Associations of Post-Diagnosis Lifestyle with Prognosis in Women with Invasive Breast Cancer

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ABSTRACT

Background: Lifestyle habits can impact breast cancer development, but its impact on breast cancer prognosis remains unclear. We investigated associations of post-diagnosis lifestyle with mortality and recurrence in 1,964 women with invasive breast cancer enrolled in the Kaiser Permanente Northern California Pathways Study shortly after diagnosis with lifestyle information at baseline (2005–2013) and the 2-year follow-up.

Methods: We calculated a post-diagnosis lifestyle score (range, 0–18) based on 9 diet, physical activity, and body weight recommendations from the American Cancer Society/American Society of Clinical Oncology (ACS/ASCO) using follow-up data (body weight also included baseline data); higher scores indicate greater guideline concordance. Similarly, we calculated a pre-diagnosis lifestyle score using baseline data to investigate pre- to post-diagnosis changes. We estimated hazard ratios (HR) and 95% confidence intervals (CI) using Cox proportional hazard models, with follow-up through December 2018 (observing 290 deaths and 176 recurrences).

Results: The 2-year post-diagnosis lifestyle score was inversely associated with all-cause mortality (ACM; HR per 2-point increase = 0.90; 95% CI, 0.82–0.98), and breast cancer–related mortality (HR, 0.79; 95% CI, 0.67–0.95), but not recurrence. Relative to women who maintained low concordance with recommendations at both time points, women who maintained high concordance had a lower risk of ACM (HR, 0.61, 95% CI, 0.37–1.03). Improved concordance with some specific recommendations (particularly PA) may be associated with a lower hazard of ACM (HR_{PA}, 0.52; 95% CI, 0.35–0.78).

Conclusions: Results suggest that women with breast cancer may benefit from a post-diagnosis lifestyle aligned with ACS/ASCO guidelines.

Impact: This information may potentially guide lifestyle recommendations for breast cancer survivors to reduce mortality risk.

Introduction

Lifestyle-related factors, such as physical activity, diet, and obesity, are estimated to account for nearly 30% of breast cancer cases (1–3), and growing evidence suggests that post-diagnosis (defined here as >1 year after cancer diagnosis) lifestyle may also play a role in the long-term health of women diagnosed with breast cancer (4, 5). In women with breast cancer, evidence demonstrating the harms of post-diagnosis obesity on mortality and recurrence (6, 7) and the potential benefits of post-diagnosis recreational physical activity on mortality (8–11) is largely consistent. Recent meta-analyses estimate a 35% to 40% higher risk of recurrence or death in women who are obese at or after the time of breast cancer diagnosis compared with normal weight women (6, 7), and a 48% lower risk of mortality in breast cancer survivors engaging in the highest versus lowest levels of physical activity (11). Previous studies in women with breast cancer investigated dietary exposures, including dietary indices (refs. 12–19; e.g., Alternative Healthy Eating Index) and major food groups, such as fruits and vegetables (16, 20), meat (16, 21, 22), and dairy (17, 21, 22) in relation to cancer-related mortality and recurrence. However, evidence remains too limited to provide strong support for any specific dietary recommendations, given either too few studies investigated a particular exposure–outcome combination or conflicting evidence from multiple studies (23).

Understanding the role of post-diagnosis physical activity, diet, and body weight on breast cancer–related mortality and recurrence is important to inform evidence-based recommendations regarding potentially modifiable lifestyle behaviors that may improve prognosis. In addition, understanding the role of post-diagnosis lifestyle on *overall* mortality in women with breast cancer is equally important, as other causes of death often play a much greater role in their mortality (24), largely due to advances in the early detection and treatment of breast cancer. However, in addition to the limited and conflicting data regarding dietary exposures, several other gaps in the literature exist. First, although post-diagnosis physical activity, certain aspects of diet (such as saturated fat intake), and body weight have each been linked separately to breast cancer–related outcomes (7, 11, 25), lifestyle behaviors are often correlated (e.g., those who are more physically active often eat a healthier diet and are leaner) and may interact to impact health, which presents challenges when studying lifestyle habits independently. Few studies investigated their combined effect on long-term prognosis after breast cancer (26, 27); none investigated their combined impact on recurrence. Second, lifestyle may change over time, yet few studies examined post-diagnosis changes in physical activity (28–32), diet, and body weight (33, 34). Some breast cancer survivors may have engaged in "less healthy"

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behaviors (e.g., limited physical activity) before diagnosis, and it is important to understand whether adopting healthier lifestyle behaviors can impact prognosis.

In this study of women diagnosed with invasive breast cancer, we investigated the independent and combined effects of post-diagnosis body weight, physical activity, and diet on all-cause mortality (ACM), breast cancer–related mortality, and recurrence. We also investigated whether changes in lifestyle factors from pre- to post-diagnosis were associated with mortality and recurrence.

Materials and Methods

Study population and design

The Pathways Study is a prospective cohort study of 4,505 women diagnosed with invasive breast cancer during 2005 to 2013 from the Kaiser Permanente Northern California (KPNC) patient population (35). Rapid case ascertainment (35) was used to identify women shortly after diagnosis (mean, 2.3 months; range, <1–17.8). Upon enrollment, participants completed in-person interviews; field interviewers measured body weight and height and collected information regarding physical activity over the previous 6-months, using the 47-item Arizona Activity Frequency Questionnaire (36), and dietary intake over the previous year, using a 139-item modified version of the Block 2005 FFQ (35). Approximately two years later, participants completed a follow-up questionnaire, including the same physical activity and diet questionnaires and self-reported their weight.

The Pathways Study was conducted in accordance with recognized ethical guidelines (e.g., U.S. Common Rule) and an assurance filed and approved by the U.S. Department of Health and Human Services. All aspects of the Pathways Study were reviewed and approved by institutional review boards of collaborating institutions. All participants provided written informed consent.

Post-diagnosis lifestyle

We investigated 9 lifestyle components—aerobic recreational activity, strength training, sedentary behavior, consumption of fruit/vegetables, legumes, whole grains, saturated fats, and alcohol, and body weight—based on recommendations from the American Cancer Society/American Society of Clinical Oncology (ACS/ASCO) *Breast Cancer Survivorship Guidelines* (5). For each of the 9 components, we used data from the 2-year follow-up questionnaire (and the baseline questionnaire for body weight) to create a score, ranging 0–2, representing the level of concordance with the corresponding recommendation, with 0 indicating low concordance and 2 indicating high concordance (**Table 1**).

We calculated a post-diagnosis lifestyle score by summing the 9 component scores, each ranging 0–2, for a total score ranging 0–18. We used an unweighted summary score so that we could compare our findings with previous similar studies (26, 37) and because it has a more straightforward interpretation compared with weighted scores (e.g., we know the minimum unweighted score represents all "unhealthy" behaviors).

Pre- to post-diagnosis lifestyle changes

To account for the influence of pre-diagnosis lifestyle on the association of post-diagnosis lifestyle on breast cancer prognosis (and because the impact of post-diagnosis lifestyle changes on breast cancer prognosis may vary depending on prior lifestyle habits), we compared pre- to post-diagnosis concordance levels for each of the 9 components and the lifestyle score and created composite variables based on the following levels: (i) maintained high concordance; (ii) maintained partial concordance; (iii) maintained low concordance; (iv) increased (i.e., improved) concordance from baseline to follow-up; and (v) decreased (i.e., worsened) concordance from baseline to follow-up.

For the total lifestyle change score, first, we modified the body weight component so that it relied on one time-point only, to be consistent with the other components, and created separate pre- and post-diagnosis lifestyle scores. The modified body weight scoring was as follows: 0: BMI $\geq$30 kg/m^2; 1: BMI 25–$\leq$30 kg/m^2 or <18.5 kg/m^2; 2: BMI 18.5–$\leq$25.0 kg/m^2. Pre-diagnosis concordance levels were scored similarly to post-diagnosis levels except that they were based on data obtained at baseline, from a questionnaire in which much of the recall period includes the time before diagnosis, instead of the follow-up questionnaire. Second, we summed across the 9 components for each timepoint and categorized both the pre- and post-diagnosis lifestyle scores based on low (0–7), partial (8–10), and high (11–18) concordance levels. Last, we created a composite variable using the 5 levels described in the above paragraph and in Supplementary Table S1.

Outcomes assessment

Outcomes included ACM, breast cancer–specific mortality, and recurrence. Participants were contacted through follow-up interviews to ascertain recurrences. The KPNC Cancer Registry and an algorithm that searched through KPNC electronic databases on a semi-annual basis were used to identify additional recurrence-related diagnoses and care (*e.g.*, the participant reinitiated chemotherapy). Recurrences were typically of the same tumor cell type and included local (in the same breast without lymph node involvement), regional (lymph node involvement), and distant recurrences (spread to a metastatic site). Deaths were identified from the KPNC mortality linkage files that incorporate data from the electronic health record, the State of California, the Social Security Administration, and the National Death Index. All events were verified by medical record review.

