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Fish/Shellfish Intake and the Risk of Head and Neck Cancer

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Abstract

Fish intake and other dietary sources of omega-3 fatty acids have been shown to be associated with a reduced risk for some cancers. Although previous studies of head and neck cancer have reported associations with different dietary factors, including reduced risks for fruits and vegetables and putatively healthy dietary patterns, associations specific to fish intake are unclear. This study investigated the association between fish/shellfish intake and risk of squamous cell carcinoma of the head and neck (SCCHN) using data from the Carolina Head and Neck Cancer Epidemiology Study, a population-based case-control study conducted in 46 NC counties with cases recruited from 2002 through 2006. Controls were frequency matched to the cases on age, sex, and race; the final sample size was 1,039 cases and 1,375 controls. Demographic, lifestyle, and dietary information were collected using an in-person interviewer-administered structured questionnaire. Multivariable-adjusted ORs and 95% confidence intervals (CIs) were estimated with unconditional logistic regression. Subjects whose fish/shellfish intake was among the highest tertile had a 20% lower odds of SCCHN compared to those in the lowest tertile (OR: 0.80; 95% CI: 0.60, 1.07) after adjustment for the matching and other factors (income, energy intake, fruit intake, cigarette smoking, and alcohol intake). The inverse association was more pronounced for oral cavity and oropharyngeal tumors, for African Americans, and for females, but CIs were wide. To further investigate this potential risk reduction strategy for SCCHN, future studies should consider examining specific fish/shellfish, cooking practices, and other omega-3 fatty acid sources.

Keywords

head and neck cancer; risk factors; diet; fish; shellfish

INTRODUCTION

Head and neck cancers (HNCs) typically include cancers of the oral cavity, pharynx, and larynx. In 2016 there were an estimated 48,330 new cases of oral cavity/pharyngeal cancer

and 9,570 deaths in the United States (US). Additionally, 13,430 new cases of laryngeal cancer and 3,620 deaths were expected (Siegel et al., 2016). HNCs are characterized by disparities in both sex and race: males are affected more than females, and African Americans are affected more than whites (Marur and Forastiere, 2008).

Tobacco use and alcohol intake are the most well-established risk factors for HNC (Hashibe et al., 2007, Hashibe et al., 2009, Maasland et al., 2014, Rettig and D'Souza, 2015). These factors have been shown to have dose-response relationships with HNC (Hashibe et al., 2007, Maasland et al., 2014), and there is evidence of a synergistic joint effect between them (Hashibe et al., 2009, Maasland et al., 2014). In addition, approximately 60–70% of oropharyngeal squamous cell carcinoma cases are now associated with the human papillomavirus (Chaturvedi et al., 2011). Although these risk factors may be responsible for a majority of HNC cases, other nutrition-related factors, such as body mass index (BMI) and dietary factors, have been shown to be associated with HNCs. In some studies, lower BMI has been associated with higher risk of HNC when compared to ideal BMI (18.5–24.9 kg/m²), whereas higher BMI has been associated with decreased risk of HNC (Gaudet et al., 2010, Petrick et al., 2014, Maasland et al., 2015). Research on diet has primarily focused on fruit and vegetable intake, and select micronutrients typically found in fruits/vegetables (Edefonti et al., 2015, Galeone et al., 2015, Leoncini et al., 2015), where higher intake of both fruits and vegetables has been associated with decreased risk of HNC (Chainani-Wu, 2002, Freedman et al., 2008, Lucenteforte et al., 2009).

Intake of fish and shellfish, a primary source of long-chain omega-3 polyunsaturated fatty acids, is a potentially modifiable risk factor for HNC. Omega-3 fatty acids, in particular the long-chain omega-3 fatty acids, have been shown to exhibit anti-inflammatory effects (Larsson et al., 2004), which may disrupt tumor growth and progression (Balkwill and Mantovani, 2001). In laboratory studies omega-3 fatty acids have been shown to reduce tumor formation and growth in mice (Fay et al., 1997, Rose and Connolly, 1999). The human body cannot make omega-3 fatty acids, and must rely on external sources for these essential fats; consumption of fish and other marine life is the primary external source (Rose and Connolly, 1999, Calder, 2011).

