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Post-diagnosis dietary factors and survival after invasive breast cancer

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Abstract

Little is known about the effects of diet after breast cancer diagnosis on survival. We prospectively examined the relation between post-diagnosis dietary factors and breast cancer and all-cause survival in women with a history of invasive breast cancer diagnosed between 1987 and 1999 (at ages 20–79 years). Diet after breast cancer diagnosis was measured using a 126-item food frequency questionnaire. Among 4,441 women without a history of breast cancer recurrence prior to completing the questionnaire, 137 subsequently died from breast cancer within 7 years of enrollment. Hazard ratios (HR) and 95% confidence intervals (CI) were estimated for intake of macronutrients as well as selected micronutrients and food groups from Cox proportional hazards regression models. After adjustment for factors at diagnosis (age, state of residence, menopausal status, smoking, breast cancer stage, alcohol, history of hormone replacement therapy), interval between diagnosis and diet assessment, and at follow-up (energy intake, breast cancer treatment, body mass index, and physical activity), women in the highest compared to lowest quintile of intake of saturated fat and trans fat had a significantly higher risk of dying from any cause (HR = 1.41, 95% CI = 1.06 to 1.87, *P*-trend = 0.03) for saturated fat; (HR = 1.78, 95% CI = 1.35 to 2.32, *P*-trend = 0.01) for trans fat intake. Associations were similar, though did not achieve statistical significance, for breast cancer survival. This study suggests that lower intake of saturated and trans fat in the post-diagnosis diet is associated with improved survival after breast cancer diagnosis.

Keywords

breast cancer; survival; post-diagnosis diet

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INTRODUCTION

With a growing number of breast cancer survivors, there is tremendous interest in establishing whether changes in lifestyle influence breast cancer outcome. Diet after the diagnosis of breast cancer has been investigated in both observational studies and randomized controlled trials [1–5]. The Women's Intervention Nutrition Study (WINS) reported a 24% (95% confidence interval (CI) = 2% to 40%) reduction in breast cancer relapse (local, regional, or distal recurrence or contralateral breast cancer) in the low fat dietary intervention (target = 15% kcal from fat) compared with the control group after a median follow-up of 5 years, but there was no effect on overall survival (hazard ratio (HR) = 0.89, 95% CI = 0.65 to 1.21) [2]. The interpretation of findings is complicated by the substantial weight loss in the intervention group. The Women's Healthy Eating and Living (WHEL) randomized trial demonstrated no effect of a low fat dietary intervention (target = 15–20% kcal from fat) on breast cancer relapse (recurrence or new primary) or survival after a mean follow-up of 7.3 years [3].

Observational studies may help to inform the research question of diet after diagnosis by providing an opportunity to examine a wider variety of dietary factors and range of exposures. For example, both the WINS and WHEL interventions focused on reduction of total fat, rather than specific types of fat. In contrast to the general population of breast cancer survivors in the US, WHEL participants already consumed a diet that met many of the intervention goals at baseline, eating on average 7.3 servings of fruits and vegetables per day [6]. Observational studies may provide a more representative sample of women consuming diets that reflect typical diets in the US [1]. We investigated the association between post-diagnosis diet and breast cancer survival and overall survival in the Collaborative Women's Longevity Study (CWLS), a large multi-center prospective cohort designed to examine the contribution of lifestyle to survival among women with breast cancer.

METHODS

Participants and Study Description

Women of ages 20–79 years at breast cancer diagnosis were recruited into the CWLS after their participation in consecutive population-based case-control studies of breast cancer conducted in Wisconsin, Massachusetts (excluding metropolitan Boston), and New Hampshire between 1988 and 2001. Details of both the case-control studies and the CWLS are provided elsewhere [7–9]. The purpose of the CWLS was to evaluate associations between post-diagnosis lifestyle factors and survival. Briefly, 5,791 cases from the parent case-control studies participated in the CWLS study by completing a mailed questionnaire from 1998–2001. The CWLS questionnaire assessed post-diagnosis behaviors, including diet and physical activity, as well as breast cancer events and treatment.