Covariates

Information on age, race and ethnicity, education, household income, marital status, menopausal status, and family history of breast cancer were self-reported at baseline. Tumor characteristics [*e.g.*, stage at diagnosis, estrogen receptor (ER) status], cancer treatments, and clinical characteristics (*e.g.*, comorbidities) were obtained through the KPNC Cancer Registry and electronic health records. Comorbidities were assessed using the Charlson Comorbidity Index (ref. 38; range, 0–5). The following variables were initially included as covariates in models: Race/ethnicity, marital status, menopausal status, family history of breast cancer, and total energy intake. However, backwards elimination of these variables resulted in less than a 5% difference in HRs obtained from the model that excluded these variables relative to the model that included all covariates. Therefore, the presented models do not control for these covariates.

Statistical analyses

For these analyses, we excluded women according to criteria outlined in **Fig. 1**. We created two analytic cohorts, the mortality cohort of 1,964 women and the recurrence cohort of 1,924 women. The whole cohort could be followed for deaths given linkage to State and National mortality databases, but recurrences were confirmed only for those that were documented in KPNC medical records.

We summarized participant characteristics for the mortality cohort overall and within tertiles of the post-diagnosis lifestyle score with frequencies and percentages. We estimated the cumulative incidence of ACM, breast cancer–related mortality, and recurrence according to tertiles of the post-diagnosis lifestyle score, using methods accounting

Table 1. Construction of the components of the 2-year post-diagnosis lifestyle score based on recommendations from the American Cancer Society/American Society of Clinical Oncology recommendations for breast cancer survivorship.

ACS/ASCO Recommendation	Lifestyle Component	Operationalization	Categorization	Score	*N* (%)
Aim for ≥150 min of moderate or 75 min of vigorous aerobic exercise per week	Aerobic activity	Total aerobic activity, measured in metabolic equivalent of task (MET) hours per week, was calculated for each subject as follows: 1. First, for each of the 19 moderate-to-vigorous recreational activities (denoted as *h*), we estimated the MET hours per week each participant engaged in each activity as the product of the activity's corresponding MET value, the frequency in which the participant engaged in the activity each week (sessions per week), and the duration of activity sessions (hours per session). $MET - hours/week_h = MET\ value_h \times frequency_h \times duration_h,$ 2. Second, we summed across the 19 activities to estimate the total MET hours per week of recreational activity	8.75+ MET h/wk 0–8.74 MET h/wk	2 1	989 (50.4) 486 (24.7)
		The 19 moderate-to-vigorous activities included: running or jogging; swimming; bicycle riding; Stairmaster, elliptical; aerobic dance or exercise class; cross-country skiing, rowing; downhill skiing, ice skating, roller blading; hiking or backpacking; walking for pleasure at a brisk pace; walking the dog (if intense); volleyball; tennis, racquet ball, squash; soccer, basketball; baseball, softball; golf (not using cart); golf (using cart), bowling; horseback riding; fly fishing, hunting; social, folk dancing; jazz, ballet, modern tap, hip hop, ethnic dance. MET values were estimated using the Compendium of Activities (63). Scores were subsequently summed across all activities and categorized, where 8.75 MET h/wk is approximately equivalent to 150 minutes of moderate or 75 minutes of vigorous activity.	0 MET h/wk	0	489 (24.9)
Include strength training exercises ≥2 days per week	Strength training	The number of times per week each participant engaged in strength training exercises was calculated by summing the frequency in which the participant engaged weekly in (i) sit-ups, push-ups, calisthenics, floor exercise, or core strengthening exercises; and (ii) weightlifting, free weights, circuit training.	>2 times/wk 1–2 times/wk 0 times/wk	2 1 0	450 (22.9) 378 (19.2) 1,136 (57.8)
Avoid inactivity and return to normal daily activities as soon as possible following diagnosis	Sedentary behavior	The number of hours per week each participant spent participating in sedentary leisure-time activities was estimated as follows: 1. First, for each of the 6 leisure-time activities, we multiplied the frequency in which the participant engaged in that activity each week by the duration of the activity (frequency x duration). 2. Second, we summed across the 6 leisure-time activities.	0–14.4 h/wk 14.5–20.9 h/wk	2 1	656 (33.4) 640 (32.6)
		The 6-leisure time activities included: Arts and crafts projects; reading, writing, being on a computer other than at work; socializing, visiting with friends, talking on the phone; attending religious, social or service club meetings, sporting events, concerts, movies, or shows; watching TV, videos (while not doing other activities); playing board or card games. Sedentary behavior was then categorized according to distribution tertiles of the post-diagnosis sedentary behavior score.	>21–54 h/wk	0	668 (34)

(Continued on the following page)

Table 1. Construction of the components of the 2-year post-diagnosis lifestyle score based on recommendations from the American Cancer Society/American Society of Clinical Oncology recommendations for breast cancer survivorship. (Cont'd)

ACS/ASCO Recommendation	Lifestyle Component	Operationalization	Categorization	Score	*N* (%)
Achieve a dietary pattern that is high in vegetables, fruits, whole grains, and legumes; low in saturated fats; limited in alcohol consumption	Fruit/ vegetables	Fruit and vegetable consumption (servings/d) was the sum of 28 fruit and vegetable line-items (servings/d): bananas; apples or pears; oranges or tangerines; grapefruit; peaches or nectarines; cantaloupe; strawberries or other berries; watermelon; other fresh fruits like grapes, plums, honeydew, mango; canned fruit like applesauce, fruit cocktail, canned peaches, or canned pineapple; broccoli; carrots or mixed vegetables with carrots; corn; onions; garlic; green beans or peas; spinach; leafy greens; Bok choy or similar; cabbage, cauliflower; Cole slaw; sweet potatoes; green salad; tomatoes; avocados; summer squash; winter squash; other vegetables.	5.56+ servings/d	2	663 (33.8)
			3.33–5.56 servings/d	1	657 (33.5)
		Fruit and vegetable consumption was then categorized according to distribution tertiles of post-diagnosis fruit and vegetable consumption (servings/day).	0–3.33 servings/d	0	644 (32.8)
	Legumes	Legume consumption (servings/d) was the sum of the 7 line-items of the FFQ related to legumes: Edamame, boiled green soybeans; pinto beans, black beans, chili with beans, baked beans; split pea, bean, or lentil soup; peanuts; soynuts, roasted soy beans; refried beans or bean burritos.	0.32+ servings/d	2	664 (33.8)
			0.09–0.32 servings/d	1	661 (33.7)
		Legume consumption was categorized according to distribution tertiles of post-diagnosis legume consumption (servings/d).	0–0.09 servings/d	0	639 (32.5)
	Whole grains	$\%\ of\ total\ grains\ that\ were\ whole = \left(\frac{whole\ grain\ intake\ (1-ounce\ equivalents)}{total\ grain\ intake\ (1-ounce\ equivalents)}\right) \times 100$	>30.0%	2	658 (33.5)
			12.5%–30.0%	1	659 (33.6)
		Percentage of total grains that were whole was subsequently categorized it on the basis of distribution tertiles of the post-diagnosis values. Daily whole-grain intake and total grain intake were estimated by NutritionQuest (based on 1-ounce equivalents).			
		Note: We evaluated whole grains as a relative percentage of total grain intake versus absolute value because we thought the ratio of whole to refined grains was less likely to assign higher concordance scores to those who consumed larger quantities of food in general (who perhaps also consumed even larger quantities of refined grains).	0%–12.5%	0	647 (32.9)
	Saturated fats	$\%\ of\ energy\ intake\ from\ saturated\ fats = \left(\frac{saturated\ fat\ (g)*9\ kcal/g}{total\ energy\ (kcal)}\right) \times 100$	<9.5%	2	656 (33.4)
			9.5%–11.8%	1	668 (34)
		Total energy intake (kcal/d) and total saturated fat intake were estimated by NutritionQuest.	>11.8%	0	640 (32.6)
	Alcohol	We divided grams of ethanol intake by 14 to estimate the number of alcoholic beverages per day and categorized as indicated.	no alcohol	2	191 (9.7)
			≤1 drink/d	1	1422 (72.4)
		$alcoholic\ drinks/day = \left(\frac{ethanol\ (g/day)}{14\ (g)/drink}\right)$	>1 drink/d	0	351 (17.9)
Achieve and maintain a healthy weight;	Obesity	Calculated using BMI at baseline and 2-years post-diagnosis.	Healthy weight (18.5≤25.0 kg/m^2) at both time points	2	656 (33.4)
		Body weight and height were measured by the field interviewer at baseline, and weight was self-reported by the participant at each follow-up. Missing measures were backfilled using data from electronic health records.	Other combinations	1	755 (38.4)
			Obese (≥30 kg/m^2) at both time points or Overweight (25≤30 kg/m^2)-obese	0	553 (28.2)

Abbreviations: BMI, body mass index; d, day; h, hour; wk, week.