The limited evidence for the relationship between fish/shellfish consumption and HNCs has been gleaned from the analysis of dietary indices and patterns (Samoli et al., 2010, Toledo et al., 2010, Bradshaw et al., 2012, Edefonti et al., 2012, De Stefani et al., 2013, Filomeno et al., 2014, Li et al., 2014). These studies have suggested that fish/shellfish intake may reduce risk, but are considered as part of an overall “healthy” diet (plenty of fruits and vegetables, lean meats, etc.). Thus, the specific relationship of fish/shellfish consumption with HNC risk is unclear.

The objective of the study reported here was to estimate the association between fish/shellfish intake and the risk of squamous cell carcinoma of the head and neck (SCCHN). Secondary aims were to examine if these associations varied by SCCHN cancer sites, race, and sex.

METHODS

The Carolina Head and Neck Cancer Epidemiology (CHANCE) Study, a population-based case-control study of SCCHN, was conducted between 2002 and 2006 in central and eastern North Carolina (NC). The institutional review boards of participating institutions approved the study protocol. Details of the study have been published previously (Divaris et al., 2010), and are summarized below.

Study population

Cases were adults aged 20–80 with newly diagnosed first primary invasive squamous cell carcinoma of the oral cavity, oropharynx, hypopharynx, and larynx between January 1, 2002 and February 28, 2006 in a 46-county area of NC. Cases were ascertained through the NC Central Cancer Registry, which contacted the registrars of 54 area hospitals on a monthly basis to identify potentially eligible cases.

Controls were adults aged 20–80 who had never been diagnosed with HNC and were residents of the same 46-county area of NC. Potentially eligible controls were identified using the NC Department of Motor Vehicle records; and controls were frequency matched to the cases using random sampling with stratification on age group (20–49, 50–54, 55–59, 60–64, 65–69, 70–74, 75–80 years), sex (male and female), and race (white, African American, and other).

Of the eligible cases, contact was made with 98%, and 82% agreed to participate in the study; and of the eligible controls, contact was made with 80% and 61% agreed to participate.

Cases of lip cancer (due to the etiological differences), SCCHN cases with a site designation of “not otherwise specified,” and cases with proxy interviews were excluded. The final analysis sample included 1,039 cases (90% of case participants) and 1,375 controls (98% of control participants).

The subset of the CHANCE study population used here is similar to the overall CHANCE population (Divaris et al., 2010). This subset has a median age of 59 and 63 for cases and controls, respectively. It is also predominantly white (74% of cases, 80% of controls), male (78% of cases, 69% of controls), and of lower socioeconomic status (61% of cases, 45% of controls with annual household income < \$40,000).

Previous studies conducted using the CHANCE study population have shown that former and current tobacco use was associated with increased risk of SCCHN (in both African Americans and whites, but the effect estimate was more pronounced among African Americans) (Stingone et al., 2013); increasing lifetime alcohol use (ml of ethanol) was associated with increased risk of SCCHN (more pronounced among African Americans than whites) (Stingone et al., 2013); and leanness is associated with increased risk of SCCHN in both African Americans and whites, while overweight and obesity is associated with decreased risk in African Americans only, when compared to ideal BMI (Petrick et al., 2014).

Data collection

During an in-home visit a study nurse administered a structured questionnaire, which was completed by the subject, or by a proxy if the subject was deceased. The questionnaire assessed demographic, lifestyle, oral health, and dietary information. Dietary factors were assessed using a version of the National Cancer Institute's (NCI) Diet History Questionnaire (DHQ) (NIH, 2007), which assessed servings per day, per week, or per month of various food items one year prior. The dietary data was then processed with the Diet*Calc analysis program (Applied Research Program, 2005) to attain information on total energy intake per day (kcal/day) and intake of individual food items per day (g/day).

