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Tea, coffee, carbonated soft drinks and upper gastrointestinal tract cancer risk in a large United States prospective cohort study

JS Ren[1], **ND Freedman**[1], **F Kamangar**[1], **SM Dawsey**[1], **AR Hollenbeck**[2], **A Schatzkin**[1], and **CC Abnet**[1]

[1]Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health, Department of Health and Human Services, Bethesda, Maryland, United States

[2]AARP, Knowledge Management, Washington, D.C., United States

Abstract

The authors investigated the relationship between hot tea, iced tea, coffee and carbonated soft drinks consumption and upper gastrointestinal tract cancers risk in the NIH-AARP Study. During 2,584,953 person-years of follow-up on 481,563 subjects, 392 oral cavity, 178 pharynx, 307 larynx, 231 gastric cardia, 224 gastric noncardia cancer, 123 esophageal squamous cell carcinoma (ESCC) and 305 esophageal adenocarcinoma (EADC) cases were accrued. Hazard ratios (HRs) and 95% Confidence Intervals (95%CIs) were calculated by multivariate-adjusted Cox regression. Compared to non-drinking, the hazard ratio for hot tea intake of ≥1 cup/day was 0.37 (95%CI: 0.20, 0.70) for pharyngeal cancer. The authors also observed a significant association between coffee drinking and risk of gastric cardia cancer (compared to <1 cup/day, the hazard ratio for drinking >3 cups/day was 1.57 (95%CI: 1.03, 2.39)), and an inverse association between coffee drinking and EADC for the cases occurring in the last three years of follow-up (compared to <1 cup/day, the hazard ratio for drinking >3 cups/day was 0.54 (95%CI: 0.31, 0.92)), but no association in earlier follow-up. In summary, hot tea intake was inversely associated with pharyngeal cancer, and coffee was directly associated with gastric cardia cancer, but was inversely associated with EADC during some follow-up periods.

Keywords

tea; coffee; carbonated beverages; upper gastrointestinal tract; cancer

INTRODUCTION

Upper gastrointestinal (UGI) tract cancers are an important burden on human health. Collectively, they accounted for about 18% of all new cancer cases worldwide, including 274,000 oral cavity, 130,000 oro- and hypo-pharynx, 159,000 larynx, 462,000 esophagus and 934,000 stomach cancers in 2002.[1]

Correspondence to: Christian Abnet, PhD, MPH, Nutritional Epidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, 6120 Executive Blvd, Suite 320, Rockville, MD, 20852-7236, USA, Phone: +1 (301) 594-1511, Fax: +1 (301) 496-6829, abnetc@mail.nih.gov.

CONFLICT OF INTEREST STATEMENT
None declared.

Tea, coffee, and carbonated soft drinks are among the most popular beverages worldwide. Most people drink at least one of these beverages daily. Several studies investigating the association of tea and coffee with upper digestive tract cancers have reported inconsistent results, with some studies showing a direct association with very hot tea and an inverse association with coffee.[2–7] Carbonated soft drinks have been hypothesized to increase the risk of gastric reflux and the risk of esophageal adenocarcinoma, but case-control studies have reported inverse or null associations with laryngeal or esophageal cancers.[8–11] Most previous studies have had case-control designs, which can be affected by selection and recall bias. Little prospective data is available.

To further evaluate the relationship of tea, coffee and carbonated soft drinks with risk of UGI tract cancers (including oral, oro- and hypo- pharyngeal, laryngeal, esophageal and gastric cancers), we examined these associations in a population-based prospective cohort, the NIH-AARP Diet and Health Study.

MATERIALS AND METHODS

Study population

The design and establishment of NIH-AARP Diet and Health Study have been described previously.[12] Between 1995 and 1996, a questionnaire on demographic characteristics, diet, and health-related behaviors was mailed to AARP members aged 50–71 years who resided in 8 US states (California, Florida, Louisiana, New Jersey, North Carolina and Pennsylvania, Georgia and Michigan). There were 566,407 respondents (339,671 men and 226,736 women) who filled out the survey in satisfactory detail and consented to participate in the study. We excluded subjects with cancer at baseline (n=51,205), proxy respondents (n=15,760), and those who were outliers for calorie/energy intake (n=4,419). Because results differed after excluding those with less than two years of follow-up (13,455 subjects, including 643 cases), and early stage tumors may affect beverage intake, we excluded those with less than two years of follow-up from our analysis. The research cohort included 481,563 participants: 286,402 men and 195,161 women. For the analysis of hot tea, iced tea and coffee, some subjects were further excluded from our study because of unreadable answers about their intake of hot tea (901 subjects), iced tea (491 subjects) or coffee (1,021 subjects). The NIH-AARP Diet and Health Study was approved by the Special Studies Institutional Review Board of the US National Cancer Institute (NCI).

