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Original Contribution

Fruit and Vegetable Intake in Relation to Risk of Breast Cancer in the Black Women's Health Study

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The authors prospectively examined the relation of fruit and vegetable intake to breast cancer risk among 51,928 women aged 21–69 years at enrollment in 1995 in the Black Women's Health Study. Dietary intake was assessed by using a validated food frequency questionnaire. Cox proportional hazards models were used to estimate incidence rate ratios and 95% confidence intervals, adjusted for breast cancer risk factors. During 12 years of follow-up, there were 1,268 incident cases of breast cancer. Total fruit, total vegetable, and total fruit and vegetable intakes were not significantly associated with overall risk of breast cancer. However, total vegetable consumption was associated with a decreased risk of estrogen receptor-negative/progesterone receptor-negative breast cancer (incidence rate ratio = 0.57, 95% confidence interval: 0.38, 0.85, for ≥2 servings/day relative to <4/week; P_{trend} = 0.02). In addition, there was some evidence of inverse associations with breast cancer risk overall for cruciferous vegetable intake (P_{trend} = 0.06) and for carrot intake (P_{trend} = 0.02). Study findings suggest that frequent consumption of vegetables is inversely associated with risk of estrogen receptor-negative/progesterone receptor-negative breast cancer, and that specific vegetables may be associated with a decreased risk of breast cancer overall.

African Americans; Brassicaceae; breast neoplasms; carotenoids; fruit; risk; vegetables; women

Abbreviations: CI, confidence interval; ER, estrogen receptor; FFQ, food frequency questionnaire; IRR, incidence rate ratio; NCI, National Cancer Institute; PR, progesterone receptor; +, positive; −, negative.

Fruits and vegetables are rich sources of carotenoids, flavonoids, and glucosinolates, which are potentially protective against cancer (1–3). Numerous studies have examined the association between fruit and vegetable consumption and breast cancer risk, but results have been inconclusive. A pooled analysis of 8 cohort studies found no overall association between fruit and vegetable intake and breast cancer risk (4). The European Prospective Investigation into Cancer and Nutrition study also had null findings for total fruit and vegetable intake (5). However, there is some evidence that specific subclasses of vegetables, such as cruciferous and carotenoid-rich vegetables, may be inversely associated with risk of breast cancer (6–8).

Molecular subtypes of breast cancer may have biologically distinct etiologies (9, 10), and there is increasing evidence that breast cancer risk factors may differ by breast cancer subtype (11–14). Four epidemiologic studies have examined the association between intake of fruits and vegetables and breast cancer risk according to estrogen receptor (ER) or progesterone receptor (PR) status. Two cohort studies reported an inverse association between fruits and vegetables and ER-negative (−) but not ER-positive (+) breast cancer (15, 16), whereas 2 case-control studies observed an inverse association with ER+ but not with ER− breast cancer (17, 18).

African-American women are more likely than white women to be diagnosed with ER−/PR− tumors, which are associated with increased 5-year mortality (19). Although black women consume fewer vegetables overall than white women (20), they tend to consume greater amounts of cruciferous vegetables (21). No epidemiologic studies have assessed breast cancer risk in relation to fruit and vegetable intake separately among African-American women. However, in our report from the Black Women's Health Study, we found that a ''prudent'' dietary pattern—rich in vegetables, fruits, whole grains, and fish—was inversely associated with both premenopausal breast cancer and ER−/PR− breast cancer among African-American women (22), consistent with results from previous studies (23). In the present report, we investigated whether fruit and vegetable intake accounted for the association of breast cancer risk with a prudent dietary pattern in the Black Women's Health Study. In addition, because specific fruits and vegetables may have an important protective effect, we evaluated the relation between subclasses of fruits and vegetables and breast cancer risk.

MATERIALS AND METHODS

Study population

The Black Women's Health Study is an ongoing prospective follow-up study of black women in the United States. The study was established in 1995 when women from all regions of the United States were enrolled through postal questionnaires (24). The baseline questionnaire collected information on lifestyle factors and medical history, and usual diet was assessed through a food frequency questionnaire (FFQ). A total of 59,000 women aged 21–69 years have been followed through mailed questionnaires every 2 years. Follow-up questionnaires update exposure information and identify incident cancers and other illnesses. Follow-up has averaged over 80% of the baseline cohort over 6 questionnaire cycles. We excluded women with a history of breast cancer ($n = 732$) or other cancer except nonmelanoma skin cancer ($n = 743$) at baseline, as well as participants who had left more than 10 FFQ items blank ($n = 1,954$), had missing or implausible energy intake values (<500 or >3,800 kcal) ($n = 3,536$), or were missing all fruit or vegetable items ($n = 134$). After these exclusions, 51,928 women remained in the present analysis.

Assessment of breast cancer

Incident cases of breast cancer were ascertained through self-report on biennial follow-up questionnaires between 1995 and 2007. We obtained medical record or cancer registry data for 85% of cases, and of these, 99% were confirmed. Given the high confirmation rate, we included all self-reported cases, except those that were disconfirmed. We learned of deaths from family members, the US Postal Service, and searches of the National Death Index for nonrespondents. Information on ER and PR status was obtained through abstraction of medical records and cancer registry data and was available for 59% of cases.

Dietary assessment

We assessed usual diet at baseline in 1995 with a 68-item modified version of the National Cancer Institute (NCI)–Block FFQ and, in 2001, with an 85-item version (25). The 9 frequency responses ranged from never or <1 serving/month to ≥2/day. In 1995, we asked participants to specify a small, medium, or large portion size. A medium portion size was defined for each item (e.g., 0.5 cup (71 g) of broccoli), and small and large servings were weighted as 0.5 and 1.5 times a medium serving size, respectively. In 2001, a super-sized portion, equivalent to 2 or more times the size of medium, was added. Nutrients were calculated by using NCI's DIETSYS software (26) for the 1995 FFQ and by using NCI's Diet*Calc software (27) for the 2001 FFQ. The FFQ was validated among 408 participants by using a 3-day dietary record and up to 3 telephone 24-hour recalls (28). Energy-adjusted and deattenuated Pearson's correlation coefficients for the FFQ compared with diet records and recalls were 0.60, 0.60, and 0.64 for vitamin C, folate, and β-carotene, respectively.

