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Alcohol types and sociodemographic characteristics as risk factors for Barrett's esophagus

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Abstract

Background & Aims—Little is known about the effects of alcohol use and sociodemographics on the risk of Barrett's esophagus, a precursor to esophageal adenocarcinoma. We evaluated the association between alcohol use, alcohol type, sociodemographic profiles, other lifestyle factors and the risk of Barrett's esophagus.

Methods—Using a case-control study within the Kaiser Permanente Northern California membership, patients with a new diagnosis of Barrett's esophagus (n=320) diagnosed between 2002–2005 were matched to persons with gastroesophageal reflux disease (GERD) (n=316) and to population controls (n=317). We collected information using validated questionnaires during direct in-person interviews. Analyses used multivariate unconditional logistic regression.

Results—Total alcohol use was not significantly associated with the risk of Barrett's esophagus, although stratification by beverage type showed an inverse association for wine drinkers compared to nondrinkers (7+ drinks wine/week vs. none: OR=0.44, 95%CI (0.20–0.99); multivariate analysis). Among population controls, those who preferred wine were more likely to have college degrees and regularly take vitamin supplements than those who preferred beer or liquor, although adjustment for these factors or GERD symptoms did not eliminate the inverse association between wine consumption and Barrett's esophagus. Education status was significantly inversely associated with the risk of Barrett's esophagus.

Conclusions—There are associations between alcohol types, socioeconomic status and the risk of Barrett's esophagus. Although choice of alcoholic beverages was associated with several factors, multiple adjustments (including for GERD) did not eliminate the association between alcohol and Barrett's esophagus. Further research to evaluate the associations among socioeconomic status, GERD, and Barrett's esophagus is warranted.

Background

The incidence of esophageal adenocarcinoma has increased by greater than 500% in the last three decades, more rapidly than any other malignancy in the United States.[1–6] The rate of

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increase is most predominant among Caucasian males, suggesting that environmental or lifestyle factors may play important roles in the change in incidence. Alcohol drinking is of substantial importance in the causation of esophageal squamous cell carcinoma;[4, 7] however, an association between alcohol use and esophageal adenocarcinoma has not been well established. Previous studies have been somewhat conflicting and there are minimal data analyzing specific alcohol types (e.g. wine, hard liquor, etc.)[8–16] In addition, if alcohol (or certain types of alcohol) are associated with cancer risk, it is unclear where alcohol may act in the carcinogenic pathway; it could increase the chance of having some strong cancer risk factors such as gastroesophageal reflux disease (GERD),[17, 18] augment the risk of precancerous conditions (such as Barrett's esophagus) among persons with GERD, or enhance the rate of progression from Barrett's esophagus progresses to esophageal adenocarcinoma. The identification of risk factors for Barrett's esophagus may provide information on early events in the carcinogenic pathway for esophageal adenocarcinoma[19] that could lead to effective intervention strategies.

Barrett's esophagus, a metaplastic transformation of the esophageal squamous epithelium into specialized intestinal columnar epithelium,[20] is of considerable interest from clinical and public health perspectives. Persons with Barrett's esophagus have a 30–125 fold increased risk of developing esophageal adenocarcinoma compared to the general population.[21] Little is known regarding the effect of alcohol on Barrett's esophagus, especially related to alcohol types: a few studies reported an adverse effect of total alcohol intake[22] or liquor intake,[23, 24] others found no association,[25–27] and few studies had true population-type control groups that are recommended for risk factor studies. The only population-based studies we identified, conducted in Sweden,[22, 27] had few cases (21 and 16, respectively).

Thus, we conducted a large community-based case-control study within the Northern California Kaiser Permanente population to investigate the association between alcohol use, alcohol type, sociodemographic factors, and Barrett's esophagus. We used two control groups: general membership controls (to evaluate for Barrett's esophagus risk factors among the general population) and patients diagnosed with GERD (to evaluate for risk factors among subjects with GERD). In addition, we examined for potential confounding by numerous sociodemographic and lifestyle factors, as well as the association between these factors and the consumption of different types of alcoholic beverages.

Methods

Study Population

Details of the study design have been described previously.[28] Briefly, this was a case-control study conducted within the Kaiser Permanente, Northern California (KPNC) population, an integrated health services delivery organization. The KPNC membership contains approximately 3.3 million persons whose demographics closely approximate the underlying census population of Northern California.[29, 30] Potentially eligible subjects for this study were all adult (ages 18–79 years) KPNC members who were continuously enrolled for at least 2 years prior to their index period, met the case or control definitions outlined below, and were able to understand spoken and written English. The index date for cases was the date of Barrett's esophagus diagnosis. The index date for controls was the midpoint of each 2–3 month selection interval for the cases. The membership population and GERD comparison groups were frequency matched to the cases by gender (given the high proportion of males among Barrett's esophagus patients), age at the index date, and geographic region (each subject's home facility).

