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Grilled, Barbecued, and Smoked Meat Intake and Survival Following Breast Cancer

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Abstract

Background: Grilled, barbecued, and smoked meat intake, a prevalent dietary source of polycyclic aromatic hydrocarbon (PAH) carcinogens, may increase the risk of incident breast cancer. However, no studies have examined whether intake of this PAH source influences survival after breast cancer.

Methods: We interviewed a population-based cohort of 1508 women diagnosed with first primary invasive or in situ breast cancer in 1996 and 1997 at baseline and again approximately five years later to assess grilled/barbecued and smoked meat intake. After a median of 17.6 years of follow-up, 597 deaths, of which 237 were breast cancer related, were identified. Multivariable Cox regression was used to estimate adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) for mortality as related to prediagnosis intake, comparing high (above the median) to low intake, as well as postdiagnosis changes in intake, comparing every combination of pre-/postdiagnosis intake to low pre-/postdiagnosis intake. All statistical tests were two-sided.

Results: High prediagnosis grilled/barbecued and smoked meat intake was associated with increased risk of all-cause mortality (HR = 1.23, 95% CI = 1.03 to 1.46). Other associations were noted, but estimates were not statistically significant. These include high prediagnosis smoked beef/lamb/pork intake and increased all-cause (HR = 1.17, 95% CI = 0.99 to 1.38, P_{trend} = .10) and breast cancer–specific (HR = 1.23, 95% CI = 0.95 to 1.60, P_{trend} = .09) mortality. Also, among women with continued high grilled/barbecued and smoked meat intake after diagnosis, all-cause mortality risk was elevated 31% (HR = 1.31, 95% CI = 0.96 to 1.78). Further, breast cancer–specific mortality was decreased among women with any pre- and postdiagnosis intake of smoked poultry/fish (HR = 0.55, 95% CI = 0.31 to 0.97).

Conclusion: High intake of grilled/barbecued and smoked meat may increase mortality after breast cancer.

In the United States, there are over 3.1 million women who are survivors of breast cancer; these women represent approximately 40% of female cancer survivors (1). After a diagnosis of breast cancer, survivors are faced with making behavioral and dietary choices as they attempt to improve their long-term prognoses. Dietary changes are one area in which breast cancer survivors may choose to make more healthful changes. To aid in this decision-making, recommendations and guidelines are available for cancer survivors in general (2) and, more recently, for breast cancer survivors specifically (3). For example, the American Cancer Society, together with the American Society of Clinical Oncology, recently released their breast cancer

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survivorship care guidelines, which recommend that survivors be counseled to "achieve a dietary pattern that is high in vegetables, fruits, whole grains, and legumes, and limit alcohol intake to no more than one drink per day" (3). These recommendations are based on limited, but suggestive, evidence of improved survival among women with such diets (4,5). No recommendations exist for breast cancer survivors that specifically address intake of high-temperature cooked meat, including intake of grilled/barbecued and smoked meat, although, in relation to primary prevention of breast cancer incidence, it is recommended (6) that women limit intake of processed meats and high-temperature cooked meat because of the formation of polycyclic aromatic hydrocarbons (PAHs) and other carcinogenic chemicals during the cooking process (7).

Grilled/barbecued and smoked meat intake is a highly prevalent source of PAHs among US women (8) and has been associated with breast cancer incidence (9), but whether intake is related to survival after breast cancer is unknown. This study examined whether grilled, barbecued, and smoked meat intake prior to breast cancer diagnosis, as well as postdiagnosis changes in intake, is associated with long-term all-cause and breast cancer–specific mortality among a population-based sample of women with first primary breast cancer.

Methods

Study Population

Adult female residents of Nassau and Suffolk counties on Long Island, New York, with a first diagnosis of in situ or invasive breast cancer between August 1, 1996, and July 31, 1997, were identified for inclusion in the Long Island Breast Cancer Study Project (LIBCSP) (10). Identification of patients was done via active daily or weekly contact with local hospitals and confirmed by physicians and medical records. After providing written informed consent, the cohort of 1508 women with breast cancer was interviewed at home by trained interviewers via structured questionnaire at baseline, on average within three months of breast cancer diagnosis.