The 1995 FFQ included 5 questions on fruit consumption and 8 questions on vegetable consumption. We summed daily intakes of those fruits and vegetables on the 1995 and 2001 FFQs to calculate total intake. We also evaluated specific groups of fruits and vegetables classified according to botanical taxonomy (29). Cruciferous vegetables included broccoli, collard or mustard greens, and cabbage or cole slaw; green leafy vegetables included spinach and green salad; yellow-orange vegetables included carrots, tomatoes or tomato juice, and sweet potatoes or yams. Citrus fruit comprised grapefruit and oranges; other fruit comprised apples or pears, bananas, and cantaloupe.

Assessment of nondietary exposures

Information on education, age at menarche, weight at age 18 years, and height was obtained at baseline. Data on current weight, physical activity, smoking status, alcohol intake, parity, age at first birth, oral contraceptive use, age at menopause, menopausal hormone use, and multivitamin use were obtained at baseline and have been updated on biennial follow-up questionnaires. First-degree family history of breast cancer was asked on the 1995 and 1999 questionnaires. Women who reported a hysterectomy but retained 1 or both ovaries were classified as premenopausal if their current age was less than the 10th percentile of age at natural menopause in the Black Women's Health Study (43 years), as postmenopausal if their age was greater than the 90th percentile of age at natural menopause in the cohort (56 years), and as uncertain menopausal status between the ages of 43 and 56 years.

Statistical analysis

Participants contributed person-years from the beginning of follow-up on March 1, 1995, until diagnosis of breast cancer, death, loss to follow-up, or end of follow-up on March 1, 2007, whichever occurred first. Cox proportional hazards models, jointly stratified by age in 1-year intervals and by questionnaire cycle, were used to estimate incidence rate ratios and 95% confidence intervals for breast cancer risk in relation to fruit and vegetable intake. To reduce within-person variation and better represent long-term intake, we assessed cumulative average intake (30). Consumption at baseline was assessed in relation to breast cancer incidence between 1995 and 2001, and the average of 1995 and 2001 consumption was assessed in relation to breast cancer incidence between 2001 and 2007; results using baseline diet only were similar. Separate items for grapefruit and oranges on the 1995 FFQ were included as a single item on the 2001 FFQ, and therefore in analyses of individual fruits and vegetables, incidence rate ratios for grapefruit and oranges were estimated by using the baseline diet only.

Multivariable models were adjusted for energy intake (quintiles), age at menarche (<12, 12–13, ≥14 years), body mass index at age 18 years (<20, 20–24, ≥25 kg/m^2), family history of breast cancer (mother or sister), education (≤12, 13–15, ≥16 years), geographic region (Northeast, South, Midwest, West), parity (0, 1, 2, ≥3 births), age at first birth (<20, 20–24, ≥25 years), oral contraceptive use (never, use in previous 5 years, use ≥5 years ago), menopausal status (postmenopausal, premenopausal, uncertain), age at menopause (<45, 45–49, ≥50 years), menopausal hormone use (never, ever use <5 years' duration, ≥5 years' duration), vigorous activity (none, 1–4, ≥5 hours/week), smoking status (never, past, current), alcohol intake (none, 1–3, 4–6, ≥7 drinks/week), and multivitamin use (current, not current). Parity, oral contraceptive use, menopausal status, menopausal hormone use, vigorous activity, smoking status, alcohol intake, and multivitamin use were treated as time-dependent variables in the analysis.

"Prudent" and "Western" dietary patterns were derived by factor analysis, as described previously (22). The prudent dietary pattern, which was most highly correlated with intakes of vegetables, fruit, whole grains, and fish, was inversely associated with breast cancer risk among some subgroups of women in the Black Women's Health Study (22). Therefore, in sensitivity analyses, we adjusted the multivariable models assessing fruit and vegetable intake in relation to breast cancer risk for the other major components of a prudent dietary pattern, that is, for quintiles of whole grains and fish.

Tests for trend were conducted by using the median of each category modeled as a continuous variable. We assessed whether the association between fruit and vegetable intake and breast cancer risk was modified by menopausal status (premenopausal, postmenopausal), age (<50, ≥50 years), body mass index (<25, 25–29, ≥30 kg/m^2), smoking status (never, past, current), and multivitamin use (current, not current). Tests for interaction were performed by using a likelihood ratio test that compared models with and without interaction terms.

RESULTS

Baseline characteristics of the study participants according to total fruit intake and total vegetable intake are presented in Table 1. Women who consumed more fruits or vegetables were more likely to be older, to live in the northeastern and western regions of the United States, to be physically active and nonsmokers, and to take multivitamins. Educational level was positively associated with vegetable consumption.

During 554,528 person-years of follow-up, we identified 1,268 cases of breast cancer; 562 cases (44%) were premenopausal, 570 (45%) were postmenopausal, and 136 (11%) had uncertain menopausal status. Among 745 cases with known hormone receptor status, 366 (49%) were ER+/PR+, 103 (14%) were ER+/PR−, 12 (2%) were ER−/PR+, and 264 (35%) were ER−/PR−. Among 310 premenopausal cases with known receptor status, 47% were ER+/PR+, 12% were ER+/PR−, 2% were ER−/PR+, and 39% were ER−/PR−; among 341 postmenopausal cases with known receptor status, the corresponding percentages were 50%, 16%, 2%, and 32%. Cases with known and unknown hormone receptor status were similar with respect to fruit and vegetable intake, age, education, and other lifestyle and reproductive factors.