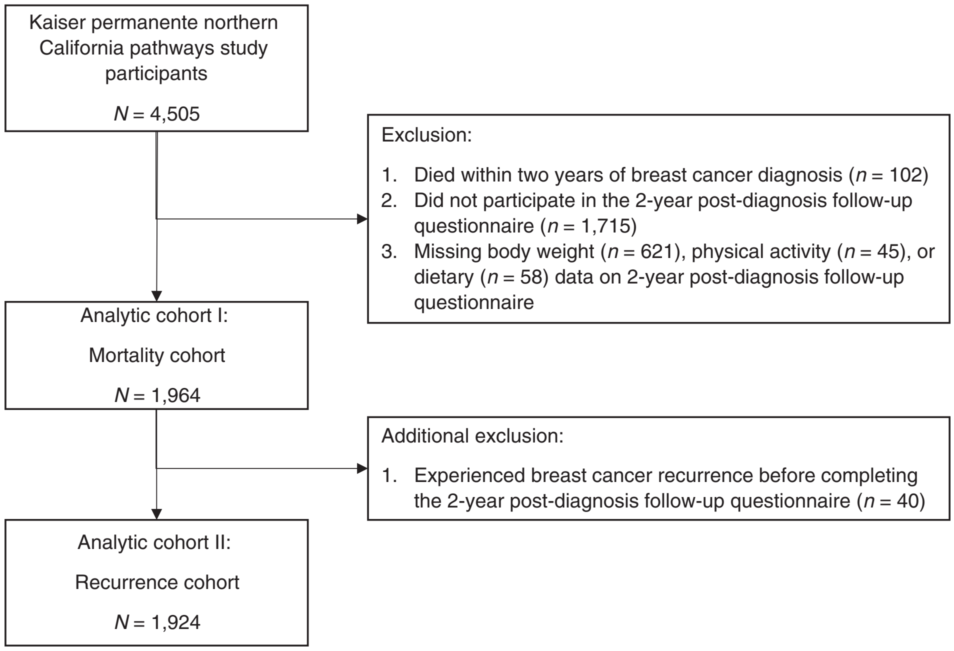

Figure 1.
Exclusion flowchart among women diagnosed with breast cancer from 2005 to 2013 in the Kaiser Permanente Northern California Pathways Study. Kaiser Permanente Northern California (KPNC) Pathways Study participants were women diagnosed with breast cancer from 2005 to 2013 who were enrolled in KPNC. All women were: (i) ≥21 years; (ii) a current KPNC member; (iii) not previously diagnosed with a malignant cancer; (iv) able to speak English, Spanish, Cantonese, or Mandarin; and (v) living within a 65-mile radius of a field interviewer

for competing events (39). Using multivariable Cox proportional hazards regression models, we estimated the separate and combined associations of the 9 lifestyle components with ACM, breast cancer–related mortality, and recurrence with cause-specific hazard ratios (HR) and 95% confidence intervals (CI). To estimate the separate associations of each of the 9 components, we included all components simultaneously, as well as other confounding factors, in a single model. The estimated associations of pre- to post-diagnosis concordance level changes for components with the outcomes were calculated in a similar manner. Proportional hazards assumptions were assessed through covariate interactions with time via the likelihood ratio test and visual assessment of log-log survival curves. No serious violations were observed. Collinearity was assessed in the component model that included all 9 components together in a model (additionally adjusted for the potential confounder variables specified below) through inspection of condition indices as well as the regression coefficients variance-decomposition proportion. All condition indices were less than 4, suggesting no major collinearity issues.

All multivariable models controlled for age at diagnosis (continuous); stage (I, II, III/IV); ER status (positive, negative); receipt of chemotherapy (yes, no), trastuzumab (yes, no), or radiotherapy (yes, no); Charlson comorbidity index (continuous); smoking status (never, former, current); education level (high-school graduate or less, some college, college graduate, post-graduate); and household income (<$25,000, ≥$25,000). Other variables were considered but did not substantially impact results (see Covariates section in Materials and Methods). Follow-up began on the completion date of the 2-year post-diagnosis survey using delayed-entry models. For mortality models, follow-up ended on the death date or December 31, 2018. For recurrence models, follow-up ended on the date of the recurrence, death, disenrollment from KPNC, or December 31, 2018, whichever came first.

We conducted several supplemental analyses to (i) examine potential heterogeneity across participant characteristics; (ii) investigate the potential for bias due to the high proportion of missing follow-up data and (iii) reverse causation bias; (iv) address competing events; and (v) exclude women diagnosed with stage IV breast cancer (see Supplementary Materials and Methods for details).

R software (version 4.0.3; R Foundation) was used to estimate cumulative incidence functions and the Bayesian selection model, the latter was fit using Just Another Gibbs Sampler software *via* the "rjags" package (RRID: SCR_017573). All other analyses were conducted using SAS statistical software (version 9.4; SAS Statistical Institute).

Data availability

Analytic datasets for this study were generated at KPNC. Derived data (e.g., lifestyle guideline scores) created for these analyses are available from the corresponding author upon request.

Results

The post-diagnosis lifestyle score ranged 0−18 [median = 9; interquartile range (IQR) = 4]. Participant characteristics according to tertiles of the post-diagnosis guideline score are shown in **Table 2**. Participants with greater guideline concordance were more likely to be Asian, have higher educational attainment, and have a higher income. We observed 290 deaths ($n = 80$ breast cancer–related deaths) over a median follow-up of 9.7 years (IQR = 3.8) in the mortality cohort, and 176 recurrences over a median follow-up of 9.5 years (IQR = 3.9) years in the recurrence cohort. Surveys administered at baseline and at follow-up were completed a median of 0.2 years (IQR = 0.1) and 2.1 years (IQR = 0.1) after diagnosis, respectively.

Post-diagnosis lifestyle

The 10-year cumulative incidence of ACM was almost twice as high in participants in the lowest tertile of the lifestyle score (21%) compared with those in the highest (11%; Supplementary Fig. S1). The 10-year cumulative incidence of breast cancer–related mortality was also higher in participants in the lowest tertile of the lifestyle score (7%) compared with those in the highest (2%). No meaningful differences in the cumulative incidence of recurrence by lifestyle score tertile were observed.

Table 2. Baseline characteristics of women diagnosed with invasive breast cancer in the Pathways Study according to tertiles of the 2-year post-diagnosis lifestyle score, 2006–2013 ($n = 1{,}964$).

Variable	Categories	Total $N = 1{,}964$ N (%)	2-year Post-Diagnosis Lifestyle Score[a] Tertile 1 – Lowest concordance $N = 656$ N (%)	2 $N = 693$ N (%)	3 – Highest concordance $N = 615$ N (%)
Race/ethnicity					
	White	1,403 (71.4)	494 (75.9)	485 (70.2)	424 (68.2)
	Black	91 (4.6)	35 (5.4)	32 (4.6)	24 (3.9)
	Asian	236 (12)	43 (6.6)	92 (13.3)	101 (16.2)
	Hispanic	187 (9.5)	59 (9.1)	69 (10)	59 (9.5)
	Other	47 (2.4)	20 (3.1)	13 (1.9)	14 (2.3)
Education Status					
	HS grad or Less	264 (13.5)	119 (18.3)	79 (11.5)	66 (10.6)
	Some college	635 (32.4)	262 (40.3)	227 (32.9)	146 (23.5)
	College grad	564 (28.8)	168 (25.8)	207 (30)	189 (30.4)
	Post-graduate	498 (25.4)	101 (15.5)	176 (25.5)	221 (35.5)
Household Income					
	<$25K	160 (9.1)	74 (13)	45 (7.2)	41 (7.3)
	$25K–69K	671 (38.3)	253 (44.5)	239 (38.4)	179 (31.9)
	≥$70K	923 (52.6)	242 (42.5)	339 (54.4)	342 (60.9)
Marital Status					
	Married/Marriage-like	1,262 (64.5)	374 (57.1)	460 (66.8)	428 (69.8)
	Single/separated/divorced	695 (35.5)	281 (42.9)	229 (33.2)	185 (30.2)
Menopausal Status					
	Premenopausal	469 (23.9)	99 (15.2)	159 (23)	211 (33.9)
	Postmenopausal	1,495 (76.1)	552 (84.8)	532 (77)	411 (66.1)
Family hx of breast cancer					
	No	1,549 (79.2)	502 (77.5)	562 (81.6)	485 (78.2)
	Yes	408 (20.8)	146 (22.5)	127 (18.4)	135 (21.8)
Tumor Stage					
	Stage I	1,131 (57.9)	363 (55.8)	399 (58)	369 (59.8)
	Stage II	640 (32.7)	218 (33.5)	220 (32)	202 (32.7)
	Stage III	172 (8.8)	64 (9.8)	63 (9.2)	45 (7.3)
	Stage IV	12 (0.6)	5 (0.8)	6 (0.9)	1 (0.2)
Tumor Subtype					
	Luminal A	979 (51.7)	346 (54.9)	323 (48.6)	310 (51.7)
	Luminal B	644 (34)	205 (32.5)	234 (35.2)	205 (34.2)
	Her2-Enriched	84 (4.4)	21 (3.3)	37 (5.6)	26 (4.3)
	Triple Negative	188 (9.9)	58 (9.2)	71 (10.7)	59 (9.8)
Chemotherapy					
	No	1,099 (56.2)	384 (59.4)	374 (54.2)	341 (55)
	Yes	858 (43.8)	263 (40.6)	316 (45.8)	279 (45)
Radiotherapy					
	No	1,042 (53.1)	384 (59.4)	374 (54.2)	341 (55)
	Yes	922 (46.9)	263 (40.6)	316 (45.8)	279 (45)
Herceptin					
	No	1,790 (91.5)	602 (93)	617 (89.4)	571 (92.1)
	Yes	167 (8.5)	45 (7)	73 (10.6)	49 (7.9)
Smoking Status	Never	1,142 (58.2)	341 (52.4)	397 (57.5)	404 (65)
	Former	763 (2.8)	285 (43.8)	273 (39.5)	205 (33)
	Current	5 (0.3)	24 (3.7)	18 (2.6)	12 (1.9)
		Mean (SD)	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**
Age at diagnosis		61.2 (11.54)	64.1 (11.1)	61.3 (11.39)	58 (11.36)
Charlson comorbidity index		0.2 (0.64)	0.3 (0.85)	0.2 (0.6)	0.1 (0.31)

Note: The following variables had missing values: education (0.2%), income (10.7%), marital status (0.4%), family history of breast cancer (0.4%), tumor stage (0.5%), tumor subtype (3.5%), chemotherapy (0.4%), and Herceptin (0.4%).
[a]See Table 1 for additional details on calculation.

