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Diet quality indices and postmenopausal breast cancer survival

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Abstract

Research on diet in breast cancer survival has been focused on single nutrients or foods, particularly dietary fat, fruits, vegetables, fiber, and alcohol. We hypothesized that diet quality indices decrease the risk of total and non breast cancer related deaths in women diagnosed with breast cancer. We evaluated 4 dietary quality scores: Alternate Healthy Eating Index (AHEI), Diet Quality Index-Revised (DQIR), Recommended Food Score (RFS), and the alternate Mediterranean Diet Score (aMED), among 2729 women from the Nurses' Health Study with invasive stage I–III breast cancer diagnosed between 1978 and 1998 with follow up through 2004. In multivariate adjusted analyses, no association was found between diet quality indices and either total or non breast cancer related deaths. However, a higher aMED score was associated with a lower risk of non-breast cancer death in women with low physical activity; the RR comparing the highest to lowest tertile was 0.39 (95% CI, 0.20 – 0.75, P trend = 0.0004). Our results suggest that a higher quality diet after breast cancer diagnosis does not considerably change the risk of death from breast cancer. However, healthy dietary choices may be important because women are at risk of death from non breast cancer-related causes affected by diet.

Introduction

Limited information exists on the role of diet in breast cancer survival from observational studies. Most research has been restricted to investigating single nutrients or foods, with the focus on dietary fat, fruits and vegetables, and fiber^{1,2,3,4,5,6,7}. Mixed results have been reported between fat intake and breast cancer survival^{2,3,4}. Additionally, there is little consensus on fruit or vegetable intake or micronutrients related to fruits and vegetables, such as beta carotene and vitamin C, and breast cancer survival^{2,6}. No study thus far has found an association of alcohol and survival⁸. Furthermore, the 2 randomized clinical trials investigating dietary intervention and breast cancer survival have shown conflicting results^{9,10}. The Women's Healthy Eating and Living (WHEL) study examining a diet very high in vegetables (5 servings per day), fruits (3 servings per day), fiber (30 grams per day) and low fat (15% to 20% of total calories) found no reduction in breast cancer mortality or recurrence after 7 years of follow up⁹. The Women's Intervention Nutrition Study (WINS) however only examined whether a low fat diet (15% of total calories) affects breast cancer survival and recurrence. After 5 years of follow up, interim results indicate that a diet low in fat demonstrated a significant decrease in breast cancer survival (p=0.03)¹⁰. Interpreting existing data on the relationship between diet and breast cancer survival is complex since measurement of diet has been pre-diagnosis, post-diagnosis, and/or at diagnosis and treatment.

We examined post-diagnosis dietary patterns and breast cancer survival in the Nurses' Health Study, and found that a prudent diet that was high in fruit, vegetables, whole grains, and low-fat dairy products was associated with lower total mortality but not breast cancer specific mortality¹¹. Additionally, a post diagnosis Western diet high in refined grains, processed meat, red meat, high-fat dairy, and desserts was associated with a higher mortality from non-breast cancer related causes. However, the relationship between a priori defined diet quality indices and breast cancer survival has not yet been examined. Diet quality indices are based on recommended dietary guidelines as compared to dietary patterns that are derived from existing eating patterns.

Therefore, in this analysis we examined diet quality indices that are based on recommended dietary guidelines among breast cancer survivors. Diet quality scores evaluated were the Alternate Healthy Eating Index (AHEI), Diet Quality Index-Revised (DQIR), Recommended Food Score (RFS), and the alternate Mediterranean Diet Score (aMed). This study may provide information useful in both public health and clinical settings women treated for breast cancer and their clinicians, search for ways to reduce their risk of recurrence and mortality.

Methods

Study population

Established in 1976, the Nurses' Health Study is a prospective cohort study consisting of 121,701 registered nurses aged 30 to 55 years at baseline. At enrollment, women completed a mailed questionnaire regarding their medical histories and lifestyles. Follow-up questionnaires are mailed every 2 years to update information on participants' health and lifestyle. In 1980, a 61-item food frequency questionnaire was added, and in 1984 and subsequently, the food frequency questionnaire was expanded to include approximately 130 items.

