



## Original Contribution

# Associations Between Dietary Patterns and Head and Neck Cancer

## The Carolina Head and Neck Cancer Epidemiology Study

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Few studies have examined the associations between dietary patterns and head and neck squamous cell carcinoma (SCC) or whether they differ by race. This was evaluated using data from a population-based case-control study (2002–2006) including 1,176 cases of head and neck SCC and 1,317 age-, race-, and gender-matched controls from central and eastern North Carolina whose diets had been assessed by food frequency questionnaire. Factor analysis identified 2 patterns of intake: 1) high consumption of fruits, vegetables, and lean protein and 2) high consumption of fried foods, high-fat and processed meats, and sweets. Associations were estimated using logistic regression, adjusting for matching factors and confounders. Heterogeneity by tumor site (oral/pharyngeal vs. laryngeal) and effect-measure modification were also evaluated. Reduced odds of head and neck SCC were found for the fruit, vegetable, and lean protein pattern (for highest quartile vs. lowest, odds ratio = 0.53, 95% confidence interval: 0.39, 0.71). The fried foods, high-fat and processed meats, and sweets pattern was positively associated only with laryngeal cancer (odds ratio = 2.12, 95% confidence interval: 1.21, 3.72). These findings underline the importance of a dietary pattern rich in fruits and vegetables and low in high-fat and processed meats and sweets for prevention of head and neck cancer.

carcinoma, squamous cell; diet; factor analysis, statistical; fruit; head and neck neoplasms; meat; vegetables

Abbreviations: CHANCE, Carolina Head and Neck Cancer Epidemiology; CI, confidence interval; OR, odds ratio; SCC, squamous cell carcinoma.

Cancers of the head and neck, which generally include squamous cell carcinomas (SCCs) of the oral cavity, pharynx, and larynx, represent a significant cancer burden in the United States and worldwide (1, 2). In the United States alone, 40,250 diagnoses of oral and pharyngeal cancer and 12,360 diagnoses of laryngeal cancer are expected in the year 2012 (3). Incidence rates for these cancers are typically higher for men than for women; black men in particular have the greatest incidence of cancer at both sites (4).

Tobacco and alcohol use remain the strongest behavioral risk factors for head and neck SCC (1, 2); however, the additional importance of dietary exposures is emerging (5). Although many investigators have noted reduced risks for

consumption of fruits and vegetables, as well as their related micronutrients (6–8), only a few studies have explored the association between dietary patterns and head and neck SCC (9–14). Additionally, studies examining effect modification of diet by race, gender, or body size have been lacking, and these results may have significant implications for public health interventions.

To investigate the association between dietary patterns and risk of head and neck SCC, we examined data from a large, population-based case-control study carried out in central and eastern North Carolina. We additionally evaluated whether these associations were similar across tumor sites and whether they differed by race, gender, smoking, or alcohol consumption.

## MATERIALS AND METHODS

The Carolina Head and Neck Cancer Epidemiology (CHANCE) Study is a population-based case-control study of head and neck SCC carried out among 46 counties in central and eastern North Carolina (15). The study protocol was approved by the institutional review boards of all participating institutions.

### Study population

Cases for this study were adults between the ages of 20 and 80 years who resided within a 46-county region in central and eastern North Carolina and were diagnosed with a new first primary invasive SCC of the oral cavity or pharynx (*International Classification of Diseases for Oncology*, Third Edition, topography codes C0.00–C14.8) or larynx (codes C32.0–C32.9) between January 1, 2002, and February 28, 2006. A rapid case ascertainment system was utilized through the North Carolina Cancer Registry and included monthly contact with the cancer registrars of 54 hospitals within the study area to identify potentially eligible cases. Potential controls who resided in the same counties were identified through North Carolina Department of Motor Vehicle records and were frequency-matched with cases on age group, race, and gender. Potential study subjects were contacted by mail, and in-home interviews were conducted for those who consented in writing. Contact was made with 98% of eligible cases, of whom 82% agreed to participate, while 80% of eligible controls were contacted, with 61% agreeing to take part in the study.

### Exposure assessment

A structured questionnaire administered by trained interviewers was completed during the in-home visit to assess information on demographic, lifestyle, and dietary behaviors. Questionnaires collected information on factors associated with head and neck SCC, including cigarette smoking, alcohol use, anthropometric measures, and education. Dietary intakes were assessed through a modified version of the National Cancer Institute's Diet History Questionnaire (16) that assessed servings per day, week, or month of various foods. The diet questionnaire was modified to account for the dietary and cooking practices of the region. Data from the modified Diet History Questionnaire were processed with the Diet\*Calc analysis program (17) to obtain information on total energy intake per day and consumption of 72 individual food items (in g/day). To eliminate the influence of outliers, we excluded subjects for whom total energy intake was below the 2.5th percentile (944.86 kcal/day) or above the 97.5th percentile (4,324.22 kcal/day) among all subjects ( $n = 135$ ). The final sample for this analysis included 1,176 cases and 1,317 controls.