Approximately five years after the initial diagnosis of breast cancer, the 1414 women who at baseline consented to continued contact were recontacted for the follow-up interview. Of these, 143 refused, no proxy was identified for 96 women who were not alive at follow-up, and 55 could not be located, resulting in 1120 women providing consent and 1033 women completing the follow-up questionnaire (11). The follow-up interview was conducted over the telephone by trained interviewers using a structured questionnaire that assessed information similar to that obtained at baseline, but regarding the time period since the initial diagnosis of breast cancer. Institutional review board approval was obtained from all participating institutions.

Outcome Assessment

Date of death and cause of death were determined using the National Death Index (12). Indicators for death from any cause and those associated with breast cancer were created with breast cancer deaths identified using International Statistical Classification of Diseases codes 174.9 and C-50.9 listed on the death certificate. Follow-up for mortality occurred from the date of diagnosis in 1996 or 1997 until December 31, 2014. Among the 1508 case women, 597 deaths were identified, 237 (39.7%) of which were related to breast cancer, after a median duration of follow-up was 17.6 years (range = 0.2–18.4 years).

Grilled, Barbecued, and Smoked Meat Intake Assessment

As part of the main baseline questionnaire, participants were asked about their intake (number of times per week, month, or year) of four types of grilled/barbecued and smoked meats: 1) grilled/barbecued beef, lamb, and pork, 2) smoked beef, lamb, and pork, such as bacon or ham, 3) grilled/barbecued poultry and fish, and 4) smoked poultry and fish, such as smoked turkey or lox. The women were asked about their intake in each decade of life (<20 years, 20–29 years, 30–39 years, 40–49 years, 50–59 years, ≥60 years) and were asked to specify the seasons in which the foods were most frequently consumed (8,13). At baseline, intake during the decade prior to breast cancer diagnosis was used to represent the average intake before diagnosis; we also examined whether lifetime intake of grilled/barbecued and smoked meat was associated with mortality. At the five-year follow-up, participants responded to the same questions, which asked about the time period since the baseline questionnaire.

Responses given as per week or per month were first multiplied by 52 or by 12, respectively, and then multiplied by the proportion of the year that the foods were consumed (ie, 25% if they were consumed during one season, 50% if they were consumed during two seasons, etc.) to obtain measures of intake in number of times per year. The continuous measures were dichotomized at the median for each of the four meat types: grilled/barbecued beef/lamb/pork (low = 0–10 vs high = 11+ times/year prediagnosis; low = 0–8 vs high = 9+ times/year postdiagnosis), grilled/barbecued poultry/fish (low = 0–9 vs high = 10+ times/year prediagnosis; low = 0–6 vs high = 7+ times/year postdiagnosis), smoked barbecued beef/lamb/pork (low = 0–4 vs high = 5+ times/year prediagnosis and postdiagnosis), and smoked poultry/fish (none = 0 vs any intake = 1+ times/year prediagnosis and postdiagnosis), separately. Intake of the four meat types were also summed to create an overall measure of intake of grilled/barbecued and smoked meat (times/year), which was dichotomized at the median (low = 0–43 vs high = 44+ times/year prediagnosis; low = 0–35 vs high = 36+ times/year postdiagnosis). Lifetime intake of each of the four types of meat was dichotomized at the median as low = 0–4724 vs high = 4725+ times throughout the lifetime. In the analysis of postdiagnosis intake of grilled/barbecued and smoked meat, every combination of prediagnosis/postdiagnosis annual intake was examined (ie, low/low intake, low/high intake, etc.).

Covariate Assessment

Most covariates were assessed by interviewer-administered questionnaire. Potential confounders included age at diagnosis (years), menopausal status (premenopausal vs postmenopausal), annual household income (<$15 000–$24 999, $25 000–$49 999, and ≥$50 000), education (<high school/high school graduate, some college/college graduate, and postcollege), marital status (married or living as married vs not married, divorced, or widowed), body mass index (continuous, kg/m^2), at-diagnosis physical activity (never, former, and current physical activity of least one hour per week for three months or more), at-diagnosis intake of alcoholic beverages such as beer, wine, or liquor (never, former, and current intake at least once a month for six months or more), at-diagnosis consumption of energy (kcal/day), at-diagnosis fruit and vegetable intake (servings/day), and at-diagnosis multivitamin supplement use (ever/never).

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Other covariates, including estrogen receptor status and nodal involvement, were determined by medical record review, and tumor size was obtained from the New York State Cancer Registry. At baseline, women were interviewed after surgery but before initiation of most other components of the first course of treatment for the first primary breast cancer. Therefore, treatment received (radiation therapy, chemotherapy, or hormone therapy) was assessed by self-report at the follow-up questionnaire, which showed high agreement with medical record data (kappas ranged from 0.92 to 0.97) (14) but was more complete.