Exposure and Outcome Assessment

Usual diet over the past year was assessed using a validated 126-item food frequency questionnaire (FFQ) [10]. Macronutrients, expressed as a percentage of total energy intake, and select micronutrients were computed from FFQ data. Participants were categorized into quintiles based on individual macronutrient, vitamin A, carotenoid, fiber, calcium, and vitamin D intake including intake from both diet and supplements. Analyses were repeated restricting to micronutrients from diet alone to consider whether source of intake was affecting associations.

Number of servings of meat, dairy, fruit, and vegetable intake was summed based on questionnaire items and grouped into quartiles. Meat and dairy food groups were also

grouped based on their fat content (<30% vs. ≥30% kcal from fat), and meat was examined separately by type (poultry, fish, beef, and processed).

Overall, 42% of women completed the CWLS questionnaire within 5 years of diagnosis of breast cancer (range: 1–16 years). We assessed all breast cancer cases for vital status regardless of whether they completed the CWLS questionnaire. We linked cases to the National Death Index records to obtain date and underlying cause of death, which has been shown to be a reliable source [11].

Study Population

For this analysis, women were excluded if: energy intake was <500 or >5000 kcal per day as measured by the FFQ (N = 20), disease or treatment interfered with diet (N = 128), there was breast cancer metastases (N = 34) or unknown disease stage at diagnosis (N = 615), or women recorded any recurrence of breast cancer before entry into the CWLS (N = 553). Following these exclusions, the final analytic cohort comprised of 4,441 women.

Statistical Analysis

Person-time of follow-up was calculated from the date of return of the CWLS questionnaire (1998–2001) until the date of death or December 31, 2005. Cox proportional hazards regression was used to estimate HRs and 95% CI for all-cause and breast cancer survival according to nutrient and food intake and to adjust for covariates potentially associated with both diet and mortality. Fully-adjusted models included *factors at diagnosis*: age (four categories), state of residence, menopausal status (pre/post), smoking (never, former, current), breast cancer stage (local or regional), alcohol (quintiles), history of hormone replacement therapy (never, former, current), and *factors at follow-up*: energy intake (continuous), breast cancer treatment (surgery, radiation, chemotherapy, tamoxifen), body mass index (BMI, < 24.9, 25.0–29.9, ≥30.0 kg/m^2), and physical activity metabolic equivalents (MET-h/wk, quartiles). Models further adjusted for years between diagnosis and diet assessment, and were energy-adjusted using the multivariate nutrient density method for macronutrients and the standard approach for micronutrients [12]. Tests of linear trend were conducted by including the median intake for each exposure category as an ordinal term in models.

Analyses were repeated restricting the outcome to each of the top three causes of death: breast cancer, cardiovascular disease, and cancer at any site. To evaluate the possibility that severity of illness affected diet, we performed a subgroup analysis excluding: women who died within two years of completing the CWLS survey, women reporting recent unintentional weight loss (5% or more of body weight), and women without a mammogram or physician breast exam after their diagnosis. All reported P-values are two-tailed without consideration of multiple comparisons; P-values < 0.05 were considered statistically significant. Analyses were conducted using SAS version 9.1 (SAS Institute Inc., Cary, NC).

RESULTS

The majority of women were white (99%) and postmenopausal at diagnosis (76%). After a mean follow-up of 5.5 (SD 1.1) years after returning the questionnaire, we documented 525 deaths, of which 26.1% were attributed to breast cancer. The other most common causes of death were cardiovascular disease (25.1%) and cancer at other sites (24.6%). The proportion of women dying was higher among women who were older, had more advanced disease, were postmenopausal at diagnosis, and had a history of smoking, whereas the proportion dying was lower among those who reported being more physically active (Table 1). In contrast to all-cause survival, breast cancer survival was higher among younger women.