### Statistical analysis

Dietary patterns were derived using factor analysis, an established method of data reduction that is frequently used in analyses of multiple dietary variables (18). Factor analysis

was conducted on the 72 food variables (expressed in g/day of intake), and the retained factors were made orthogonal through varimax rotation (19). Retention of derived factors was determined through consideration of the pattern of the eigenvalues, as well as interpretability of the factors. Factors with eigenvalues greater than 2.0 were retained for final analysis, resulting in a 2-factor solution. Each of the derived dietary patterns was named according to the strongest factor loadings of the foods found in that pattern and categorized according to quartiles of the distribution among the control subjects.

We employed unconditional logistic regression (20), adjusting for matching strata defined by the combination of age (20–49, 50–54, 55–59, 60–64, 65–69, 70–74, or  $\geq 75$  years), race (black, white, other), and gender (male, female) (21), to estimate odds ratios and 95% confidence intervals for the association between dietary patterns and head and neck SCC. Potential confounders included those variables thought to be associated with risk of head and neck cancer or levels of dietary intake: body mass index (weight in kilograms divided by squared height in meters;  $<25$ , 25–29.9, or  $\geq 30$ ), total energy intake (kcal/day; continuous), duration of cigarette smoking (never smoker or 1–19, 20–39, or  $\geq 40$  years), number of 12-ounce (0.4-L) servings of beer consumed per week (none,  $<1$ , 1–4, 5–14, 15–29, or  $\geq 30$ ), number of 1.5-ounce (44.4-mL) servings of hard liquor consumed per week (none,  $<1$ , 1–4, 5–14, 15–29, or  $\geq 30$ ), and education (high school completion or less, some college, college completion or more). Residual confounding by smoking was explored using alternative parameterizations of the smoking variable, and results were nearly identical (data not shown).

Confounders that altered any odds ratio by more than 10% were included in the final model; total energy intake, number of years of cigarette smoking, number of servings of beer per week, number of servings of liquor per week, and education met this criterion. Tests for linear trend were performed by including the derived factor as a continuous variable in the logistic model. Multinomial logistic regression was used to estimate effects across tumor types (oral/pharyngeal vs. control and laryngeal vs. control). Homogeneity of effect across tumor sites was evaluated by testing equality of corresponding coefficients on dietary pattern variables for the 2 equations in the model with the likelihood ratio test, which compared the model allowing the effects to vary across tumor site with the model in which the effects were constrained to be the same across tumor site. Heterogeneity of effect was determined at a significance level of  $P < 0.05$ .

Multiplicative interaction (21) between dietary patterns and race, gender, smoking, alcohol use, and body mass index was assessed using the likelihood ratio test to compare models with and without interaction terms; these interactions were deemed significant for  $P$  values less than 0.05. When examining interactions by race, subjects in the "other race" category were omitted from the analysis. For the purposes of evaluating effect modification, we collapsed the categories for the liquor and beer variables into 0,  $<1$ –4, and  $\geq 5$  drinks/week, the categories for cigarette smoking into never,  $<1$ –19.9, and  $\geq 20$  years, and the categories for body mass index into overweight ( $\geq 25$ ) and nonoverweight ( $<25$ ), in order to reduce the imprecision caused by small strata.

**Table 1.** Distribution of Sociodemographic and Anthropometric Factors Among Cases With Head and Neck Squamous Cell Carcinoma and Controls, CHANCE Study, North Carolina, 2002–2006

Variable	Controls (n = 1,317)		Cases (n = 1,176)	
	No.	%	No.	%
Age group, years				
<50	146	11.1	230	19.6
50–54	154	11.7	188	16.0
55–59	200	15.2	188	16.0
60–64	199	15.1	203	17.3
65–69	236	17.9	160	13.6
70–74	223	16.9	131	11.1
≥75	159	12.1	76	6.5
Race				
White	1054	80.0	880	74.8
Black	246	18.7	274	23.3
Other	17	1.3	22	1.9
Gender				
Male	909	69.0	899	76.5
Female	408	31.0	277	23.6
Body mass index <sup>a</sup>				
<18.5	10	0.8	35	3.0
18.5–24.9	396	30.1	439	37.3
25.0–29.9	534	40.6	400	34.0
≥30.0	375	28.5	302	25.7
Education				
High school or less	518	39.3	707	60.1
Some college	388	29.5	291	24.7
College graduation or more	411	31.2	178	15.1
Liquor consumption, 1.5-ounce (44.4-mL) servings per week				
0	462	35.3	246	21.0
<1	271	20.7	181	15.5
1–4	285	21.8	215	18.4
5–14	161	12.3	184	15.7
15–29	70	5.3	138	11.8
≥30	61	4.7	207	17.7
Beer consumption, 12-ounce (0.4-L) servings per week				
0	478	36.5	222	19.0
<1	185	14.1	98	8.4
1–4	281	21.4	177	15.1
5–14	227	17.3	259	22.2
15–29	69	5.3	149	12.7
≥30	71	5.4	264	22.6
Duration of cigarette smoking, years				
Never smoker	505	38.4	160	13.6
1–19	281	21.4	110	9.4
20–39	317	24.1	449	38.2
≥40	211	16.1	455	38.8

