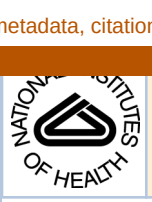

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Inverse relationship between moderate alcohol intake and rectal cancer: Analysis of the North Carolina Colon Cancer Study

Seth D. Crockett, MD[1,2], **Millie D. Long, MD MPH**[2], **Evan S. Dellon, MD MPH**[2], **Christopher F. Martin, MSPH**[2], **Joseph A. Galanko, PhD**[2], and **Robert S. Sandler, MD MPH**[2]

[1]Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina

[2]Division of Gastroenterology and Hepatology, University of North Carolina School of Medicine

Abstract

Background—The relationship between alcohol intake and rectal cancer is uncertain

Objective—We sought to evaluate whether alcohol consumption is associated with distal colorectal cancer and rectal cancer specifically.

Design—Data on alcohol intake were examined from the North Carolina Colon Cancer Study, a population-based case control study of distal colorectal cancer.

Setting—33 counties in the central and eastern part of North Carolina

Patients—Cases had adenocarcinoma of the rectum, rectosigmoid, and sigmoid colon. Controls were frequency-matched on age, race, and gender.

Interventions—Demographic and dietary intake data were collected using a validated questionnaire.

Corresponding author: Seth D. Crockett MD, Department of Medicine, Division of Gastroenterology and Hepatology, University of North Carolina School of Medicine, CB#7080, Chapel Hill, NC 27599-7080, seth_crockett@med.unc.edu, Phone: (919) 966-2514, Fax: (919) 843-2508.

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Author	Specific contributions
SD Crockett	Planned & conducted the data analysis and interpretation, drafted manuscript, revised manuscript for publication, approved final draft of manuscript
MD Long	Participated in data analysis and interpretation, participated in drafting of manuscript, revised manuscript for publication, approved final draft of manuscript
ES Dellon	Participated in data analysis and interpretation, revised manuscript for publication, approved final draft of manuscript
CF Martin	Supervised the original study, participated in data collection, participated in data analysis and interpretation, approved final draft of manuscript
JA Galanko	Participated in data collection and data management, approved final draft of manuscript
RS Sandler	Planned & conducted the original study, obtained funding, revised manuscript for publication, approved final draft of manuscript

Main outcome measures—Logistic regression was used to estimate odds ratios for the relationship between alcohol consumption and distal colorectal cancer.

Results—1,033 cases and 1,011 controls participated. The odds ratio for rectal cancer comparing any vs. no alcohol intake was 0.73 (95% confidence interval 0.60, 0.90), adjusted for age, gender, race, smoking status, obesity, education, red meat intake, use of non-steroidal anti-inflammatory medications and family history of colorectal cancer. The odds ratio for moderate alcohol (≤14 grams/day) was 0.66 (0.53, 0.82), while the odds ratio for heavy alcohol (>14 grams/day) was 0.93 (0.70, 1.23). Moderate beer and wine intakes were also inversely associated with distal colorectal cancer: odds ratios 0.76 (0.60, 0.96) and 0.69 (0.56, 0.86) respectively.

Limitations—This was a retrospective, observational study. Residual confounding is possible.

Conclusions—In this study, moderate alcohol intake (especially wine) was inversely associated with distal colorectal cancer.

Keywords

Colorectal cancer; Rectal cancer; Alcohol; Case-control; Epidemiology; Wine; Beer

Introduction

Colorectal cancer (CRC) ranks 3rd in both incidence and cancer mortality among men and women in the US, with roughly 150,000 people diagnosed and 50,000 attributable deaths each year.[1] Rectal cancer accounts for a substantial portion of all CRC, approximately 30% of cases.[2] Optimal treatment for rectal cancer requires coordinated, multi-specialty care, and is associated with higher with healthcare utilization and costs compared to colon cancer.[3] In addition to differences in management, rectal cancer and colon cancer also have different risk factor profiles.[4, 5]

Alcohol is a potentially modifiable risk factor that has been linked to multiple cancers of the gastrointestinal tract including oropharyngeal and squamous esophageal cancer.[6–10] With respect to CRC, the evidence is conflicting. Previous studies have reported a weak positive association between alcohol and CRC, especially for higher alcohol intakes.[11, 12] Some studies, however suggest an inverse relationship between alcohol and CRC, especially wine.[13, 14] The effect of beer intake on CRC is uncertain. Few studies focus on the relationship between alcohol and rectal cancer specifically. Furthermore, many studies of this association have taken place in European countries, where drinking patterns and social determinants of alcohol consumption may differ from the US.