In multivariable Cox models, the post-diagnosis lifestyle score was inversely associated with ACM (HR, 0.90; 95% CI, 0.82–0.98; per 2-point increase), and breast cancer–related mortality (HR, 0.79; 95% CI, 0.67–0.95; per 2-point increase; **Table 3**). We observed no meaningful associations of the post-diagnosis lifestyle score with recurrence.

In our component model that included each of the 9 recommendations together in a multivariable model, higher intake of legumes (HR,

Table 3. Hazard ratios and 95% confidence intervals for the association of the 2-year post-diagnosis lifestyle score with all-cause mortality, breast cancer-mortality, and breast cancer recurrence.

		Complete Case Analysis			
		Model 1[a]		Model 2[b]	
		# Events	HR (95% CI)	# Events	HR (95% CI)
		All-Cause Mortality			
Score tertile (range)	1 (0–7)	132	1.00 (—)	108	1.00 (—)
	2 (8–10)	99	0.79 (0.61–1.03)	88	0.91 (0.69–1.22)
	3 (11–18)	59	0.63 (0.46–0.85)	46	0.72 (0.50–1.03)
Continuous[c], per 2-point increase			0.86 (0.80–0.94)		0.90 (0.82–0.98)
		Breast Cancer-Specific Mortality			
Score tertile (range)	1 (0–7)	49	1.00 (—)	42	1.00 (—)
	2 (8–10)	20	0.47 (0.28–0.79)	17	0.50 (0.28–0.88)
	3 (11–18)	11	0.40 (0.21–0.78)	11	0.65 (0.32–1.31)
Continuous[c], per 2-point increase			0.75 (0.64–0.87)		0.79 (0.67–0.95)
		Breast Cancer Recurrence			
Score tertile (range)	1 (0–7)	55	1.00 (—)	49	1.00 (—)
	2 (8–10)	64	1.07 (0.74–1.53)	56	1.10 (0.74–1.62)
	3 (11–18)	57	1.06 (0.73–1.55)	47	1.09 (0.72–1.66)
Continuous[c], per 2-point increase			1.00 (0.90–1.11)		0.98 (0.88–1.10)

Abbreviations: CI, confidence interval; HR, hazard ratio.
[a]Model 1 adjusts for age only. Mortality cohort (n = 1,964); Recurrence cohort (n = 1,924).
[b]Model 2 adjusts for age, tumor stage, ER status, chemotherapy, Herceptin, radiotherapy, comorbidities, smoking status, income, and education level. Observations were additionally excluded due to missing covariates in the mortality cohort (n = 228) and the recurrence cohort (n = 219). Mortality cohort (n = 1,736); Recurrence cohort (n = 1,705).
[c]We examined the potentially non-linear relationships between the lifestyle score and the outcomes of interest non-parametrically by fitting models using restricted cubic splines. We tested non-linearity using the likelihood ratio test, comparing a model with only the linear term for the lifestyle score to the model with the linear and cubic spline terms. The relationships between the lifestyle score and the outcomes of interest were approximately linear.

0.40; 95% CI, 0.18–0.89; per 2 serving/d increase) as well as higher levels of aerobic physical activity (e.g., 8.75+ MET h/wk vs. 0: HR, 0.55; 95% CI, 0.39–0.76) and engaging in strength training exercises 1–2 times/wk, relative to no strength training (HR, 0.63; 95% CI, 0.41–0.98), were inversely related to ACM (**Table 4**). Participants who went from being categorized as overweight at baseline to obese 2-years post-diagnosis or those who were obese at both time points, relative to healthy weight, had a higher risk of breast cancer–related mortality (HR, 2.50; 95% CI, 1.27–4.91). Higher levels of aerobic physical activity (HR, 0.98; 95% CI, 0.94–1.01; per 3.5 MET h/wk increase) appeared inversely associated with recurrence. We did not observe meaningful associations between the other components with outcomes. No substantial differences were observed when only one component was included in the ACM model at a time, adjusting for the other confounders (Supplementary Table S2).

Change models

In multivariable models, women who maintained high concordance with the lifestyle guidelines at both baseline (representing pre-diagnosis lifestyle) and approximately 2-years post-diagnosis had a lower risk of ACM, relative to women who maintained low concordance (HR, 0.61; 95% CI, 0.37–1.03; **Table 5**). Relative to women who maintained low concordance, the risk of ACM was lower among women who maintained partial concordance (HR, 0.89; 95% CI, 0.61–1.30), and women who decreased concordance (e.g., went from high to low concordance; HR, 0.78; 95% CI, 0.54–1.13). Somewhat similar trends were observed for breast cancer–related mortality and recurrence, although associations tended to be weaker for the latter [e.g., the HRs for maintained partial, maintained high, and decreased concordance relative to maintained low concordance were 0.87 (95% CI, 0.52–1.43], 0.86 [95% CI, 0.49–1.52], and 0.77 [95% CI, 0.47–1.26), respectively].

In models examining changes in concordance with each of the recommendations, the hazard of ACM in women who maintained partial or high concordance levels with aerobic physical activity recommendations at both baseline and post-diagnosis and in women who decreased their concordance levels was less than half that of women who reported low concordance at both time points (e.g., maintained high concordance HR, 0.38; 95% CI, 0.25–0.57; Supplementary Table S3). In addition, women who increased their concordance levels with aerobic physical activity recommendations had approximately half the hazard of ACM compared with those who maintained low concordance (HR, 0.52; 95% CI, 0.35–0.78). Similar trends were observed for recommendations related to achieving a dietary pattern that is high in legumes and low in saturated fat, though associations were weaker and less precise than those for aerobic physical activity (*e.g.*, increased concordance for legumes: HR, 0.84; 95% CI, 0.57–1.24). The hazard of ACM was lower in women who maintained partial concordance with the strength training recommendation (HR, 0.39; 95% CI, 0.16–0.97) or decreased concordance levels (HR, 0.65; 95% CI, 0.43–0.96), though results were based on few events in those who engaged in any strength training exercises. In contrast with these findings, for alcohol, relative to women who maintained low concordance with the alcohol recommendation, those who maintained partial concordance or increased/decreased concordance levels appeared to have a higher hazard of ACM (e.g., increased concordance, HR, 2.02; 95% CI, 1.17–3.48). Trends regarding changes in concordance levels for recommendations regarding high intake of fruits/vegetables and whole grains, as well as limited sedentary behavior with ACM, were less clear. We were unable to examine the component change models with breast cancer–related mortality due to few events. In recurrence models, we observed somewhat similar trends to our ACM results for legumes and saturated fats. The hazard of recurrence appeared somewhat lower in those who maintained

Table 4. Hazard ratios and 95% confidence intervals for associations[a] of each of the 9 components of the 2-year post-diagnosis lifestyle score with all-cause mortality, breast cancer–related mortality, and breast cancer recurrence.