Cohort follow-up and case identification

The cohort follow-up methods have been described previously.13 Follow-up time extended from subject entry into the cohort (between 1995 and 1996) to the diagnosis of the first upper-gastrointestinal tract cancer (oral, pharyngeal, laryngeal, esophageal or gastric cancers, as a diagnosis of one of these cancers would be associated with increased surveillance of the other sites), the date of death, the end of the study (December 31, 2003), or the date the subject moved out of the registry ascertainment area. Incident cases of cancer were identified by linkage between the NIH-AARP cohort membership files and 11 state cancer registry databases (the registries of participating states plus Arizona, Nevada and Texas).13 Cancer sites were identified by anatomic site and histologic code of the International Classification of Disease for Oncology (ICD-O, third edition).14 Cancers of the oral cavity, oro-and hypo- pharynx and larynx were restricted to squamous cell carcinomas, and gastric cancers were restricted to adenocarcinomas. We classified tumors with site codes C00.1-C06.9 as oral cavity cancer. Oro- and hypo- pharyngeal cancers included tumours of the tonsil (C09.0 – C09.9), oropharynx (C10.0 – C10.9), pyriform sinus (C12.9), hypopharynx (C13.0 – C13.9), and pharynx not otherwise specified (NOS) (C14.0). Tumors with site codes C32.0-C32.9 were classified as laryngeal cancer. Esophageal cancers (C15.0–C15.9) were further subclassified as esophageal

squamous cell carcinoma (ESCC) or esophageal adenocarcinoma (EADC) based on their histology. Gastric cancers were classified as gastric cardia cancer (C16.0) or gastric noncardia cancer (C16.1–C16.9).

Assessment of tea, coffee and carbonated soft drinks intake

The baseline questionnaire included a 124-item food frequency questionnaire and questions about demographics, height, weight, alcohol intake, tobacco use and physical activity. Participants were asked to report their usual frequency of beverage intake over the last 12 months, using 10 frequency categories ranging from 'never' to '6+ times per day' and 3 categories of portion size. We classified intake categories for hot tea, iced tea and coffee in cups, and intake categories for carbonated soft drinks in 12 ounce cans.

Statistical analysis

Analyses were performed with SAS version 9.1.3 (SAS Institute, Cary, NC). An alpha level of less than 0.05 was considered statistically significant, and all tests were two-sided. Hazard ratios (HRs) and 95% confidence intervals (95%CI) were calculated using Cox proportional hazards regression.[15] As noted, we deleted the first two-years of follow-up for the entire cohort. We tested the proportional hazards assumption by including an interaction term for person-years and each beverage variable for the remaining six years of follow-up time. The proportional hazards assumption failed for the association of hot tea with ESCC, coffee with EADC, and carbonated soft drinks with oral cavity cancer. Risk estimates for hot tea with ESCC and carbonated soft drinks with oral cavity cancer from the Cox models using all six years of follow-up appeared similar in logistic regression analyses (data not shown). Furthermore, risk estimates for cancers occurring in the first three years of follow-up were similar to those for the last three years of follow-up. Therefore, we present results for all six years of follow-up for these associations. In contrast, risk estimates for the association of coffee with EADC risk appeared different for cases occurring in the first three years of follow-up compared to the last three years of follow-up. Therefore, for this association we present risk estimates by three year follow-up period.

All models included adjustment for continuous variables of age, body mass index (BMI), calorie intake, intake of vegetables, fruit, white meat and red meat, and categorical variables of sex, education (< high school education, completion of high school, some post-high school training, completion of college, or completion of graduate school), smoking (never cigarette smokers, quit ≤ 1 pack/day, quit >1 pack/day, currently smoking ≤ 1 pack/day, or currently smoking >1 pack/day), alcohol drinking (none, >0–1 drink/day, >1–3 drinks/day or >3 drinks/day), vigorous physical activity (never, rarely, 1–3 times/month, 1–2 times/week, 3–4 times/week, or 5 or more times per week), usual physical activity throughout the day (sitting during the day/little walking, sitting during the day/walking a fair amount, standing/walking a lot/no lifting, lifting/carrying light loads or often climbing stairs or hills, or doing heavy work/carrying heavy loads), and ethnicity (non-Hispanic white, non-Hispanic black, Hispanic or Asian/Pacific Islander/Native American). Models were also mutually adjusted for the categorical intake of hot tea, iced tea, coffee, and carbonated soft drinks.