Exposure assessment

Fish/shellfish intake was self-reported using the DHQ described in the previous paragraph, and asked how often participants ate "fish sticks, fish, other seafood and shellfish", where answers ranged from never, 1–6 times per year, to 2 times per day. Using the information on frequency of fish/shellfish consumption, the number of oz. per day consumed for each participant was calculated. Fish/shellfish intake was then categorized using tertiles of intake (oz/day) based on intake distribution of the controls with cutpoints of 0.07, 0.07–0.14, and >0.14 oz/day.

Covariate assessment

Annual household income was self-reported and categorized as follows: \$20,000, \$20,001–\$40,000, \$40,001–\$60,000, \$60,001–\$80,000, and >\$80,000. Self-reported weight and height were used to calculate BMI (weight (kg)/height (m)²), which was categorized using the standard World Health Organization classifications (WHO, 1987,1995): 18.5 kg/m², 18.5–24.9 kg/m², 25.0–29.9 kg/m², and 30.0 kg/m². Cigarette smoking duration was assessed as lifetime years of smoking and categorized into never smokers, and quartiles based on the control distribution: 1–14 years, 15–27 years, 28–40 years, >40 years. Alcohol intake was assessed as lifetime consumption of ethanol (ml) and categorized into never drinkers, and tertiles based on the controls' distribution: 1–66,268.8 ml, 66,268.8–331,344 ml, >331,344 ml. Fruit intake and vegetable intake were both modeled continuously in servings per day. Total energy intake was modeled continuously in kcal/day, centered at the standard dietary recommendation of 2,000 kcal/day (US Department of Health Human Services, 2015).

Statistical methods

Unconditional logistic regression (Hosmer Jr et al., 2013) was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for associations between fish/shellfish intake and SCCHN, and all models included terms for the matching factors of age, sex, and race. In secondary analyses we estimated site-specific associations for oral cavity, oropharyngeal, and laryngeal cancer (compared to controls) in a single model using polytomous logistic regression (Kleinbaum and Klein, 2002); heterogeneity by tumor site was evaluated using a Wald test at the 0.10 significance level (Hosmer Jr et al., 2013). Hypopharyngeal cases were excluded from this analysis due to small sample size. Effect measure modification (EMM) on the multiplicative scale was assessed for race and sex at the 0.10 significant level using

the likelihood ratio test comparing models with and without the interaction term (Breslow et al., 1982, Rothman et al., 2008, Hosmer Jr et al., 2013).

Potential confounders were selected *a priori* using directed acyclic graph (Greenland et al., 1999) analysis and backwards elimination strategy with significance level of 0.10. Potential confounders included: annual household income, BMI, cigarette smoking duration, lifetime alcohol intake, fruit intake, vegetable intake, and total energy intake. After assessment of confounders, models were adjusted for the matching factors of age, sex, and race, as well as annual household income, duration of cigarette smoking, lifetime alcohol intake, fruit intake, and total energy intake. SAS version 9.3 (SAS Institute, Cary, NC) was used for all analyses.

RESULTS

The distribution of select participant characteristics, including BMI, smoking, alcohol intake, and energy intake, is shown by case/control status in Table 1. The mean age of controls was slightly higher than for the cases. The vast majority of participants, both cases and controls, were male and white. Controls were more likely to be college graduates or higher, compared to cases. Cases reported higher levels of both cigarette smoking and alcohol intake, and reported higher energy intakes from the FFQ. The majority of SCCHN cases were diagnosed with cancer of the larynx or oropharynx.

As shown in Table 2, after adjustment for the matching factors of age, sex, and race, as well as annual household income, duration of cigarette smoking, lifetime alcohol intake, and fruit intake, the highest tertile of fish/shellfish intake compared to the lowest tertile was associated with a 20% decrease in risk of SCCHN ($OR_{T3 \text{ vs. } T1}=0.80$; 95% CI: 0.60, 1.07), but confidence intervals included the null value. The odds ratio was similar when adjusted only for the matching factors.