Utilizing data from the North Carolina Colon Cancer Study, a large population-based case-control study, we aimed to determine the association between alcohol intake and the risk of distal CRC. We were particularly interested in the effect of moderate alcohol intake and the effects of different beverages (beer, wine, and liquor) on risk of rectal cancer.

Materials and Methods

Study design & population

The North Carolina Colon Cancer Study-Phase II (NCCCS-II) was a population-based case-control study of incident distal large bowel cancer (rectal, recto-sigmoid, or sigmoid cancer) in 33 counties in the central and eastern part of North Carolina.[15] These counties included urban, suburban, and rural areas and a diverse socioeconomic population. Study data were collected by trained nurse interviewers during in-person interviews. In order to confirm the diagnosis of invasive adenocarcinoma of sigmoid, rectosigmoid, or rectum, pathology

reports were obtained and reviewed by the study pathologist for each case. The study was designed and reported in accordance with the STROBE guidelines [16].

Identification of cases and controls

Participants (cases and controls) were eligible for the study if they were residents of the selected counties, aged between 40 and 80 years, had a North Carolina driver's license or identification card, were able to complete an interview in English, and were not deaf or hard of hearing, too ill to be interviewed, legally incompetent or currently incarcerated.

A total of 1831 potentially eligible patients with a first diagnosis of invasive adenocarcinoma in sigmoid, rectosigmoid, and rectum were identified through the rapid case ascertainment system of the North Carolina Central Cancer Registry between May 2001 and September 2006.[17] Of the 1,831 potentially eligible cases identified, 57 (3%) were excluded for physician refusal, and 357 (19%) were found ineligible. Of the remaining 1,417 eligible cases, 118 (8%) were not able to be contacted, 242 (17%) refused to participate, and 1,058 (75%) completed an in-person interview. Subsequently, 25 cases were excluded as they had no data on alcohol intake, the exposure of interest.

Using a randomized recruitment technique,[18] controls without a previous diagnosis of CRC were randomly selected from North Carolina Division of Motor Vehicle records (for controls age <65) or from Health Care Financing Administration (HCFA) records (for controls age ≥65), based on sampling probabilities within blocks defined by sex, race, and 5-year age group. African Americans were oversampled in order to enhance their proportion. A total of 2,345 subjects were initially identified as eligible controls, but 518 (22%) were later determined to be ineligible according to the above criteria (e.g. they did not reside in the 33 county study area, etc.). Of the 1,827 remaining eligible controls, 325 (18%) were not able to be contacted, and 483 (26%) refused to participate. A total of 1,019 (56% of eligible controls) completed an interview. Subsequently, 8 controls were excluded because they had no data on alcohol intake. This study was approved by the Institutional Review Board of the University of North Carolina, and all subjects provided written informed consent prior to participation.

Assessment of main exposure and covariates of interest

Information on alcohol intake was obtained during the interview. Participants were asked whether they drank beer, wine, or liquor, and the frequency and amount of consumption 1 year prior to diagnosis (cases) or at the time of interview (controls). From responses to these questions, consumption of beer (ounces/day), wine (ounces/day) and liquor (shots/day) were calculated. Alcohol intake (grams (g)/day) was also determined from these questions. Alcoholic beverage consumption was subsequently categorized into none, moderate, and heavy intake based on accepted definitions.[19] Non-beverage alcohol consumption (e.g. trace amounts of alcohol used in cooking) was disregarded.