Case Definition

Cases were eligible KPNC members with a new diagnosis of Barrett's esophagus between October, 2002 and September, 2005, using the International Classification of Disease, 9th revision (ICD-9) code 530.2 (which at KPNC is uniquely coded as "Barrett's esophagitis"), or the College of American Pathologists code 73330 ("Barrett's esophagus"). A single Board-certified gastroenterologist (DAC) then reviewed the endoscopy and pathology records of potentially eligible cases. Subjects were included if the endoscopist clearly described a visible length of columnar-type epithelium proximal to the gastroesophageal junction/gastric folds, this area was biopsied, and the pathologist described specialized intestinal epithelium.[19] The following patients were excluded: patients with only gastric-type metaplasia of the esophagus on all pathologic evaluations; patients with columnar metaplasia without features of intestinal metaplasia on all pathology readings; patients without a biopsy of esophageal origin; biopsies of only a mildly irregular squamocolumnar junction (i.e. an "irregular z-line"); and patients with a prior Barrett's esophagus diagnosis. Pathology slides underwent a separate manual review by a gastrointestinal pathologist (GJR).

Membership Population Controls

Membership population controls were randomly selected from among all members who lacked an electronic diagnosis of Barrett's esophagus at the time the Barrett's esophagus cases were identified.

GERD Comparison Group

GERD comparison group members were randomly selected from among all members with the following characteristics prior to their index date: a GERD-related diagnosis code (ICD-9 codes 530.11 [reflux esophagitis] or 530.81 [gastroesophageal reflux]); a prescription for at least a 90 days supply of a histamine-2 receptor antagonist or a proton pump inhibitor (medications used for treating GERD symptoms) in the previous year (from electronic pharmacy records); no prior diagnosis of Barrett's esophagus; and an esophagogastroduodenoscopy close to the index date that did not demonstrate esophageal columnar metaplasia of any type.

Exposure Measurements

Each subject underwent an in-person interview and physical examination, most commonly at their home. During the interview, a structured questionnaire was administered by trained interviewers, and information was collected on GERD symptoms, medication use, income and education, medical history, and tobacco use. The questionnaires asked participants to report exposures in the year prior to their index date. Anthropometric measurements and blood samples were also taken during the interview. Additional data regarding demographic information, medical history, and medication use were collected from electronic databases. Alcohol use during the year prior to the index date was assessed using a validated food frequency questionnaire (Block 98, 110-food items) that recorded the type of alcohol used (wine, beer, liquor), amount consumed, and the frequency of use. The term 'drink' is defined as 1 glass for wine (4–5oz), 12oz for beer, and one shot (1 ¼Oz) for liquor; each contains approximately 13g of ethanol.

Prior heavy alcohol use was also captured using the question "Did you or someone else ever feel you drank too much alcohol before (the index date)?" Since individuals who answer "yes" to this question may have had drinking problems before and quit drinking (and been erroneously classified as nondrinkers), we excluded these individuals from the non-drinking category.

Other dietary information including fruit and vegetable intakes, total caloric intake, and vitamin supplement use was also collected using the same food frequency questionnaire. Long-term vitamin use was defined as persons who indicated >2 years use of any vitamin supplements (single or multiple) prior to the index date.

Statistical Analysis

First, we utilized unconditional logistic regression to calculate odds ratios (ORs) as an estimate of the relative risk to evaluate the associations between alcohol use, socio-demographic characteristics and the risk of Barrett's esophagus.[31–33]

We compared Barrett's esophagus cases vs. population controls *and* cases vs. GERD controls; the latter group permitted the evaluation of risk factors for Barrett's esophagus among persons with GERD. The following additional variables were evaluated as potential confounders: race/ethnicity (classified as Caucasian vs. non-Caucasian due to small sample sizes in the subgroups), education (highest level achieved), body mass index (BMI=kg/m^2), smoking (ever/never), types of alcohol, serum *Helicobacter Pylori* (*H. Pylori*) antibody status, aspirin or nonsteroidal anti-inflammatory drug (NSAID) use, total energy intake (kcal/day), long-term (>2years) vitamin use, and a co-morbidity index (the DxCg score, which creates a predictive comorbidity score based on demographic data, medical coding, and pharmacy utilization).[34, 35] Potential confounders were included in the final model if their inclusion altered the β coefficient by >10%.