Table continues

**Table 1.** Continued

Variable	Controls (n = 1,317)		Cases (n = 1,176)	
	No.	%	No.	%
Total energy intake, kcal/day				
944.9–1,440.0	263	20.0	116	9.9
1,440.1–1,763.5	263	20.0	127	10.8
1,763.6–2,056.5	264	20.0	157	13.4
2,056.6–2,474.4	263	20.0	240	20.4
2,474.5–4,324.22	264	20.0	536	45.6
Cancer site				
Oral/pharyngeal	N/A	N/A	757	64.4
Laryngeal	N/A	N/A	419	35.6

Abbreviations: CHANCE, Carolina Head and Neck Cancer Epidemiology; N/A, not applicable.

<sup>a</sup> Weight (kg)/height (m)<sup>2</sup>.

Analyses were conducted using Stata, version 11.0 (Stata-Corp LP, College Station, Texas).

**RESULTS**

The distributions of sociodemographic and anthropometric characteristics, as well as smoking, alcohol use, and total energy intake, by case-control status are given in Table 1. The average ages among the case and control subjects were 58.8 years and 61.6 years, respectively. Slightly more cases than controls were black (23.3% cases, 18.9% controls) and male (76.5% cases, 69.0% controls), while fewer cases (15.1%) than controls (31.2%) were college graduates. Liquor and beer intake and smoking were much more common among cases than among controls, reflecting the importance of these variables in the etiology of head and neck SCC. Total energy intake was also greater among the cases. Cancers of the oral cavity and pharynx accounted for the majority of the cases.

The first 2 derived factors explained over half of the variation in the data (53.6%) and yielded meaningful interpretations. The remaining variability in dietary intake was spread across the other 70 factors, with no discernable pattern to the factor loadings. For the 2 patterns used in this analysis, rotated factor loadings with absolute values greater than 0.20 for the individual food items are presented in Table 2. The first factor, explaining 27.0% of the variation in the data, loaded highly on fruits (bananas; strawberries; fruit salad; apples, pears, and applesauce; grapes, peaches, and cantaloupes; oranges and grapefruit), vegetables (carrots; string beans; cooked spinach, turnip greens, and collard greens; zucchini and squash; broccoli and cauliflower; salad), and sources of lean protein (light-meat chicken, not fried; seafood, not fried) and was deemed the “fruit, vegetable, and lean protein” pattern. The second pattern, explaining 26.6% of the variation, which we call the “fried foods, high-fat and processed meats, and sweets” pattern, loaded highly on beef (roast beef, burgers, ground beef), fried chicken (dark and light meat), candy and chocolate, ice cream, desserts, sugar-sweetened

**Table 2.** Rotated Factor Loadings for Food Items, CHANCE Study, North Carolina, 2002–2006<sup>a</sup>

Food Item	Factor 1 (Fruits, Vegetables, and Lean Protein)	Factor 2 (Fried Foods, High-fat and Processed Meats, and Sweets)
Milk, low-fat	0.21	
Beef, roast		0.24
Beef, burgers		0.22
Beef, ground	−0.22	0.30
Hot dogs		0.46
Chicken, fried, light meat		0.32
Chicken, fried, dark meat		0.27
Chicken, light meat (not fried)	0.32	−0.21
White bread	−0.30	0.40
Whole-grain bread	0.32	
Cornbread		0.36
Pretzels		
Hot cereals		0.25
Cereal, ready to eat	0.26	
Rice and grains		0.27
Pasta with meatless red sauce	0.21	0.20
Macaroni and cheese		0.42
Bananas	0.47	
Strawberries	0.43	
Fruit salad and other fruits	0.61	
Beans, no fat added	0.24	
Beans, fat added		0.43
Potatoes, fried		0.40
Sweet potatoes	0.28	0.25
Carrots	0.52	
Tomatoes, raw	0.40	
Mayonnaise, regular		0.33
Lard		0.28
Candy and chocolate		0.20
Gravy		0.43
Coleslaw and cabbage		0.30
Fruit juice	0.29	
Sugar-sweetened beverages	−0.24	0.27
String beans	0.28	0.24
Potatoes		0.30
Ketchup and salsa		0.26
Peanuts	0.21	
Sausage and bacon		0.50
Chips and popcorn		0.24
Ice cream		0.24
Desserts		0.24
Mustard greens		0.31
Cooked spinach, turnip greens, or collard greens	0.31	0.31