Median intakes of total fruit and total vegetables were 0.7 servings/day and 1.0 servings/day, respectively. Total fruit, total vegetable, and total fruit and vegetable intakes were not significantly associated with breast cancer risk overall (Table 2). The multivariable incidence rate ratios were 0.87 (95% confidence interval (CI): 0.71, 1.07) for ≥4 servings/day of fruits and vegetables relative to <1/day, 0.87 (95% CI: 0.73, 1.05) for ≥2 servings/day of vegetables compared with <4/week, and 0.91 (95% CI: 0.74, 1.11) for ≥2 servings/day of fruits relative to <2/week. However, there was an inverse association with cruciferous vegetable intake; the incidence rate ratios for 1–2, 3–5, and ≥6 servings/week compared with <1/week were 0.94 (95% CI: 0.80, 1.11), 1.01 (95% CI: 0.84, 1.21), and 0.80 (95% CI: 0.65, 0.99), respectively ($P_{\text{trend}} = 0.06$). The association was stronger among premenopausal women (incidence rate ratio (IRR) = 0.59, 95% CI: 0.42, 0.83, for ≥6 servings/week relative to <1/week), whereas there was no evidence of an association among postmenopausal women ($P_{\text{interaction}} = 0.007$). However, when we excluded women who had ever used menopausal hormones, there was a nonsignificant inverse association between cruciferous vegetable intake and risk of postmenopausal breast cancer (IRR = 0.74, 95% CI: 0.43, 1.26, for ≥6 servings/week relative to <1/week). There was also some evidence of an inverse association between yellow-orange vegetable intake and breast cancer risk overall; the incidence rate ratio was 0.87 (95% CI: 0.72, 1.05) for ≥6 servings/week compared with <1/week ($P_{\text{trend}} = 0.13$). Results for yellow-orange vegetable intake did not differ significantly by menopausal status ($P_{\text{interaction}} = 0.88$).

Because of the previous finding of an inverse association between a prudent dietary pattern and breast cancer risk among subgroups of women in the Black Women's Health Study (22), in a subanalysis of fruit and vegetable intake in relation to breast cancer risk, we controlled for the other major components of a prudent dietary pattern, that is, whole grains and fish. The results were unchanged (data not shown).

There was no evidence of effect modification of fruit and vegetable intake in relation to breast cancer risk according to age, body mass index, smoking status, or multivitamin use (data not shown).

Table 3 presents results for individual vegetables and fruit in relation to breast cancer risk overall and according to menopausal status. The incidence rate ratios for the highest

Table 1. Baseline Characteristics According to Intake of Fruits and Vegetables in the Black Women's Health Study, 1995

Characteristic[a]	Total Fruit Intake, Servings											
	<2/Week			2–6/Week			1/Day			≥2/Day		
	No.	%	Mean	No.	%	Mean	No.	%	Mean	No.	%	Mean
No.	13,142			18,282			13,178			7,326		
Age, years			35.5			38.0			40.6			42.3
Age at menarche, years			12.3			12.3			12.3			12.3
Body mass index at age 18 years, kg/m^2			21.2			21.5			21.5			21.6
Body mass index, kg/m^2			27.7			28.0			27.9			27.9
Family history of breast cancer		6.5			6.2			6.7			6.4	
Education ≥16 years		42.5			46.8			48.2			45.7	
Region[b]												
Northeast		26.8			26.7			27.7			30.5	
South		31.3			30.4			30.5			28.4	
Midwest		24.6			23.8			22.2			21.4	
West		17.3			19.0			19.4			19.6	
Nulliparous		36.4			35.9			36.5			35.2	
Age at first birth ≥25 years[c]		27.3			30.5			30.5			29.1	
Oral contraceptive use ≥5 years		32.0			32.9			32.0			28.5	
Vigorous activity ≥5 hours/week		8.5			11.9			16.9			21.2	
Current smoker		21.7			16.1			12.7			12.3	
Alcohol ≥7 drinks/week		7.9			5.6			4.4			4.2	
Multivitamin use		41.0			48.1			55.3			59.7	
Total energy, kcal			1,439			1,553			1,670			1,872

Characteristic[a]	Total Vegetable Intake, Servings											
	<4/Week			4–6/Week			1/Day			≥2/Day		
	No.	%	Mean	No.	%	Mean	No.	%	Mean	No.	%	Mean
No.	14,509			11,698			15,441			10,280		
Age, years			35.6			38.2			39.9			41.5
Age at menarche, years			12.4			12.3			12.3			12.3
Body mass index at age 18 years, kg/m^2			21.3			21.4			21.5			21.6
Body mass index, kg/m^2			27.9			27.9			27.9			27.9
Family history of breast cancer		6.4			6.3			6.4			6.8	
Education ≥16 years		40.4			45.0			48.7			50.5	
Region[b]												
Northeast		22.9			26.3			29.2			32.8	
South		33.3			31.4			29.2			26.8	
Midwest		26.4			24.3			21.9			19.7	
West		17.4			17.8			19.6			20.5	
Nulliparous		35.4			35.7			36.1			37.8	
Age at first birth ≥25 years[c]		26.1			28.7			31.0			30.8	
Oral contraceptive use ≥5 years		32.3			32.5			32.7			28.7	
Vigorous activity ≥5 hours/week		9.4			11.1			14.4			21.0	
Current smoker		17.3			16.7			15.0			14.6	
Alcohol ≥7 drinks/week		5.3			5.7			5.6			5.7	
Multivitamin use		42.7			47.3			52.7			58.4	
Total energy, kcal			1,355			1,507			1,675			1,924

[a] All characteristics, with the exception of age, are standardized to the age distribution of the cohort at baseline.
[b] Percentages do not total 100% because of missing data.
[c] Restricted to parous women.