First, we compared the risk of Barrett's esophagus by total alcohol use categorizing into doses defined *a priori* (any type; never, <7drinks/week, 7–13 drinks/week, ≥14 drinks/week). Second, we evaluated use of each alcohol type (wine, beer, and liquor), adjusted for the total volume of other types consumed. For example, to analyze the independent effect of wine use, we included in the model beer and liquor consumption (numbers of drinks/week). We also evaluated whether the effects differed by the Barrett's segment lengths (<3 centimeters vs. ≥3 centimeters). Tests for interaction used cross products in the logistic model, and were considered significant if $p<0.1$. The reference group for all the analyses was non-alcohol users.

Third, we re-classified alcohol users (anyone who reported use of alcoholic beverages) by the preference of alcohol types, by creating mutually exclusive variables. We defined a person as "wine-preferred" if wine intake exceeded 50% of all servings of alcohol consumed. Among alcohol users, if no single type exceeded 50% of all servings, the person was classified as an alcohol user with "no preference".

Third, we explored the associations between alcohol preference and other demographic and lifestyle factors using population controls. For this descriptive analysis, we tabulated alcohol types by factors such as sex, race, income, education, smoking status, long-term vitamin supplement use, television watching, diet, and BMI.

Lastly, we examined the associations between each socio-demographic and lifestyle factor and the risk of Barrett's esophagus using unconditional logistic regression.

All data were analyzed using SAS statistical software (SAS institute, Cary, NC), and all tests of statistical significance are two sided. The study and analyses were approved by the KPNC institutional review board.

RESULTS

Baseline Characteristics

Selected baseline characteristics of study participants are shown in Table 1. Compared with the cases, the population controls were generally more likely to have a greater educational status, higher income and to be light or moderate drinkers. More cases preferred beer, while more population controls preferred wine. Among the cases, the length of the Barrett's esophagus segment was <3 centimeters in 118 subjects (37%), ≥3 centimeters in 151 subjects (47%), and the length was not reported in 51 subjects (16%).

Total Alcohol Use and Barrett's esophagus—When cases were compared to population controls, total alcohol intake was not consistently associated with the risk of Barrett's esophagus (Table 2), though there were trends for a lower risk among subjects with moderate intakes and higher risk for those with heavier intakes. Moderate drinking (7–13 drinks/week) had a borderline inverse association [OR=0.52 95% CI (0.26–1.08)], after controlling for age, race, gender, smoking, *H. pylori* status, BMI, income, and location of diagnosis.

Alcohol Types and Barrett's esophagus—Associations varied by alcohol type (Table 2). These models adjusted for all the variables mentioned above as well as other alcoholic beverage types. When cases were compared to population controls, subjects who consumed a glass of wine a day on average (≥7 glasses of wine a week) had less than half risk of Barrett's esophagus compared to non-alcohol drinkers [OR=0.44 95%CI (0.20–0.99)]. In contrast, there was no association between beer drinking and Barrett's esophagus, and a non-significant trend for an adverse association between heavy liquor drinking (≥7/week) and Barrett's esophagus [OR=1.67, 95%CI (0.49–5.73)].

Alcohol Preference and Barrett's esophagus—The directions of the associations were similar when subjects were categorized into mutually exclusive categories for alcohol preferences (i.e. alcohol type >50% of all alcohol consumed): individuals who preferred wine were at lower risk of having Barrett's esophagus, while those who preferred liquor had a non-significant trend for a slightly higher risk, though the estimates were less precise due to the smaller numbers of subjects in each category. The estimates were weakened and the confidence intervals included 1.0 after adjusting for potential confounding variables (Table 3).

Alcohol Preference and sociodemographic and lifestyle characteristics

We qualitatively explored how choice of alcoholic beverages was related to other potential confounders (Table 4). Among the population controls, subjects with a wine preference (>50% of all alcohol consumed) had a greater tendency (at least 15% difference in frequency) to have had at least four years of college education and regular vitamin supplement intake compared with those who preferred beer or liquor. Those who preferred beer tended to be male, and liquor drinkers to be obese and consume fewer fruits and vegetables.

Sociodemographic and lifestyle characteristics and Barrett's esophagus

The associations between certain demographic and lifestyle variables and the risk of Barrett's esophagus are presented in Table 5. Compared to population controls, patients with Barrett's esophagus had lower levels of education; for example, individuals who completed at least 4 years of college had half the risk of developing Barrett's esophagus [OR=0.47 95% CI(0.27–0.82)] compared to those who had less than a high school education. In addition, consumption of more fruits and vegetables was inversely associated with risk [OR=0.90 95% CI (0.84–0.96), per serving/day]. Current smoking, the amount of television watching (a proxy for physical activity level) and income were not associated with the risk of Barrett's esophagus. Past smoking and long-term supplement use were associated with a higher risk of Barrett's

esophagus, though of borderline statistical significance (Table 5). Similar results were observed when cases were compared to GERD controls, though the associations were not statistically significant.