		All-Cause Mortality		Breast Cancer–Specific Mortality		Breast Cancer Recurrence	
Recommendation	**Category**	**# Events**	**HR (95% CI)**	**# Events**	**HR (95% CI)**	**# Events**	**HR (95% CI)**
Fruits/Vegetables	Tertile 1 (0–3.33 svg/d)	84	1.00 (—)	30	1.00 (—)	45	1.00 (—)
	Tertile 2 (3.33–5.56 svg/d)	89	1.25 (0.92–1.70)	26	0.95 (0.54–1.67)	52	1.23 (0.82–1.86)
	Tertile 3 (5.56+ svg/d)	69	1.20 (0.85–1.69)	14	0.79 (0.40–1.58)	55	1.49 (0.97–2.28)
	per 2 svg/d increase		1.02 (0.92–1.12)		0.94 (0.76–1.16)		1.09 (0.98–1.21)
Legumes	Tertile 1 (0–0.09 svg/d)	103	1.00 (—)	38	1.00 (—)	53	1.00 (—)
	Tertile 2 (0.09–0.32 svg/d)	79	0.92 (0.68–1.25)	17	0.53 (0.10–2.75)	56	0.97 (0.66–1.43)
	Tertile 3 (0.32+ svg/d)	60	0.66 (0.47–0.94)	15	0.57 (0.29–1.11)	43	0.67 (0.43–1.02)
	per 2 svg/d increase		0.40 (0.18–0.89)		0.53 (0.10–2.75)		0.48 (0.20–1.14)
Percentage of grains that are whole	Tertile 1 (0%–12.5%)	83	1.00 (—)	26	1.00 (—)	49	1.00 (—)
	Tertile 2 (12.5%–30.0%)	79	1.15 (0.84–1.59)	20	1.08 (0.57–2.03)	55	1.09 (0.73–1.62)
	Tertile 3 (>30.0%)	80	1.14 (0.83–1.59)	24	1.24 (0.67–2.28)	48	0.99 (0.65–1.51)
	Per 2% increase		1.00 (0.99–1.02)		1.00 (0.97–1.03)		1.00 (0.98–1.02)
Percentage of calories from saturated fats	Tertile 1 (<9.5%)	77	1.00 (—)	22	1.00 (—)	47	1.00 (—)
	Tertile 2 (9.5%–11.8%)	76	0.86 (0.62–1.20)	16	0.47 (0.23–0.93)	52	1.05 (0.70–1.58)
	Tertile 3 (>11.8%)	89	1.05 (0.75–1.46)	32	1.14 (0.63–2.07)	53	1.13 (0.74–1.71)
	Per 2% increase		1.03 (0.92–1.14)		1.12 (0.93–1.35)		1.03 (0.90–1.17)
Alcohol	Nondrinker	32	1.00 (—)	10	1.00 (—)	17	1.00 (—)
	≤1 drink/d	172	0.81 (0.54–1.20)	48	0.74 (0.36–1.55)	104	0.74 (0.44–1.25)
	>1 drink/d	38	0.70 (0.42–1.15)	12	0.72 (0.29–1.81)	31	0.88 (0.47–1.64)
	Per 2 drinks/d increase		0.95 (0.69–1.29)		0.99 (0.55–1.79)		1.01 (0.70–1.48)
Aerobic	0 MET h/wk	112	1.00 (—)	35	1.00 (—)	39	1.00 (—)
	0 ≤ 8.75 MET h/wk	49	0.58 (0.41–0.83)	12	0.65 (0.32–1.32)	38	0.85 (0.53–1.37)
	8.75+ MET h/wk	81	0.55 (0.39–0.76)	23	1.07 (0.58–1.98)	75	0.84 (0.54–1.31)
	Per 3.5 MET h/wk increase		0.97 (0.94–1.00)		1.03 (0.97–1.09)		0.98 (0.94–1.01)
Strength	None	174	1.00 (—)	57	1.00 (—)	89	1.00 (—)
	1–2x/wk	24	0.63 (0.41–0.98)	3	0.26 (0.08–0.86)	24	0.81 (0.50–1.29)
	>2x/wk	44	0.99 (0.69–1.42)	10	0.84 (0.40–1.76)	39	1.26 (0.84–1.90)
Sedentary	Tertile 1 (0–14.4 h/wk)	73	1.00 (—)	21	1.00 (—)	54	1.00 (—)
	Tertile 2 (14.5–20.9 h/wk)	76	0.91 (0.65–1.27)	19	0.64 (0.33–1.24)	46	0.90 (0.60–1.35)
	Tertile 3 (>21–54 h/wk)	93	0.93 (0.67–1.30)	30	0.88 (0.48–1.62)	52	0.97 (0.64–1.46)
	Per 2 h/wk increase		0.98 (0.95–1.01)		0.97 (0.91–1.03)		1.00 (0.96–1.04)
Body Weight[b]	Normal–Normal	61	1.00 (—)	11	1.00 (—)	38	1.00 (—)
	Other	97	1.17 (0.84–1.63)	26	1.07 (0.53–2.17)	70	1.30 (0.87–1.92)
	Obese–obese or overweight–obese	84	1.21 (0.85–1.73)	33	2.50 (1.27–4.91)	44	1.14 (0.73–1.79)

Abbreviations: CI, confidence intervals; d, days; HR, hazard ratio; h, hours; svg, servings; wk, week.

[a]Model includes all 9 recommendations together in a multivariable Cox model and additionally adjusts for age, tumor stage, ER status, chemotherapy, Herceptin, radiotherapy, comorbidities, smoking status, income, and education level. Mortality cohort ($n = 1{,}736$); Recurrence cohort ($n = 1{,}705$). No collinearity issues were identified.

[b]Body weight at baseline and 2-years post-diagnosis.

concordance with aerobic physical activity recommendations, relative to those who maintained low concordance, though results were weaker with wider CIs than those with ACM (e.g., maintained high HR, 0.74; 95% CI, 0.42–1.29). Relative to maintained low concordance with fruit/vegetable recommendations, maintained partial or high concordance as well as increased concordance were associated with a higher hazard of recurrence (e.g., maintained high: HR, 1.76; 95% CI, 0.98–3.18).

Supplemental analyses

Associations of the total lifestyle score with ACM, breast cancer–related mortality, and recurrence appeared mostly similar across participant characteristics (Supplementary Table S4) that had >5 events within each strata, with some exceptions. The lifestyle score was inversely associated with ACM and breast cancer–related mortality in former and never smokers but was positively and paradoxically associated with ACM and breast cancer–related mortality in current smokers [e.g., HRs per 2-point increase in lifestyle score for breast cancer–related mortality in never, former, and current smokers were 0.66 (95% CI, 0.49–0.88), 0.80 (95% CI, 0.62–1.02), and 1.52 (95% CI, 0.94–2.48), respectively]. Associations of the total lifestyle score with ACM and breast cancer–related mortality were somewhat stronger among women with a Charlson Comorbidity Index score of 0, indicating no comorbidities were found, than among those with scores ≥1. For example, the lifestyle score was inversely related to ACM among women with a comorbidity score of 0 (e.g., HR per 2-point increase was 0.87; 95% CI, 0.79–0.96) but the association was null among women with higher comorbidity scores (e.g., HR per 2-point increase was 1.00; (95% CI, 0.82–1.22). In addition, we observed somewhat stronger associations of a reduced score (excluding the BMI component) with breast cancer–related mortality among women who were overweight and obese than among healthy weight women, though CIs were wide and overlapping [e.g., HRs per 2-point increase

Table 5. Multivariable Cox proportional hazards models for the associations of changes in lifestyle on all-cause mortality, breast cancer–related mortality, and breast cancer recurrence in the Pathways Study.

	All-Cause Mortality		Breast Cancer–Specific Mortality		Breast Cancer Recurrence	
Concordance Level	**# Events**	**HR[a] (95% CI)**	**# Events**	**HR[a] (95% CI)**	**# Events**	**HR[a] (95% CI)**
Maintained Low[b]	69	1.00 (—)	24	1.00 (—)	34	1.00 (—)
Maintained Partial[c]	45	0.89 (0.61–1.30)	9	0.66 (0.30–1.43)	29	0.87 (0.52–1.43)
Maintained High[d]	19	0.61 (0.37–1.03)	4	0.51 (0.17–1.49)	20	0.86 (0.49–1.52)
Increased[e]	57	0.91 (0.64–1.31)	17	0.98 (0.52–1.86)	39	0.89 (0.56–1.42)
Decreased[f]	52	0.78 (0.54–1.13)	16	0.70 (0.37–1.33)	30	0.77 (0.47–1.26)

Abbreviations: CI, confidence intervals; HR, hazard ratio.
[a]Adjusts for age, tumor stage, ER status, chemotherapy, Herceptin, radiotherapy, comorbidities, smoking status, income, and education level.
[b]Participant in lowest category of guideline concordance (lifestyle score <7) at both baseline and 2 years post-diagnosis.
[c]Participant in the middle category of guideline concordance (lifestyle score 8–10) at both baseline and 2 years post-diagnosis.
[d]Participant in the highest category of guideline concordance (lifestyle score 11+) at both baseline and 2 years post-diagnosis.
[e]Participant increased category of guideline concordance from baseline to 2 years post-diagnosis (e.g., participant went from being in the lowest category of concordance at baseline to being in the middle category 2 years post-diagnosis).
[f]Participant decreased category of guideline concordance from baseline to 2 years post-diagnosis (e.g., participant went from being in the highest category of concordance at baseline to being in the middle category 2 years post-diagnosis).

in reduced lifestyle score for breast cancer–related mortality in healthy weight, overweight, and obese women were 0.91 (95% CI, 0.67–1.25), 0.82 (95% CI, 0.58–1.17), and 0.69 (95% CI, 0.49–0.96)].

Results from models accounting for data not missing at random to calculate the lifestyle score were mostly comparable with those from our complete case analysis (the main results), albeit somewhat stronger for breast cancer–related mortality (Supplementary Table S5). Findings were similar after excluding deaths occurring within two years of the post-diagnosis survey in efforts to mitigate the potential for bias due to reverse causation (Supplementary Table S6). In models accounting for competing events, subdistribution HRs estimating the association of the overall lifestyle score with breast cancer–related mortality and recurrence were mostly consistent with our cause-specific HRs (Supplementary Table S7). Excluding women diagnosed with stage IV breast cancer ($n = 12$) had minimal impact on our results (Supplementary Table S8).