While all associations between energy and macronutrients with breast cancer survival were null, some associations with all-cause survival were statistically significant (Table 2). Total fat intake was not associated with all-cause or breast cancer survival, but type of fat intake did appear to influence risk of death from any cause. Women with a median intake of 13% of calories from saturated fat had a 41% increased risk of death from any cause compared to women consuming a median of 7% calories from saturated fat (HR = 1.41, 95% CI = 1.06 to 1.87, *P*-trend = 0.03). Furthermore, those in the upper quintile of trans fat intake had a 78% increased risk of all-cause survival compared to those in the lowest quintile (HR = 1.78, 95% CI = 1.35 to 2.32, *P*-trend = 0.01). Though similar HRs for saturated and trans fat intake were observed for cause-specific survival (breast cancer, any cancer, cardiovascular disease), the associations were not statistically significant. No consistent associations were observed between all-cause or breast cancer survival and monounsaturated or polyunsaturated fat intake.

Carbohydrate and protein intakes were not associated with all-cause or breast cancer survival. We observed a trend toward lower risk of death from any cause with higher alcohol consumption (*P*-trend = 0.01), but this trend was not present for breast cancer survival (*P*-trend = 0.50). When restricting analyses to deaths related to cardiovascular disease (*N* = 123), there was a non-statistically significant (*P*-trend = 0.11) positive association between trans fat intake and survival, and inverse associations with polyunsaturated fat (*P*-trend = 0.05) and alcohol intakes (*P*-trend = 0.14) with cardiovascular disease survival (data not shown).

Sensitivity analyses were conducted restricting attention to women who survived at least two years after completing the CWLS survey, reported no recent unintentional weight loss (5% or more of body weight), and had a mammogram or physician breast exam after their diagnosis (*N* = 3,977). For all-cause survival, the associations with saturated fat (HR for highest vs. lowest quintile = 1.52, 95% CI = 1.07–2.16, *P*-trend = 0.09) and trans fat (HR = 1.56, 95% CI = 1.11–2.17, *P*-trend = 0.01) were robust, but the association with alcohol was null (HR = 0.99, 95% CI = 0.72–1.36, *P*-trend = 0.51).

There was a non-statistically significant trend towards decreased risk of death from breast cancer with higher calcium and a positive association with lycopene intake; no association was observed for the other selected micronutrients (Table 3). Associations between diet and all-cause and breast cancer survival were similar to those presented after excluding supplements. There was a non-significant inverse trend (*P*-trend = 0.09) between calcium intake and breast cancer death, but there were no other associations between consumption of the selected micronutrients and breast cancer survival (data not shown).

Meat and dairy are two of the largest contributors to saturated fat intake. No significant associations were observed between all-cause and breast cancer survival and intakes of meat and dairy products (Table 4). We also examined meat and dairy servings/day according to fat intake (<30% vs. ≥30% kcal from fat) as well as type of meat (poultry, fish, beef, and processed), but there were no associations for all-cause or breast cancer specific survival. Because fruits and vegetables, particularly cruciferous vegetables, may be associated with a reduced risk of cancer, we also examined the relation between produce intake and all-cause and breast cancer survival; no association was observed.

DISCUSSION

In this large cohort of breast cancer survivors, post-diagnosis diets high in saturated and trans fat were associated with decreased all-cause survival. Though there were suggestive dietary associations for breast cancer survival, none were statistically significant.

Women who consumed the highest quartile of saturated fat (median of 13% kcal) had a 41% statistically significant higher risk of all-cause survival compared to women in the lowest quartile, who consumed a median of 7% calories from saturated fat (*P*-trend = 0.03). Doubling percentage of energy from trans fat was associated with a 78% statistically significantly greater risk of death (*P*-trend = 0.01).

A recent report from the Center for Disease Control and Prevention indicated that saturated fat intake as a percentage of energy intake decreased between 1971–2000 among US women from 13% to 11% (*P*-trend = 0.01), but energy intake has increased over this period, suggesting similar exposure to absolute amounts of saturated fat over time [13]. Average trans fat intake in the United States during the enrollment period for this study was approximately 2% to 3% of energy, which is greater than reported by participants of this study [14]. Despite a large body of evidence that alcohol increases risk of breast cancer [15], there was no association between alcohol intake and breast cancer survival. Others have recently reported either no association between alcohol intake and survival or an inverse relation between alcohol intake and survival, so this area warrants further study [16–18].