The models for sociodemographic and lifestyle characteristics were adjusted for age, race (white vs. non-white), gender, location of diagnosis, fruit and vegetables intake, *H. Pylori* status, income and education (Table 5). Other potential confounders such as alcohol, smoking, BMI, and supplement use did not confound these associations.

Supplemental Analysis

Evaluation of confounding variables—Inclusion of education, income, *H. pylori* status, BMI, vitamin supplement use, and smoking changed the effect estimate when included in the logistic models. We did not observe any evidence of confounding by most of the factors that were associated with alcohol preference, such as fruit and vegetable intake, and the overall influence of detectable confounding on the estimates was modest. For example, the unadjusted estimate for ≥7 glasses of wine per week compared to no use was OR=0.49 95% CI (0.25–0.97) (case vs. population control comparison). This was similar to both an adjusted odds ratio that included education, smoking (ever vs. never), *H. pylori* status, income, use of other types of alcohol (for alcohol type analysis only), and location of diagnosis [OR=0.44 95% CI (0.20–0.99)] and to a model that also contained fruit and vegetable intake, vitamin supplement use, BMI, comorbidity score, NSAIDs use, and total caloric intake [OR=0.40 95% CI (0.20–0.88)]. Similar results were found for other alcohol variables.

History of heavy alcohol use—A history of heavy alcohol use was reported for 58 cases, 53 GERD controls, and 60 population controls who answered “yes” to the question “Did you or someone else feel you drank too much alcohol (before the index date)?” When cases were compared to population controls, a potential history of heavy alcohol use itself was not associated with the risk of Barrett’s esophagus [OR=0.97 95% CI (0.60–1.56)]. Similar findings were seen when cases were compared to GERD controls (data not shown).

Lengths of Barrett’s segment—There were no substantial differences in the magnitude of the associations observed by the length of Barrett’s segment. Comparing cases to population controls, those who drank wine (7+drinks/week) were at significantly lower risk of having both long-segment [OR=0.38; 95% CI (0.15–0.99)] and short-segment Barrett’s esophagus [OR=0.35; 95% CI (0.14–0.83)]. The reason for these stronger effect estimates compared to the overall association between wine drinking and Barrett’s esophagus is due to weaker associations among people without information on the segment length.

Alcohol and GERD—The analyses did not indicate that GERD symptoms alone, a strong risk factor for Barrett’s esophagus, explained the associations between alcohol types and the risk of Barrett’s esophagus. First, adjustment for at least weekly GERD symptoms did not change the magnitude of the association for moderate wine consumption [OR=0.44, 95% CI (0.20–0.99) without adjustment vs. OR=0.49, 95% CI (0.14–1.79) with adjustment; cases vs. population controls], although the association was no longer statistically significant. Adjustment for GERD symptoms strengthened the associations for liquor drinking (≥7/week) [from OR=1.67, 95% CI (0.49–5.73) to OR=4.64, 95% CI (0.67–21.1)] and for beer drinking from OR=1.05, 95% CI (0.37–2.93) to OR=1.93, 95% CI (0.44–8.52), respectively.] Adjustment weakened the trend for moderate total alcohol consumption, from OR=0.52 95% CI (0.26–1.08) to OR=1.10 95%CI (0.35–3.44).

Second, we evaluated whether alcohol was a risk factor for Barrett’s esophagus among persons with GERD by comparing cases to GERD controls who lacked Barrett’s esophagus on

endoscopy (Table 2). These analyses effectively helped "match" for a GERD-type diagnosis and for health-care seeking behaviors leading to an endoscopy. For this comparison, total alcohol consumption was positively, though not always significantly, associated with the risk of Barrett's esophagus and there was no evidence of risk differences between the dose categories. Beer and liquor use had trends of positive association where drinkers were at higher risk compared to non alcohol users (Table 2). There was no inverse association between wine drinking and Barrett's esophagus for this comparison.

Effect modification—The associations between total alcohol use and Barrett's esophagus differed between users vs. nonusers of vitamin supplements (p-value interaction term=0.07). Long-term supplement users who drank alcohol moderately had one-third the risk of Barrett's esophagus compared with non-drinking supplement users [OR=0.30, 95% CI (0.10–0.86) case vs. population control comparison], while among non-supplement users, there was no association [OR=1.37 95%CI (0.41–4.57)]. In contrast, supplement non-users who were heavy drinkers (14+ drinks/week) were at 4 times higher risk compared with nondrinkers/non-supplement users, though with borderline statistical significance [OR=4.34 95% CI (1.07–17.7)], while among supplement users, there was no association [OR=0.82 95%CI (0.27–2.48)].