Table continues

**Table 2.** Continued

Food Item	Factor 1 (Fruits, Vegetables, and Lean Protein)	Factor 2 (Fried Foods, High-fat and Processed Meats, and Sweets)
Zucchini and squash	0.34	
Pork products		0.46
Hash and Spam <sup>b</sup>		0.35
Bologna and ham		0.32
Apples, pears, and applesauce	0.51	
Grapes, peaches, and cantaloupes	0.47	
Broccoli and cauliflower	0.52	
Oranges and grapefruit	0.47	
Soups	0.26	
Eggs		0.41
Seafood, not fried	0.38	
Seafood, fried		0.40
Salad	0.51	

Abbreviation: CHANCE, Carolina Head and Neck Cancer Epidemiology.

<sup>a</sup> Only factor loadings  $\geq 0.20$  in absolute value are displayed. Food items with factor loadings  $< 0.20$  for both factors have been omitted.

<sup>b</sup> Hormel Foods Corporation, Austin, Minnesota.

beverages, sausage and bacon, pork products, hash and Spam (Hormel Foods Corporation, Austin, Minnesota), bologna and ham, and fried seafood.

The fruit, vegetable, and lean protein pattern was associated with decreased risk of head and neck SCC overall (Table 3), with decreasing risk being observed across increasing levels of intake (for quartile 4 vs. quartile 1, odds ratio (OR) = 0.53, 95% confidence interval (CI): 0.39, 0.71) and a significant linear trend ( $P < 0.0005$ ). Although the association between the highest intake of this pattern and oral and pharyngeal cancer (OR = 0.45, 95% CI: 0.32, 0.63) was somewhat stronger than for laryngeal cancer (OR = 0.73, 95% CI: 0.48, 1.10), this heterogeneity of effect failed to reach statistical significance ( $P$ -heterogeneity = 0.24).

In contrast, the dietary pattern characterized by fried foods, high-fat meats, and sweets was associated with an increased risk of head and neck SCC (OR = 1.24, 95% CI: 0.84, 1.82;  $P$ -trend = 0.02). The elevated risk for this dietary pattern was essentially limited to laryngeal cancer (OR = 2.12, 95% CI: 1.21, 3.72), because a nearly null relation was observed when oral and pharyngeal cancers were considered (OR = 0.96, 95% CI: 0.63, 1.47;  $P$ -heterogeneity = 0.05).

As Table 4 shows, the pattern characterized by high fruit, vegetable, and lean protein intake showed similar effects regardless of prediagnosis body mass index ( $P$ -interaction = 0.24), gender ( $P$ -interaction = 0.28), smoking duration ( $P$ -interaction = 0.18), liquor consumption ( $P$ -interaction = 0.99), and beer consumption ( $P$ -interaction = 0.50). Although an inverse association of this pattern with head and neck SCC risk was noted among all participants, the effect of higher



**Table 3.** Risk of Head and Neck Cancer According to Quartile of Dietary Pattern (Determined Among Control Subjects), Overall and by Cancer Site, CHANCE Study, North Carolina, 2002–2006

Dietary Pattern	No. of Controls	Overall			Oral/Pharyngeal Cancer			Laryngeal Cancer		
		No. of Cases	OR <sup>a</sup>	95% CI	No. of Cases	OR	95% CI	No. of Cases	OR	95% CI
Fruits, vegetables, and lean protein										
Q1	329	505	1		325	1		180	1	
Q2	329	294	0.77	0.60, 1.00	186	0.77	0.59, 1.01	108	0.78	0.56, 1.09
Q3	329	221	0.71	0.54, 0.94	148	0.71	0.52, 0.95	73	0.70	0.48, 1.03
Q4	330	156	0.53	0.39, 0.71	98	0.45	0.32, 0.63	58	0.73	0.48, 1.10
<i>P</i> -trend			<0.0005			<0.0005			0.08	
<i>P</i> -heterogeneity <sup>b</sup>					0.24					
Fried foods, high-fat and processed meats, and sweets										
Q1	329	133	1		101	1		32	1	
Q2	329	179	0.94	0.69, 1.29	126	0.90	0.64, 1.26	53	1.10	0.66, 1.83
Q3	329	264	1.02	0.74, 1.42	164	0.86	0.60, 1.24	100	1.53	0.93, 2.52
Q4	330	600	1.24	0.84, 1.82	366	0.96	0.63, 1.47	234	2.12	1.21, 3.72
<i>P</i> -trend			0.02			<0.005			0.01	
<i>P</i> -heterogeneity					0.05					

Abbreviations: CHANCE, Carolina Head and Neck Cancer Epidemiology; CI, confidence interval; OR, odds ratio; Q, quartile.