Breast cancer case identification

Diagnoses of breast cancer were ascertained from self-reports on the questionnaire, and confirmed by physician review of medical and pathology records obtained after the participant or next of kin gave permission. Overall, 99% of self-reported invasive breast cancers for which medical records were obtained have been confirmed. Only invasive stage I–III breast cancer cases between 1978 and 1998 were included. Women with stage 4 breast cancer at diagnosis were excluded because their diet is unlikely to affect prognosis. In addition, women with 4 or more positive lymph nodes without a complete negative metastatic workup were also excluded. A complete metastatic workup was comprised of a negative chest x-ray (or chest computed tomographic scan), bone scan, and liver function tests (or liver scan) or documentation from a treating physician that the patient did not have metastatic disease. Furthermore, women with missing disease stage, and any death or recurrence within one year of diagnosis were excluded. Of the 6,367 women diagnosed with breast cancer, we excluded women for the following reasons: cancer before 1978 (470), stage IV at diagnosis or missing stage (620), stage III but lacking a complete metastatic work-up (369), death or recurrence within one year of diagnosis (140), diet assessment during treatment or calculated recurrence date (354), and missing diet (1685). There were 2,729 women remaining for the analysis.

Endpoints

Distant breast cancer recurrence was determined using supplemental 2003 and 2005 questionnaires. We performed a validation of this method by reviewing the medical records of 39 women with stage III disease who had answered the 2003 supplemental questionnaire,

13 of whom had reported distant recurrence and 26 of whom had reported no recurrence. Sensitivity and specificity of self-reported distant recurrence were 92%. However, if a participant did not answer the supplemental questionnaire, but on a routine follow up questionnaire reported a second cancer, that was brain, bone, or liver cancer, it was assumed to have been a breast cancer recurrence. If the second cancer reported was lung cancer, records were obtained to determine whether it was primary lung cancer or metastatic breast cancer. Finally, for all women dying from breast cancer but not reporting recurrence, her recurrence date was defined as occurring 2 years before her death. The number of cases of recurrent breast cancer calculated using this method for participants with follow up questionnaires were similar to the numbers expected given the recurrence rates found in a large (N=5569) trial of early stage breast cancer¹². In addition, only 12% of the recurrences came from the supplemental questionnaire as opposed to the calculation used based on follow up and deaths. Median survival of stage 4 disease is 22 months and since we only ask every 2 years, the majority of women who have recurred have died before they can answer a supplemental questionnaire or are too sick¹³.

Deaths were reported by family members or the postal service, or were identified from a search of the National Death Index¹⁴; the ascertainment of death is estimated to be 98% complete¹⁵. Mortality in this study was defined as breast cancer mortality if cause of death was listed on the death certificate as breast cancer. All-cause mortality was defined as death from any cause. Mortality from causes other than breast cancer was determined by excluding mortality from breast cancer. The primary cause of death was determined by physicians reviewers.

Dietary Assessment

The food frequency questionnaires (FFQ) used to assess diet have been described in detail elsewhere and were completed in 1984, 1986, 1990, 1994, and 1998. Each food was assigned a commonly consumed portion size, such as one apple; women were asked how often they consumed each food on average over the past year, with answers ranging from never consumed to six or more times per day. The validity and reliability of this FFQ in terms of nutrient and food consumption have been documented in detail¹⁶.

The AHEI was adapted from the original Healthy Eating Index based on the 1992 Food Guide Pyramid and the 1995 Dietary Guidelines for Americans¹⁷. The AHEI was adapted to this cohort by McCullough et al and contained 9 components including vegetables (potatoes were removed), fruits, nuts and soy, cereal fiber, ratio of white to red meat, trans fat, polyunsaturated:saturated fat ratio, and alcohol, each of which contributed 0 to 10 points, with 10 indicating that the recommendations were fully met¹⁸. Duration of multivitamin use was scored dichotomously: 7.5 points for ≥ 5 y regular use and 2.5 for all others to avoid overly emphasizing this component. The possible score ranged from 2.5 (worst) to 87.5 (best), and was designed to target food choices associated with reduced risk for chronic diseases.