Table 2. Intake of Fruits and Vegetables in Relation to Risk of Breast Cancer in the Black Women's Health Study, 1995–2007

	All Women					Premenopausal Women			Postmenopausal Women		
	Cases, No.	Person-Years	IRR[a]	IRR[b]	95% CI	Cases, No.	IRR[b]	95% CI	Cases, No.	IRR[b]	95% CI
Total fruits and vegetables, servings											
<1/day	222	125,279	1.00	1.00	Referent	121	1.00	Referent	78	1.00	Referent
1/day	365	164,217	1.01	1.00	0.85, 1.19	186	1.08	0.86, 1.37	133	0.80	0.60, 1.06
2–3/day	474	184,590	0.98	0.97	0.82, 1.15	186	0.98	0.77, 1.25	244	0.89	0.68, 1.16
≥4/day	207	80,442	0.87	0.87	0.71, 1.07	69	0.90	0.65, 1.23	115	0.76	0.56, 1.04
P_{trend}					0.14			0.31			0.24
$P_{interaction}$								0.40			
Total vegetables, servings											
<4/week	261	140,397	1.00	1.00	Referent	141	1.00	Referent	95	1.00	Referent
4–6/week	283	128,079	0.97	0.96	0.81, 1.14	136	0.97	0.76, 1.23	114	0.87	0.66, 1.15
1/day	449	175,086	1.00	0.99	0.84, 1.16	187	0.97	0.77, 1.22	209	0.91	0.71, 1.17
≥2/day	275	110,965	0.88	0.87	0.73, 1.05	98	0.82	0.62, 1.08	152	0.86	0.65, 1.14
P_{trend}					0.14			0.15			0.47
$P_{interaction}$								0.82			
Cruciferous, servings											
<1/week	202	109,756	1.00	1.00	Referent	113	1.00	Referent	67	1.00	Referent
1–2/week	526	233,548	0.94	0.94	0.80, 1.11	243	0.93	0.75, 1.17	227	0.93	0.71, 1.23
3–5/week	350	128,914	1.00	1.01	0.84, 1.21	155	1.12	0.87, 1.44	156	0.89	0.66, 1.20
≥6/week	190	82,310	0.80	0.80	0.65, 0.99	51	0.59	0.42, 0.83	120	0.94	0.68, 1.28
P_{trend}					0.06			0.01			0.86
$P_{interaction}$								0.007			
Green leafy, servings											
<1/week	275	140,934	1.00	1.00	Referent	138	1.00	Referent	113	1.00	Referent
1–2/week	402	179,738	0.97	0.96	0.82, 1.12	183	0.94	0.75, 1.17	172	0.92	0.72, 1.16
3–5/week	379	150,169	0.98	0.96	0.82, 1.13	164	0.99	0.79, 1.26	168	0.84	0.66, 1.07
≥6/week	212	83,687	0.91	0.90	0.75, 1.09	77	0.84	0.62, 1.12	117	0.92	0.70, 1.21
P_{trend}					0.32			0.34			0.65
$P_{interaction}$								0.45			

Table continues

categories of consumption of each cruciferous vegetable (broccoli, collard greens, and cabbage), though not significant, were each compatible with a decreased risk of breast cancer overall. Carrot intake was inversely associated with overall breast cancer risk; the incidence rate ratio was 0.83 (95% CI: 0.67, 1.04) for ≥3 servings/week relative to <1/month ($P_{trend} = 0.02$).

Total vegetable intake was associated with a significant reduction in risk of ER−/PR− breast cancer (Table 4); the incidence rate ratios were 0.71 (95% CI: 0.50, 1.01), 0.79 (95% CI: 0.57, 1.10), and 0.57 (95% CI: 0.38, 0.85) for 4–6 servings/week, 1/day, and ≥2/day, respectively, compared with <4/week ($P_{trend} = 0.02$). Conversely, for ER+/PR+ breast cancer, the incidence rate ratios for total vegetable intake were above 1; the corresponding incidence rate ratios were 1.40 (95% CI: 0.99, 1.99), 1.54 (95% CI: 1.11, 2.14), and 1.41 (95% CI: 0.97, 2.04). For ER−/PR− breast cancer, there was a reduced risk for higher levels of intake for each vegetable subclass, but the confidence intervals were compatible with 1. For ER+/PR+ and ER+/PR− breast cancer, there was no consistent pattern by type of vegetable. Neither citrus fruit nor other fruit was materially associated with risk of breast cancer subtypes. Results are not presented for ER−/PR+ breast cancer because the number of cases was too small for meaningful interpretations. Results for ER− breast cancer were similar to those for ER−/PR− breast cancer, and results for ER+ breast cancer were similar to those for ER+/PR+ breast cancer (data not shown). We had limited power to evaluate associations jointly by ER/PR status and menopausal status, but results for breast cancer hormone receptor subtypes appeared to be similar across menopausal status (data not shown).

When individual vegetables and fruit were considered in relation to breast cancer risk according to ER/PR status