Statistical Analysis

Age-adjusted and multivariable-adjusted Cox proportional hazards models were fit for each of the four types of grilled and smoked meat intake, separately, and for the total measure of annual intake and for all-cause and breast cancer–specific mortality. The proportional hazards assumption was verified using exposure interactions with time. For analyses using breast cancer–specific mortality as the outcome, non–breast cancer deaths were censored at time of death. We estimated hazard ratios (HRs) and 95% confidence intervals (CIs) for the associations between prediagnosis, lifetime and average annual intake, as well as postdiagnosis changes in grilled, barbecued, and/or smoked meat intake and all-cause and breast cancer–specific mortality. Tests for trend used continuous measures of grilled/barbecued and smoked intake in the proportional hazards models. Survival time began at the date of breast cancer diagnosis in the analyses of prediagnosis grilled/barbecued and smoked meat intake and at the date of the follow-up interview for the corresponding analyses on postdiagnosis intake. Survival time for all analyses ended at the date of death or, if alive, date of censoring. We also restricted the analysis to women with invasive cancer only, but results did not differ substantially from those among all women, so only the latter is shown. All analyses were done using the Cox Regression function in IBM SPSS Statistics Version 22.0 (IBM Corp., Armonk, NY).

In the analyses of postdiagnosis changes in grilled/barbecued, and smoked meat intake and survival, we employed multiple imputation to account for the missing exposure data after excluding 169 women who died within five years of diagnosis; 377 (28.2%) participants were lost to follow-up and thus were missing data on intake of grilled/barbecued and smoked meat. Missing values were imputed using SPSS, which employs a fully conditional specification algorithm, an iterative Markov Chain Monte Carlo procedure that sequentially imputes missing values starting from the first variable with missing values (15). SPSS applies linear regression to continuous scale variables, and logistic or multinomial logistic regression to categorical variables. We used 25 imputations with 1000 iterations and included demographics (age at diagnosis, menopausal status, income, education, marital status, BMI, physical activity, and alcohol intake, smoking status), prediagnosis and postdiagnosis grilled and smoked meat intake, disease characteristics (stage, tumor size, nodal involvement estrogen receptor status), treatment (radiation therapy, chemotherapy, and hormone therapy), and the outcome (the event indicator and the Nelson-Aalen estimator of the cumulative hazard) (16). As a sensitivity analysis, we also conducted a complete-case analysis, where the missing exposure data are ignored. This alternative approach is commonly employed in follow-up studies with multiple exposure assessments over time. However, the imputation approach is designed to reduce the bias associated with the complete case analysis (17). In analyses that used follow-up data, survival time began at the date of completion of the follow-up questionnaire to the date of death or December 31, 2014, if alive.

All statistical tests were two-sided, and a P value of less than .05 was considered statistically significant.

Results

Participant demographic characteristics, as well as disease, tumor, and treatment characteristics, are presented in Table 1. Women with high intake of total grilled/barbecued and smoked meat were younger at diagnosis (56.7 years vs 60.9 years), and a higher proportion had an annual income of $50 000 or more (57.0% vs 40.4%) compared with women with low intake. Women with high intake were also more likely to be married (77.2% vs 60.4%). A higher proportion of women with high intake reported being current alcohol drinkers (51.9% vs 43.2%). Disease and treatment characteristics were similar across total intake of grilled/barbecued and smoked meat, except for chemotherapy; receipt of chemotherapy was reported by 45.8% of women with high intake compared with 36.7% of women with low intake.

Prediagnosis Intake of Grilled/Barbecued and Smoked Meat

Table 2 shows the associations between prediagnosis annual intake of grilled/barbecued and smoked meat and mortality. Compared with low intake, high intake of grilled/barbecued and smoked meat prior to diagnosis was associated with a 23% increased hazard (HR = 1.23, 95% CI = 1.03 to 1.46, P_{trend} = .02) of all-cause mortality. High vs low intake of smoked beef/lamb/pork intake was associated with a 17% increased hazard (HR = 1.17, 95% CI = 0.99 to 1.38, P_{trend} = .10) of all-cause and a 23% increased hazard (HR = 1.23, 95% CI = 0.95 to 1.60, P_{trend} = .09) of breast cancer–specific mortality, but the confidence intervals include the null value. Lifetime grilled/barbecued and smoked meat intake and prediagnosis annual intake of grilled/barbecued beef/lamb/pork and poultry/fish were not associated with mortality (Table 2).