Data on potential confounders including non-steroidal anti-inflammatory drug (NSAID) use, physical activity, red meat intake, smoking, and family history of colorectal cancer were also obtained in the interview. In addition to age, race, and sex, demographic information such as education, household income, and insurance status was also collected. All participants were asked their weight 1 year prior to diagnosis (case) or interview (control) in order to calculate body mass index from a weight that was unaffected by the cancer diagnosis or treatment. Physical activity was assessed via a validated 7 day physical activity recall questionnaire.[20, 21] Dietary intake was assessed via a validated Diet History Questionnaire [22, 23]. Daily intakes of nutrients and other food components (including

alcohol) were calculated with DietCalc software obtained from the National Cancer Institute (http://riskfactor.cancer.gov/DHQ/dietcalc).

Statistical analysis

Bivariate analysis of exposure variables was performed using chi-squared tests. Alcohol intake was examined using variables that accounted for different levels of intake, beverage type, and combination of beverages consumed. All covariates were assessed for confounding and effect measure modification. Because folate intake was felt to be a causal intermediate on the pathway from alcohol to CRC, it was not included as a covariate in multivariate analyses.[24] Multivariate logistic regression modeling was performed to estimate odds ratios (OR) and 95% confidence intervals (CI) for the association between alcohol intake and distal CRC. All logistic regression models included indicator variables for the matching strata (determined by sex, age and race) as well as an offset term to adjust for sampling probability.[18, 25]

To determine which covariates should be included in the final multivariable models, we constructed a full model with all potential confounders, and assessed the change in beta coefficients for those with any vs. no alcohol intake in relation to distal CRC when covariates were removed using backwards elimination with a threshold of <10% change in beta coefficients and a likelihood ratio test p value of >0.10. The final model contained the exposure (alcohol intake), educational level, smoking status, obesity, family history of colon cancer, red meat consumption and NSAID use.

We also constructed logistic regression models for each exposure subtype of interest (e.g. beer, wine, or spirits), and with a categorical exposure variable accounting for different combinations of beverages consumed. Finally, polytomous regression (using the same exposure variables) was subsequently used to evaluate whether the observed effects were similar amongst those with cancer of the rectum, and rectosigmoid and sigmoid colon. Because polytomous models cannot incorporate weights, the offset term was not included for these analyses. All analyses were performed with STATA version 10.1 (College Station, TX).

Results

Participants

The final study population included 1,033 cases and 1,011 controls. Cases and controls differed significantly by age, race, red meat intake, NSAID use, education level, insurance status, and household income (Table 1). Significant differences also existed between cases and controls with respect to overall alcohol intake and quantities of specific alcoholic beverages consumed. In general, cases had a higher proportion of non drinkers and a lower proportion of moderate drinkers for beer, wine, and liquor (Table 2).

Primary analyses

The OR for distal CRC for those with any alcohol intake compared to nondrinkers was 0.73 (95% CI 0.60, 0.90). We further analyzed the effect of different levels of alcohol consumption. The adjusted OR for distal CRC associated with moderate alcohol intake was 0.66 (95% CI 0.53, 0.82), indicating that the odds of distal CRC were decreased for moderate alcohol users. There was no statistically significant association between heavy alcohol use and distal CRC (Table 3).

Beverage type

After adjusting for confounders, moderate beer intake was associated with an OR for distal CRC of 0.76 (95% CI 0.60, 0.96). Moderate wine intake was also inversely related to distal CRC: OR 0.69 (95% CI 0.56, 0.86). Neither heavy beer nor heavy wine intake were significantly associated with distal CRC. There were no statistically significant associations between liquor intake and CRC, though the highest level of liquor consumption (>1 shot/day) did appear to be associated with an elevated risk of CRC: OR 1.46 (95% CI 0.92, 2.36) (Table 3).

Because of overlapping consumption of different alcoholic beverages, we sought to estimate the effects of both isolated consumption of each beverage type, and different combinations of beverages consumed. Wine intake, whenever it was included in beverage combinations, was associated with the lowest OR of CRC (for wine only: OR 0.64 (95% CI 0.45, 0.93), for wine and beer: OR 0.60 (95% CI 0.41, 0.88); and for wine, beer and liquor: 0.74 (95% CI 0.54, 1.00)) (Figure 1).