Similar to our findings, qualitative reviews reported no consistent association between total fat consumption either pre- or post-diagnosis and breast cancer survival after energy adjustment [19,20]. None of the studies reviewed by Rock and Demark-Wahnefried reported an association between total dietary fiber intake and breast cancer recurrence or overall survival; only three studies reported an inverse association between fruit and vegetable consumption and survival [21].

Strengths of our study include the prospective design, its large sample size, and detailed information on diet obtained after the diagnosis of breast cancer. In addition, we were able to assess many potential confounding variables. The relation between saturated and trans fat intake and all-cause survival that we observed is consistent with observational and controlled-feeding studies of cardiovascular disease and other chronic diseases [22–24]. This also supports the ability of our dietary assessment to detect moderate associations with survival.

When restricting attention to deaths related to cardiovascular disease (*N* = 123), there were suggestive (*P*-trend = 0.11) inverse associations between trans fat and survival, and positive associations between polyunsaturated fat (*P*-trend = 0.05) as well as alcohol (*P*-trend = 0.14) with survival, although these associations likely did not reach statistical significance, possibly because of the limited number of observed deaths.

Nonetheless, some limitations should be considered when interpreting these results. Though we used a validated self-reported measure of diet adapted from the Nurses' Health Study (NHS), measurement error is a pervasive problem in dietary assessment [25–27]. Because measurement error is likely non-differential with respect to outcome, this should lead to attenuation in risk estimates. We lacked information on the clinical status of breast cancer at the time of the CWLS questionnaire, but we excluded women who reported any recurrence of breast cancer at that time. Also, survival may depend upon hormone responsiveness [28], but steroid receptor status was not available from state cancer registries for all CWLS participants.

The CWLS involved women that were previously enrolled in our sequential case-control studies of breast cancer, and thus women were not immediately followed from the initial diagnosis of their breast cancer. One practical limitation of the data is that our results may only be applicable to women who survive the first several years after breast cancer diagnosis. A potential concern is that the observed inverse associations with survival might reflect reverse causation if increased saturated and trans fat intakes are associated with

worsening health and poor prognosis. The relatively short interval, however, between diagnosis and subsequent entry into the cohort for the majority of women minimizes the likelihood of bias caused by selective survival. Also, information was available on a number of surrogate measures including treatment interfering with diet, recent unintentional weight loss, general health status, and frequency of mammogram or physician breast or chest wall examination after diagnosis, and hazard ratios were essentially unchanged in analyses restricted to women in apparent good health at the time of CWLS entry and who had undergone screening since diagnosis. Taken together, these results suggest that reverse causation is unlikely to account for the inverse association of saturated and trans fat intake with overall survival in these data.

Finally, our study did not consider diet prior to breast cancer diagnosis, or the pre- to post-diagnosis change in dietary patterns. Our study, instead, was designed to inform how a woman's post-diagnosis diet influences survival. This research provides little evidence for an association between dietary intake and breast cancer survival, but provides additional support for an adverse relationship between saturated and trans fat intake and overall survival following a breast cancer diagnosis.

ABBREVIATIONS

BMI	body mass index
CI	confidence interval
CWLS	Collaborative Women's Longevity Study
FFQ	food frequency questionnaire
HR	hazard ratio
MET	metabolic equivalent of task
NHS	Nurses' Health Study
WHEL	Women's Healthy Eating and Living
WINS	Women's Intervention Nutrition Study