Gender, race, education, income, or fruits and vegetables intake did not modify the association significantly.

DISCUSSION

The current study is the first community or population-based study in the United States to evaluate alcohol and socio-demographic factors as risk factors for Barrett's esophagus. There were a few important findings. First, when cases were compared to population controls, we observed an inverse association between wine consumption and the risk of Barrett's esophagus, no associations were found for liquor or beer consumption. Second, education, which is likely related to numerous health-seeking behaviors, was strongly associated with a lower risk of Barrett's esophagus. Third, although the choice of alcoholic beverages was related to other demographic and health-seeking behavioral factors (such as vitamin use), adjustment for these factors did not eliminate the inverse association observed between wine consumption and Barrett's esophagus.

The current results extend knowledge from prior studies of esophageal adenocarcinoma and Barrett's esophagus. Approximately a dozen previous studies examined the association between alcohol and the risk of esophageal adenocarcinoma, although little information is available about different types of alcohol. A US population-based study reported an inverse association between wine drinking and the risk of esophageal adenocarcinoma[16] and a Swedish study reported inverse associations for subjects liquor and wine (ever vs. never used) and the risk of esophageal adenocarcinoma.[15] For Barrett's esophagus, two hospital-based studies reported an adverse effect of liquor intake.[23, 24]

There are several potential mechanisms through which alcohol (and alcohol types) may be associated with Barrett's esophagus, a potential early event in the carcinogenic pathway for esophageal adenocarcinoma. First, there are differences in drinking patterns: wine drinkers are more likely than liquor drinkers to consume their alcoholic beverage with food. Consumption of alcohol with food may reduce the direct damage the lining of esophagus, reducing the carcinogenesis process. Second, red wine contains compounds such as polyphenol that have important protective action on biomarkers of oxidative stress.[36] Human and animal data suggest anti-oxidants may decrease the risk of Barrett's esophagus and esophageal adenocarcinoma.[37–39] Drinking wine may reduce the oxidative damage caused by GERD,

thereby either decreasing the risk of esophagitis among GERD patients, or decreasing the chance of Barrett's esophagus among patients with esophagitis.

In contrast, higher alcohol contained in liquor may cause a direct irritation to the esophageal tissue, which may already have been injured by frequent reflux: a previous study of esophageal adenocarcinoma reported that those who consumed more straight liquor were at higher risk of developing cancer, while mixed liquor consumption (which tends to be more diluted) did not increase the risk.[10] Though our results were of borderline statistical significance, the slightly increased risk among heavy liquor users may be explained by this mechanism.

Another possibility is that moderate alcohol consumption and wine drinking are proxies for some unmeasured lifestyle factors, which in turn explain the significant inverse associations. Among our population controls, wine drinkers were more likely to be educated and have other markers of a healthy lifestyle such as a better diet and vitamin use, while beer and liquor drinkers were more likely to engage in unhealthier lifestyles such as eating fewer servings of fruits and vegetables and having higher BMIs. This corroborates previous alcohol research reporting that the frequency of general alcohol consumption and type of beverage are related to many factors.[40–42] Although demographic and lifestyle factors were associated with Barrett's esophagus, these factors did not appear to explain the inverse association between wine consumption and Barrett's esophagus. The association between wine drinking and Barrett's esophagus remained even after controlling for income, education, smoking, BMI, *H. Pylori*, fruits and vegetables intake, or vitamin supplement intake. Further adjustment of the model with NSAIDs use, television watching, or a co-morbidity score also made little change to the effect estimates.

Our data also showed that individuals with higher education were at a significantly lower risk of Barrett's esophagus. This contrasts with a report from England that suggested those with higher socioeconomic status were at a higher risk of Barrett's esophagus,[43] though it is similar to studies of esophageal adenocarcinoma in the United States that demonstrated inverse associations between higher education or income and cancer risk.[9, 16] Lower socio-economic status is associated with GERD,[44] but adjustment for GERD symptoms in the current study did not substantially diminish the association between alcohol and Barrett's esophagus. The results for cases vs. GERD controls, however, were mostly weaker than population control comparisons. The presence of GERD may partially mediate the association between socioeconomic status and the risk of Barrett's esophagus, though there are likely other pathways through which alcohol and socioeconomic status affect the risk of Barrett's esophagus. Further study examining what components of socioeconomic status are associated with higher risk of GERD is warranted.