Effect of race, sex, and smoking status

When stratified by race, the OR for distal CRC associated with moderate alcohol intakes was similar for Blacks and non-Blacks. Similarly, males and females had similar odds of distal CRC associated with moderate intake. When stratified by smoking status, never smokers had the lowest ORs associated with moderate wine and liquor consumption, while current smokers had the highest ORs, but this OR heterogeneity was not statistically significant ($p = 0.6$) (Table 4).

Site of cancer

Because this study included cases of distal CRC including cancers of the rectum, rectosigmoid and sigmoid colon, we sought to estimate the ORs for each site specifically. For moderate overall alcohol intake, the OR of rectal cancer specifically was 0.69 (95% CI 0.51, 0.93). For moderate wine intake, the OR for rectal cancer was similar: 0.69 (95% CI 0.51, 0.93) (Table 5).

Discussion

In this case control study, we found that alcohol use and especially wine intake was inversely associated with distal colorectal cancer. This effect was consistent for cancers of the rectum, recto-sigmoid and sigmoid colon, was not modified by age, race, sex, or smoking status, and persisted after accounting for multiple potential confounding factors. The protective effect appeared confined primarily to the moderate consumption strata across alcohol types.

Some previous studies have shown a positive association between alcohol intake (particularly heavy alcohol use) and rectal cancer, generally of fairly low magnitude. A meta-analysis of 27 studies relating consumption of alcoholic beverages to risk of colorectal cancer found a weak positive association for consumption of 2 or more alcoholic drinks (24 g) daily and rectal cancer (relative risk (RR) 1.10 (95% CI 1.02, 1.18)).[12] A pooled analysis of 8 cohort studies addressing this topic found that only high alcohol intakes (30 to <45 g/day and ≥45 g/day) were significantly associated with increased risk of rectal cancer: RR 1.42 (95% CI 1.07, 1.88) and 1.49 (95% CI 1.04, 2.12) respectively.[11] An analysis from the multicenter European Prospective Investigation into Cancer and Nutrition (EPIC) cohort study reported an elevated risk of rectal cancer only for those with very high average lifetime alcohol intakes: hazard ratio (HR) for those consuming (>60g/day) compared to the lowest level of consumption was 2.59 (95% CI 1.62, 4.13). However, other studies have

reported both null and inverse associations between alcohol consumption and CRC.[13, 14, 26] Nevertheless, previous reports that heavy alcohol consumption is associated with increased risk of CRC are not necessarily inconsistent with our findings.

We focused on moderate intake but also found evidence that heavy intake of alcohol may be associated with increased risk of distal CRC. Heavy alcohol consumption was relatively rare in our sample; 109 participants (5.3%) had alcohol intakes ≥ 45grams/day and 70 participants (3.4%) had alcohol intakes >60 g/day. Given the small numbers of heavy alcohol consumers in our study, it is certainly possible that higher levels of alcohol consumption are associated with an elevated risk of CRC. Indeed, in this study heavy beer and liquor intakes were associated with ORs greater than 1, though they were not statistically significant. This finding points to the possibility that there may be a "J-shaped" dose-response curve for alcohol and CRC, in which moderate intakes are associated with reduced risk of CRC, but the risk increases for those with heavy use as others have postulated.[13] Our findings may also differ somewhat from previous studies because of changes in folate intake over time. Since alcohol interferes with folate metabolism and folate has been shown to have a protective effect for CRC,[27–29] changes in folate intake could impact the total effect of alcohol on rectal cancer. Indeed, some studies have suggested that adequate folate is a necessary precursor for a beneficial effect of alcohol in CRC.[27, 30] Since 1996, the US Food and Drug Administration has required the addition of folic acid to enriched breads, cereals, flours, corn meals, pastas, rice, and other grain products,[31] which may be one reason why some American studies conducted prior to the late 1990s found that alcohol was associated with an elevated risk of CRC.