Missing values for adjusting covariates were included as dummy variables in the models. Linear trend tests across intake categories of hot tea, iced tea, coffee and carbonated soft drinks were conducted by assigning participants the category for their intake and entering it as an ordinal term in the regression model.

RESULTS

During 2,584,953 person-years of follow-up on 481,563 subjects we accrued the following cancer case numbers: 392 oral cavity, 178 pharynx, 307 larynx, 123 ESCC, 305 EADC, 231 gastric cardia, and 224 gastric noncardia.

In our cohort, about 30% of the cohort did not drink hot tea, 19% drank less than 1 cup per month, 17% drank 1–3 cups per month, 18% drank 1–6 cups per week, and 16% drank at least 1 cup of hot tea every day. Compared to non-drinkers, hot tea drinkers were more likely to be women, to never smoke, to drink alcohol, to have more years of education and higher intake of fruit, white meat, and iced tea, and to have less intake of red meat and carbonated soft drinks.

Coffee was consumed by more people in the cohort than any other beverage that was analyzed in this study. Only 10% did not drink any coffee, 16% drank less than 1 cup of coffee per day, 17% drank 1 cup per day, 41% drank 2–3 cups per day, and 16% drank 3 or more cups per day. Coffee drinkers tended to be men, use more tobacco and alcohol, eat more red meat and less fruits and vegetables, and drink less tea than non-drinkers.

We found that greater consumption of hot tea was significantly inversely associated with pharyngeal cancer risk (Table 1). Compared with participants who did not drink hot tea, hazard ratios (95%CIs) were 0.52 (0.30, 0.87) for the participants who drank 1–6 cups of hot tea per week and 0.37 (0.20, 0.70) for those who drank more than 1 cup per day (*P* for trend = 0.0003). We also found a suggestion of a protective effect of hot tea for ESCC. Compared with those who did not drink hot tea, the hazard ratios (95%CIs) for the groups who drank <1 cup/month, 1–3 cups/month, 1–6cups/week and ≥1 cup/day were 0.61 (0.36, 1.03), 0.61 (0.34, 1.09), 0.84 (0.50, 1.44) and 0.57 (0.30, 1.07) (*P* for trend = 0.10). There were no significant associations between hot tea and the other five UGI tract cancer sites.

Eighty-one percent of the cohort drank iced tea, including 21% who drank 3 or fewer cups per month, 30% who drank 1–6 cups per week, and 30% who drank at least one cup each day (Table 2). Iced tea intake was not associated with the risk of any of the upper digestive tract cancers. Except for ESCC, all hazard ratio estimates were close to 1.00. For ESCC, compared with those who drank no iced tea, the hazard ratio (95%CI) was 0.49 (0.28, 0.86) for those who drank ≤3 cups/month, but this association was not found among subjects who drank iced tea more frequently. For the iced tea intake groups of 1–6 cups/week and ≥1 cup/day, the hazard ratios (95%CIs) were 0.80 (0.50, 1.28) and 0.69 (0.42, 1.12), respectively (*P* for trend = 0.37).

We observed a significant positive association between coffee intake and gastric cardia cancer risk (Table 3). As coffee intake increased from 0–1 cup/day, to 1 cup/day, 2–3 cups/day and >3 cups/day, the hazard ratios (95%CIs) for gastric cardia cancer also increased, from 1.00 (reference) to 1.13 (0.71, 1.78), 1.24 (0.86, 1.79) and 1.57 (1.03, 2.39), respectively (*P* for trend = 0.039). We found no significant association between coffee intake and EADC risk for the cases occurring over all six years or the first three years of follow-up, but observed a significant inverse association between coffee intake and EADC risk for the cases occurring in the last three years of follow-up. The Harzard ratios (95%CIs) for the associations between coffee intake and EADC risk during the last three years of follow-up were 0.78 (0.47, 1.30), 0.69 (0.46, 1.04) and 0.54 (0.31, 0.92), respectively (*P* for trend = 0.017). We found no significant associations between coffee intake and cancer at the other five sites.