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Table 1

CWLS participant characteristics

	***N* (%) *N* = 4,441[a]**	**All-cause Deaths, % *N* = 525**	**Breast cancer Deaths, % *N* = 137**
Characteristics at breast cancer diagnosis			
Age, y			
<40	172 (3.9%)	1.5%	5.8%
40–49	686 (15.4%)	7.4%	18.3%
50–59	1,377 (31.0%)	17.9%	34.3%
60–69	1,669 (37.6%)	40.2%	35.8%
70–79	537 (12.1%)	33.0%	5.8%
Breast cancer stage			
Local	3,233 (72.8%)	10.3%	1.8%
Regional	1,208 (27.2%)	16.0%	6.6%
Postmenopausal[b]			
No	1,011 (22.8%)	4.9%	3.5%
Yes	3,254 (73.3%)	14.4%	3.0%
Alcohol, drinks/d			
None	702 (15.8%)	13.8%	3.0%
<1	2,946 (66.3%)	11.2%	3.0%
1–2	530 (11.9%)	11.7%	2.8%
>2	239 (5.4%)	14.2%	4.6%
Hormone replacement therapy, duration			
None	2,527 (56.9%)	11.9%	3.0%
<2 years	357 (8.0%)	14.9%	3.6%
≥2 years	1,120 (25.2%)	9.0%	3.2%
Smoking history			
Never	2,136 (48.1%)	9.2%	2.8%
Former	1,536 (34.6%)	13.1%	2.8%
Current	752 (16.9%)	17.0%	4.5%
Education			
< 12 years	388 (8.7%)	18.6%	2.6%
≥ 12 years	4,041 (91.0%)	11.2%	3.1%
Breast cancer treatment[c]			
Surgery	4,346 (97.9%)	11.5%	3.1%
Radiation	2,210 (49.8%)	9.7%	3.5%
Hormonal therapy	2,568 (57.8%)	10.9%	3.4%
Chemotherapy	1,417 (31.9%)	9.7%	5.3%
Characteristics at follow-up			
Body mass index, kg/m^2			
<20	209 (4.7%)	19.6%	1.9%
20–24.9	1,485 (33.4%)	10.2%	2.2%

	***N* (%)** ***N* = 4,441[a]**	**All-cause Deaths, %** ***N* = 525**	**Breast cancer Deaths, %** ***N* = 137**
25–29.9	1,452 (32.7%)	10.7%	2.8%
≥30	1,038 (23.4%)	12.9%	4.9%
Physical activity, MET-h/wk			
≤2.7	1,064 (24.0%)	20.4%	4.0%
2.8–7.9	1,038 (23.4%)	10.2%	2.6%
8.0–20.9	1,147 (25.8%)	8.8%	2.8%
≥ 21.0	1,091 (24.6%)	7.2%	3.0%

[a] Numbers may not sum to total because of missing values

[b] Women with unknown menopausal status are excluded

[c] Can reflect more than one treatment type

Table 2

Association of total energy and macronutrient intake with all-cause (N = 525) and breast cancer (N = 137) survival, CWLS

