–1.32)	0.79 (0.53–1.19)	0.78 (0.52–1.17)	0.178
Age and energy-adjusted HR (95% CI)	1.00	0.89 (0.60–1.32)	0.79 (0.53–1.19)	0.78 (0.52–1.16)	0.173
Multivariate-adjusted HR (95% CI)[a]	1.00	0.99 (0.66–1.50)	0.93 (0.61–1.43)	0.91 (0.60–1.40)	0.627
Death from causes other than breast cancer (*n*)	66	57	58	46	
Unadjusted HR (95% CI)	1.00	0.80 (0.56–1.14)	0.79 (0.56–1.13)	0.59 (0.40–0.86)	0.008
Age and energy-adjusted HR (95% CI)	1.00	0.79 (0.55–1.12)	0.77 (0.54–1.10)	0.52 (0.36–0.76)	0.001
Multivariate-adjusted HR (95% CI)[a]	1.00	0.83 (0.58–1.20)	0.79 (0.54–1.15)	0.58 (0.38–0.87)	0.011

[a]Adjusted for age at screening visit (continuous), WHI component (WHI-DM-intervention, WHI-DM-control, or OS), ethnicity (White non-Hispanic, Black/African American, Hispanic/Latino, other, missing), income (<20,000, 20,000–49,999, ≥50,000, missing), education (high school or below, some college, college, postgraduate, missing), stage (localized, regional, distant, unknown), estrogen receptor status (positive, negative, unknown), progesterone receptor status (positive, negative, unknown), time since diagnosis (continuous), energy intake in kcals (continuous), physical activity in MET-h/wk (0, 0.1–3, 3.1–8.9, 9+, unknown), servings of alcohol per week (continuous), and use of postmenopausal hormone therapy (never, former, current).

dietary indices and mortality by clinically important subgroups, like calendar year of treatment, will be important to advance scientific evidence in this research area.

This is the first study to show results of the HEI-2005 mortality relationship by survivors' ER status. Our secondary analysis suggested a stronger association among women whose breast cancers were ER^+, suggesting that the effects of diet quality may differ by tumor subtype, but the interaction between HEI-2005 score and ER status was not statistically significant. One explanation for this finding is that ER^+ survivors generally have better prognosis than survivors of ER^- breast cancer and thus may be more likely to die of causes other than breast cancer (38, 39), and for these women, postdiagnosis diet quality may play a larger role in promoting longevity. Alternatively, dietary quality may have a more important role for cardiovascular health than on breast cancer progression in breast cancer survivors, especially in older women. It is also possible that this finding by ER status is due to chance, due to the smaller number of ER^- cases in this study. In the only other study to report on a potential diet quality–ER status interaction, the Women's Intervention Nutrition study, a stronger effect of a low-fat diet was observed among ER^- patients, but the focus of that analysis was breast cancer recurrence not overall mortality, and the interaction was also not significant ($P = 0.15$). Replication of our findings in future studies is needed.

Advantages of the present study include use of the multidimensional HEI-2005, which is able to capture the potentially synergistic nature of multiple important dietary components (40), is energy adjusted, facilitates the classification of survivors with better versus poor quality diets, and can be compared between study populations. Furthermore, given that the HEI-2005 measure reflects adherence to U.S. federal food and nutrition guidance, evaluating its association with mortality risk among breast cancer survivors has public health relevance. Further strengths include our large sample size, prospective nature of evaluations, and long mortality follow-up. We also had data allowing us to make simultaneous adjustments for factors known to alter mortality risk after breast cancer and risk of death from any cause in general populations thereby providing a thorough analysis of HEI-2005 score and its potential role in survival after breast cancer.

Study limitations include measurement error inherent to the FFQ. Also, our results may not be generalizable to the very earliest deaths after diagnosis, because of our study's focus on the population who lived until a postdiagnosis FFQ. Furthermore, although we had detailed data allowing us to carefully control for the major confounders and to show that associations were unlikely to be artifacts of reverse causation, given the observational nature of this study, it remains possible that those who chose a better quality diet had better prognoses for

Table 3. Multivariate associations between diet quality and death from any cause, stratified analysis by ER status

	Poor-quality diet	Mixed-quality diet		Better-quality diet		
	Healthy Eating Index-2005 Score Quartile 1 (34–63)	Healthy Eating Index-2005 Score Quartile 2 (63–71)	Healthy Eating Index-2005 Score Quartile 3 (71–77)	Healthy Eating Index-2005 Score Quartile 4 (77–91)	P_{trend}	$P_{interaction}$
ER-positive						
N	429	455	451	423		
Death from any cause (*n*)	81	74	71	57		
Multivariate-adjusted HR of all-cause mortality (95% CI)[a]	1.00	0.82 (0.59–1.13)	0.71 (0.51–0.99)	0.55 (0.38–0.79)	0.0009	
ER-negative						0.449
N	90	65	72	90		
Death from any cause (*n*)	25	16	15	20		
Multivariate-adjusted HR of all-cause mortality (95% CI)[a]	1.00	0.90 (0.46–1.76)	0.92 (0.46–1.83)	1.14 (0.58–2.23)	0.811	

NOTE: For 2,075 participants with known ER status.

[a]Adjusted for age at screening visit (continuous), WHI component (WHI-DM-intervention, WHI-DM-control, or OS), ethnicity (White non-Hispanic, Black/African American, Hispanic/Latino, other, missing), income (<20,000, 20,000–49,999, ≥50,000, missing), education (high school or below, some college, college, postgraduate, missing), stage (localized, regional, distant, unknown), progesterone receptor status (positive, negative, unknown), time since diagnosis (continuous), energy intake in kcals (continuous), physical activity in MET-h/wk (0, 0.1–3, 3.1–8.9, 9+, unknown), servings of alcohol per week (continuous), and use of postmenopausal hormone therapy (never, former, current).

reasons that we did not examine. Importantly, we did not have data on cancer treatment; however, we did control for cancer stage which did not affect multivariate HRs in our study and was similar across quintile of HEI-2005 scores. Although not a proxy for treatment, cancer stage has been correlated with treatment in survivors in other studies of early-stage breast cancer survivors (28). During the years that WHI participants were diagnosed with early-stage breast cancer, the proportion of women diagnosed with stage I and II breast cancer who received breast-conserving surgery and radiation treatment increased substantially (41), and the use of concurrent chemotherapy and tamoxifen increased for node-positive women (41, 42). We also were able to control for ER/PR status of tumors, which would help predict who gets adjuvant hormonal therapy. Future large studies with treatment data are needed to determine whether the associations we observed differ by treatment regimens.

In summary, in this large cohort of postmenopausal breast cancer survivors, a better quality postdiagnosis diet was associated with a reduced risk of dying overall and from causes other than breast cancer, but not from breast cancer death. Our study suggests that breast cancer survivors may improve survival through choosing postdiagnosis diets that reflect adherence to U.S. dietary guidance. Because a great deal of user-friendly individual guidance is available for interpreting U.S. dietary guidelines (www.choosemyplate.gov; ref. 43), this study provides results that, with replication, may be useful for survivors in both educating themselves about healthy eating and tracking their diets. A priority for future research will be investigating this relationship among subgroups based on postdiagnosis physical activity level, BMI category, and race, due to the importance of this information in both risk stratification and corresponding lifestyle prescriptions (30).

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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Additional Information: A full list of all the investigators who have contributed to Women's Health Initiative science appears at https://cleo.whi.org/researchers/Documents%20%20Write%20a%20Paper/WHI%20Investigator%20Long%20List.pdf.

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