Carbonated soft drinks were also commonly consumed by cohort members. Only 12% did not drink any soft drinks, 31% drank one or fewer cans per week, 41% drank 2–6 cans per week, and 16% drank at least one can each day (Table 4). We observed no evidence for a dose-response association between soft drink consumption and any of the UGI tract cancer risks, although risk estimates for some categories and cancer sites were significantly different from

the null. For oral cavity cancer, compared with those who drank no carbonated soft drinks, the hazard ratios (95%CIs) for drinking ≤1 can/week, 2–6 cans/week, and ≥1 can/day were 0.62 (0.46, 0.85), 0.66 (0.49, 0.89) and 0.77 (0.54, 1.09), respectively (*P* for trend = 0.31). For pharyngeal cancers, the hazard ratio (95%CI) was 0.56 (0.36, 0.87) for 2–6 cans/week, but no significant association was observed with higher intake. We found a borderline insignificant association between carbonated soft drinks intake and EADC for those who drank ≤1 can/week, with a hazard ratio (95%CI) of 1.52 (0.97, 2.38). But for those with the greatest intake, with ≥1 can/day, the hazard ratio (95%CI) was 1.11 (0.66, 1.85). For ESCC, laryngeal, gastric cardia, and gastric noncardia cancers, all of the hazard ratio estimates were less than 1.00, but not significant.

DISCUSSION

We investigated the relationship between upper gastrointestinal tract cancers (including cancers of the oral cavity, pharynx, larynx, esophagus, and stomach) and consumption of hot tea, iced tea, coffee and carbonated soft drinks in the NIH-AARP Diet and Health Study. We found an inverse association between hot tea intake and pharyngeal cancer risk and a direct association between coffee intake and gastric cardia cancer risk. There were no associations observed between hot tea or coffee consumption and the other cancer sites, or between iced tea or carbonated soft drinks and any of the UGI tract cancers.

The possible preventive effect of tea on cancer has received much attention in recent years.[16] Tea polyphenols may act at numerous points of carcinogenesis including cancer cell growth, apoptosis, and metastasis.[17] On the other hand, chronic thermal injury from drinking very hot beverages may be a risk factor for carcinogenesis in some UGI sites,[7,18,19] and black tea may acquire carcinogenic contaminants, such as benzo[*a*]pyrene (BaP) or mycotoxins, when being processed.[20,21]

We found an inverse association between hot tea intake and pharyngeal cancer. Our results are consistent with a previous case-control study conducted in Southern Brazil, which found pharyngeal cancer risk was significantly decreased by 69% when comparing tea drinkers with non-drinkers.22 On the other hand, another case-control study conducted in India found a significant positive dose-response association between tea drinking and pharyngeal cancer.[23] Comparing subjects who drank three, four, or five or more cups per day with those who drank two cups or less per day, a significant increase in risk for pharyngeal cancer was found (relative risks (RRs): 1.1, 1.8, and 2.3, respectively, *P* for trend = 0.035). Studies that have analyzed both pharyngeal and oral cavity tumors together have shown no association between hot tea consumption and the risk of these tumors.[5,24–26] We found no significant associations between hot tea intake and cancers of the oral cavity or larynx. This is consistent with three previous case-control studies.[22,27,28] Since the oral cavity, pharynx and larynx are adjacent, connected structures and have similar squamous epithelium, the associations between hot tea and pharyngeal cancer alone that were found in our and other studies could be due to chance.

We found a suggestion of a protective effect of hot tea drinking for ESCC and no association between hot tea consumption and EADC risk. As noted above, these results probably reflect the combined effects of the tea constituents themselves, tea processing techniques, and thermal injury. A recent review of epidemiological studies evaluating the effects of green tea reported inconsistent findings between case-control and cohort studies of esophageal cancer.[29] Three case-control studies found a protective effect for green tea against esophageal cancer.[30–32] However, two cohort studies demonstrated positive associations between drinking green tea and mortality from esophageal cancer among men,[33,34] and a randomized controlled trial with 400 participants showed no benefit for decaffeinated green tea against precancerous lesions or abnormal cell proliferation. 35 Since black tea may acquire potentially carcinogenic

contaminants during processing, attention has also been paid to the association between black tea consumption and esophageal cancer risk.20,21 A recent case-control study conducted in Iran showed no association between the frequency of drinking black tea and ESCC risk.[19] However, a hospital-based case-control study in China, including 1,248 ESCC cases and 1,248 controls, reported an inverse association between drinking Congou tea (a grade of Chinese black tea) and ESCC risk.[36] In the current study, we didn't distinguish between the consumption of green, black or herbal tea, and we did not assess the drinking temperature of hot tea. Also, only 16% participants in our cohort drank ≥1cups of hot tea each day, a lower intake than in most Asian populations. These differences may contribute to the heterogeneity of results.