Postdiagnosis Changes in Intake Grilled, Barbecued, and Smoked Meat

Table 3 shows the associations between postdiagnosis changes in annual intake of grilled/barbecued and smoked meat and mortality after imputation of missing covariates. Compared with women with low prediagnosis and low postdiagnosis intake of grilled/barbecued and smoked meat, continued high intake was associated with a 31% increased hazard (HR = 1.31, 95% CI = 0.96 to 1.78) of all-cause mortality. The increase in risk of death from any cause was similar in magnitude (HR = 1.28, 95% CI = 0.97 to 1.68) among women who reported high prediagnosis and low postdiagnosis intake of grilled/barbecued and smoked meat. Smoked beef/lamb/pork intake was positively associated with all-cause (HR = 1.36, 95% CI = 1.01 to 1.82) and breast cancer–specific mortality (HR = 1.71, 95% CI = 1.00 to 2.92) among women who had high intake at prediagnosis and low postdiagnosis intake, relative to low pre- and low postdiagnosis intake, but not among women with continued high postdiagnosis intake. Additionally, women who reported any pre- and postdiagnosis intake of smoked poultry and fish had a reduced risk of breast cancer mortality (HR = 0.55, 95% CI = 0.31

Table 1. Distribution of participant characteristics at diagnosis among the LIBCSP women diagnosed with first primary breast cancer in 1996 and 1997, overall and by grilled, barbecued, and smoked meat intake (n = 1508)*

		Prediagnosis grilled, barbecued, and smoked meat intake†	
	Total (n = 1508)	Low (n = 732)	High (n = 726)
At-diagnosis characteristic	No. (%)	No. (%)	No. (%)
Age at diagnosis, y			
<50	407 (27.0)	160 (21.9)	233 (32.1)
50–64	582 (38.6)	271(37.0)	295 (40.6)
≥65	519 (34.4)	301 (41.1)	198 (27.3)
Mean (SD)	58.8 (12.7)	60.9 (12.7)	56.7 (12.3)
Menopausal status			
Premenopausal	472 (31.9)	180 (25.1)	276 (38.9)
Postmenopausal	1006 (68.1)	538 (74.9)	434 (61.1)
Income			
<$15 000–$24 999	286 (19.0)	165 (22.7)	110 (15.2)
$25 000–$49 999	488 (32.4)	269 (36.9)	202 (27.8)
≥$50 000	730 (48.5)	294 (40.4)	414 (57.0)
Education			
<HS/HS graduate	721 (48.0)	355 (48.8)	338 (46.6)
Some college/college graduate	551 (36.7)	271 (37.3)	264 (36.4)
Postcollege	230 (15.3)	101 (13.9)	123 (17.0)
Marital atatus			
Married or living as married	1029 (68.3)	442 (60.4)	560 (77.2)
Not married	478 (31.7)	290 (39.6)	165 (22.8)
BMI at diagnosis, kg/m^2			
<25.0	683 (45.8)	343 (47.4)	321 (44.6)
25–29.9	476 (31.9)	237 (32.8)	225 (31.3)
≥30.0	332 (22.3)	143 (19.8)	174 (24.1)
Mean (SD)	26.6 (5.7)	26.3 (5.5)	26.8 (5.8)
Physical activity‡			
Never	334 (22.5)	176 (24.4)	140 (19.6)
Former	253 (17.0)	122 (16.9)	124 (17.3)
Current	900 (60.5)	424 (58.7)	452 (63.1)
Alcohol intake§			
Never	588 (39.0)	297 (40.6)	263 (36.3)
Former	212 (14.1)	119 (16.3)	86 (11.9)
Current	707 (46.9)	316 (43.2)	376 (51.9)
Stage			
Invasive	1273 (84.4)	608 (83.1)	622 (85.7)
In situ	235 (15.6)	124 (16.9)	104 (14.3)
Nodal involvement‖	622 (74.5)	286 (73.0)	320 (76.9)
Tumor size, cm‖			
≤2.0	622 (75.5)	299 (76.9)	302 (73.5)
>2.0	202 (24.5)	90 (23.1)	109 (26.5)
Mean (SD)	1.7 (1.6)	1.7 (1.7)	1.7 (1.5)
Estrogen receptor status‖			
Negative	264 (26.7)	129 (27.3)	127 (25.9)
Positive	726 (73.3)	343 (72.7)	363 (74.1)
Treatment received‖			
Radiation	625 (60.9)	295 (59.5)	313 (62.2)
Chemotherapy	423 (41.4)	181 (36.7)	230 (45.8)
Hormone therapy	616 (61.1)	292 (59.8)	308 (62.2)

*LIBCSP participants diagnosed with breast cancer between August 1, 1996, and July 31, 1997, followed-up for vital status through December 31, 2014. BMI = body mass index; HS = high school; LIBCSP = Long Island Breast Cancer Study Project.