<sup>a</sup> Odds ratios were adjusted for matching strata (gender, race, age), total energy intake (continuous), tobacco use (number of years of cigarette smoking: never, 1–19, 20–39, or ≥40), beer consumption (number of 12-ounce (0.4-L) servings per week: none, <1, 1–4, 5–14, 15–29, or ≥30), liquor consumption (number of 1.5-ounce (44.4-mL) servings per week: none, <1, 1–4, 5–14, 15–29, or ≥30), and education (high school or less, some college, college or more).

<sup>b</sup> *P* value for test of heterogeneity of effect across tumor sites, assessed using the likelihood ratio test and a multinomial logistic regression model.

intake appeared to have more reduced odds among black subjects (OR = 0.28, 95% CI: 0.14, 0.59) than among white subjects (OR = 0.58, 95% CI: 0.42, 0.81; *P*-interaction = 0.14); however, this difference was not statistically significant. Linear trends were significant within strata of each of the effect modifiers considered here.

Although the interactions concerning the fried foods, high-fat and processed meats, and sweets pattern did not meet the criteria for heterogeneity, several patterns emerged. This pattern appeared to be more strongly associated with head and neck SCC risk among overweight persons (Table 5; OR = 1.70, 95% CI: 1.10, 2.62), with a nearly null effect being seen among those who were not overweight (OR = 0.89, 95% CI: 0.52, 1.52; *P*-interaction = 0.13). The association between high consumption of fried foods, high-fat meats, and sweets and cancer was stronger among blacks (OR = 1.92, 95% CI: 0.81, 4.58) than among whites (OR = 1.31, 95% CI: 0.88, 1.95) and stronger among persons who had smoked for a longer amount of time (for never smokers, OR = 0.97 (95% CI: 0.54, 1.75); for those who had smoked for <1–19 years, OR = 1.20 (95% CI: 0.60, 2.41); for those who had smoked for ≥20 years, OR = 1.94 (95% CI: 1.23, 3.07)). A stronger association was also noted for decreasing intake of beer (for 0 drinks/day, OR = 1.82 (95% CI: 1.01, 3.30); for <1–4 drinks/day, OR = 1.28 (95% CI: 0.75, 2.17); for ≥5 drinks/day, OR = 1.02 (95% CI: 0.60, 1.76)), but a similar pattern was not evident for liquor consumption. Linear trends were significant among overweight persons (*P*-trend = 0.004),

males (*P*-trend = 0.01), long-term smokers (*P*-trend < 0.0005), persons consuming 5 or more liquor-based drinks per day (*P*-trend = 0.002), and persons who consumed no beer (*P*-trend = 0.005).

The effect of dietary pattern was similar within cancer site (oral/pharyngeal vs. laryngeal) for most variables (data not shown), with the exception of race (*P*-interaction = 0.005). For oral and pharyngeal cancer, a stronger effect of the fruit, vegetable, and lean meat pattern was more evident among blacks (for quartile 4 vs. quartile 1, OR = 0.38, 95% CI: 0.19, 0.75) than among whites (OR = 0.54, 95% CI: 0.37, 0.78).

## DISCUSSION

Through factor analysis of food groups assessed using a food frequency questionnaire, using data from a large, population-based case-control study (CHANCE), we identified 2 dominant dietary patterns: 1) high consumption of fruits, vegetables, and lean protein and 2) high consumption of fried foods, high-fat and processed meats, and sweets. Our analysis of these patterns in relation to risk of head and neck SCC revealed that the fruit, vegetable, and lean protein pattern was associated with reduced risk of head and neck SCC. In contrast, the fried foods, high-fat and processed meats, and sweets pattern was associated with an increase in risk, but this association was limited to laryngeal cancer. Although we failed to detect heterogeneity, there

**Table 4.** Effect Modification of the Association of the Fruit, Vegetable, and Lean Protein Dietary Pattern With Risk of Head and Neck Squamous Cell Carcinoma by Anthropometric, Sociodemographic, and Lifestyle Factors, CHANCE Study, North Carolina, 2002–2006