We found no association between hot tea consumption and stomach cancer (both gastric cardia and non-cardia cancers). A meta-analysis of 13 epidemiologic studies found a significant inverse association between green tea consumption and risk of stomach cancer (RR: 0.82, 95% CI: 0.70, 0.96).[37] Summary relative risks (95%CI) were 0.73 (0.64, 0.83) for case-control studies and 1.04 (0.93, 1.17) for cohort studies, respectively. A recent case-control study conducted in Italy, including 999 gastric cancer patients and 2,628 controls, also reported black tea consumption was unlikely to be associated with gastric cancer.38

This is the first study to examine the association between iced tea consumption and risk of upper digestive tract cancers. We found no consistent dose-response associations that suggested a link between iced tea intake and upper GI cancer risk.

Similar to hot tea, coffee is drunk at high temperatures and it contains compounds that may reduce UGI tract cancer risk. We found that drinking >3 cups of coffee per day was associated with increased risk of gastric cardia cancer but was not associated with gastric non-cardia cancer risk. Results from the few previous studies of these associations have been null.[39,40] Therefore, it is not clear whether the difference we found by anatomic subsite in our study reflects a true difference or the effects of chance. For EADC, we found an inverse association during the last three years of follow-up but no association during the first three years. This difference by follow-up time could reflect chance or it may be that early cancer symptoms might alter coffee intake. We did not find associations between coffee consumption and ESCC or squamous cancers at other sites. Both case-control[5,18,22,28,40–46] and cohort studies[2–4] have previously explored these associations, but no consistent patterns have emerged.

The association between carbonated soft drinks consumption and UGI tract cancers has received little attention overall, but several reports have evaluated a possible association with esophageal adenocarcinoma. Carbonated beverages have been shown to increase gastric reflux, and thus could be associated with an increased risk of esophageal adenocarcinoma.[9] Three previous case-control studies have examined this possibility. One US study showed an inverse association[9] but the other two studies, from Australia[10] and the US[11], showed no association. In our study we also found no association between carbonated beverage intake and EADC risk.

We also found no association between carbonated soft drinks consumption and risk of gastric cardia or non-cardia cancers. Gastric cardia cancer showed no association with carbonated soft drinks intake in two earlier case-control studies.10,11 The only previous prospective study of carbonated soft drinks and UGI tract cancers was conducted in Japan.[47] After 8 years of follow-up of 1,524 men and 1,634 women, no association was found between cola or carbonated drink intake and stomach cancer in men (RR: 0.8, 95%CI: 0.4–1.8), but a significant positive association was found between carbonated drink intake and stomach cancer in women (RR: 3.9, 95%CI: 1.4, 11.1).

The current study has a number of strengths and limitations. It is a large prospective analysis with exposure information collected before cancer diagnosis. Furthermore, we performed lag

analysis to examine whether reverse causation affected our results. The associations for UGI tract cancers were examined by anatomic sub-sites and different tumor histology types. To limit confounding, we adjusted our models for most of the major risk factors for UGI tract cancers, including alcohol and cigarette use. Nevertheless, confounding by these or other exposures, such as *Helicobacter pylori* infection and esophageal reflux disease, could still affect results. We also lacked information on types of tea consumed (green, black, herbal, etc.) and we did not collect any information on the usual temperature of tea and coffee consumption, which may be an important risk factor for ESCC.[7] In addition, we had limited power for several cancer sites because of small case numbers. Finally, because we examined multiple exposures and multiple endpoints, significant associations could be due to chance.

In summary, in this large prospective study that included 1,760 cases of oral, laryngeal, pharyngeal, esophageal and gastric cancers, we observed an inverse association between hot tea intake and pharyngeal cancer, a direct association between coffee intake and gastric cardia cancer and an inverse association between coffee intake and EADC during some follow-up periods.