Several studies have reported either a null or an inverse association between wine consumption and CRC, particularly with moderate wine intake.[12–14, 32, 33] In a study of 41,837 post-menopausal women in the US, wine consumption was found to be inversely associated with distal colon cancer: RR 0.64 (95% CI 0.40, 0.98).[14] A Danish cohort study found that wine consumption lowered the risk of rectal cancer, even in combination with other alcoholic beverages.[33] In a recent analysis from a British cohort study involving 25,639 participants, daily consumption of 1 or more glasses of wine was associated with a decreased risk of CRC (HR 0.61 (95% CI 0.40, 0.94).[13] Interestingly, wine intake has also been demonstrated to be inversely associated with other gastrointestinal cancers, namely gastric[34] and esophageal adenocarcinoma.[8]

Apart from its relationship to cancer, moderate alcohol intake is associated with a variety of salutatory effects such as protection from coronary heart disease,[35, 36] stroke,[37, 38] diabetes,[39] dementia,[36] and even reduced overall mortality.[40] The biologic mechanism by which alcohol may mitigate the risk of cancer is unknown, but may be related to antioxidant properties. Wine in particular has antioxidant and antithrombotic properties related to its flavonoid and phenolic components.[41] One of these compounds, resveratrol, has been shown to have cancer chemopreventive effects.[42]

This study has important strengths. We used a validated questionnaire for measurement of exposure and covariates of interest. The outcome (distal CRC) was determined via a cancer registry and was independently verified by the study team, making measurement error unlikely. In comparison with other published studies on this topic, we enrolled a relatively large number of CRC cases, and thus our statistical power allowed for more precise estimates. The population-based sampling of this study avoids the selection bias that occurs when cases are drawn from a single hospital. African Americans represented 21% of our study population (because of over-sampling), which is substantially higher than other studies on this topic. We were able to evaluate a large number of covariates for possible

confounding, and all recognized important confounders of the relationship between alcohol and CRC were controlled for in our multivariate analysis.

The limitations of this study are primarily related to potential misclassification of the exposure. Alcohol intake was self-reported as recorded on the nurse-administered study questionnaire. It is well known that self-reported alcohol intake is subject to under or misreporting, and as with all retrospective studies, there is potential for recall bias. Because of the manner in which the study questionnaire was structured, we obtained average daily consumption, and could not account for patterns of use such as binge drinking or changes in drinking patterns over time, or for lifetime alcohol consumption. Furthermore, the definitions of moderate and heavy alcohol use may not apply equally to all participants because of body weight and/or genetic differences, though we did adjust for elevated body mass index in our analyses. Another issue with all observational trials of alcohol intake relates to the fact that abstainers may be systematically different from non-abstainers. The nondrinker category may contain former drinkers including recovered alcoholics, and those who stop drinking due to illness or concern for medication interactions. Moderate drinking also may be a marker of higher socioeconomic status, a healthier lifestyle, or both. For this reason, we evaluated several different measures of socioeconomic status for confounding (education level, insurance status, and income). Nevertheless, we cannot exclude the possibility that drinking in moderation is so tightly coupled to other cancer-protective behaviors that multivariate analysis was unable to completely isolate the effect of alcohol intake alone, and that residual confounding exists. Though we did not find statistically-significant results in some smaller subgroups (e.g. heavy drinkers of wine and liquor) this may be due to a lack of statistical power, and thus these results should be interpreted with caution.

In conclusion, moderate alcohol intake, especially wine, was inversely associated with distal colorectal cancer in this population-based case-control study. These results should not be interpreted as an endorsement of alcohol, because excessive alcohol consumption has been clearly linked to other health problems such as accidents and injuries,[43] teratogenicity,[44] cardiomyopathy,[45] pancreatitis,[46] liver disease,[47] and premature death,[48] and there are some individuals for whom no amount of alcohol is safe (e.g. people with alcoholism or cirrhosis). Nevertheless, our findings add to the growing body of literature suggesting that drinking alcohol in moderation may have a beneficial role for some cancers, including rectal cancer.