	No. of Controls	No. of Cases	Quartile of Fruit, Vegetable, and Lean Protein Dietary Pattern								<i>P</i> <sub>trend</sub> <sup>a</sup>	<i>P</i> <sub>interaction</sub> <sup>b</sup>
			Q1	Q2		Q3		Q4				
				OR <sup>c</sup>	95% CI	OR	95% CI	OR	95% CI			
Body mass index <sup>d</sup>												
<25	496	474	1	0.61	0.40, 0.94	0.49	0.30, 0.79	0.41	0.25, 0.67	<0.0005		0.24
≥25	909	742	1	0.88	0.65, 1.19	0.85	0.61, 1.18	0.58	0.41, 0.83	<0.0005		
Gender												0.28
Male	909	899	1	0.88	0.60, 1.18	0.79	0.58, 1.08	0.55	0.38, 0.79	<0.0005		
Female	408	277	1	0.51	0.30, 0.85	0.52	0.31, 0.89	0.42	0.25, 0.70	<0.0005		
Race												0.14
White	1,054	880	1	0.87	0.60, 1.16	0.74	0.55, 1.01	0.58	0.42, 0.81	<0.0005		
Black	246	274	1	0.50	0.27, 0.82	0.58	0.32, 1.07	0.28	0.14, 0.59	<0.0005		
Smoking duration, years												0.18
Never smoker	505	160	1	1.08	0.63, 1.85	0.88	0.51, 1.50	0.39	0.21, 0.71	<0.0005		
<1–19	281	110	1	0.74	0.38, 1.45	0.74	0.38, 1.44	0.40	0.20, 0.83	0.03		
≥20	528	904	1	0.67	0.50, 0.92	0.56	0.39, 0.78	0.56	0.38, 0.81	<0.0005		
Liquor consumption, drinks/day												0.99
0	462	246	1	0.71	0.45, 1.13	0.63	0.37, 1.06	0.50	0.28, 0.80	0.001		
<1–4	556		1	0.81	0.54, 1.22	0.76	0.50, 1.15	0.55	0.35, 0.86	0.002		
≥5	292	529	1	0.78	0.51, 1.20	0.73	0.45, 1.15	0.51	0.31, 0.85	0.005		
Beer consumption, drinks/day												0.50
0	478	222	1	0.58	0.35, 0.96	0.65	0.39, 1.08	0.41	0.24, 0.70	<0.0005		
<1–4	466	275	1	0.66	0.42, 1.04	0.57	0.36, 0.94	0.46	0.28, 0.75	0.001		
≥5	367	672	1	0.96	0.66, 1.38	0.82	0.54, 1.24	0.61	0.38, 0.96	0.007		

Abbreviations: CHANCE, Carolina Head and Neck Cancer Epidemiology; CI, confidence interval; OR, odds ratio; Q, quartile.

<sup>a</sup> *P* value from test for linear trend.

<sup>b</sup> *P* value from likelihood ratio test of interaction.

<sup>c</sup> Odds ratios were adjusted for matching strata (gender, race, age), total energy intake (continuous), tobacco use (number of years of cigarette smoking: never, 1–19, 20–39, or ≥40), beer consumption (number of 12-ounce (0.4-L) servings per week: none, <1, 1–4, 5–14, 15–29, or ≥30), liquor consumption (number of 1.5-ounce (44.4-mL) servings per week: none, <1, 1–4, 5–14, 15–29, or ≥30), and education (high school or less, some college, college or more). Models for interaction by smoking duration, liquor consumption, and beer consumption included only the grouped version of the respective variable.

<sup>d</sup> Weight (kg)/height (m)<sup>2</sup>.

was a suggestive association of a reduced effect for the fruit, vegetable, and lean meat pattern that was stronger among blacks compared with whites, which was significant when oral and pharyngeal cancer were considered. The increased risk for the fried foods, high-fat meat, and sweets pattern also appeared somewhat stronger among overweight subjects. These findings underline the importance of intake of fruits and vegetables for prevention of head and neck cancer, while potentially implicating the carcinogenic potential of high-fat and processed foods for these tumor types.

Our findings are in agreement with previous work that has shown that dietary patterns involving greater consumption of fruits and vegetables are inversely associated with a lower cancer risk and that high consumption of fatty meat and animal products is positively associated with head and neck

cancer. In a recent hospital-based case-control study that examined the effect of dietary patterns derived from nutrient intakes on risks of oral and pharyngeal cancer, Edefonti et al. (12) found that the pattern typified by high intake of vitamins and fiber (which correlated highly with fruit and vegetable intake) was inversely associated with oral and pharyngeal cancer with a magnitude similar to that which we observed here (for quintile 5 vs. quintile 1, OR = 0.47, 95% CI: 0.34, 0.65); inverse associations were also found for patterns that loaded highly on unsaturated dietary fats and starches. Conversely, an increase in risk was noted for high consumption of a pattern that loaded highly on animal products (animal protein, animal fat, cholesterol, and saturated fatty acids) (OR = 1.56, 95% CI: 1.13, 2.15), which we did not observe with our pattern of high-fat and processed

**Table 5.** Effect Modification of the Association of the Fried Foods, High-Fat and Processed Meats, and Sweets Dietary Pattern With Risk of Head and Neck Squamous Cell Carcinoma by Anthropometric, Sociodemographic, and Lifestyle Factors, CHANCE Study, North Carolina, 2002–2006