There are numerous strengths of these analyses. The subjects came from the diverse KPNC membership base that closely approximates the region's census demographics and the results can likely be generalized to similar large populations. This is the first community-based study restricted to patients with a new diagnosis of Barrett's esophagus and the study identified all patients with a new diagnosis of Barrett's esophagus within a community-based population. The use of prevalent cases or referral cases may select for patients with a different risk profile, clinical course or patient compliance with follow-up; prevalent cases may also have initiated changes in diet or other behaviors after their Barrett's esophagus diagnosis.[45] The use of new diagnoses thus decreased selection bias and provided the most valid evaluation of the entire population of Barrett's esophagus patients. Lastly, the availability of a GERD comparison group provided information on the risk of Barrett's esophagus among patients with GERD.

There are several potential limitations of these analyses. Case-control studies cannot definitively establish cause and effect[33] and observational studies in general are subject to

confounding by other unmeasured variables. Although detailed analyses provided little evidence of confounding, we cannot exclude the possibility that unmeasured (or inadequately measured) socioeconomic or lifestyle factors might have influenced the results or that interactions between measured confounders were not completely adjusted for in the logistic models. We also cannot exclude the possibility that some of the associations between alcohol use and Barrett's esophagus are mediated by GERD, given the imperfect correlation between GERD symptoms and acid reflux. To explain the results by alcohol type, however, confounding by GERD may require that different types of alcohol influence GERD differently, with less GERD induced by wine than by equivalent amounts of alcohol from beer or hard liquor. We did not collect information on lifetime alcohol use. However, previous studies have reported a strong association between recent alcohol use from a food frequency questionnaire and long-term consumption from lifetime alcohol use questionnaires.[1] In addition, to avoid biases due to those who quit drinking for health or other reasons, we asked subjects a question about prior heavy alcohol use that may not have been captured by the food frequency questionnaire and excluded these patients from the "non-drinker" category, as appropriate. Of note, however, we found no differences between the effect estimates with and without these individuals (data not shown). We also evaluated whether there was a reverse causation bias whereby GERD symptoms may have lead the subjects to quit alcohol use. There was no difference in the estimates between those who had GERD symptoms for longer than one year prior to the index date, and those who had symptoms for shorter durations (data not shown). In addition, if reverse causation was causing our observed inverse association between wine and Barrett's esophagus, we might expect similar patterns for other types of alcohol (i.e., if subjects were to quit drinking due to symptoms, they may be likely to quit all types of alcohol). Finally, the presence of non-responders may lead to bias. However, electronic data suggested that non-responders were similar to responders on major demographic variables and were slightly healthier than the responders (i.e., slightly lower co-morbidity scores), which would tend to bias the results towards the null if such a bias was present. In addition, if the alcohol use rate among our sample of population controls was artificially different than the "true" average rate among our membership, the observed association may be biased. However, a recent Kaiser Permanente Northern California stratified random sample survey of over 18,000 members found that 27% of males 45–64 years of age were "non-drinkers";[46] this number is almost identical to the 26% proportion of non-drinkers found among males ages 45–64 in the current study's population control group.

In summary, in a community-based population, we found associations between alcohol types and a new diagnosis of Barrett's esophagus, and the effects were modified by the presence of vitamin supplement use. The observed associations were independent of demographic and life style factors that were related to choice of alcoholic beverages, including vitamin supplement use. Higher education level was also inversely related to the risk. Future studies examining the interaction between vitamin supplement and alcohol types, and how socioeconomic status may affect GERD and Barrett's esophagus are needed.

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Abbreviations

GERD
gastroesophageal reflux disease

KPNC
Kaiser Permanente, Northern California

NSAID
nonsteroidal anti-inflammatory drug

BMI
body mass index

BE
Barrett's esophagus

OR
odds ratio

95%CI
confidence interval

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Table 1

Characteristics of study groups

	Cases	GERD controls	Population controls
	Number or Mean (% or standard deviation)	Number or Mean (% or standard deviation)	Number or Mean (% or standard deviation)
Number of subjects	320	316	317
Age (years)			
20–39	9 (3)	12 (4)	9 (3)
40–59	120 (38)	116 (37)	105 (33)
60–79	191 (59)	188 (59)	203 (64)
Race			
White	261 (82)	249 (79)	264 (83)
Hispanic	25 (8)	20 (6)	13 (4)
Black	5 (2)	21 (7)	17 (5)
Asian	19 (6)	11 (3)	12 (4)
Others/Mixed/Unknown	10 (3)	15 (5)	11 (4)
Gender			
Male	234 (73)	218 (69)	214 (68)
Education			
High school or less	83 (26)	78 (25)	60 (19)
Some college	144 (45)	133 (42)	120 (38)
College and beyond	93 (29)	105 (33)	137 (43)
Income[1]			
<50k	136 (46)	110 (41)	106 (36)
50–75	66 (22)	61 (23)	68 (23)
75k+	94 (32)	99 (37)	121 (41)
Smoking status			
Never smoker	108 (34)	129 (41)	140 (44)
Current smoker	51 (16)	40 (13)	39 (12)
Ever smoker	212 (66)	187 (59)	176 (56)
Alcohol use status			
Non drinker	99 (31)	114 (36)	85 (27)
Light drinker (<7 drinks[2]/wk)	155 (48)	133 (42)	158 (50)
Moderate drinker (7–13 drinks/wk)	27 (8)	27 (9)	48 (15)
Heavy drinker (14+drinks/wk)	39 (12)	42 (13)	26 (8)
Alcohol type preference (among drinkers)			
Wine	75 (23)	74 (23)	104 (33)
Beer	74 (23)	44 (14)	50 (16)
Liquor	39 (12)	36 (11)	30 (9)
No preference	33 (10)	48(15)	48 (15)
Body mass index (kg/m^2)	29.5 (0.3)	28.9 (0.3)	29.5 (0.3)