For the analysis of SCCHN tumor sites (Table 3), the inverse association for the highest intake was more pronounced for oral cavity ($OR_{T3 \text{ vs. } T1}=0.71$; 95% CI: 0.44, 1.17) and oropharyngeal cancers ($OR_{T3 \text{ vs. } T1}=0.78$; 95% CI: 0.53, 1.13) than for laryngeal cancers ($OR_{T3 \text{ vs. } T1}=0.92$; 95% CI: 0.64, 1.33). The differences by tumor site were not statistically significant ($p_{\text{heterogeneity}}=0.86$).

With regards to race (Table 4), the decreased risk for SCCHN was more pronounced among African Americans ($OR_{T3 \text{ vs. } T1}=0.66$; 95% CI: 0.37, 1.16) than whites ($OR_{T3 \text{ vs. } T1}=0.88$; 95% CI: 0.64, 1.22), but the difference was not statistically significant on the multiplicative scale ($p_{\text{interaction}}=0.67$). The inverse association for fish/shellfish intake varied by sex (Table 4) with effect estimates more pronounced among females ($OR_{T3 \text{ vs. } T1}=0.67$; 95% CI: 0.38, 1.17) than among males ($OR_{T3 \text{ vs. } T1}=0.85$; 95% CI: 0.61, 1.17), although the difference was non-significant ($p_{\text{interaction}}=0.72$).

DISCUSSION

Among this population-based sample of NC residents, higher intake of fish/shellfish was associated with a non-statistically significant 20% decrease in risk of SCCHN, which is consistent with our hypothesis of an inverse association with omega-3 food sources. The

association with fish/shellfish intake may be more pronounced for cancers of the oral cavity and oropharynx, and perhaps among African Americans and females, but the precision of these comparisons are limited by sample size.

Previous epidemiologic studies examining the relationship between fish/shellfish intake and HNC are inconsistent. The INHANCE Consortium, of which CHANCE is a member, has previously shown an association between higher levels of seafood intake and lower risk of overall HNC (OR_{Q4 vs. Q1}=0.83; 95% CI: 0.74, 0.94) with a significant linear dose-response relationship ($p=0.02$), but EMM by race and other factors was not considered separately for seafood (Chuang et al., 2012). Also, INHANCE included Asian populations, where seafood intake is substantially higher than it is in the U.S. (FAOU, 2014); thus our study provides estimates among a bi-racial NC population which is more generalizable to the U.S. population. In the NIH-AARP cohort, there was a slightly decreased but non-statistically significant effect between fish intake and cancer of the oral cavity (HR_{Q5 vs. Q1}=0.90; 95% CI: 0.75, 1.09), but a null association with laryngeal cancer (HR_{Q5 vs. Q1}=1.03; 95% CI: 0.79, 1.36 (Daniel et al., 2011). In another study conducted in Italy and Switzerland, Bravi et al. found results similar to our own, including inverse relationships with higher levels of fish intake among oral and pharyngeal cancers (OR_{T3 vs. T1}=0.81; 95% CI: 0.60, 1.09) (Bravi et al., 2013). In another Italian study, however, Garavello et al. did not find any consistent relationship between fish and oral and pharyngeal cancer (Garavello et al., 2008). Similarly, a Spanish study found no association between fish and oral/oropharyngeal cancer (Sanchez et al., 2003). Finally, the most recent study using the Netherlands Cohort Study (Perloy et al., 2017) found no associations between fish intake and HNC overall or by cancer site. The inconsistencies between these studies and our analyses may be due to the differences in seafood intake, either differences in absolute intake, differences in type of fish/shellfish consumed (Mahaffey, 2004), or differences in cooking practices (Strobel et al., 2012) among country-specific populations, or the number of food line items specific to fish/shellfish on these FFQs.