†Low intake = 0–43 vs high intake = 44+ times/year in the most recent decade prior to diagnosis.

‡At-diagnosis recreational physical activity was defined as never, former, and current physical activity of least one hour per week for three months or more.

§At-diagnosis intake of alcoholic beverages was defined as never, former, and current intake of alcoholic beverages such as beer, wine, or liquor at least once a month for six months or more.

‖Variables with >2% missing values include (n missing): nodal involvement (n = 673), tumor size (n = 684), estrogen receptor status (n = 518), radiation treatment (n = 482), chemotherapy (n = 486), and hormone therapy (n = 499).

Table 2. Cox regression hazard ratios and 95% confidence intervals for the association between prediagnosis lifetime and annual intake of grilled, barbecued, and smoked meat and mortality in the LIBCSP women diagnosed with breast cancer in 1996 and 1997 and followed for 18+ years (n = 1508)*

	All-cause mortality (n = 597 deaths)				Breast cancer–specific mortality (n = 237 deaths)			
			Age-adjusted	Multivariable-adjusted†			Age-adjusted	Multivariable-adjusted†
Type of meat intake prediagnosis	Deaths	Censored	HR (95% CI)	HR (95% CI)	Deaths	Censored	HR (95% CI)	HR (95% CI)
Lifetime grilled, barbecued, and smoked meat intake‡								
Low	280	441	1 (ref.)	1 (ref.)	117	604	1 (ref.)	1 (ref.)
High	285	436	0.99 (0.84 to 1.17)	1.02 (0.86 to 1.21)	105	616	0.88 (0.68 to 1.15)	0.89 (0.68 to 1.17)
P_{trend}			.34	.16			.47	.59
Annual grilled, barbecued, and smoked meat intake§								
Low	297	435	1 (ref.)	1 (ref.)	112	620	1 (ref.)	1 (ref.)
High	279	447	1.14 (0.96 to 1.34)	1.23 (1.03 to 1.46)	114	612	1.03 (0.79 to 1.34)	1.11 (0.85 to 1.46)
P_{trend}			.06	.02			.17	.07
Annual grilled, barbecued beef, lamb, and pork intake‖								
Low	323	422	1 (ref.)	1 (ref.)	118	627	1 (ref.)	1 (ref.)
High	262	478	1.02 (0.86 to 1.21)	1.09 (0.91 to 1.30)	113	627	0.94 (0.72 to 1.22)	1.04 (0.79 to 1.37)
P_{trend}			.21	.10			.50	.10
Annual smoked beef, lamb, and pork intake¶								
Low	288	453	1 (ref.)	1 (ref.)	106	635	1 (ref.)	1 (ref.)
High	302	441	1.13 (0.96 to 1.33)	1.17 (0.99 to 1.38)	127	616	1.20 (0.93 to 1.55)	1.23 (0.95 to 1.60)
P_{trend}			.06	.10			.10	.09
Annual grilled, barbecued poultry, and fish intake#								
Low	330	403	1 (ref.)	1 (ref.)	115	618	1 (ref.)	1 (ref.)
High	254	492	0.95 (0.80 to 1.12)	1.06 (0.89 to 1.26)	114	632	0.94 (0.72 to 1.23)	1.07 (0.81 to 1.41)
P_{trend}			.95	.38			.59	.31
Annual smoked poultry and fish intake**								
None	428	556	1 (ref.)	1 (ref.)	169	815	1 (ref.)	1 (ref.)
Any	161	341	0.80 (0.67 to 0.97)	0.89 (0.74 to 1.08)	66	436	0.72 (0.54 to 0.96)	0.80 (0.59 to 1.07)
P_{trend}			.43	.09			.99	.63

*Long Island Breast Cancer Study Project participants diagnosed with breast cancer between August 1, 1996, and July 31, 1997, followed-up for vital status through December 31, 2014. CI = confidence interval; HR = hazard ratio; LIBCSP = Long Island Breast Cancer Study Project.