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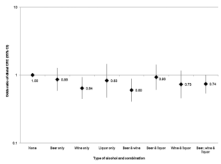

Figure 1.
Odds ratio of distal colorectal cancer by type and combination of alcohol consumed, demonstrating consistent inverse relationship with wine consumption vs. other beverage types.
Odds ratios obtained via logistic regression, adjusted for age, sex, race, red meat intake, NSAID use, family history of CRC, obesity, smoking status, and education level. CRC: colorectal cancer; NSAID: non-steroidal anti-inflammatory drug.

Table 1

Characteristics of study participants

Covariate	Cases n=1,033 n (%) or mean ± SD	Controls n=1,011 n (%) or mean ± SD
Age (in years)†		
40–49	149 (14.4)	101 (10.0)
50–59	285 (27.6)	239 (23.6)
60–69	313 (30.3)	324 (32.1)
70–79	286 (27.7)	347 (34.3)
Sex		
Female	449 (43.5)	414 (41.0)
Race‡		
White	747 (73.7)	818 (82.3)
Black	257 (25.4)	169 (17.0)
Other	9 (0.9)	7 (0.7)
Positive family history of CRC§	128 (12.7)	100 (10.1)
Smoking status		
Never smoked	377 (37.5)	379 (38.5)
Former smoker	447 (44.5)	463 (47.1)
Current smoker	181 (18.0)	142 (14.4)
Obese	320 (33.2)	306 (31.7)
Physical activity (met-min/day)	2249.2 ± 662.2	2162.3 ± 487.1
Total folate intake		
<400 mcg/day	247 (23.9)	233 (23.1)
≥400 mcg/day	786 (76.1)	778 (76.9)
Red meat intake (grams/day)	83.6 ± 69.4	73.7 ± 58.2
NSAID use		
<15 uses/month	684 (68.0)	579 (58.5)
≥15 uses/month	322 (32.0)	410 (41.5)
Education		
≤High school graduate	540 (53.7)	422 (42.6)
Some college	244 (24.3)	257 (26.0)
≥College graduate	222 (22.1)	311 (31.4)
Uninsured	52 (5.2)	27 (2.7)
Household income		
<$25,000/year	337 (35.7)	281 (30.2)
≥$25,000/year	607 (64.3)	649 (69.8)

† Age at diagnosis for cases, or at time of interview for controls.

‡ Self-reported race differs slightly from the administrative race definition used for matching.

§ Family history of colorectal cancer in a 1st degree relative.

NSAID: non-steroidal anti-inflammatory drug

Table 2

Bivariate analysis of alcohol intake and beverage type by case or control status

Exposure variables	Cases n = 1,033 n (%)	Controls n = 1,011 n (%)	p*
All alcohol			<0.0001
None	548 (53.1)	435 (43.0)	
Moderate (>0 & ≤14 g/day)	304 (29.4)	390 (38.6)	
Heavy (>14 g/day)	181 (17.5)	186 (18.4)	
Beer intake			0.001
None	689 (66.7)	620 (61.4)	
Moderate (>0 & ≤12 oz/day)	260 (25.2)	325 (32.2)	
Heavy (>12 oz/day)	84 (8.1)	65 (6.4)	
Wine intake			<0.0001
None	726 (70.4)	592 (58.6)	
Moderate (>0 & ≤6 oz/day)	271 (26.3)	374 (37.0)	
Heavy (>6 oz/day)	35 (3.4)	45 (4.5)	
Liquor intake			0.01
None	764 (74.0)	692 (68.5)	
Moderate (>0 & ≤1 shot/day)	222 (21.5)	275 (27.2)	
Heavy (>1 shot/day)	47 (4.6)	44 (4.4)	

* p values determined via chi-squared tests.

g: grams; oz: ounces

Table 3

Unadjusted and adjusted odds ratios for distal colorectal cancer by type of alcohol consumed*