The DQIR addressed diet diversity and moderation and are based on methods by Haines et al¹⁹. It was adapted for our FFQ by Newby et al and was based on 10 components including grains, vegetables, fruits, total fat, saturated fat, cholesterol, iron, calcium, diet diversity, and added fat and sugar moderation²⁰. Each component was scored from 0 to 10 based on the recommended range of intakes. The maximum possible score was 100. The *Diet Quality Index Revised* (DQI-R) was updated from the original DQI, which is based on recommendations made in *Diet and Health: Implications for Reducing Chronic Disease Risk*. Additional aspects of diet quality included variety and moderation.

The RFS was originally developed by Kant et al and used a 62-item FFQ that included 23 different recommended foods²¹. 1 point was given for each recommended foods that participants ate weekly. The RFS was modified for our FFQ; since our dietary questionnaire were longer, the highest possible RFS score ranged from 49 to 56²² depending on the FFQ year. Recommended foods were from 5 categories: fruits, vegetables, whole grains, low saturated fat proteins, and low fat dairy products, and provides a simple summary of healthy foods listed on the dietary questionnaire.

The aMed Diet Score was adapted from the original Mediterranean score developed by Trichopoulou et al which contained 9 components including vegetables, legumes, fruits and nuts, dairy, cereals, meat and meat products, fish, alcohol, and the monounsaturated:saturated fat ratio^{23, 24}. The aMed was modified to exclude potato products from the vegetable group, separated fruits and nuts into 2 groups, eliminated the dairy group, included whole-grain products only, included only red and processed meats for the meat group. Participants who consumed greater than the median intake of vegetables, legumes, fruits, nuts, whole grains, fish and monounsaturated:saturated fat ratio received 1 point, and otherwise received 0 points for the particular food group. Participants received 1 point for consuming less than the median intake of meat and dairy. 1 point was assigned for alcohol intake between 5 and 15g/d. The maximum possible score for aMed was 9. These modifications were based on dietary patterns and eating behaviors associated with reduced risks of chronic disease.

Statistical Analysis

We considered diet measured at least 12 months after breast cancer diagnosis as baseline diet to allow time of completion from active treatment which may affect diet. Cumulative updating of diet indices after diagnosis was not used because of potential bias of decreased intake or changes in diet due to a recurrence. Furthermore, prediagnosis diet indices and breast cancer mortality, total mortality, non breast cancer related mortality and recurrences were examined using the single most recent diet indices before diagnosis.

Simple models were stratified by time since diagnosis and adjusted for age and energy intake. Multivariate models were adjusted for known risk factors for breast cancer and/or total survival². These include disease stage (I, II, III), treatment (radiation, chemotherapy and tamoxifen in mutually exclusive categories) provided by medical records. Prior to breast cancer diagnosis, age, smoking status (never, past, current), physical activity (5 categories assessed in total MET-hours per week e.g. an average pace walking is 3 METS/hr therefore 9 METS/wk is equivalent to 3 hrs of walking per week), menopausal status and hormone therapy use (13 categories), age at first birth and parity, oral contraceptive use (yes/no), body mass index (BMI – 5 categories), weight change (BMI at time of diet minus BMI just prior to diagnosis – 5 categories), energy intake (quintiles), multivitamin use (yes/no, except for AHEI because it is a component), alcohol (4 categories, only for RFS because alcohol is a component in the other 3 diet quality indices) were obtained as covariates.