However, studies examining *a posteriori* dietary patterns that include fish as a contributor or studies using *a priori* patterns, such as the Mediterranean diet, have shown reduced risk of HNCs with higher adherence. A study by Bradshaw et al. also using the CHANCE data found a reduction in risk (OR=0.53; 95% CI: 0.39, 0.71) for HNC with highest adherence to a “healthy” dietary pattern, which included non-fried seafood (Bradshaw et al., 2012). The estimate for oral/pharyngeal cancer was slightly more pronounced (OR=0.45; 95% CI: 0.32, 0.63), whereas the estimate for laryngeal cancer was attenuated (OR=0.73; 95% CI: 0.48, 1.10). A study from Uruguay (De Stefani et al., 2013) created a “prudent” dietary pattern in which fish was a contributor. For overall HNC in men only, this study found a 48% reduction in risk for highest adherence to the pattern (OR=0.52; 95% CI: 0.34, 0.76) (De Stefani et al., 2013). For male HNC by cancer site, the estimates were similar for oral/pharyngeal cancer and laryngeal cancer. A Brazilian study with a “prudent” dietary pattern, of which fish was a contributor, found a similar reduction in risk comparing those with the highest adherence to the lowest (OR=0.44; 95% CI: 0.25, 0.75) (Toledo et al., 2010).

In the Mediterranean diet, fish intake is a primary component for creating these diet scores (Trichopoulou et al., 2003). A Greek study examining upper aerodigestive tract cancers

found a reduction in risk (OR=0.59; 95% CI: 0.39, 0.89) with a three-unit increase in Mediterranean diet score (MDS) (Samoli et al., 2010). A study from Italy and Switzerland found an OR=0.73 (95% CI: 0.68, 0.78) for every 1-unit increase in MDS for oral and pharyngeal cancer (Filomeno et al., 2014). Li et al used the NIH-AARP cohort study to examine the alternate MDS (aMDS) and HNC, and by cancer site (Li et al., 2014). For men, there was a reduction in risk for HNC (HR=0.80; 95% CI: 0.64, 1.01) comparing the highest aMDS to the lowest, and for women a more pronounced reduction (HR=0.42; 95% CI: 0.24, 0.74). In men, higher aMDS was associated with reduced risk of laryngeal (HR=0.68; 95% CI: 0.45, 1.03) and oropharyngeal cancers (HR=0.54; 95% CI: 0.38, 0.79). In women, an association was only seen with oral cavity cancer (HR=0.47; 95% CI: 0.24, 0.93).

These dietary pattern studies support the results from our study, however the patterns represent an overall health-conscious diet consisting of fruits, vegetables, lean proteins, etc. in addition to fish intake. Our study is examining a more distinct exposure than the pattern represented by overall intake.

A component of fish/shellfish that could be a factor in the inverse associations noted by ours and some studies is long-chain omega-3 fatty acids, specifically eicosapentaenoic and docosahexaenoic fatty acids (Rose and Connolly, 1999, Stephenson et al., 2013, Fabian et al., 2015). These long-chain omega-3 fatty acids which are found in fish have been hypothesized to reduce cancer risk (Chavarro et al., 2007, Zheng et al., 2013) through several mechanisms including suppressing mutations (Larsson et al., 2004), reducing inflammation (Larsson et al., 2004), inhibiting cell growth (Larsson et al., 2004, Stephenson et al., 2013), and enhancing apoptosis (Larsson et al., 2004, Stephenson et al., 2013). There has also been suggestion that these fatty acids may be associated with increased immune function through this enhancement of apoptosis (Troyer and Fernandes, 1996, Avula et al., 2000, Johnson, 2002). Lastly, fish intake could reduce cancer risk by replacing less healthy options (such as red meat) with fish/shellfish; which can displace intake of some pro-inflammatory omega-6 fatty acids, which are hypothesized to increase cancer risk (Rose and Connolly, 1990, Brown et al., 2006), with omega-3 fatty acids. Thus, fish/shellfish intake should be considered for further examination as a risk reduction strategy for HNC because of its high content (relative to other food items) of omega-3 fatty acids.