Type of alcohol	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
All alcohol intake		
None	1.00	1.00
Moderate (>0 & ≤14 g/day)	0.60 (0.49, 0.73)	0.66 (0.53, 0.82)
Heavy (>14 g/day)	0.78 (0.61, 1.01)	0.93 (0.70, 1.23)
Beer intake		
None	1.00	1.00
Moderate (>0 & ≤12 oz/day)	0.69 (0.56, 0.85)	0.76 (0.60, 0.96)
Heavy (>12 oz/day)	1.14 (0.79, 1.64)	1.16 (0.79, 1.70)
Wine intake		
None	1.00	1.00
Moderate (>0 & ≤6 oz/day)	0.60 (0.49, 0.73)	0.69 (0.56, 0.86)
Heavy (>6 oz/day)	0.68 (0.43, 1.09)	0.83 (0.50, 1.36)
Liquor intake		
None	1.00	1.00
Moderate (>0 & ≤1 shot/day)	0.72 (0.58, 0.89)	0.83 (0.66, 1.05)
Heavy (>1 shot/day)	1.11 (0.72, 1.72)	1.46 (0.92, 2.36)

* Regardless of other alcoholic beverage consumption. ORs obtained via logistic regression, adjusted for age, sex, race, red meat intake, NSAID use, family history of colorectal cancer, obesity, smoking status, and education level.

Table 4

Adjusted odds ratios for distal colon cancer for moderate alcohol, beer, wine, and liquor consumption, stratified by race, sex, and smoking status

Strata of covariate	Moderate alcohol OR (95% CI)	Moderate beer OR (95% CI)	Moderate wine OR (95% CI)	Moderate liquor OR (95% CI)
Race				
Black	0.62 (0.38, 1.02)	0.63 (0.37, 1.06)	0.75 (0.45, 1.27)	0.70 (0.40, 1.22)
Nonblack	0.67 (0.53, 0.86)	0.81 (0.63, 1.04)	0.68 (0.54, 0.87)	0.86 (0.67, 1.11)
Sex				
Female	0.59 (0.43, 0.82)	0.80 (0.55, 1.17)	0.65 (0.47, 0.90)	0.74 (0.50, 1.08)
Male	0.71 (0.53, 0.95)	0.74 (0.56, 0.98)	0.73 (0.55, 0.96)	0.89 (0.67, 1.18)
Smoking				
Never	0.60 (0.43, 0.85)	0.77 (0.53, 1.13)	0.55 (0.39, 0.78)	0.68 (0.45, 1.01)
Former	0.71 (0.52, 0.99)	0.80 (0.58, 1.09	0.76 (0.55, 1.03)	0.89 (0.64, 1.24)
Current	0.66 (0.38, 1.15)	0.65 (0.38, 1.11)	0.92 (0.55, 1.56)	1.02 (0.60, 1.76)

ORs obtained via logistic regression, adjusted for age, sex, race, red meat intake, NSAID use, family history of colorectal cancer, obesity, smoking status, and education level. P values for likelihood ratio tests for models with interaction terms for race, sex, and smoking status all>0.10 indicating lack of strong effect measure modification.

Table 5

Adjusted odds ratios for cancer of the rectum, rectosigmoid and sigmoid cancer for moderate alcohol, beer, wine, and liquor consumption.

Cancer site	Moderate alcohol OR (95% CI)	Moderate beer OR (95% CI)	Moderate wine OR (95% CI)	Moderate liquor OR (95% CI)
Rectum (n=386)	0.69 (0.51, 0.93)	0.79 (0.58, 1.08)	0.69 (0.51, 0.93)	0.77 (0.55, 1.06)
Rectosigmoid (n=166)	0.55 (0.36, 0.84)	0.64 (0.41, 1.00)	0.66 (0.44, 1.01)	0.84 (0.54, 1.30)
Sigmoid (n=468)	0.68 (0.51, 0.91)	0.77 (0.57, 1.03)	0.70 (0.53, 0.93)	0.88 (0.66, 1.19)

ORs obtained via polytomous logistic regression, adjusted for age, sex, race, red meat intake, NSAID use, family history of CRC, obesity, smoking status, and education level. Cases with site recorded as “colon not otherwise specified” not included in this analysis (n=13).