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Table 1

The Association between Hot Tea Intake and Risk of Incident Upper Gastrointestinal Cancers in the NIH-AARP Diet and Health Study Cohort

Sites[†]	**Total**	**None**	**<1 cup/month**	**1–3 cups/month**	**1–6cups/week**	**≥1 cup/day**	***P* for trend**[§]
Oral cavity							
No.	391	153	80	57	57	44	
HR[†]		1.00	0.96	0.84	0.88	0.75	0.083
95%CI[†]			0.73, 1.26	0.61, 1.14	0.65, 1.21	0.53, 1.06	
Pharynx							
No.	178	93	31	26	17	11	
HR[†]		1.00	0.67	0.72	0.52	0.37	0.0003
95%CI[†]			0.44, 1.01	0.46, 1.12	0.30, 0.87	0.20, 0.70	
Larynx							
No.	307	123	57	56	37	34	
HR[†]		1.00	0.98	1.20	0.87	0.92	0.69
95%CI[†]			0.71, 1.34	0.87, 1.65	0.60, 1.27	0.63, 1.36	
Esophagus (ESCC[‡])							
No.	123	58	19	15	19	12	
HR[†]		1.00	0.61	0.61	0.84	0.57	0.10
95%CI[†]			0.36, 1.03	0.34, 1.09	0.50, 1.44	0.30, 1.07	
Esophagus (EADC[‡])							
No.	305	115	57	46	49	38	
HR[†]		1.00	0.93	0.91	1.04	0.97	0.98
95%CI[†]			0.67, 1.28	0.64, 1.29	0.74, 1.47	0.67, 1.41	
Gastric Cardia							
No.	231	86	47	36	34	28	
HR[†]		1.00	1.05	0.98	0.99	0.97	0.85
95%CI[†]			0.74, 1.51	0.66, 1.46	0.66, 1.49	0.63, 1.50	
Gastric noncardia							
No.	224	74	40	36	35	39	

Sites[†]	Total	None	<1 cup/month	1–3 cups/month	1–6cups/week	≥1 cup/day	*P* for trend[§]
HR[†]		1.00	1.02	1.02	0.96	1.21	0.52
95%CI[†]			0.69, 1.50	0.68, 1.53	0.64, 1.46	0.81, 1.81	

[†]Hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated in Cox proportional hazards models adjusted for age, sex, tobacco smoking, alcohol drinking, BMI, education, ethnicity, usual physical activity throughout the day, vigorous physical activity, and the daily intake of fruit, vegetables, red meat, white meat, and calories.

[‡]ESCC = Esophageal Squamous Cell Carcinoma, EADC = Esophageal Adenocarcinoma

[§]*P* values for trend were calculated by representing intake as an ordinal variable for each category in the adjusted models described above.

Table 2

The Association between Iced Tea Intake and Risk of Incident Upper Gastrointestinal Cancers in the NIH-AARP Diet and Health Study Cohort

Sites[†]	**Total**	**None**	**≤3 cups/month**	**1–6 cups/week**	**≥1 cup/day**	***P* for trend**[§]
Oral cavity						
No.	392	79	85	114	114	
HR[†]		1.00	0.98	0.96	0.89	0.42
95%CI[†]			0.72, 1.34	0.72, 1.29	0.67, 1.19	
Pharynx						
No.	177	34	33	63	47	
HR[†]		1.00	0.95	1.37	0.99	0.68
95%CI[†]			0.58, 1.53	0.90, 2.09	0.63, 1.55	
Larynx						
No.	307	69	77	72	89	
HR[†]		1.00	1.05	0.74	0.86	0.13
95%CI[†]			0.76, 1.46	0.53, 1.03	0.62, 1.18	
Esophagus (ESCC[‡])						
No.	123	35	19	38	31	
HR[†]		1.00	0.49	0.80	0.69	0.37
95%CI[†]			0.28, 0.86	0.50, 1.28	0.42, 1.12	
Esophagus (EADC[‡])						
No.	305	55	58	90	102	
HR[†]		1.00	0.94	1.01	1.12	0.38
95%CI[†]			0.65, 1.36	0.72, 1.42	0.80, 1.57	
Gastric Cardia						
No.	231	45	48	73	65	
HR[†]		1.00	0.97	1.04	0.90	0.65
95%CI[†]			0.65, 1.47	0.72, 1.52	0.61, 1.32	
Gastric noncardia						
No.	224	52	48	69	55	

Sites[†]	Total	None	≤3 cups/month	1–6 cups/week	≥1 cup/day	*P* for trend[§]
HR[†]		1.00	0.90	0.96	0.73	0.16
95%CI[†]			0.60, 1.33	0.67, 1.39	0.50, 1.08	

[†]Hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated in Cox proportional hazards models adjusted for age, sex, tobacco smoking, alcohol drinking, BMI, education, ethnicity, usual physical activity throughout the day, vigorous physical activity, and the daily intake of fruit, vegetables, red meat, white meat, and calories.