Discussion

In this cohort of breast cancer survivors, we found that overall, a healthier lifestyle, assessed by concordance with the ACS/ASCO breast cancer survivorship guidelines approximately 2 years after breast cancer diagnosis, was associated with a lower risk of ACM and breast cancer–related mortality, but not with recurrence. Many of the individual lifestyle behaviors we considered appeared to contribute to the inverse association of the lifestyle score, especially aerobic physical activity and legume intake for mortality, and body weight and legume intake for breast cancer–related mortality. Importantly, women who reported healthier lifestyle behaviors both around and after the time of diagnosis (i.e., maintained high concordance with guidelines, relative to maintained low concordance) had the lowest risk of mortality, but there also appeared to be some survival advantage when certain behaviors, such as increasing aerobic physical activity levels, were changed after diagnosis.

Combined lifestyle

To our knowledge, only two previous studies examined the combined effects of post-diagnosis lifestyle on breast cancer prognosis, both of which largely support our findings that a healthier post-diagnosis lifestyle may be associated with lower mortality (26, 27). In the first, conducted in early-stage breast cancer survivors, women with both high fruit/vegetable consumption and high levels of physical activity had a lower hazard of mortality compared with those with low consumption and low physical activity, regardless of obesity (27). In the second, conducted by Inoue-Choi and colleagues (26), breast cancer survivors who were more concordant with the World Cancer Research Fund's cancer prevention guidelines, assessed a median of 8.6 years after diagnosis, had a lower risk of overall mortality, but not breast cancer–related mortality. Our findings supporting a positive association between post-diagnosis lifestyle and breast cancer–related mortality contrast with previous findings from Inoue-Choi and colleagues (26), though findings from both studies were based on few breast cancer–related deaths. Differences in findings could also be attributed to our definition of breast cancer–related mortality, which was broad and included deaths in which breast cancer was a contributing and not solely the primary cause of death, and differences in lifestyle scores (e.g., ours included additional physical activity components and different dietary components). Diet, physical inactivity, and obesity could plausibly effect breast cancer progression and survival through changes in sex and metabolic hormones, body composition, and inflammation (40–43).

Several factors might explain our largely null findings for overall lifestyle and recurrence. First, most breast cancer recurrences were classified as distant recurrences (53%) and occurred within 5 years of diagnosis (55%). As distant and early recurrences are often indicative of more aggressive tumor types (44, 45), it is possible that they may be more related to tumor biology than post-diagnosis lifestyle. We had too few recurrence events to explore detailed differences by tumor subtype or menopausal status. In addition, we were unable to investigate late recurrences, which may be particularly susceptible to lifestyle. Second, the positive association of fruit/vegetable intake with recurrence (the opposite direction of what we hypothesized) may have negated any potential benefits of the remaining components (e.g., legume intake). Third, it is possible that that the cumulative effects of a healthy lifestyle over time are more important than lifestyle measured just at one time point, as we observed a lower risk of breast cancer recurrence among women who maintained partial or high concordance (or had a higher level of concordance during at least one time point considered in this study) with guidelines relative to those who maintained low concordance.

Physical activity

In our study, recreational aerobic physical activity had the strongest impact on the lifestyle score-mortality association. We observed lower risks of mortality in those who partially and fully met the recommended levels of physical activity, relative to those who were inactive, indicating that any level of physical activity may be beneficial. Importantly, we found that women who reported increasing levels of physical activity after diagnosis had approximately half the risk of mortality of those who reported being inactive at both time points, supporting the idea that improving behaviors after diagnosis may influence survival. Most (28–31), but not all (32), previous studies largely support our current findings regarding the benefits of maintained activity on mortality in breast cancer survivors. Findings regarding the benefits of increasing physical activity after a breast cancer diagnosis are more mixed, with some studies (28, 30, 32), but not all (29, 31), supporting our current findings. We also observed a lower mortality risk in women who decreased their physical activity levels, which is in contrast with most (29–32), but not all (28), previous studies. Most women in our study who decreased aerobic activity concordance at follow-up reported high concordance at baseline (98%) and may have been active for much of their lives. Persisting benefits of physical activity in individuals who decreased levels were previously observed in the general population (46).

We also found that engaging in some strength training activities (1–2 days per week) may be associated with a lower mortality risk, though we had too few events in this group to draw strong conclusions. Though strength training is less studied than aerobic activity, findings from a recent meta-analysis, conducted in the general population, suggest that strength training, separately and in combination with aerobic activity, may be associated with lower mortality (47). In a secondary analysis of a randomized controlled trial, breast cancer survivors assigned to one year of resistance exercise, compared with a stretching control group, had lower levels of biomarkers associated with cancer progression (48), providing further support for our findings. Strength training exercises may be particularly important in women treated with chemotherapy, as low muscle mass may be associated with poorer tolerance to chemotherapy and reduced survival (49, 50).

Diet

In our study, post-diagnosis legume intake appeared strongly and inversely associated with mortality, and possibly breast cancer–related mortality and recurrence, though CIs were wide due to few events. The benefits of legume intake on mortality, and possibly recurrence, were even more apparent when habitual intake of legumes (pre- to post-diagnosis) was considered (for mortality and recurrence only). Moreover, those who increased legume intake after diagnosis also appeared to have some survival benefit. The inverse association between legume intake and mortality was previously observed in the general population (51, 52). Regarding the recommendation to consume a diet low in saturated fats, whereas our models that examined pre- to post-diagnosis changes in saturated fat intake appeared to suggest benefits to limiting saturated fat intake, these findings were inconsistent with our largely null findings from post-diagnosis models and should be interpreted with caution. Previous studies that examined post-diagnosis saturated fat intake with mortality in breast cancer survivors had mixed findings (21, 22), one of which suggests a possible positive association with mortality due to all causes and breast cancer (21). Similar to previous studies in cohorts of breast cancer survivors (16, 27), post-diagnosis fruit and vegetable consumption as well as the percentage of total grain that is whole did not appear associated with the risk of mortality.

We observed a lower hazard of ACM, breast cancer–related mortality, and recurrence among those who consumed alcohol approximately 2-years after being diagnosed with breast cancer, relative to those who did not consume alcohol, though CIs were wide and overlapping due to few events (especially for breast cancer–related mortality and recurrence) among non-drinkers, who represented a small proportion of our total sample ($\sim$10%). Our results regarding mortality are consistent with many (21, 53–56), but not all (57, 58), previous studies investigating post-diagnosis alcohol intake in relation to mortality outcomes among women with breast cancer. The suggested inverse associations between alcohol consumption and total mortality could partly reflect the J-shaped association between alcohol consumption and cardiovascular disease often observed in the general population (59). Alternatively, women with more advanced disease may have been more likely to stop drinking and be categorized as "non-drinkers" according to the 2-year post-diagnosis follow-up survey (making this category appear more high risk than it truly is), which could also potentially explain our observed inverse association, particularly for recurrence, as associations did not generally uphold when pre- to post-diagnosis changes were considered. Previous studies investigating post-diagnosis alcohol intake and breast cancer recurrence found largely null (54, 60) or positive (61) associations. In a pooled analysis by Kwan and colleagues (54), results suggested although there was no association with recurrence overall, there was a positive association in postmenopausal women. One additional study found post-diagnosis alcohol intake associated with late recurrence in ER^{+} breast cancers (55).

Body weight

Although we had too few breast cancer–related deaths to draw strong conclusions, it appeared that relative to women who were of a healthy weight both pre- and post-diagnosis, women who were obese at both time points or who went from being overweight to obese had a higher risk of breast cancer–related mortality, and possibly ACM, though our findings for the latter were imprecise and included the null. These results are somewhat consistent with a previous meta-analysis that found that both pre- and post-diagnosis obesity were associated with higher risk of ACM [pre-diagnosis BMI (21 studies): HR, 1.41; 95% CI, 1.29–1.53; post-diagnosis BMI (5 studies): HR, 1.21; 95% CI, 1.06–1.38] and breast cancer–related mortality [pre-diagnosis BMI (22 studies): HR, 1.35; 95% CI, 1.24–1.47; post-diagnosis BMI (2 studies): HR, 1.68; 95% CI, 0.90–3.15; ref. 7].