Table 2. Continued

	All Women					Premenopausal Women			Postmenopausal Women		
	Cases, No.	Person-Years	IRR[a]	IRR[b]	95% CI	Cases, No.	IRR[b]	95% CI	Cases, No.	IRR[b]	95% CI
Yellow-orange, servings											
<1/week	359	169,476	1.00	1.00	Referent	182	1.00	Referent	132	1.00	Referent
1–2/week	463	198,255	0.91	0.90	0.78, 1.03	210	0.91	0.74, 1.11	204	0.88	0.70, 1.10
3–5/week	267	116,244	0.82	0.81	0.68, 0.95	103	0.76	0.59, 0.98	138	0.84	0.66, 1.08
≥6/week	179	70,552	0.88	0.87	0.72, 1.05	67	0.83	0.62, 1.12	96	0.92	0.70, 1.22
P_{trend}					0.13			0.12			0.77
$P_{interaction}$								0.88			
Total fruits, servings											
<2/week	239	129,616	1.00	1.00	Referent	137	1.00	Referent	77	1.00	Referent
2–6/week	440	208,291	0.94	0.94	0.80, 1.10	205	0.87	0.70, 1.08	179	0.94	0.72, 1.23
1/day	404	145,174	1.05	1.04	0.88, 1.23	150	0.97	0.76, 1.23	215	1.09	0.83, 1.43
≥2/day	185	71,446	0.89	0.91	0.74, 1.11	70	1.00	0.74, 1.35	99	0.86	0.63, 1.18
P_{trend}					0.69			0.66			0.55
$P_{interaction}$								0.57			
Citrus, servings											
<1/week	585	277,050	1.00	1.00	Referent	270	1.00	Referent	244	1.00	Referent
1–2/week	321	138,685	1.01	1.00	0.88, 1.16	153	1.11	0.91, 1.35	141	0.96	0.78, 1.18
3–5/week	250	89,114	1.10	1.15	0.99, 1.34	86	1.03	0.81, 1.32	135	1.19	0.96, 1.47
≥6/week	112	49,678	0.88	0.90	0.73, 1.11	53	1.20	0.88, 1.62	50	0.74	0.54, 1.01
P_{trend}					0.83			0.30			0.27
$P_{interaction}$								0.05			
Other fruit, servings											
<2/week	345	190,232	1.00	1.00	Referent	191	1.00	Referent	116	1.00	Referent
2–4/week	361	155,521	1.05	1.04	0.89, 1.21	160	0.97	0.78, 1.20	159	1.07	0.84, 1.36
5–8/week	308	120,172	1.00	1.00	0.85, 1.17	128	1.04	0.83, 1.31	146	0.93	0.72, 1.19
≥9/week	254	88,603	1.00	1.01	0.85, 1.19	83	1.02	0.78, 1.33	149	1.02	0.79, 1.32
P_{trend}					0.91			0.75			0.88
$P_{interaction}$								0.63			

Abbreviations: CI, confidence interval; IRR, incidence rate ratio.
[a] Adjusted for age and energy intake.
[b] Adjusted for age, energy intake, age at menarche, body mass index at age 18 years, family history of breast cancer, education, geographic region, parity, age at first birth, oral contraceptive use, menopausal status, age at menopause, menopausal hormone use, vigorous activity, smoking status, alcohol intake, and multivitamin use.

(data not shown), the incidence rate ratios were less than 1 for the association of ER−/PR− breast cancer with the highest intake categories of broccoli, collard greens, cabbage, spinach, green salad, and yams, but only the incidence rate ratio for intake of yams ≥1/week relative to <1/month was statistically significant (IRR = 0.59, 95% CI: 0.35, 0.98). There were no consistent trends for ER+/PR+ or ER+/PR− breast cancer.

DISCUSSION

In this large prospective study of African-American women, total vegetable intake was associated with a significant decrease in risk of ER−/PR− breast cancer, and inverse associations were observed for most vegetable types. There was also evidence suggesting that intakes of cruciferous vegetables and carrots may be inversely associated with risk of breast cancer overall.

Our findings are consistent with those from the few prospective studies that have reported on the association between total fruit and vegetable intake and breast cancer by ER or ER/PR status. Among postmenopausal women in the Nurses' Health Study, the fruit and vegetable components of dietary patterns were associated with a decreased risk of ER− breast cancer (15, 31). A cohort study of postmenopausal women in Denmark showed an inverse association between fruit and vegetable intake and ER− but not ER+

Table 3. Intake of Individual Fruits and Vegetables in Relation to Risk of Breast Cancer in the Black Women's Health Study, 1995–2007

	All Women					Premenopausal Women			Postmenopausal Women		
	Cases, No.	Person-Years	IRR[a]	IRR[b]	95% CI	Cases, No.	IRR[b]	95% CI	Cases, No.	IRR[b]	95% CI
Cruciferous vegetables											
Broccoli, servings											
<1/month	88	46,088	1.00	1.00	Referent	44	1.00	Referent	34	1.00	Referent
1–3/month	485	226,018	0.94	0.92	0.74, 1.16	235	0.96	0.69, 1.33	204	0.90	0.62, 1.30
1–2/week	436	168,646	1.02	0.99	0.79, 1.25	189	1.00	0.71, 1.39	195	0.93	0.64, 1.34
≥3/week	259	113,776	0.87	0.85	0.67, 1.09	94	0.74	0.51, 1.07	137	0.91	0.62, 1.34
P_{trend}					0.19			0.03			0.92
$P_{interaction}$									0.37		
Collard greens, servings											
<1/month	152	96,375	1.00	1.00	Referent	86	1.00	Referent	50	1.00	Referent
1–3/month	746	309,578	1.13	1.14	0.96, 1.36	348	1.22	0.96, 1.55	317	1.07	0.79, 1.45
1–2/week	267	99,724	1.10	1.11	0.91, 1.37	95	1.11	0.82, 1.49	145	1.14	0.82, 1.58
≥3/week	103	48,851	0.81	0.84	0.65, 1.08	33	0.81	0.54, 1.21	58	0.85	0.57, 1.25
P_{trend}					0.03			0.11			0.22
$P_{interaction}$									0.70		
Cabbage, servings											
<1/month	241	136,035	1.00	1.00	Referent	124	1.00	Referent	87	1.00	Referent
1–3/month	781	324,155	1.05	1.05	0.91, 1.22	361	1.17	0.95, 1.43	340	0.95	0.75, 1.21
1–2/week	191	71,823	0.99	0.99	0.81, 1.20	58	0.91	0.66, 1.25	113	1.02	0.77, 1.36
≥3/week	55	22,515	0.87	0.88	0.66, 1.19	19	0.99	0.61, 1.62	30	0.80	0.52, 1.22
P_{trend}					0.26			0.41			0.49
$P_{interaction}$									0.25		
Green leafy vegetables											
Spinach, servings											
<1/month	349	175,829	1.00	1.00	Referent	179	1.00	Referent	130	1.00	Referent
1–3/month	563	237,574	0.96	0.96	0.83, 1.10	236	0.91	0.75, 1.11	264	0.98	0.79, 1.21
1–2/week	267	95,879	1.08	1.08	0.91, 1.27	111	1.03	0.81, 1.32	132	1.14	0.89, 1.46
≥3/week	89	45,245	0.78	0.79	0.62, 1.00	36	0.73	0.51, 1.05	44	0.84	0.59, 1.19
P_{trend}					0.24			0.27			0.68
$P_{interaction}$									0.94		
Green salad, servings											
<1/week	392	199,755	1.00	1.00	Referent	186	1.00	Referent	167	1.00	Referent
1–2/week	399	170,078	1.03	1.01	0.88, 1.16	183	1.06	0.86, 1.30	174	0.94	0.76, 1.16
≥3/week	477	184,694	1.01	0.99	0.86, 1.14	193	1.03	0.83, 1.27	229	0.89	0.72, 1.10
P_{trend}					0.80			0.86			0.29
$P_{interaction}$									0.50		
Yellow-orange vegetables											
Carrots, servings											
<1/month	138	72,624	1.00	1.00	Referent	80	1.00	Referent	47	1.00	Referent
1–3/month	601	244,640	1.02	0.99	0.82, 1.20	270	0.89	0.69, 1.15	259	1.02	0.75, 1.40
1–2/week	315	140,185	0.87	0.84	0.68, 1.03	123	0.69	0.51, 0.92	158	0.93	0.67, 1.30
≥3/week	214	97,078	0.86	0.83	0.67, 1.04	89	0.71	0.52, 0.97	106	0.94	0.66, 1.33
P_{trend}					0.02			0.03			0.49
$P_{interaction}$									0.65		
Yams, servings											
<1/month	316	161,377	1.00	1.00	Referent	151	1.00	Referent	128	1.00	Referent
1–3/month	797	333,851	0.99	0.99	0.86, 1.13	356	1.09	0.90, 1.32	353	0.86	0.70, 1.06
≥1/week	155	59,300	0.90	0.90	0.74, 1.10	55	1.04	0.76, 1.43	89	0.82	0.62, 1.08
P_{trend}					0.27			0.88			0.30
$P_{interaction}$									0.20		