Cox proportional hazards models were used to compute failure-time data to evaluate associations of diet quality scores and time to outcome^{25, 26}. In the main analysis, death from breast cancer was the end point, and deaths from any other cause were censored. In additional analyses, death from any cause, death from causes other than breast cancer, and recurrence were the end points. Person-months of follow-up were counted from the date of breast cancer diagnosis until the date of death or age at end of follow-up in June 2004, whichever came first. P values for linear trends were calculated using continuous values. Interaction was assessed by multiplying the two variables and entering them into the relevant models with likelihood ratio tests calculated to determine statistical significance. In addition, we stratified our results by physical activity, overweight (Body Mass Index ≥ 25)

vs normal weight, stage of breast cancer, and estrogen receptor status. For BMI & physical activity, we were interested in how diet might work in various states of insulin sensitivity^{27, 28}. For stratification on stage, we wanted to investigate if diet may influence survival in the continuum of cancer development. For example, if diet improved survival in Stage I disease but not Stages II, III, then diet may likely prevent lymph node metastases. For estrogen receptor status, we anticipated a difference in how diet may affect non hormonal (estrogen receptor negative) breast cancers compared to hormone responsive (estrogen receptor positive) breast cancers

Results

We included 2377 women with invasive stage I–III breast cancer diagnosed between 1978 and 1998, with information on diet. Participants were then followed through 2004 during which 572 women died; 302 women died from breast cancer and 270 women died from causes other than breast cancer. Of the 270 non breast cancer related deaths, 139 deaths were from cardiovascular disease (51%), 33 deaths from respiratory disease, and 21 deaths were from primary lung cancer.

Women who scored higher on diet quality scores were less likely to be smokers, more likely to use multivitamins, currently use postmenopausal hormones, exercise more and have higher energy intakes (Table 1). The 4 diet quality indices were strongly correlated with each other (spearman correlation coefficient r ranging from 0.50 to 0.76), with the strongest correlation between RHEI and aMED, ($r = 0.76$).

For prediagnosis diet, diet quality indices based on a single dietary questionnaire prior to breast cancer diagnosis were not associated with total mortality, breast cancer mortality, distant recurrences or non breast cancer mortality (data not shown).

For post diagnosis diet, in simple and multivariate adjusted analyses, diet quality scores were not associated with all cause mortality (Table 2), or non breast cancer related mortality (Table 3). Smoking was the main confounder in both all cause mortality and non breast cancer mortality. Diet quality scores as measured by RFS were associated with a borderline increase in breast cancer mortality and RFS; the RR comparing the highest to lowest quintiles of RFS score was 1.54 (95% CI, 0.95 – 2.47, P trend = 0.02) (Table 4). In addition, higher RFS scores were associated with an increase in distant recurrences; the RR comparing the highest to lowest quintiles of RFS score was 1.45 (95% CI, 0.94 – 2.23, P trend = 0.001). However, investigation of each component of RFS did not indicate any significant relationships with either breast cancer mortality or recurrences (data not shown).

The association between diet quality indices and non-breast cancer mortality appeared to differ by physical activity level. We defined high physical activity as more than 9 METs/wk and low physical activity as equal to or less than 9 METs/wk. In women with low physical activity, DQIR and aMED were associated with a decrease in non breast cancer related mortality after multivariate adjustment; the RR comparing the highest to lowest tertiles was 0.52 (95% CI, 0.28 – 0.96, P trend = 0.05) and 0.39 (95% CI, 0.20 – 0.75, P trend = 0.004) respectively (Table 5). P -value for the interaction between AHEI and aMED, and physical activity was 0.02. In women with low physical activity, we also found a decrease in total mortality in AHEI and aMED; the RR comparing the highest to lowest tertiles was 0.71 (95% CI, 0.46 – 1.08, P trend = 0.02) and 0.63 (95% CI, 0.41 – 0.97, P trend = 0.02) respectively.

Moreover, no difference was observed between diet quality indices and breast cancer mortality or recurrence comparing stage 1 and stage 2/3 breast cancer. Furthermore, association did not differ between normal weight and overweight subjects and their

relationship to diet quality indices and breast cancer mortality, recurrence, total mortality or non breast cancer mortality. We were unable to investigate difference by estrogen receptor status and breast cancer mortality due to the small number of estrogen receptor negative breast cancers in our analysis.