[1] Total responses for each exposure category may not equal total for the study group due to missing data for some questions.

[2] The term ‘drink’ was defined as 1 glass for wine (4–5oz), 12oz for beer, and one shot (1¼) for liquor, all containing approximately 13g of ethanol. <7 drinks approximately equals to <91g ethanol/day, 7–13 to 91–181g ethanol/day, and 14+ to 182+g ethanol/day.

Table 2

The risk of Barrett's esophagus in relation to total alcohol use and types of alcohol

	N (Cases/GERD/Population)	Odds Ratio (95%CI)[1] Case vs. Population controls	Odds Ratio (95%CI) [1] Case vs. GERD controls
Any alcohol[2]			
No alcohol use	99/114/85	1.0 (ref)	1.0 (ref)
<7 drinks/week	149/130/157	0.94 (0.60–1.45)	1.58 (1.03–2.41)
7–13 drinks/week	45/55/65	0.52 (0.26–1.08)	1.56 (0.75–3.22)
14+ drinks/week	27/17/10	1.44 (0.68–3.04)	1.53 (0.80–2.92)
Wine			
No alcohol use	99/114/85	1.0 (ref)	1.0 (ref)
<7 drinks/week	128/125/147	0.81 (0.51–1.31)	1.44 (0.90–2.29)
7+ drinks/week	29/37/44	0.44 (0.20–0.99)	1.03 (0.45–2.34)
Beer			
No alcohol use	99/114/85	1.0 (ref)	1.0 (ref)
<7 drinks/week	139/117/157	1.00 (0.62–1.63)	1.84 (1.15–2.95)
7+ drinks/week	27/28/17	1.05 (0.37–2.93)	2.14 (0.82–5.64)
Liquor			
No alcohol use	99/114/85	1.0 (ref)	1.0 (ref)
<7 drinks/week	92/101/114	0.81 (0.51–1.30)	1.54 (0.96–2.46)
7+ drinks/week	23/18/13	1.67 (0.49–5.73)	1.81(0.62–5.33)

[1]The model was controlled for age, race (white vs. non-white), gender, education, smoking (ever vs. never), *H. pylori* status, BMI, income, use of other types of alcohol (for alcohol type analysis only), and location of diagnosis

[2]The term 'drink' was defined as 1 glass for wine (4–5oz), 12oz for beer, and one shot (1 ¼Oz) for liquor, all containing approximately 13g of ethanol. <7 drinks approximately equals to <91g ethanol/day, 7–13 to 91–181g ethanol/day, and 14+ to 182+g ethanol/day.

Table 3

The association between alcohol preference and the risk of Barrett's esophagus (cases vs. population controls)

Beverage preference[1]	**Wine drinker**	**Beer drinker**	**Liquor drinker**	**No preference**	**Non drinker**
Number of subjects	104	50	30	48	85
OR (95% CI): Crude	0.55 (0.33–0.93)	1.03 (0.54–1.99)	1.27 (0.60–2.70)	0.69 (0.28–1.67)	1 (ref)
OR (95% CI): Adjusted[2]	0.78 (0.47–1.31)	1.43 (0.80–2.57)	1.07 (0.53–2.16)	0.77 (0.41–1.44)	1 (ref)

[1]Preference of beverage was defined as follows: wine drinker if amount of wine comprised >50% of the total servings of alcohol consumed. Among alcohol users, if no beverage type exceeded 50% the person was classified as "no preference".

[2]The model was controlled for age, race (white vs. non-white), gender, education, smoking (ever vs. never), *H. pylori* status, BMI, income, use of other types of alcohol (for alcohol type analysis only), and location of diagnosis

Table 4

The demographic and lifestyle characteristics by alcohol preference among population controls.