Table continues

Table 3. Continued

	All Women					Premenopausal Women			Postmenopausal Women		
	Cases, No.	Person-Years	IRR[a]	IRR[b]	95% CI	Cases, No.	IRR[b]	95% CI	Cases, No.	IRR[b]	95% CI
Tomatoes, servings											
<1/month	355	169,123	1.00	1.00	Referent	172	1.00	Referent	136	1.00	Referent
1–3/month	495	222,613	0.94	0.92	0.80, 1.06	224	0.90	0.73, 1.10	222	0.99	0.80, 1.23
1–2/week	275	112,208	0.95	0.93	0.79, 1.10	120	0.97	0.76, 1.23	127	0.91	0.71, 1.17
≥3/week	143	50,583	1.06	1.04	0.85, 1.27	46	0.84	0.60, 1.18	85	1.27	0.96, 1.68
P_{trend}					0.56			0.56			0.13
$P_{interaction}$								0.17			
Citrus fruit											
Grapefruit, servings[c]											
<1/month	646	299,263	1.00	1.00	Referent	300	1.00	Referent	271	1.00	Referent
1–3/month	386	165,269	0.93	0.93	0.82, 1.06	174	1.06	0.88, 1.28	178	0.86	0.71, 1.04
1–2/week	125	48,279	0.90	0.91	0.75, 1.11	45	0.98	0.72, 1.35	64	0.78	0.59, 1.03
≥3/week	111	41,717	0.94	0.95	0.78, 1.17	43	1.17	0.84, 1.61	57	0.81	0.61, 1.09
P_{trend}					0.70			0.42			0.21
$P_{interaction}$								0.21			
Oranges, servings[c]											
<1/month	252	115,467	1.00	1.00	Referent	107	1.00	Referent	113	1.00	Referent
1–3/month	492	216,910	1.09	1.09	0.94, 1.27	223	1.06	0.84, 1.34	216	1.18	0.94, 1.48
1–2/week	247	108,490	1.01	1.02	0.85, 1.21	118	1.10	0.85, 1.44	105	0.96	0.73, 1.26
≥3/week	277	113,660	1.01	1.03	0.87, 1.23	114	1.09	0.83, 1.42	136	1.01	0.79, 1.31
P_{trend}					0.80			0.58			0.42
$P_{interaction}$								0.39			
Other fruit											
Apples, servings											
<1/month	130	68,431	1.00	1.00	Referent	63	1.00	Referent	51	1.00	Referent
1–3/month	447	210,573	1.04	1.02	0.84, 1.25	213	1.01	0.76, 1.34	182	1.02	0.74, 1.39
1–2/week	321	137,210	1.01	0.99	0.80, 1.22	146	1.03	0.76, 1.39	145	0.96	0.69, 1.33
≥3/week	370	138,314	1.03	1.02	0.83, 1.25	140	1.04	0.76, 1.41	192	0.99	0.72, 1.36
P_{trend}					0.98			0.79			0.87
$P_{interaction}$								0.85			
Bananas, servings											
<1/month	145	81,143	1.00	1.00	Referent	77	1.00	Referent	52	1.00	Referent
1–3/month	365	176,005	1.09	1.08	0.89, 1.31	191	1.05	0.81, 1.37	133	1.10	0.80, 1.52
1–2/week	347	145,259	1.07	1.06	0.87, 1.29	142	0.94	0.71, 1.25	168	1.16	0.84, 1.58
≥3/week	411	152,121	1.03	1.03	0.85, 1.26	152	1.08	0.82, 1.43	217	1.01	0.74, 1.37
P_{trend}					0.79			0.66			0.47
$P_{interaction}$								0.40			
Cantaloupe, servings											
<1/month	307	172,631	1.00	1.00	Referent	167	1.00	Referent	110	1.00	Referent
1–3/month	548	232,151	1.03	1.02	0.88, 1.17	238	1.00	0.82, 1.23	250	0.99	0.79, 1.24
1–2/week	258	96,244	1.04	1.03	0.87, 1.22	104	1.05	0.82, 1.35	127	0.97	0.75, 1.26
≥3/week	155	53,502	1.11	1.11	0.91, 1.35	53	1.05	0.76, 1.43	83	1.10	0.82, 1.46
P_{trend}					0.30			0.68			0.51
$P_{interaction}$								0.89			

Abbreviations: CI, confidence interval; IRR, incidence rate ratio.