Our population-based study among blacks and whites included a comprehensive assessment of dietary habits, and both known and suspected risk factors for SCCHN. However, there are a few limitations to consider when interpreting our findings. There was a lower response rate among the controls as compared to the cases, but is typical of population-based studies conducted among racially diverse populations (Hall et al., 2000). Using an FFQ as the dietary assessment method, allows for the possibility of measurement error, but is reliable for ranking individuals by relative intake (Willett, 2013). Due to the retrospective nature of the study, there is the potential for recall bias. However, overall intake of fish/shellfish among our population-based biracial sample was similar to the average intake in the US (NCI). Thus, recall of fish/shellfish does not appear to be a strong concern in our study. Nonetheless, nationally only about 10% of individuals meet or exceed recommendations for seafood intake. Fish is a substantially stronger source of dietary omega-3 than is shellfish (US Department of Health Human Services, 2007), however due to the wording of the

CHANCE questionnaire, we were unable to examine associations with fish separately, which would likely have increased the magnitude of the reduced effect estimates reported here. Finally, like all previous studies of SCCHN, we were not able to account for any possible omega-3 dietary supplement use.

In summary, our results suggest that higher consumption of fish/shellfish may be associated with a lower risk of SCCHN, and this association may be more pronounced for oral cavity and oropharyngeal cancer, for African Americans, and for females, although confidence intervals were wide. Our findings are consistent with some previous studies. To further investigate this potential association for SCCHN, future studies should consider examining fish and shellfish separately, specific fish/shellfish (such as white vs. dark, oily fish), cooking methods, and other omega-3 fatty acid sources including dietary supplements.

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Table 1

Demographic characteristic distribution by case control status among the CHANCE study participants, 2002–2006

	Cases (N=1,039) N (%)	Controls (N=1,375) N (%)
Age		
<50 yrs	196 (18.9)	156 (11.4)
50–54.9 yrs	164 (15.8)	163 (11.9)
55–59.9 yrs	180 (17.3)	206 (15.0)
60–64.9 yrs	174 (16.8)	208 (15.1)
65–69.9 yrs	141 (13.6)	246 (17.9)
70–74.9 yrs	118 (11.4)	231 (16.8)
75 yrs	66 (6.4)	165 (12.0)
Sex		
Male	808 (77.8)	946 (68.8)
Female	231 (22.2)	429 (31.2)
Race		
White	768 (73.9)	1,099 (79.9)
African American	249 (24.0)	259 (18.8)
Other	22 (2.1)	17 (1.2)
Income		
\$20,000	366 (36.4)	255 (19.3)
\$20,001–\$40,000	251 (25.0)	335 (25.3)
\$40,001–\$60,000	172 (17.1)	284 (21.4)
\$60,001–\$80,000	89 (8.9)	174 (13.1)
\$80,001	127 (12.6)	277 (20.9)
Education		
High School or Less	656 (63.1)	541 (39.4)
Some College	243 (23.4)	411 (30.0)
College Graduation or More	140 (13.5)	423 (30.8)
BMI		
<18.5 kg/m ²	35 (3.4)	11 (0.8)
18.5–24.9 kg/m ²	379 (36.5)	411 (29.9)
25.0–29.9 kg/m ²	364 (35.0)	553 (40.3)
30.0 kg/m ²	261 (25.1)	398 (29.0)
Cigarette Smoking Duration		
Never Smokers	118 (11.4)	525 (38.3)
14 yrs	59 (5.7)	214 (15.6)
15–27 yrs	131 (12.6)	215 (15.7)
28–40 yrs	347 (33.4)	209 (15.2)
>40 yrs	383 (36.9)	209 (15.2)
Alcohol Intake (lifetime)		