Beverage preference*	Wine drinker	Beer drinker	Liquor drinker	No preference	Non drinker
	Number or Mean (% or standard deviation)	Number or Mean (% or standard deviation)	Number or Mean (% or standard deviation)	Number or Mean (% or standard deviation)	Number or Mean (% or standard deviation)
Number of subjects	104	50	30	48	85
Education					
<11years	2 (2)	4 (8)	1 (3)	2 (4)	5 (6)
High school	13 (13)	9 (18)	6 (20)	6 (13)	12 (14)
Some college	32 (31)	19 (38)	11 (37)	20 (42)	38 (45)
College/Univ	19 (18)	9 (18)	7 (23)	11 (23)	15 (18)
Graduate school	38 (37)	9 (18)	5 (17)	9 (19)	15 (18)
Income					
<$50k	32 (32)	17 (39)	9 (32)	14 (30)	34 (44)
$50–75	23 (23)	9 (20)	6 (21)	12 (26)	18 (23)
>+$75	45 (45)	18 (41)	13 (46)	20 (43)	25 (33)
Gender					
Male	68 (65)	41 (82)	17 (57)	35 (73)	49 (62)
Race					
White	93 (89)	43 (86)	26 (87)	40 (83)	62 (73)
BMI					
Underweight (<18.5)	0 (0)	1 (2)	0 (0)	1 (2)	0 (0)
Normal (18.5–24.9)	31 (30)	11 (22)	4 (13)	7 (15)	17 (20)
Overweight (25–29.9)	40 (39)	24 (48)	12 (40)	19 (40)	23 (27)
Obese (30+)	33(32)	14 (28)	14 (47)	21 (44)	45 (53)
Television					
<1hr/day	25 (24)	9 (18)	3 (10)	6 (12)	17 (22)
1–2hr//day	36 (35)	15 (30)	13 (43)	20 (42)	22 (26)
3+hr/day	43 (41)	26 (52)	14 (47)	22 (46)	39 (46)
Smoking					
Never	42 (40)	16 (32)	10 (33)	26 (54)	46 (55)
Former	51 (49)	30 (60)	13 (43)	17 (35)	29 (34)

Beverage preference*	Wine drinker	Beer drinker	Liquor drinker	No preference	Non drinker
	Number or Mean (% or standard deviation)	Number or Mean (% or standard deviation)	Number or Mean (% or standard deviation)	Number or Mean (% or standard deviation)	Number or Mean (% or standard deviation)
Current	11 (11)	4 (8)	7 (23)	5 (10)	9 (11)
Fruit & vegetables intake (servings/day)	5.0 (2.6)	4.3 (2.5)	3.8 (2.4)	4.6 (3.1)	4.4 (2.9)
Long term vitamin use	61 (64)	18 (41)	12 (48)	20 (48)	42 (53)

*Preference of beverage was defined as follows: wine drinker if amount of wine comprised >50% of the total servings of alcohol consumed. If none of the beverage type exceeded 50% the person was classified as having no preference.

Table 5

The association between demographic and lifestyle factors and the risk of Barrett's esophagus

	# BE/GERD/Pop controls	Cases vs. Population controls OR (95% CI)[1]	Cases vs. GERD controls OR (95% CI)[1]
Education			
High school or less	83/78/60	1 (ref)	1 (ref)
Some college	144/133/120	0.94 (0.57–1.54)	0.94 (0.59–1.49)
College and beyond	93/105/137	0.47 (0.27–0.82)	0.65 (0.38–1.14)
Household Income			
<50k	136/110/106	1 (ref)	1 (ref)
50–75k	66/61/68	0.83 (0.51–1.36)	1.10 (0.68–1.80)
75k+	94/99/121	0.68 (0.42–1.11)	1.09 (0.67–1.75)
Smoking			
Never	108/129/140	1 (ref)	1 (ref)
Former	170/155/140	1.46 (0.95–2.23)	1.19 (0.79–1.81)
Current	42/32/36	1.10 (0.58–2.08)	1.28 (0.68–2.40)
Fruits and vegetables intake (per serving)		0.90 (0.84–0.96)	0.99 (0.92–1.06)
Television			
<1hr/day	63/51/67	1 (ref)	1 (ref)
1–2hr/day	93/103/106	1.12 (0.65–1.91)	0.78 (0.45–1.36)
3+hr/day	164/162/144	1.37 (0.80–2.33)	0.82 (0.48–1.39)
Supplement use			
Non users	103/133/124	1 (ref)	1 (ref)
Long-term users	154/142/153	1.42 (0.95–2.14)	1.43 (0.96–2.14)

[1]The model was controlled for age, race (white vs. non-white), gender, location of diagnosis, fruit and vegetables intake, *H. Pylori* status, income and education