[a] Adjusted for age and energy intake.

[b] Adjusted for age, energy intake, age at menarche, body mass index at age 18 years, family history of breast cancer, education, geographic region, parity, age at first birth, oral contraceptive use, menopausal status, age at menopause, menopausal hormone use, vigorous activity, smoking status, alcohol intake, and multivitamin use.

[c] Baseline diet only.

Table 4. Intake of Fruits and Vegetables in Relation to Risk of Breast Cancer by ER/PR Status in the Black Women's Health Study, 1995–2007

	ER+/PR+ Cases			ER+/PR− Cases			ER−/PR− Cases		
	Cases, No.	IRR[a]	95% CI	Cases, No.	IRR[a]	95% CI	Cases, No.	IRR[a]	95% CI
Total fruits and vegetables, servings									
<1/day	52	1.00	Referent	14	1.00	Referent	53	1.00	Referent
1/day	106	1.20	0.86, 1.69	28	1.13	0.59, 2.17	75	0.90	0.63, 1.29
2–3/day	155	1.31	0.94, 1.82	37	1.10	0.58, 2.09	100	0.97	0.68, 1.38
≥4/day	53	0.96	0.64, 1.46	24	1.43	0.69, 2.94	36	0.79	0.50, 1.24
P_{trend}			0.62			0.33			0.40
Total vegetables, servings									
<4/week	53	1.00	Referent	16	1.00	Referent	71	1.00	Referent
4–6/week	84	1.40	0.99, 1.99	20	1.03	0.53, 2.00	56	0.71	0.50, 1.01
1/day	142	1.54	1.11, 2.14	41	1.34	0.74, 2.45	93	0.79	0.57, 1.10
≥2/day	87	1.41	0.97, 2.04	26	1.20	0.61, 2.36	44	0.57	0.38, 0.85
P_{trend}			0.25			0.59			0.02
Cruciferous vegetables, servings									
<1/week	49	1.00	Referent	11	1.00	Referent	49	1.00	Referent
1–2/week	157	1.16	0.83, 1.60	41	1.24	0.63, 2.44	109	0.83	0.59, 1.18
3–5/week	115	1.36	0.96, 1.93	32	1.57	0.77, 3.18	67	0.86	0.59, 1.26
≥6/week	45	0.80	0.52, 1.23	19	1.38	0.63, 3.01	39	0.81	0.52, 1.26
P_{trend}			0.17			0.47			0.56
Green leafy vegetables, servings									
<1/week	66	1.00	Referent	18	1.00	Referent	61	1.00	Referent
1–2/week	109	1.03	0.76, 1.41	30	1.03	0.57, 1.86	100	1.08	0.78, 1.49
3–5/week	125	1.25	0.92, 1.71	37	1.27	0.71, 2.28	65	0.77	0.54, 1.11
≥6/week	66	1.14	0.80, 1.63	18	1.00	0.51, 1.99	38	0.80	0.52, 1.22
P_{trend}			0.36			0.94			0.09

Table continues

tumors (16). ER+/PR+ breast cancer has been shown to be more strongly associated with hormonal risk factors than are ER−/PR− tumors (11, 32). Therefore, modest associations between dietary intake and breast cancer may be more readily detected for ER−/PR− breast cancer, given that these tumors are less influenced by hormonal factors.

On the other hand, 2 case-control studies observed associations for fruit and vegetable intake with ER+ breast cancer. The Long Island Breast Cancer Study Project case-control study found an inverse association among postmenopausal women between fruit and vegetable intake and ER+/PR+ but not ER−/PR− breast cancer (17), and a case-control study in Poland reported an inverse association between fruit intake and breast cancer that was stronger for ER+ tumors than for ER− tumors (18).

We previously reported a significant inverse association between a prudent dietary pattern and ER−/PR− breast cancer in the Black Women's Health Study (22). The food groups most highly correlated with a prudent dietary pattern were vegetables, fruit, whole grains, and fish. In our current analyses, the association between vegetable intake and risk of ER−/PR− breast cancer persisted after adjustment for other major components of a prudent dietary pattern, suggesting that the vegetable component of the prudent dietary pattern is driving the inverse association of a prudent dietary pattern with ER−/PR− breast cancer.

Most previous studies of the relation between intakes of vegetables and fruit and breast cancer risk have been conducted among predominantly white populations (4, 5). Although a greater range of fruit and vegetable intake was observed in prior studies in comparison to the Black Women's Health Study, evidence suggests that African-American women consume more cruciferous vegetables than do white women (21). Consumption of specific fruits and vegetables, rather than total fruit and vegetable intake, may play a greater role in breast cancer risk (6–8), and therefore we focused our analysis on fruit and vegetable subgroups.