†Adjusted for age at diagnosis, marital status, income, alcohol intake, body mass index, and physical activity.

‡Low intake = 0–4724 vs high intake = 4725+ times throughout the lifetime.

§Low intake = 0–43 vs high intake = 44+ times/year in the most recent decade prior to diagnosis.

‖Low intake = 0–10 vs high intake = 11+ times/year in the most recent decade prior to diagnosis.

¶Low intake = 0–4 vs high intake = 5+ times/year in the most recent decade prior to diagnosis.

#Low intake = 0–9 vs high intake 10+ times/year in the most recent decade prior to diagnosis.

**None = 0 vs any intake = 1+ times/year in the most recent decade prior to diagnosis.

Table 3. Cox regression hazard ratios and 95% confidence intervals for the association between prediagnosis/postdiagnosis annual intake of grilled, barbecued, and smoked meat and mortality in the LIBCSP women diagnosed with breast cancer in 1996 and 1997 and followed for 18+ years (n = 1339)*

	All-cause mortality (n = 428 deaths)				Breast cancer–specific mortality (n = 126 deaths)			
			Age- adjusted	Multivariable-adjusted†			Age-adjusted	Multivariable-adjusted†
Type of meat intake prediagnosis/postdiagnosis	Deaths	Censored	HR (95% CI)	HR (95% CI)	Deaths	Censored	HR (95% CI)	HR (95% CI)
Total grilled, barbecued, and smoked meat intake‡								
Low/low	160	295	1 (ref.)	1 (ref.)	42	413	1 (ref.)	1 (ref.)
Low/high	60	156	1.05 (0.73 to 1.50)	1.10 (0.75 to 1.62)	16	201	0.78 (0.38 to 1.63)	0.77 (0.36 to 1.64)
High/low	101	158	1.24 (0.96 to 1.62)	1.28 (0.97 to 1.68)	28	231	1.18 (0.71 to 1.98)	1.14 (0.67 to 1.93)
High/high	108	302	1.18 (0.88 to 1.58)	1.31 (0.96 to 1.78)	41	169	1.09 (0.66 to 1.80)	1.08 (0.63 to 1.83)
Grilled, barbecued beef, lamb, and pork intake§								
Low/low	183	291	1 (ref.)	1 (ref.)	43	430	1 (ref.)	1 (ref.)
Low/high	52	137	0.98 (0.68 to 1.40)	1.00 (0.69 to 1.45)	16	174	0.93 (0.48 to 1.81)	0.88 (0.45 to 1.75)
High/low	81	156	1.06 (0.80 to 1.40)	1.10 (0.83 to 1.46)	19	219	0.86 (0.48 to 1.56)	0.88 (0.48 to 1.61)
High/high	112	327	1.10 (0.84 to 1.43)	1.14 (0.87 to 1.51)	48	390	1.25 (0.78 to 1.98)	1.24 (0.76 to 2.03)
Smoked beef, lamb, and pork intake‖								
Low/low	142	326	1 (ref.)	1 (ref.)	36	432	1 (ref.)	1 (ref.)
Low/high	66	138	1.25 (0.87 to 1.80)	1.18 (0.81 to 1.71)	20	185	1.29 (0.65 to 2.58)	1.22 (0.60 to 2.50)
High/low	93	148	1.34 (1.01 to 1.77)	1.36 (1.01 to 1.82)	31	210	1.75 (1.04 to 2.94)	1.71 (1.00 to 2.92)
High/high	126	299	1.20 (0.92 to 1.56)	1.20 (0.91 to 1.59)	40	386	1.25 (0.76 to 2.04)	1.19 (0.71 to 1.99)
Grilled, barbecued poultry, and fish intake¶								
Low/low	201	302	1 (ref.)	1 (ref.)	45	459	1 (ref.)	1 (ref.)
Low/high	41	110	1.01 (0.64 to 1.59)	1.04 (0.65 to 1.65)	13	138	0.97 (0.43 to 2.19)	0.95 (0.41 to 2.19)
High/low	93	180	1.01 (0.78 to 1.31)	1.03 (0.78 to 1.34)	29	244	1.21 (0.73 to 2.02)	1.22 (0.72 to 2.05)
High/high	93	318	0.98 (0.73 to 1.30)	1.06 (0.79 to 1.43)	39	373	1.06 (0.64 to 1.76)	1.11 (0.66 to 1.88)
Smoked poultry and fish intake#								
None/none	275	489	1 (ref.)	1 (ref.)	83	682	1 (ref.)	1 (ref.)
None/any	32	76	0.82 (0.52 to 1.30)	0.84 (0.51 to 1.37)	8	100	0.62 (0.27 to 1.45)	0.56 (0.23 to 1.34)
Any/none	51	122	0.89 (0.64 to 1.24)	0.97 (0.69 to 1.35)	19	154	0.96 (0.56 to 1.63)	0.97 (0.57 to 1.67)
Any/any	70	224	0.79 (0.59 to 1.06)	0.88 (0.64 to 1.20)	18	277	0.52 (0.30 to 0.92)	0.55 (0.31 to 0.97)