	No. of controls	No. of Cases	Quartile of Fried Foods, High-Fat and Processed Meats, and Sweets Dietary Pattern								<i>P</i> <sub>trend</sub> <sup>a</sup>	<i>P</i> <sub>interaction</sub> <sup>b</sup>
			Q1	Q2		Q3		Q4				
				OR <sup>c</sup>	95% CI	OR	95% CI	OR	95% CI			
Body mass index <sup>d</sup>												
<25	496	474	1	0.65	0.39, 1.08	0.85	0.51, 1.43	0.89	0.52, 1.52	0.19	0.13	
≥25	909	742	1	1.20	0.81, 1.77	1.27	0.86, 1.88	1.70	1.10, 2.62	0.004		
Gender												
Male	909	899	1	0.98	0.67, 1.43	1.11	0.75, 1.62	1.38	0.90, 2.12	0.01	0.99	
Female	408	277	1	0.94	0.55, 1.59	1.08	0.64, 1.84	1.25	0.70, 2.24	0.17		
Race												
White	1,054	880	1	0.93	0.67, 1.30	1.11	0.79, 1.57	1.31	0.88, 1.95	0.02	0.65	
Black	246	274	1	1.44	0.54, 3.83	1.22	0.49, 3.04	1.92	0.81, 4.58	0.05		
Smoking duration, years												
Never smoker	505	160	1	0.77	0.45, 1.32	0.68	0.39, 1.19	0.97	0.54, 1.75	0.65	0.45	
<1–19	281	110	1	1.08	0.53, 2.17	1.10	0.54, 2.22	1.20	0.60, 2.41	0.36		
≥20	528	904	1	1.17	0.76, 1.80	1.51	0.99, 2.32	1.94	1.23, 3.07	<0.0005		
Liquor consumption, drinks/day												
0	462	246	1	0.79	0.43, 1.45	1.19	0.66, 2.13	1.30	0.70, 2.40	0.13	0.69	
<1–4	556	396	1	1.02	0.66, 1.58	1.07	0.68, 1.67	1.13	0.70, 1.83	0.32		
≥5	292	529	1	1.10	0.60, 2.04	1.04	0.58, 1.86	1.66	0.92, 2.98	0.002		
Beer consumption, drinks/day												
0	478	222	1	1.13	0.63, 2.06	1.31	0.73, 2.32	1.82	1.01, 3.30	0.005	0.47	
<1–4	466	275	1	1.16	0.71, 1.91	1.28	0.77, 2.13	1.28	0.75, 2.17	0.31		
≥5	367	672	1	0.67	0.39, 1.14	0.80	0.48, 1.34	1.02	0.60, 1.76	0.05		

Abbreviations: CHANCE, Carolina Head and Neck Cancer Epidemiology; CI, confidence interval; OR, odds ratio; Q, quartile.

<sup>a</sup> *P* value from test for linear trend.

<sup>b</sup> *P* value from likelihood ratio test of interaction.

<sup>c</sup> Odds ratios were adjusted for matching strata (gender, race, age), total energy intake (continuous), tobacco use (number of years of cigarette smoking: never, 1–19, 20–39, or ≥40), beer consumption (number of 12-ounce (0.4-L) servings per week: none, <1, 1–4, 5–14, 15–29, or ≥30), liquor consumption (number of 1.5-ounce (44.4-mL) servings per week: none, <1, 1–4, 5–14, 15–29, or ≥30), and education (high school or less, some college, college or more). Models for interaction by smoking duration, liquor consumption, and beer consumption included only the grouped version of the respective variable.

<sup>d</sup> Weight (kg)/height (m)<sup>2</sup>.

meats. We have no specific explanation for the lack of association in our study population. A high-fruit and -vegetable intake pattern was also found to be inversely associated with oral and pharyngeal cancer risk in 2 other case-control studies (9, 14). In a third study, Marchioni et al. (13) also reported a positive association between risk of oral cancer and a low-fruit and -vegetable intake pattern.

With regard to laryngeal cancer, Edefonti et al. (11) recently reported a strong protective effect of a vitamin and fiber pattern on laryngeal cancer risk (for quartile 4 vs. quartile 1, OR = 0.35, 95% CI: 0.24, 0.52), yet the magnitude of our association with a similar pattern was more modest. However, their report of a positive association between laryngeal cancer and an animal-products pattern was similar in magnitude to ours (OR = 2.34, 95% CI: 1.59, 3.45).

Similar to our findings, De Stefani et al. (10) recently found that a healthy dietary pattern (fish, fresh vegetables, fruit, and tea) was associated with lower risk of laryngeal cancer, while a Western pattern (fried meat, barbecued meat, processed meat, and fried eggs) was associated with an increase in risk.