Discussion

We found a borderline positive association between RFS and increased breast cancer mortality of unclear significance. This association is contrary to our hypothesis and to all other previous studies that a higher quality diet would have no effect on breast cancer survival. It is possible that this association is due to chance. Our results are largely consistent with a previous study between dietary patterns and breast cancer survival in the Nurses Health Study¹¹ and suggest that overall diet does not affect breast cancer survival. The previous study with dietary patterns however did indicate a lower non breast cancer mortality which was not demonstrated in this analysis. This may be due to the variation in composition of foods included using factor analysis to create a western vs prudent pattern in the previous study which is data driven and allows for inclusion of all possible dietary exposures within a population. Diet quality indices on the other hand have been previously standardized and are based on *a priori* criteria for optimal diets for chronic diseases including heart disease and diabetes, however, may not reflect the existing eating behaviors²⁹. Furthermore, a recent review of lifestyle changes in breast cancer survivors concluded that data suggest limited evidence to support the benefits of a high fruit and vegetable intake and low fat intake on breast cancer survival³⁰.

In contrast to our study, recent results from the Women's Intervention Nutrition Study (WINS) randomized trial suggested that a lower fat diet improves relapse free survival in breast cancer patients⁹. However, the intervention group in the WIN study lost a significant amount of weight (6lbs), and since lower BMI and less weight gain predicts better breast cancer survival^{28, 31, 32}, the potential increase in overall survival in women in the WINS may be confounded by weight loss during the intervention.

In addition, we found a lack of association between diet quality scores and total mortality or non breast cancer mortality. However, higher diet quality indices in DQIR and aMed were beneficial for a decreased risk of non breast cancer related mortality in women with low physical activity. This is likely due to the large number of non breast cancer related deaths attributed by cardiovascular and respiratory illnesses. Other studies in the US and Europe indicate that an adherence to the dietary guidelines, even those aimed at lowering cancer risk were more strongly related to coronary heart disease mortality than to cancer mortality²². In our study almost all of the components of the DQIR and aMED diet quality score have been associated with a lower risk of coronary heart disease^{18, 33}. However, only about half have been associated with reduced cancer incidence and even less with cancer mortality^{7, 8, 34}. This may explain why the DQIR and aMED score was associated with non breast cancer specific mortality, which included mortality from cardiovascular diseases. In addition, a higher Mediterranean diet quality has also been associated with a significant decrease in cardiovascular mortality in a Greek population³⁵. Furthermore, AHEI also excludes dairy from the scoring and therefore if dairy significantly impacted the results seen with aMED, we would have likely seen similar results with AHEI. Additionally, a recent WHEL study observed an increase in breast cancer survival with high physical activity and high fruits and vegetable intake³⁶. However, we did not observe any effect of physical activity between diet quality indices and breast cancer related deaths.

The strengths of this study include the ability to control for many possible confounders as well as the large sample size. In addition, we were able to study prediagnosis diet quality

indices as well as postdiagnosis diet quality indices. We limited our study to women with confirmed stage 1 through 3 breast cancer, and excluded over half the women initial analysis of breast cancer diagnosis. This was important because women who were undergoing treatment during the collection of the FFQ, and women in late or terminal stages of their cancer were likely to have diets that do not impact survival. In addition, women missing dietary assessment, and those excluded for other reasons, were similar to women included in the analysis in terms of age at diagnosis, BMI, and treatment (data not shown). Limitations include self reported recurrences which were not confirmed by record review. Additionally, it is possible that despite physician's review of medical records, the cause of death may have been misclassified. However, given our findings with non breast cancer specific mortality, it is unlikely that a great deal of misclassification occurred.

In conclusion, our results suggest that dietary quality after breast cancer diagnosis does not appreciably change the risk of total death or death from breast cancer. However, healthy dietary choices may still be important for women after breast cancer, particularly inactive women, because they are still at risk of death from nonbreast cancer-related causes, such as cardiovascular diseases, which are affected by dietary choices.

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Table 1

Age-standardized covariates according to quintiles of diet quality index scores after breast cancer diagnosis.