*Long Island Breast Cancer Study Project participants diagnosed with breast cancer between August 1, 1996, and July 31, 1997, followed-up for vital status through December 31, 2014. Missing data analyses exclude women who died within five years of breast cancer diagnosis (n = 169). CI = confidence interval; HR = hazard ratio; LIBCSP = Long Island Breast Cancer Study Project.

†Adjusted for age at diagnosis, marital status, income, alcohol intake, body mass index, physical activity, tumor size, lymph node involvement, and estrogen receptor status.

‡Low intake = 0–43 vs high intake = 44+ times/year prediagnosis in the most recent decade prior to diagnosis and low intake = 0–35 vs high intake = 36+ times/year postdiagnosis.

§Low intake = 0–10 vs high intake = 11+ times/year prediagnosis in the most recent decade prior to diagnosis and low intake = 0–8 vs high intake = 9+ times/year postdiagnosis.

‖Low intake = 0–4 vs high intake = 5+ times/year prediagnosis in the most recent decade prior to diagnosis and postdiagnosis.

¶Low intake = 0–9 vs high intake 10+ times/year prediagnosis in the most recent decade prior to diagnosis and low intake = 0–6 vs high intake = 7+ times/year postdiagnosis.

#None = 0 vs any intake = 1+ times/year in the most recent decade prior to diagnosis and postdiagnosis.

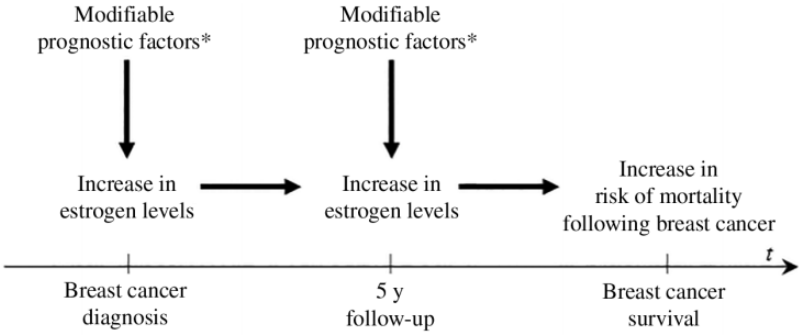

Figure 1. Conceptual model linking at-diagnosis and postdiagnosis changes in modifiable prognostic factors (indicated with an asterisk) including obesity, physical activity, fat intake, smoking, and intake of grilled/smoked foods and survival following breast cancer.

to 0.97) compared with no intake at pre- and postdiagnosis. Postdiagnosis changes in intake of grilled/barbecued poultry/fish were not associated with all-cause and breast cancer–specific mortality. Age-adjusted results from the complete-case analyses are presented in Supplementary Table 1 (available online), which are mostly similar to the imputation-based results, except for total grilled/barbecued and smoked meat intake, which are null in the complete-case analysis.

Discussion

In this population-based prospective study of grilled/barbecued and smoked meat intake and mortality among a cohort of women diagnosed with first primary breast cancer, high prediagnosis annual intake of total grilled/barbecued and smoked meat was statistically significantly associated with an elevated risk of all-cause mortality. Additionally, when considering postdiagnosis changes in intake, we observed that women who continued to consume a high amount of grilled/barbecued and smoked meat after diagnosis had a 31% increased risk of all-cause mortality. When each of the four types of grilled/barbecued and smoked meat were examined individually, some associations were noted, but the estimates were not statistically significant and include the following. Prediagnosis annual intake of smoked beef/lamb/pork was positively associated with all-cause and breast cancer–specific mortality. Postdiagnosis smoked beef/lamb/pork intake was also positively associated with all-cause and breast cancer mortality, with risk of mortality highest among women who reported high prediagnosis and low postdiagnosis intake. Risk of breast cancer–specific mortality was inversely associated with any pre- and postdiagnosis intake of smoked poultry/fish.