	Cases (N=1,039) N (%)	Controls (N=1,375) N (%)
Never Drinkers	96 (9.7)	292 (21.9)
<66,268.8 ml	108 (11.0)	348 (26.1)
66,268.8 –331,344 ml	187 (19.0)	341 (25.6)
>331,344 ml	595 (60.3)	351 (26.4)
Total Energy Intake (kcal/day) *	2,572.3 (1,027.4)	1,970.4 (701.9)
Fruit Intake (servings/day) *	2.1 (1.7)	2.6 (1.7)
Vegetable Intake (servings/day) *	2.4 (1.4)	2.1 (1.0)
Cancer Site		
Larynx	446 (42.9)	N/A
Oral Cavity	195 (18.8)	N/A
Oropharynx	343 (33.0)	N/A
Hypopharynx	55 (5.3)	N/A

* Mean (SD)

Table 2

Association between fish/shellfish intake and SCCHN in CHANCE participants, 2002–2006

Fish/shellfish intake (oz. per day)	Cases N (%)	Controls N (%)	Matching only[*] OR (95% CI)	Adjusted^{**} OR (95% CI)
0.07	444 (42.7)	598 (43.5)	1	1
0.07–0.14	386 (37.2)	462 (33.6)	1.10 (0.92, 1.33)	1.13 (0.89, 1.42)
>0.14	209 (20.1)	315 (22.9)	0.83 (0.67, 1.04)	0.80 (0.60, 1.07)

^{*} Adjusted for matching factors of age, sex, and race

^{**} Adjusted for matching factors of age, sex, and race; income; smoking; drinking; total energy intake; fruit intake

Table 3

Association between fish/shellfish intake and SCC/HN by cancer site^{*}, 2002–2006

Fish/shellfish intake (oz. per day)	Controls N (%)	Larynx		Oral Cavity		Oropharynx	
		N (%)	OR (95% CI) ^{**}	N (%)	OR (95% CI) ^{**}	N (%)	OR (95% CI) ^{**}
0.07	598 (43.5)	188 (42.2)	1	89 (45.6)	1	143 (41.7)	1
0.07–0.14	462 (33.6)	165 (37.0)	1.21 (0.90, 1.63)	70 (35.9)	1.02 (0.69, 1.51)	125 (36.4)	1.09 (0.80, 1.49)
>0.14	315 (22.9)	93 (20.9)	0.92 (0.64, 1.33)	36 (18.5)	0.71 (0.44, 1.17)	75 (21.9)	0.78 (0.53, 1.13)
P _{heterogeneity} =0.86							

^{*} 55 hypopharynx cancer cases were not included in this analysis

^{**} Adjusted for: matching factors of age, sex, and race; income; smoking; drinking; total energy intake; fruit intake

Table 4

Association between fish/shellfish intake and SCCN by race* and sex, 2002–2006

Fish/shellfish intake (oz. per day)	White			African American		
	Cases	Controls	OR (95% CI)**	Cases	Controls	OR (95% CI)**
0.07	355 (46.2)	501 (45.6)	1	78 (31.3)	93 (35.9)	1
0.07–0.14	287 (37.4)	364 (33.1)	1.18 (0.91, 1.53)	94 (37.8)	93 (35.9)	1.02 (0.60, 1.75)
>0.14	126 (16.4)	234 (21.3)	0.88 (0.64, 1.22)	77 (30.9)	73 (28.2)	0.66 (0.37, 1.16)
P _{heterogeneity} =0.67						
Fish/shellfish intake (oz. per day)	Males			Females		
	Cases	Controls	OR (95% CI)***	Cases	Controls	OR (95% CI)***
0.07	333 (41.2)	399 (42.2)	1	111 (48.1)	199 (46.4)	1
0.07–0.14	309 (38.2)	331 (35.0)	1.17 (0.90, 1.54)	77 (33.3)	131 (30.5)	1.01 (0.63, 1.60)
>0.14	166 (20.5)	216 (22.8)	0.85 (0.61, 1.17)	43 (18.6)	99 (23.1)	0.67 (0.38, 1.17)
P _{heterogeneity} =0.72						

* 39 participants classified as “other” race were not included in this analysis

** Adjusted for: matching factors of age and sex; income; smoking; drinking; total energy intake; fruit intake

*** Adjusted for: matching factors of age and race; income; smoking; drinking; total energy intake; fruit intake