	Quintiles of diet score														
	AHEI					DQIR					RFS				
	Q1	Q3	Q5	Q1	Q5	Q1	Q3	Q5	Q1	Q5	Q1	Q3	Q5	Q1	Q5
BMI, mean (kg/m ²)	26.7	26.2	24.6	26.5	25.7	25.7	25.7	25.0	25.7	25.8	25.8	25.8	25.8	26.0	25.9
Current smoker (%)	20.5	11.4	7.4	21.6	13.2	13.2	13.2	6.1	20.3	11.4	7.5	22.3	11.7	7.7	7.7
Physical activity (METs/wk)	10.3	14.8	20.6	9.90	15.0	15.0	15.0	18.3	10.5	14.0	20.7	10.6	14.9	19.6	19.6
Calories, mean (kcal)	1447	1666	1985	1499	1700	1700	1700	1881	1353	1697	2040	1424	1687	2031	2031
Alcohol (g)	5.0	5.2	6.7	5.9	6.8	6.8	6.8	4.7	6.5	5.9	5.2	6.1	5.2	6.7	6.7
Multivitamin use (%)	35.0	45.9	70.8	44.9	49.8	49.8	49.8	60.6	47.9	55.2	59.2	47.0	53.5	59.1	59.1
Oral contraceptives, ever (%)	42.9	41.3	48.8	44.4	43.2	43.2	43.2	43.7	44.1	47.1	43.9	42.8	41.5	44.5	44.5
Postmenopausal hormone therapy, current use (%)	2.9	3.2	4.0	2.9	2.3	2.3	2.3	3.1	2.1	3.1	2.9	2.5	3.0	4.1	4.1
Chemotherapy (%)	37.8	42.9	32.9	40.0	35.2	35.2	35.2	37.1	35.9	37.7	36.7	36.0	40.0	36.1	36.1
Radiation (%)	39.8	48.8	45.2	46.0	46.8	46.8	46.8	42.4	41.6	47.7	39.6	39.5	45.0	45.0	45.0
Tamoxifen (%)	65.9	59.2	65.2	63.5	62.7	62.7	62.7	62.3	65.9	56.7	67.2	64.1	65.3	60.2	60.2
Cancer Stage (%)															
1	57.1	57.9	56.7	58.0	56.9	56.9	56.9	57.0	60.6	54.9	56.3	57.1	56.1	56.8	56.8
2	33.8	31.6	36.4	30.9	34.7	34.7	34.7	34.1	32.0	37.3	34.2	35.0	34.0	33.9	33.9
3	9.1	10.5	6.9	11.1	8.4	8.4	8.4	8.9	7.4	7.8	9.5	7.9	9.9	9.3	9.3

Table 2

Relative risks of total deaths (Total=572) by quintiles of diet quality scores after breast cancer diagnosis (N=2729).

Score	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	P Trend
AHEI Deaths, n	111	100	110	135	116	
TSD and Age adjusted*	1.00 (ref)	0.78 (0.59, 1.04)	0.77 (0.57, 1.02)	0.85 (0.65, 1.13)	0.67 (0.50, 0.89)	0.008
Multivariate**	1.00 (ref)	0.82 (0.61, 1.10)	0.83 (0.62, 1.12)	0.98 (0.73, 1.32)	0.85 (0.63, 1.17)	0.46
DQR Deaths, n	103	88	105	133	143	
TSD and Age adjusted*	1.00 (ref)	0.69 (0.51, 0.94)	0.59 (0.44, 0.80)	0.77 (0.58, 1.02)	0.63 (0.47, 0.83)	0.004
Multivariate**	1.00 (ref)	0.78 (0.57, 1.07)	0.64 (0.47, 0.88)	0.89 (0.66, 1.20)	0.78 (0.58, 1.07)	0.18
RFS Deaths, n	111	89	117	137	118	
TSD and Age adjusted*	1.00 (ref)	0.79 (0.58, 1.07)	0.85 (0.64, 1.14)	0.93 (0.70, 1.24)	0.87 (0.64, 1.18)	0.38
Multivariate**	1.00 (ref)	0.83 (0.60, 1.14)	0.92 (0.68, 1.24)	1.05 (0.78, 1.42)	1.03 (0.74, 1.42)	0.85
aMed Deaths, n	117	99	109	124	123	
TSD and Age adjusted*	1.00 (ref)	0.88 (0.66, 1.18)	0.64 (0.48, 0.85)	0.81 (0.61, 1.07)	0.74 (0.55, 0.99)	0.02
Multivariate**	1.00 (ref)	0.86 (0.64, 1.16)	0.67 (0.50, 0.91)	0.86 (0.65, 1.15)	0.87 (0.64, 1.17)	0.34