Grilled and smoked meat intake is a source of polycyclic aromatic hydrocarbons, including benzo[a]pyrene, chrysene, and fluoranthene, and is the primary route of PAH exposure among nonsmokers (18). PAHs, a group of over 100 different chemicals, are formed during the incomplete combustion or pyrolysis of organic substances (19). Specifically, during grilling and barbecuing, PAHs are formed when fat and juices from meat grilled directly over an open fire drip onto the fire, creating flames and smoke. The PAHs adhere to the surface of the meat upon contact (20). Wood smoke, which is used to cook and preserve foods, contains a large number of PAHs, which also contaminate the foods upon contact (21).

Although we could not definitively rule out chance as an explanation for some of our findings, a link between dietary sources of PAH and breast cancer prognosis is biologically plausible and epidemiologically consistent. First, these foods have been previously associated with increased risk of breast cancer incidence; effect estimates range from 1.5 to 2.2 when comparing the highest to the lowest quantiles of intake of well-done meat (8,22–25). Second, dietary PAH exposures are hypothesized to be etiologically related to breast carcinogenesis as PAHs are known to form DNA adducts, which can cause mutations during DNA replication and may alter promoter methylation or promoter binding, leading to inheritable abnormal gene expression, early steps in carcinogenesis (7). Third, PAHs are also likely to influence breast cancer development and prognosis through endocrine disruption (26). Several PAHs or derivatives including chrysene and fluoranthene show estrogenic activity in vitro, while others, such as benzo[k]fluoranthene, benzo[a]pyrene, and benz[a]anthracene, can be anti-estrogenic (27–29). Thus, as shown in Figure 1, our study hypothesis is that dietary PAH sources (and other modifiable factors) may influence breast cancer prognosis through an estrogen pathway.

Our findings of a possible positive association with death and intake for smoked beef/lamb/pork may possibly be explained by the higher saturated fat content of these meats compared with poultry and fish. Though results are inconsistent, higher risk of mortality has been observed among women with high intake of total fat, saturated fat, and monounsaturated fat (30–32). Furthermore, higher fat content may also result in the formation of more PAHs (18). However, we did not observe the same elevated risk of mortality among women with continued postdiagnosis high intake and when we examined at-diagnosis intake of these meats cooked by grilling/barbecuing. The lack of association between mortality and intake of grilled/barbecued beef/lamb/pork may be due to method of preparation; marinating meat before grilling, as is often done, may inhibit the formation of PAHs (33). Our finding of an inverse association between smoked poultry/fish intake and mortality could also be related to the different fat composition of these meats. Moreover, it has been hypothesized that the amino acid content of white meat supports proper immune system function (34), while intake of fish, a source of omega-3 polyunsaturated fatty acids, could improve survival (30,35) by reducing pro-inflammatory derivatives (36). Nonetheless, we did not observe reductions in mortality risk associated with the intake of grilled/barbecued poultry/fish intake.

Ours is the first study to examine the associations between grilled/barbecued and smoked meat intake and mortality after breast cancer. Strengths of our study include the population-based cohort design, which utilized data collected shortly after diagnosis and again five years postdiagnosis. Women were

followed for over 18 years using the National Death Index, which has accurate ascertainment of vital status (37).

However, this study also has several limitations. Women were asked to self-report their intake of grilled/barbecued and smoked meats. This could have resulted in nondifferential misclassification of the exposure, which would bias estimates towards the null (38). Given the prospective design, approximately 28% of women did not complete the follow-up assessment. Analyses using a complete-case approach could result in biased estimates (39); therefore, we used multiple imputation, a methodologically sound approach, to address the missing data. Additionally, given the missingness in the follow-up assessment, we were unable to consider time-varying covariates because of problems with model convergence. Lastly, given the complexity of diet, it is possible that our results are confounded by other correlated dietary factors; however, few dietary exposures have been consistently linked to breast cancer survival (32).

The results of our study indicate that grilled/barbecued and, particularly, smoked meat consumed prior to and after breast cancer diagnosis may influence survival. This study, with confirmation by future studies, may help to identify modifiable prognostic indicators for the more than 3 million women who are survivors of breast cancer (1).

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Notes

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