No specific group of vegetables appeared to explain the inverse association between total vegetable intake and risk of ER−/PR− breast cancer. The estimates for frequent consumption of cruciferous vegetables, green leafy vegetables,

Table 4. Continued

	ER+/PR+ Cases			ER+/PR− Cases			ER−/PR− Cases		
	Cases, No.	IRR[a]	95% CI	Cases, No.	IRR[a]	95% CI	Cases, No.	IRR[a]	95% CI
Yellow-orange vegetables, servings									
<1/week	77	1.00	Referent	16	1.00	Referent	90	1.00	Referent
1–2/week	146	1.30	0.98, 1.72	45	1.84	1.03, 3.29	88	0.69	0.51, 0.94
3–5/week	87	1.19	0.87, 1.64	26	1.63	0.85, 3.11	53	0.69	0.49, 0.99
≥6/week	56	1.31	0.91, 1.89	16	1.63	0.78, 3.38	33	0.72	0.47, 1.10
P_{trend}			0.37			0.56			0.21
Total fruits, servings									
<2/week	61	1.00	Referent	17	1.00	Referent	53	1.00	Referent
2–6/week	130	1.04	0.77, 1.42	34	0.93	0.52, 1.68	99	0.99	0.71, 1.39
1/day	122	1.18	0.86, 1.63	38	1.21	0.68, 2.21	74	0.98	0.68, 1.41
≥2/day	53	1.02	0.69, 1.50	14	0.84	0.40, 1.76	38	1.04	0.67, 1.61
P_{trend}			0.80			0.87			0.88
Citrus, servings									
<1/week	160	1.00	Referent	39	1.00	Referent	128	1.00	Referent
1–2/week	103	1.17	0.91, 1.51	29	1.32	0.81, 2.15	70	1.02	0.76, 1.38
3–5/week	76	1.28	0.97, 1.70	24	1.61	0.96, 2.71	42	0.97	0.68, 1.39
≥6/week	27	0.84	0.55, 1.28	11	1.33	0.67, 2.64	24	1.03	0.66, 1.62
P_{trend}			0.88			0.24			0.95
Other fruit, servings									
<2/week	91	1.00	Referent	30	1.00	Referent	73	1.00	Referent
2–4/week	99	1.03	0.77, 1.38	28	0.84	0.50, 1.42	84	1.20	0.87, 1.64
5–8/week	100	1.16	0.86, 1.56	25	0.81	0.47, 1.41	56	0.95	0.66, 1.36
≥9/week	76	1.12	0.81, 1.55	20	0.74	0.40, 1.35	51	1.15	0.79, 1.69
P_{trend}			0.40			0.35			0.76

Abbreviations: CI, confidence interval; ER, estrogen receptor; IRR, incidence rate ratio; PR, progesterone receptor; +, positive; −, negative.

[a] Adjusted for age, energy intake, age at menarche, body mass index at age 18 years, family history of breast cancer, education, geographic region, parity, age at first birth, oral contraceptive use, menopausal status, age at menopause, menopausal hormone use, vigorous activity, smoking status, alcohol intake, and multivitamin use.

and yellow-orange vegetables were each compatible with a reduced risk of breast cancer, but the incidence rate ratios were not statistically significant.

Some (4, 6, 33, 34) but not all (5, 15, 18, 35) studies that considered all breast cancers without regard to subtype support a protective effect of broccoli and other cruciferous vegetables on breast cancer risk. Although a pooled analysis of 8 prospective cohort studies did not find an association with breast cancer risk for intake of total vegetables or total fruit, broccoli was associated with a reduced risk that was marginally significant (4). The pooled analysis, which included mostly postmenopausal cases, did not observe effect modification by menopausal status. A population-based case-control study in Sweden, which found no association between total vegetable intake and postmenopausal breast cancer risk, observed a significant decreased risk for higher consumption of cruciferous vegetables (6). One case-control study reported a marginally significant inverse association between broccoli intake and breast cancer risk among premenopausal but not postmenopausal women (33), whereas another case-control study observed inverse associations for intakes of cruciferous vegetables with breast cancer risk primarily among postmenopausal but not premenopausal women (34). We observed a significant inverse association between cruciferous vegetable intake and breast cancer risk among premenopausal women regardless of breast cancer subtype. Although we observed no association among all postmenopausal women, there was a nonsignificant inverse association among postmenopausal women who had never used menopausal hormones, suggesting that relatively modest effects of diet may not be evident among women at increased risk of breast cancer due to the use of exogenous hormones.

Broccoli and other cruciferous vegetables are sources of glucosinolates, which are metabolized into indoles and isothiocyanates, potential chemoprotective compounds. Indoles exert antiestrogenic effects and inhibit transcription of estrogen-responsive genes (36), and it has been shown that increased cruciferous vegetable intake shifts estrogen metabolism toward metabolites with less estrogenic potential (37). Isothiocyanates induce phase II enzymes (e.g., glutathione *S*-transferases) and thereby play an important role in the detoxification of carcinogens (36).

Although the epidemiologic evidence has been inconsistent, several case-control studies have reported inverse associations for intakes of carrots and other yellow-orange vegetables with breast cancer risk (7, 8, 17, 38, 39). In the present study, carrot intake was inversely associated with breast cancer risk overall. Carrots and other yellow-orange vegetables are rich sources of carotenoids, which have also been associated with a reduced risk of breast cancer (17, 38–42). The primary mechanism by which carotenoids are proposed to prevent cancer is by reducing oxidative DNA damage (43). Some carotenoids are also converted into vitamin A, which is involved in cellular differentiation and may play a role in preventing cancer (44).

Strengths of our study include its large size, prospective design, high rate and length of follow-up, and information on breast cancer risk factors and other potential confounders. The analysis included nearly 300 ER−/PR− cases, a subtype of breast cancer with few established risk factors. Misclassification of long-term dietary intake would likely be random and would have attenuated true associations. It is possible that unknown lifestyle factors may partially account for our findings, but we were able to control for several established breast cancer risk factors, which did not appreciably influence our results. Because we examined a large number of associations in these analyses, it is more likely that a given significant finding may be due to chance, and our results need to be confirmed.

In conclusion, results from the present study of African-American women suggest that increased consumption of vegetables may decrease the risk of ER−/PR− breast cancer. Furthermore, our findings suggest that higher intakes of cruciferous and carotenoid-rich vegetables may reduce risk of breast cancer overall. Future studies investigating the association between subclasses of vegetables and subtypes of breast cancer are warranted.

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