* Time since diagnosis and age adjusted

** Multivariate models adjusted for: time since diagnosis, age (continuous), alcohol intake in grams/day (0, 0.1–1.0, 1.1–6.3, >6.3, missing), only for RFS because alcohol is a component in the other 3 diet quality indices), energy (quintiles), multivitamin use (yes, no, missing, except for AHEI because it is a component), body mass index in kg/m² (<22, 22–24.9, 25–29.9, 30–34.9, ≥35, missing), body mass index (BMI), weight change (BMI at time of diet minus BMI just prior to diagnosis), oral contraceptive use (yes/no), age, smoking status (never, past, current), physical activity in METs (0, 0.1–3.1, 3.2–9.5, 9.6–21, >21), stage (I, II, III), categories of treatment (chemotherapy=no/radiation=no/tamoxifen=no, chemotherapy=no/radiation=yes or no/tamoxifen=yes, chemotherapy=yes/radiation=no/tamoxifen=yes, chemotherapy=yes/radiation=yes/tamoxifen=no, chemotherapy=yes/radiation=yes/tamoxifen=yes, chemotherapy=yes/radiation=yes/tamoxifen=yes), age at first birth and parity (nulliparous, age <25 and 1 birth, age ≥25 and 2 births, age ≥30 and 1 birth, age ≥30 and 2 births, age ≥30 and ≥3 births, missing), menopausal status and postmenopausal hormone use (premenopausal, postmenopausal and never use, postmenopausal and past use, postmenopausal and current use, missing).

Table 3

Relative risks of non breast cancer related deaths (Total=270) by quintiles of diet quality scores after breast cancer diagnosis (N=2729).

Score	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	P Trend
AHEI Deaths, n	68	49	49	61	43	
TSD and Age adjusted*	1.00 (ref)	0.57 (0.38, 0.85)	0.60 (0.40, 0.89)	0.68 (0.47, 1.01)	0.40 (0.26, 0.61)	0.0005
Multivariate**	1.00 (ref)	0.64 (0.42, 0.98)	0.76 (0.49, 1.19)	0.95 (0.62, 1.45)	0.52 (0.32, 0.83)	0.09
DQIR Deaths, n	52	51	50	55	62	
TSD and Age adjusted*	1.00 (ref)	0.89 (0.58, 1.36)	0.58 (0.38, 0.90)	0.67 (0.44, 1.02)	0.55 (0.37, 0.84)	0.0003
Multivariate**	1.00 (ref)	1.02 (0.65, 1.61)	0.71 (0.45, 1.13)	0.87 (0.55, 1.37)	0.85 (0.54, 1.34)	0.24
RFS Deaths, n	68	46	60	47	49	
TSD and Age adjusted*	1.00 (ref)	0.67 (0.44, 1.02)	0.66 (0.45, 0.98)	0.51 (0.33, 0.78)	0.56 (0.36, 0.86)	0.001
Multivariate**	1.00 (ref)	0.78 (0.50, 1.22)	0.89 (0.58, 1.36)	0.65 (0.41, 1.03)	0.86 (0.54, 1.37)	0.31
aMed Deaths, n	66	51	53	51	49	
TSD and Age adjusted*	1.00 (ref)	0.84 (0.57, 1.26)	0.61 (0.41, 0.91)	0.57 (0.38, 0.86)	0.58 (0.38, 0.88)	0.0008
Multivariate**	1.00 (ref)	0.89 (0.59, 1.36)	0.75 (0.49, 1.14)	0.69 (0.45, 1.07)	0.80 (0.50, 1.26)	0.10

* Time since diagnosis and age adjusted

** Adjusted for the same factors in Table 2

Table 4

Relative risks of breast cancer related deaths (Total=302) by quintiles of diet quality scores after breast cancer diagnosis (N=2729).