	Macronutrient intake (quintiles)					
	1	**2**	**3**	**4**	**5**	***P*-trend**
Total energy (kcal)[a]	1,077	1,400	1,649	1,935	2,407	
All-cause survival HR (95% CI)[b]	Ref	0.78 (0.60–1.02)	0.86 (0.66–1.11)	0.78 (0.59–1.02)	0.89 (0.68–1.15)	0.33
Breast cancer survival HR (95% CI)[b]	Ref	0.91 (0.53–1.57)	0.89 (0.51–1.54)	0.94 (0.55–1.60)	1.02 (0.61–1.71)	0.89
Total fat (% kcal)[a]	23	27	30	34	39	
All-cause survival HR (95% CI)[b]	Ref	1.11 (0.84–1.47)	1.00 (0.76–1.33)	1.02 (0.78–1.35)	1.05 (0.79–1.39)	0.98
Breast cancer survival HR (95% CI)[b]	Ref	1.11 (0.65–1.91)	1.00 (0.58–1.73)	0.76 (0.43–1.35)	0.92 (0.53–1.60)	0.39
Saturated fat (% kcal)[a]	7	8	10	11	13	
All-cause survival HR (95% CI)[b]	Ref	1.06 (0.79–1.41)	1.25 (0.94–1.65)	1.05 (0.78–1.40)	**1.41 (1.06–1.87)**	**0.03**
Breast cancer survival HR (95% CI)[b]	Ref	1.56 (0.88–2.74)	1.32 (0.74–2.37)	1.01 (0.55–1.87)	1.55 (0.88–2.75)	0.50
Trans fat (% kcal)[a]	0.7	0.9	1.1	1.3	1.6	
All-cause survival HR (95% CI)[b]	Ref	1.10 (0.82–1.49)	1.14 (0.85–1.53)	1.21 (0.90–1.62)	**1.78 (1.35–2.32)**	**0.01**
Breast cancer survival HR (95% CI)[b]	Ref	1.27 (0.72–2.23)	1.25 (0.71–2.18)	1.19 (0.66–2.13)	1.42 (0.80–2.52)	0.34
Monounsaturated fat (% kcal)[a]	8	10	11	13	15	
All-cause survival HR (95% CI)[b]	Ref	1.27 (0.97–1.68)	1.27 (0.96–1.67)	0.95 (0.71–1.28)	1.14 (0.86–1.52)	0.93
Breast cancer survival HR (95% CI)[b]	Ref	1.58 (0.93–2.71)	1.10 (0.62–1.94)	1.06 (0.59–1.89)	0.89 (0.49–1.60)	0.25
Polyunsaturated fat (% kcal)[a]	4	5	5	6	8	
All-cause survival HR (95% CI)[b]	Ref	1.00 (0.77–1.32)	0.81 (0.61–1.07)	0.93 (0.71–1.22)	0.91 (0.70–1.19)	0.41
Breast cancer survival HR (95% CI)[b]	Ref	1.28 (0.76–2.17)	1.00 (0.58–1.73)	0.89 (0.51–1.57)	0.90 (0.52–1.55)	0.33
Carbohydrates (% kcal)[a]	42	49	53	57	63	
All-cause survival HR (95% CI)[b]	Ref	1.07 (0.80–1.41)	1.00 (0.75–1.33)	1.06 (0.79–1.42)	0.97 (0.72–1.30)	0.80
Breast cancer survival HR (95% CI)[b]	Ref	0.81 (0.47–1.37)	0.80 (0.47–1.35)	1.08 (0.64–1.81)	0.93 (0.54–1.62)	0.87
Protein (% kcal)[a]	13	16	17	18	21	
All-cause survival HR (95% CI)[b]	Ref	0.93 (0.72–1.20)	0.89 (0.68–1.16)	1.09 (0.84–1.42)	0.98 (0.73–1.31)	0.72

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	Macronutrient intake (quintiles)					
	1	**2**	**3**	**4**	**5**	***P*-trend**
Breast cancer survival HR (95% CI)[b]	Ref	1.37 (0.77–2.42)	1.36 (0.77–2.42)	1.60 (0.91–2.80)	1.19 (0.66–2.14)	0.49
Alcohol (% kcal)[a]	0.0	0.3	1.2	4.9	15.0	
All-cause survival HR (95% CI)[b]	Ref	0.99 (0.77–1.27)	0.83 (0.65–1.07)	**0.68 (0.51–0.90)**	0.78 (0.60–1.01)	**0.01**
Breast cancer survival HR (95% CI)[b]	Ref	0.88 (0.50–1.55)	1.21 (0.74–2.01)	0.81 (0.46–1.44)	1.27 (0.76–2.14)	0.50

[a]Median within each quintile.

[b]Hazard ratio (95% confidence interval) adjusted for factors at diagnosis (age, state of residence, menopausal status, smoking, breast cancer stage, alcohol, history of hormone replacement therapy), interval between diagnosis and diet assessment, and factors at follow-up (energy intake, breast cancer treatment, body mass index, and physical activity).