To our knowledge, our study was the first to investigate the potential for differences in the effects of dietary patterns derived by means of factor analysis according to racial group and one of the few to examine effects of these patterns according to any other factors. Examining fruit and vegetable intake individually, Day et al. (22) found reduced odds of oral and pharyngeal cancer with increasing fruit intake among whites compared with blacks and reduced odds with increasing vegetable intake among blacks

compared with whites, yet neither of these contrasts achieved statistical significance. De Stefani et al. (10) reported that the inverse effect of their healthy pattern on laryngeal cancer risk was more pronounced among former smokers, while a high-fat dietary pattern increased risk only within this group. In the study by Edefonti et al. (11), the authors mentioned that they failed to detect significant heterogeneity of effect by education, alcohol consumption, tobacco use, or body mass index, while the inverse association between the fruit and vegetable pattern and risk held only for younger subjects. The suggestions of stronger effects of our fruit, vegetable, and lean meat pattern among black subjects, especially for oral and pharyngeal tumors, and stronger effects for the fried foods, high-fat and processed meats, and sweets pattern among overweight subjects are unique findings which warrant future study.

Individual dietary components (foods or specific nutrients) have been studied far more extensively than dietary patterns with respect to oral and pharyngeal cancer risk. In a recent review of studies of diet and oral and pharyngeal cancers, Lucenteforte et al. (7) noted a consistent decrease in risk with increasing consumption of fruits and vegetables across 3 cohort and 18 case-control studies that were used to produce pooled effect estimates for each of these food groups. The effects from the case-control studies were slightly stronger than those from the cohort studies; however, the pooled estimates were significant regardless of study design. The association of oral and pharyngeal cancer with high meat consumption, a prominent element in the second dietary factor we observed, is less clear in the extant literature, as a positive association of cancer risk with increasing meat intake was observed in 18 case-control studies, while a null finding was reported in 10 others. The 2 cohort studies included in this review did not find a significant association with total meat consumption. High fruit and vegetable intake has also been inversely related to risk of laryngeal cancer (8, 23), while high consumption of red and processed meats and high-sugar foods has been associated with increased risk (23). The results from previous studies lend credence to our findings; however, the high correlation in dietary intakes, which motivated our derivation of dietary patterns, precluded the identification of individual elements of these patterns that may be associated with cancer risk.

Critical evaluation of empirically derived dietary patterns is always prudent, and our findings are strengthened by biologic plausibility. Fruits and vegetables are high in numerous compounds thought to protect against cancer development, including several antioxidants such as carotenoids and vitamins C and E, as well as nutrients involved in DNA synthesis, such as folate (5). Meats can contain compounds that promote carcinogenesis, such as nitrates and nitrites in processed meat, as well as heterocyclic amines and polycyclic aromatic hydrocarbons in cooked and smoked meats (5). Notably, our higher-risk pattern also loaded highly on desserts and sweetened beverages. High-glycemic-load foods, such as these, are believed to increase blood glucose levels (24), which would therefore be accompanied by a compensatory increase in plasma levels of insulin, a hormone believed to encourage tumor proliferation (25, 26).

Our analysis benefited from a number of strengths. Our data were obtained from a large, racially diverse population-based case-control study, which allowed us to provide estimates that are more likely representative of similar source populations. Previous studies were relatively small (9, 10, 13, 14) and utilized hospital-based controls (9–14), making generalizability of their findings a potential issue. Additionally, we were able to investigate effect-measure modification by race, a potentially important factor in head and neck SCC etiology. Our study also benefited from a comprehensive assessment of important behaviors, notably smoking and alcohol use, which allowed for thorough control of these confounders. Our use of a theoretically sound approach to dietary pattern analysis allowed for estimation of the effect of meaningful dietary behaviors, with a reduced likelihood for the spurious statistical significance observed in analyses that consider multiple foods or nutrients individually (18).

Nonetheless, our findings must be evaluated in light of a few potential limitations. The response among controls (61%) was lower than is considered desirable. Our ability to find expected associations related to key risk factors, tobacco and alcohol, suggests that selection bias was limited; nonetheless, this cannot be ruled out. The use of a food frequency questionnaire to ascertain usual diet leaves open the possibility of measurement error. Although this is a concern, food frequency questionnaires have been shown to adequately rank dietary intakes (27), which is what the corresponding data were used for in our analysis. Differential recall is possible, since cases may recall dietary behaviors before diagnosis differently than noncases, as is inaccurate assessment of remote diet by questionnaire (27). While the use of empirical methods to derive dietary patterns has a number of benefits, as outlined above, it involves a degree of subjectivity in deriving the number of significant factors and interpretation of their meaning. Additionally, the dimensions identified by factor analysis are dependent upon the patterns of food consumption observed in the data set; therefore, it is possible that they may not correspond to the best dietary behavior (18).

In summary, our results suggest that a dietary pattern high in fruits, vegetables, and lean meats may reduce the risk of head and neck SCC, while a pattern high in fried foods, high-fat and processed meats, and sweets may increase the likelihood of laryngeal cancer. The protective effect of the fruit, vegetable, and lean protein pattern appears stronger among blacks, who have a much higher incidence of these cancers than whites. This finding may indicate a potential avenue for public health intervention.

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