Score	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	P Trend
AHEI Deaths, n	43	51	61	74	73	
TSD and Age adjusted*	1.00 (ref)	1.07 (0.70, 1.64)	1.10 (0.73, 1.67)	1.17 (0.78, 1.76)	1.23 (0.82, 1.86)	0.55
Multivariate**	1.00 (ref)	1.06 (0.68, 1.66)	1.12 (0.72, 1.74)	1.28 (0.83, 1.98)	1.53 (0.98, 2.39)	0.08
DQIR Deaths, n	51	37	55	78	81	
TSD and Age adjusted*	1.00 (ref)	0.61 (0.39, 0.95)	0.67 (0.44, 1.02)	0.91 (0.62, 1.34)	0.79 (0.53, 1.16)	0.96
Multivariate**	1.00 (ref)	0.60 (0.37, 0.97)	0.62 (0.40, 0.97)	0.88 (0.58, 1.33)	0.81 (0.53, 1.24)	0.98
RFS Deaths, n	43	43	57	90	69	
TSD and Age adjusted*	1.00 (ref)	1.01 (0.64, 1.59)	1.22 (0.80, 1.87)	1.79 (1.19, 2.69)	1.53 (1.00, 2.35)	0.01
Multivariate**	1.00 (ref)	0.93 (0.57, 1.51)	1.20 (0.77, 1.88)	1.69 (1.08, 2.63)	1.54 (0.95, 2.47)	0.02
aMed Deaths, n	51	48	56	73	74	
TSD and Age adjusted*	1.00 (ref)	1.01 (0.67, 1.53)	0.79 (0.52, 1.18)	1.24 (0.84, 1.83)	1.11 (0.74, 1.66)	0.34
Multivariate**	1.00 (ref)	0.97 (0.63, 1.50)	0.72 (0.47, 1.10)	1.25 (0.83, 1.89)	1.15 (0.74, 1.77)	0.21

* Time since diagnosis and age adjusted

** Adjusted for the same factors in Table 2

Relative risks by tertiles of diet quality scores after breast cancer diagnosis (N=2729) for non breast cancer related deaths stratified by physical activity.

Table 5

Score	Low Physical Activity ≤9 METs/wk				High Physical Activity >9 METs/wk			
	Tertile 1	Tertile 2	Tertile 3	P Trend	Tertile 1	Tertile 2	Tertile 3	P Trend
	Total = 129				Total = 94			
AHEI Deaths, n	64	33	32		20	34	40	
Multivariate *	1.00 (ref)	0.77 (0.44, 1.36)	0.65 (0.35, 1.23)	0.06	1.00 (ref)	1.03 (0.48, 2.19)	0.89 (0.43, 1.84)	0.32
DQIR Deaths, n	50	45	34		17	24	53	
Multivariate *	1.00 (ref)	1.04 (0.60, 1.80)	0.52 (0.28, 0.96)	0.05	1.00 (ref)	0.60 (0.27, 1.36)	1.11 (0.52, 2.39)	0.96
RFS Deaths, n	59	39	31		17	41	36	
Multivariate *	1.00 (ref)	1.06 (0.61, 1.83)	1.08 (0.58, 2.00)	0.32	1.00 (ref)	1.02 (0.47, 2.19)	0.75 (0.34, 1.67)	0.47
aMed Deaths, n	68	28	33		24	27	43	
Multivariate *	1.00 (ref)	0.64 (0.35, 1.15)	0.39 (0.20, 0.75)	0.004	1.00 (ref)	1.29(0.64, 2.58)	0.73 (0.36, 1.46)	0.30

* Adjusted for the same factors in Table 2 except physical activity was excluded