Table 3

Association of micronutrient intake with all-cause (N = 525) and breast cancer (N = 137) survival, CWLS

	Micronutrient intake (quintiles)					
	1	**2**	**3**	**4**	**5**	***P*-trend**
Vitamin A (IU/d)[a]	4816	8070	10939	14453	21857	
All-cause survival HR (95% CI)[b]	Ref	0.97 (0.75–1.27)	1.00 (0.76–1.32)	1.05 (0.79–1.40)	1.12 (0.84–1.50)	0.38
Breast cancer survival HR (95% CI)[b]	Ref	1.40 (0.82–2.40)	1.19 (0.67–2.12)	1.18 (0.66–2.12)	1.24 (0.68–2.24)	0.74
Carotenoids						
α-Carotene (μg/d)[a]	206	406	582	864	1752	
All-cause survival HR (95% CI)[b]	Ref	1.10 (0.85–1.42)	0.97 (0.74–1.29)	0.94 (0.70–1.27)	1.08 (0.81–1.43)	0.98
Breast cancer survival HR (95% CI)[b]	Ref	0.93 (0.57–1.50)	0.63 (0.36–1.09)	0.54 (0.30–0.99)	0.98 (0.59–1.64)	0.43
β-Carotene (μg/d)[a]	1610	2549	3644	5156	8570	
All-cause survival HR (95% CI)[b]	Ref	0.98 (0.75–1.28)	1.25 (0.95–1.64)	1.05 (0.79–1.40)	1.17 (0.88–1.57)	0.25
Breast cancer survival HR (95% CI)[b]	Ref	1.06 (0.63–1.81)	1.00 (0.58–1.73)	0.93 (0.52–1.65)	1.05 (0.60–1.86)	0.97
β-Cryptoxanthin (μg/d)[a]	45	99	170	228	329	
All-cause survival HR (95% CI)[b]	Ref	1.06 (0.79–1.41)	1.18 (0.89–1.56)	1.18 (0.89–1.57)	1.25 (0.93–1.68)	0.11
Breast cancer survival HR (95% CI)[b]	Ref	0.56 (0.32–1.00)	1.22 (0.75–1.99)	0.77 (0.44–1.34)	0.81 (0.45–1.45)	0.82
Lutein/Zeaxanthin (μg/d)[a]	995	1543	2174	2950	4591	
All-cause survival HR (95% CI)[b]	Ref	0.99 (0.75–1.30)	0.98 (0.74–1.29)	1.31 (0.99–1.74)	1.05 (0.77–1.43)	0.26
Breast cancer survival HR (95% CI)[b]	Ref	1.25 (0.71–2.21)	0.99 (0.54–1.81)	1.38 (0.78–2.46)	1.16 (0.62–2.19)	0.56
Lycopene (μg/d)[a]	2102	3908	4734	6222	11479	
All-cause survival HR (95% CI)[b]	Ref	0.93 (0.72–1.21)	1.08 (0.83–1.41)	0.98 (0.73–1.31)	1.11 (0.83–1.47)	0.47
Breast cancer survival HR (95% CI)[b]	Ref	0.72 (0.39–1.34)	1.08 (0.61–1.91)	0.89 (0.49–1.63)	1.42 (0.80–2.50)	0.11
Fiber (g/d)[a]	11	15	19	23	30	
All-cause survival HR (95% CI)[b]	Ref	1.00 (0.77–1.32)	0.79 (0.58–1.08)	0.96 (0.69–1.32)	0.75 (0.52–1.09)	0.17
Breast cancer survival HR (95% CI)[b]	Ref	0.92 (0.55–1.56)	0.65 (0.35–1.18)	0.62 (0.33–1.17)	0.75 (0.38–1.49)	0.24
Whole grains (g/d)	7	16	26	37	57	