Limitations/strengths

Our study has several limitations. First, many participants were excluded from primary analyses because of missing post-diagnosis lifestyle data, potentially biasing our results, especially if the data were not missing at random (i.e., lifestyle related to responding to the questionnaire). However, our supplemental analysis suggests that this may have minimal impact on our results. Second, our lifestyle score relied on self-reported data and may have been subject to misclassification. Because of the study's prospective design, exposure misclassification, particularly for high versus low concordance comparisons, is expected to be non-differential with respect to our outcomes and likely would not account for positive findings, this includes misclassification of BMI due to self-reported weight (height was measured by a trained interviewer). For example, previous research suggests that relative to measured values, underweight people tend to overestimate their weight, whereas others tend to underestimate their weight, and this bias tends to increase with increasing BMI category (62). So, we can expect that some women who were truly underweight or overweight reported a "healthy weight" (independent of outcome status). However, we would expect that women who reported a weight categorized as obese would have truly been in our obese category, as their true weight was potentially even higher (also independent of outcome status). Therefore, bias due to misclassification is expected to bias findings toward the null (as overweight and underweight women may have a higher risk of mortality than healthy weight women, making the healthy weight group appear to have a higher risk of mortality than it truly does). However, it is important to note that in our study, the correlation between BMI based on self-reported weight and BMI based on weight from electronic health records among women in this study was high ($r = 0.96$). Third, we weighted the components of the overall lifestyle score equally (0, 1, and 2 for low, partial, and high concordance levels, respectively), despite differences in their effect sizes (e.g., a 2-point increase in our aerobic recreational activity concordance score is quite different from a 2-point increase in our fruit/vegetable concordance score). Therefore, we recommend exercising caution when interpreting summary score results without considering the results of the individual components. Fourth, underlying severe disease leading to changes in body weight and death, sometimes referred to as reverse causation, could bias our study results for BMI. Unfortunately, we lacked information on whether weight loss (if any occurred) was intentional. However, this should largely impact the "partial" concordance group, which includes those with an underweight status or BMI category combinations, indicating enough weight loss to drop a BMI category. Finally, we had too-few breast cancer–related deaths and recurrences to enable meaningful interpretation of the individual lifestyle component models. Nonetheless, our study has several strengths, including its large sample size, detailed lifestyle information collected at multiple time points, and careful consideration of several major sources of potential bias in supplemental analyses.

In summary, our results suggest that in women diagnosed with invasive breast cancer, a post-diagnosis lifestyle that is concordant with ACS/ASCO guidelines for breast cancer survivors may be associated with a lower risk of mortality and breast cancer–related mortality. Importantly, our data suggest that it is not too late for breast cancer survivors to change their behaviors and potentially improve health outcomes, particularly when it comes to aerobic physical activity. Not surprisingly, we found the strongest evidence for the potential benefits of aerobic physical activity on mortality, though several other factors appeared to contribute to our observed lifestyle-mortality association, including legume intake and possibly strength training. Perhaps our most important findings are those supporting the potential benefits of changing certain behaviors (e.g., increasing aerobic activity, and possibly increasing legume/nut intake or decreasing saturated fat intake) after a breast cancer diagnosis. Future studies, particularly well-conducted randomized controlled trials, are needed to confirm the role of post-diagnosis lifestyle on breast cancer prognosis as well as investigate ways to motivate and maintain behavior change. As breast cancer recurrence is heterogeneous by tumor and patient characteristics, future studies should also investigate the effects of lifestyle on early versus late recurrence as well as locoregional versus distant recurrences.

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Authors' Contributions

A.N. Troeschel: Conceptualization, formal analysis, investigation, visualization, methodology, writing–original draft, writing–review and editing. **T.J. Hartman:** Conceptualization, resources, data curation, supervision, methodology, project administration, writing–review and editing. **L.E. McCullough:** Conceptualization, resources, supervision, funding acquisition, investigation, methodology, project administration, writing–review and editing. **I.J. Ergas:** Data curation, investigation, methodology, writing–review and editing. **L.J. Collin:** Investigation, methodology, writing–review and editing. **M.L. Kwan:** Investigation, methodology, writing–review and editing. **C.B. Ambrosone:** Investigation, methodology, writing–review and editing. **W.D. Flanders:** Formal analysis, supervision, investigation, methodology, writing–review and editing. **P.T. Bradshaw:** Methodology, writing–review and editing. **E.M. Cespedes Feliciano:** Investigation, methodology, writing–review and editing. **J.M. Roh:** Investigation, project administration, writing–review and editing. **Y. Wang:** Supervision, methodology, writing–review and editing. **E. Valice:** Data curation, methodology, writing–review and editing. **L.H. Kushi:** Resources, data curation, supervision, investigation, methodology, project administration, writing–review and editing.

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Note

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References

1. Masala G, Bendinelli B, Assedi M, Occhini D, Zanna I, Sieri S, et al. Up to one-third of breast cancer cases in post-menopausal mediterranean women might be avoided by modifying lifestyle habits: the EPIC Italy study. Breast Cancer Res Treat 2017;161:311–20.
2. Mezzetti M, La Vecchia C, Decarli A, Boyle P, Talamini R, Franceschi S. Population attributable risk for breast cancer: diet, nutrition, and physical exercise. J Natl Cancer Inst 1998;90:389–94.
3. Harvie M, Howell A, Evans DG. Can diet and lifestyle prevent breast cancer: what is the evidence? Am Soc Clin Oncol Educ Book 2015;35:e66–73.
4. Rock CL, Doyle C, Demark-Wahnefried W, Meyerhardt J, Courneya KS, Schwartz AL, et al. Nutrition and physical activity guidelines for cancer survivors. CA Cancer J Clin 2012;62:243–74.
5. Runowicz CD, Leach CR, Henry NL, Henry KS, Mackey HT, Cowens-Alvarado RL, et al. American cancer society/American society of clinical oncology breast cancer survivorship care guideline. J Clin Oncol 2016;34:611–35.
6. Jiralerspong S, Goodwin PJ. Obesity and breast cancer prognosis: evidence, challenges, and opportunities. J Clin Oncol 2016;34:4203–16.