	Micronutrient intake (quintiles)					
	1	**2**	**3**	**4**	**5**	***P*-trend**
All-cause survival HR (95% CI)[b]	Ref	1.03 (0.79–1.33)	1.05 (0.80–1.37)	0.98 (0.74–1.30)	0.79 (0.59–1.08)	0.20
Breast cancer survival HR (95% CI)[b]	Ref	0.96 (0.58–1.60)	1.16 (0.70–1.92)	0.66 (0.37–1.20)	0.83 (0.46–1.48)	0.30
Calcium (mg/d)[a]	622	947	1302	1735	4108	
All-cause survival HR (95% CI)[b]	Ref	0.81 (0.62–1.05)	0.98 (0.75–1.28)	0.96 (0.73–1.27)	0.74 (0.53–1.02)	0.32
Breast cancer survival HR (95% CI)[b]	Ref	0.80 (0.48–1.34)	0.84 (0.50–1.44)	0.70 (0.40–1.23)	0.59 (0.32–1.08)	0.09
Vitamin D (mg/d)[a]	81	190	438	558	826	
All-cause survival HR (95% CI)[b]	Ref	1.02 (0.79–1.32)	0.87 (0.66–1.14)	1.00 (0.77–1.33)	0.86 (0.64–1.16)	0.35
Breast cancer survival HR (95% CI)[b]	Ref	1.03 (0.60–1.76)	0.96 (0.55–1.66)	1.08 (0.63–1.86)	1.02 (0.58–1.79)	0.90

[a]Median intake within each quintile. Includes intake from diet and supplements.

[b]Hazard ratio (95% confidence interval) adjusted for factors at diagnosis (age, state of residence, menopausal status, smoking, breast cancer stage, alcohol, history of hormone replacement therapy), interval between diagnosis and diet assessment, and factors at follow-up (energy intake, breast cancer treatment, body mass index, and physical activity).

Table 4

Associations of selected food group intake with all-cause (N = 525) and breast cancer (N = 137) survival, CWLS

	Food group intake (quartiles)				*P*-trend
	1	**2**	**3**	**4**	
Dairy (servings/d)[a]	0.7	1.5	2.6	4.0	
All-cause survival HR (95% CI)[b]	Ref	0.92 (0.72–1.17)	0.95 (0.74–1.23)	1.18 (0.90–1.54)	0.27
Breast cancer survival HR (95% CI)[b]	Ref	0.76 (0.46–1.27)	0.94 (0.58–1.53)	0.94 (0.56–1.59)	0.99
Meat (servings/d)[a]	0.7	1.1	1.5	2.2	
All-cause survival HR (95% CI)[b]	Ref	1.12 (0.88–1.43)	1.11 (0.85–1.44)	1.12 (0.83–1.51)	0.46
Breast cancer survival HR (95% CI)[b]	Ref	0.89 (0.53–1.52)	1.20 (0.71–2.01)	0.89 (0.50–1.60)	0.94
Vegetables (servings/d)[a]	0.4	0.8	1.0	2.5	
All-cause survival HR (95% CI)[b]	Ref	1.04 (0.83–1.31)	1.04 (0.84–1.30)	1.44 (0.91–2.27)	0.35
Breast cancer survival HR (95% CI)[b]	Ref	1.00 (0.65–1.56)	0.82 (0.54–1.25)	0.96 (0.38–2.45)	0.43
Cruciferous vegetables (servings/d)[a]	0.1	0.2	0.3	0.7	
All-cause survival HR (95% CI)[b]	Ref	0.77 (0.61–0.98)	1.11 (0.87–1.43)	1.02 (0.80–1.30)	0.35
Breast cancer survival HR (95% CI)[b]	Ref	0.83 (0.51–1.35)	1.15 (0.70–1.90)	0.95 (0.59–1.54)	0.86
Fruit (servings/d)[a]	0.1	0.4	1.0	2.5	
All-cause survival HR (95% CI)[b]	Ref	0.83 (0.62–1.11)	0.89 (0.73–1.09)	1.38 (0.88–2.17)	0.67
Breast cancer survival HR (95% CI)[b]	Ref	0.65 (0.36–1.19)	0.66 (0.45–0.97)	1.39 (0.64–2.99)	0.16

[a] Median within each quartile.

[b] Hazard ratio (95% confidence interval) adjusted for factors at diagnosis (age, state of residence, menopausal status, smoking, breast cancer stage, alcohol, history of hormone replacement therapy), interval between diagnosis and diet assessment, and factors at follow-up (energy intake, breast cancer treatment, body mass index, and physical activity).