7. Chan DSM, Vieira AR, Aune D, Bandera EV, Greenwood DC, McTiernan A, et al. Body mass index and survival in women with breast cancer-systematic literature review and meta-analysis of 82 follow-up studies. Ann Oncol 2014;25: 1901–14.
8. Beasley JM, Kwan ML, Chen WY, Weltzien EK, Kroenke CH, Lu W, et al. Meeting the physical activity guidelines and survival after breast cancer: findings from the after breast cancer pooling project. Breast Cancer Res Treat 2012;131: 637–43.
9. Spei M-E, Samoli E, Bravi F, La Vecchia C, Bamia C, Benetou V. Physical activity in breast cancer survivors: a systematic review and meta-analysis on overall and breast cancer survival. Breast Edinb Scotl 2019;44:144–52.
10. Lee J. A meta-analysis of the association between physical activity and breast cancer mortality. Cancer Nurs 2019;42:271–85.
11. Lahart IM, Metsios GS, Nevill AM, Carmichael AR. Physical activity, risk of death and recurrence in breast cancer survivors: a systematic review and meta-analysis of epidemiological studies. Acta Oncol Stockh Swed 2015;54: 635–54.
12. Kim EHJ, Willett WC, Fung T, Rosner B, Holmes MD. Diet quality indices and postmenopausal breast cancer survival. Nutr Cancer 2011;63:381–8.
13. George SM, Irwin ML, Smith AW, Neuhouser ML, Reedy J, McTiernan A, et al. Postdiagnosis diet quality, the combination of diet quality and recreational physical activity, and prognosis after early-stage breast cancer. Cancer Causes Control 2011;22:589–98.
14. George SM, Ballard-Barbash R, Shikany JM, Caan BJ, Freudenheim JL, Kroenke CH, et al. Better postdiagnosis diet quality is associated with reduced risk of death among postmenopausal women with invasive breast cancer in the women's health initiative. Cancer Epidemiol Biomarkers Prev 2014;23:575–83.
15. Izano MA, Fung TT, Chiuve SS, Hu FB, Holmes MD. Are diet quality scores after breast cancer diagnosis associated with improved breast cancer survival? Nutr Cancer 2013;65:820–6.
16. McCullough ML, Gapstur SM, Shah R, Campbell PT, Wang Y, Doyle C, et al. Pre- and postdiagnostic diet in relation to mortality among breast cancer survivors in the CPS-II nutrition cohort. Cancer Causes Control 2016;27: 1303–14.
17. Kroenke CH, Fung TT, Hu FB, Holmes MD. Dietary patterns and survival after breast cancer diagnosis. J Clin Oncol 2005;23:9295–303.
18. Kwan ML, Weltzien E, Kushi LH, Castillo A, Slattery ML, Caan BJ. Dietary patterns and breast cancer recurrence and survival among women with early-stage breast cancer. J Clin Oncol 2009;27:919–26.
19. Ergas IJ, Cespedes Feliciano EM, Bradshaw PT, Roh JM, Kwan ML, Cadenhead J, et al. Diet quality and breast cancer recurrence and survival: the pathways study. JNCI Cancer Spectr 2021;5:pkab019.
20. Dal Maso L, Zucchetto A, Talamini R, Serraino D, Stocco CF, Vercelli M, et al. Effect of obesity and other lifestyle factors on mortality in women with breast cancer. Int J Cancer 2008;123:2188–94.
21. Beasley JM, Newcomb PA, Trentham-Dietz A, Hampton JM, Bersch AJ, Passarelli MN, et al. Post-diagnosis dietary factors and survival after invasive breast cancer. Breast Cancer Res Treat 2011;128:229–36.
22. Holmes MD, Stampfer MJ, Colditz GA, Rosner B, Hunter DJ, Willett WC. Dietary factors and the survival of women with breast carcinoma. Cancer 1999; 86:826–35.
23. Jochems SHJ, Van Osch FHM, Bryan RT, Wesselius A, van Schooten FJ, Cheng KK, et al. Impact of dietary patterns and the main food groups on mortality and recurrence in cancer survivors: a systematic review of current epidemiological literature. BMJ Open 2018;8:e014530.
24. Pierre-Victor D, Pinsky PF, McCaskill-Stevens W. Other- and all-cause mortality among women with breast cancer. Cancer Epidemiol 2020;65:101694.
25. World Cancer Research Fund International/American Institute for Cancer Research Continuous Update Project Report: diet, nutrition, physical activity, and breast cancer survivors. [Internet]. 2014. Available from: www.wcrf.org/sites/default/files/Breast-Cancer-Survivors-2014-Report.pdf.
26. Inoue-Choi M, Robien K, Lazovich D. Adherence to the WCRF/AICR guidelines for cancer prevention is associated with lower mortality among older female cancer survivors. Cancer Epidemiol Biomarkers Prev 2013;22:792–802.
27. Pierce JP, Stefanick ML, Flatt SW, Natarajan L, Sternfeld B, Madlensky L, et al. Greater survival after breast cancer in physically active women with high vegetable-fruit intake regardless of obesity. J Clin Oncol 2007;25:2345–51.
28. Cannioto RA, Hutson A, Dighe S, McCann W, McCann SE, Zirpoli GR, et al. Physical activity before, during, and after chemotherapy for high-risk breast cancer: relationships with survival. J Natl Cancer Inst 2021;113:54–63.
29. Borch KB, Braaten T, Lund E, Weiderpass E. Physical activity before and after breast cancer diagnosis and survival—the Norwegian women and cancer cohort study. BMC Cancer 2015;15:967.
30. Irwin ML, McTiernan A, Manson JE, Thomson CA, Sternfeld B, Stefanick ML, et al. Physical activity and survival in postmenopausal women with breast cancer: results from the women's health initiative. Cancer Prev Res 2011;4:522–9.
31. Bertram LAC, Stefanick ML, Saquib N, Natarajan L, Patterson RE, Bardwell W, et al. Physical activity, additional breast cancer events, and mortality among early-stage breast cancer survivors: findings from the WHEL Study. Cancer Causes Control 2011;22:427–35.
32. Irwin ML, Smith AW, McTiernan A, Ballard-Barbash R, Cronin K, Gilliland FD, et al. Influence of Pre- and postdiagnosis physical activity on mortality in breast cancer survivors: the health, eating, activity, and lifestyle study. J Clin Oncol 2008;26:3958–64.
33. Caan BJ, Kwan ML, Shu XO, Pierce JP, Patterson RE, Nechuta SJ, et al. Weight change and survival after breast cancer in the after breast cancer pooling project. Cancer Epidemiol Biomarkers Prev 2012;21:1260–71.
34. Bradshaw PT, Ibrahim JG, Stevens J, Cleveland R, Abrahamson PE, Satia JA, et al. Postdiagnosis change in bodyweight and survival after breast cancer diagnosis. Epidemiol Camb Mass 2012;23:320–7.
35. Kwan ML, Ambrosone CB, Lee MM, Barlow J, Krathwohl SE, Ergas IJ, et al. The pathways study: a prospective study of breast cancer survivorship within kaiser permanente Northern California. Cancer Causes Control 2008;19:1065–76.
36. Staten LK, Taren DL, Howell WH, Tobar M, Poehlman ET, Hill A, et al. Validation of the Arizona activity frequency questionnaire using doubly labeled water. Med Sci Sports Exerc 2001;33:1959–67.
37. Pierce JP, Natarajan L, Caan BJ, Parker BA, Greenberg ER, Flatt SW, 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 2007;298:289–98.
38. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373–83.
39. Gray RJ. A class of K-sample tests for comparing the cumulative incidence of a competing risk. Ann Stat 1988;16:1141–54.
40. Rock CL, Flatt SW, Thomson CA, Stefanick ML, Newman VA, Jones LA, et al. Effects of a high-fiber, low-fat diet intervention on serum concentrations of reproductive steroid hormones in women with a history of breast cancer. J Clin Oncol 2004;22:2379–87.
41. Chlebowski RT, Aiello E, McTiernan A. Weight loss in breast cancer patient management. J Clin Oncol 2002;20:1128–43.
42. McTiernan A, Irwin M, Vongruenigen V. Weight, physical activity, diet, and prognosis in breast and gynecologic cancers. J Clin Oncol 2010;28:4074–80.
43. Lee K, Kruper L, Dieli-Conwright CM, Mortimer JE. The impact of obesity on breast cancer diagnosis and treatment. Curr Oncol Rep 2019;21:41.
44. Sestak I, Dowsett M, Zabaglo L, Lopez-Knowles E, Ferree S, Cowens JW, et al. Factors predicting late recurrence for estrogen receptor-positive breast cancer. J Natl Cancer Inst 2013;105:1504–11.
45. Sestak I, Cuzick J. Markers for the identification of late breast cancer recurrence. Breast Cancer Res BCR 2015;17:10.
46. Mok A, Khaw K-T, Luben R, Wareham N, Brage S. Physical activity trajectories and mortality: population based cohort study. BMJ 2019;365:l2323.
47. Saeidifard F, Medina-Inojosa JR, West CP, Olson TP, Somers VK, Bonikowske AR, et al. The association of resistance training with mortality: a systematic review and meta-analysis. Eur J Prev Cardiol 2019;26:1647–65.
48. Winters-Stone KM, Wood LJ, Stoyles S, Dieckmann NF. The effects of resistance exercise on biomarkers of breast cancer prognosis: a pooled analysis of three randomized trials. Cancer Epidemiol Biomarkers Prev 2018;27:146–53.
49. Ryan AM, Prado CM, Sullivan ES, Power DG, Daly LE. Effects of weight loss and sarcopenia on response to chemotherapy, quality of life, and survival. Nutrition 2019;67–68:110539.
50. Caan BJ, Cespedes Feliciano EM, Prado CM, Alexeeff S, Kroenke CH, Bradshaw P, et al. Association of muscle and adiposity measured by computed tomography with survival in patients with nonmetastatic breast cancer. JAMA Oncol 2018;4: 798–804.
51. Schwingshackl L, Schwedhelm C, Hoffmann G, Lampousi A-M, Knüppel S, Iqbal K, et al. Food groups and risk of all-cause mortality: a systematic review and meta-analysis of prospective studies. Am J Clin Nutr 2017;105:1462–73.
52. Li H, Li J, Shen Y, Wang J, Zhou D. Legume consumption and all-cause and cardiovascular disease mortality. BioMed Res Int 2017;2017:8450618.

53. Barnett GC, Shah M, Redman K, Easton DF, Ponder BAJ, Pharoah PDP. Risk factors for the incidence of breast cancer: do they affect survival from the disease? J Clin Oncol 2008;26:3310–6.
54. Kwan ML, Chen WY, Flatt SW, Weltzien EK, Nechuta SJ, Poole EM, et al. Postdiagnosis alcohol consumption and breast cancer prognosis in the after breast cancer pooling project. Cancer Epidemiol Biomarkers Prev 2013;22:32–41.
55. Nechuta S, Chen WY, Cai H, Poole EM, Kwan ML, Flatt SW, et al. A pooled analysis of post-diagnosis lifestyle factors in association with late estrogen-receptor-positive breast cancer prognosis. Int J Cancer 2016;138:2088–97.
56. Newcomb PA, Kampman E, Trentham-Dietz A, Egan KM, Titus LJ, Baron JA, et al. Alcohol consumption before and after breast cancer diagnosis: associations with survival from breast cancer, cardiovascular disease, and other causes. J Clin Oncol 2013;31:1939–46.
57. Ewertz M, Gillanders S, Meyer L, Zedeler K. Survival of breast cancer patients in relation to factors which affect the risk of developing breast cancer. Int J Cancer 1991;49:526–30.
58. Franceschi S, Dal Maso L, Zucchetto A, Talamini R. Prospective Analysis of Case-control studies on Environmental factors and health (PACE) study group. Alcohol consumption and survival after breast cancer. Cancer Epidemiol Biomarkers Prev 2009;18:1011–2.
59. Ronksley PE, Brien SE, Turner BJ, Mukamal KJ, Ghali WA. Association of alcohol consumption with selected cardiovascular disease outcomes: a systematic review and meta-analysis. BMJ 2011;342:d671.
60. Flatt SW, Thomson CA, Gold EB, Natarajan L, Rock CL, Al-Delaimy WK, et al. Low to moderate alcohol intake is not associated with increased mortality after breast cancer. Cancer Epidemiol Biomarkers Prev 2010;19:681–8.
61. Kwan ML, Kushi LH, Weltzien E, Tam EK, Castillo A, Sweeney C, et al. Alcohol consumption and breast cancer recurrence and survival among women with early-stage breast cancer: the life after cancer epidemiology study. J Clin Oncol 2010;28:4410–6.
62. Maukonen M, Männistö S, Tolonen H. A comparison of measured versus self-reported anthropometrics for assessing obesity in adults: a literature review. Scand J Public Health 2018;46:565–79.
63. Ainsworth BE, Haskell WL, Herrmann SD, Meckes N, Bassett DR, Tudor-Locke C, et al. 2011 Compendium of Physical Activities: a second update of codes and MET values. Med Sci Sports Exerc 2011;43:1575–81.