[‡]ESCC = Esophageal Squamous Cell Carcinoma, EADC = Esophageal Adenocarcinoma

[§]*P* values for trend were calculated by representing intake as an ordinal variable for each category in the adjusted models described above.

Table 3

The Association between Coffee Intake and Risk of Incident Upper Gastrointestinal Cancers in the NIH-AARP Diet and Health Study Cohort

Sites†	Total	<1 cup/day	=1 cup/day	2–3 cups/day	>3 cups/day	*P* for trend§
Oral cavity						
No.	392	89	65	157	81	
HR†		1.00	1.07	0.85	0.85	0.14
95%CI†			0.78, 1.48	0.65, 1.11	0.62, 1.16	
Pharynx						
No.	177	32	24	80	41	
HR†		1.00	1.15	1.27	1.23	0.34
95%CI†			0.68, 1.96	0.83, 1.94	0.75, 2.01	
Larynx						
No.	306	63	41	124	78	
HR†		1.00	0.90	0.88	1.01	0.95
95%CI†			0.61, 1.34	0.64, 1.21	0.71, 1.44	
Esophagus (ESCC‡)						
No.	123	19	17	59	28	
HR†		1.00	1.29	1.50	1.53	0.13
95%CI†			0.67, 2.48	0.88, 2.56	0.83, 2.82	
Esophagus (EADC‡)						
Cases in all 6 years						
No.	305	74	48	125	58	
HR†		1.00	0.87	0.78	0.81	0.14
95%CI†			0.61, 1.26	0.58, 1.04	0.57, 1.16	
Cases in the first 3 years						
No.	156	33	25	63	35	
HR†		1.00	0.99	0.88	1.17	0.78
95%CI†			0.59, 1.68	0.57, 1.36	0.71, 1.93	
Cases in the last 3 years						

Sites[†]	Total	<1 cup/day	=1 cup/day	2–3 cups/day	>3 cups/day	*P* for trend[§]
No.	149	41	23	62	23	
HR[†]		1.00	0.78	0.69	0.54	0.017
95%CI[†]			0.47, 1.30	0.46, 1.04	0.31, 0.92	
Gastric Cardia						
No.	231	43	33	100	55	
HR[†]		1.00	1.13	1.24	1.57	0.039
95%CI[†]			0.71, 1.78	0.86, 1.79	1.03, 2.39	
Gastric noncardia						
No.	223	54	36	95	38	
HR[†]		1.00	0.96	1.07	1.06	0.67
95%CI[†]			0.63, 1.47	0.76, 1.52	0.68, 1.64	

[†]Hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated in Cox proportional hazards models adjusted for age, sex, tobacco smoking, alcohol drinking, BMI, education, ethnicity, usual physical activity throughout the day, vigorous physical activity, and the daily intake of fruit, vegetables, red meat, white meat, and calories.

[‡]ESCC = Esophageal Squamous Cell Carcinoma, EADC = Esophageal Adenocarcinoma

[§]*P* values for trend were calculated by representing intake as an ordinal variable for each category in the adjusted models described above.

Table 4

The Association between Carbonated Soft Drinks Intake and Risk of Incident Upper Gastrointestinal Cancers in the NIH-AARP Diet and Health Study Cohort

Sites[†]	Total	None	≤1 can/ week	2–6 cans/week	≥1 can/day	*P* for trend[§]
Oral cavity						
No.	392	66	106	147	73	
HR[†]		1.00	0.62	0.66	0.77	0.31
95%CI[†]			0.46, 0.85	0.49, 0.89	0.54, 1.09	
Pharynx						
No.	178	31	53	59	35	
HR[†]		1.00	0.68	0.56	0.76	0.20
95%CI[†]			0.43, 1.06	0.36, 0.87	0.46, 1.25	
Larynx						
No.	307	45	91	116	55	
HR[†]		1.00	0.77	0.73	0.82	0.35
95%CI[†]			0.54, 1.11	0.51, 1.04	0.55, 1.23	
Esophagus (ESCC[‡])						
No.	123	23	37	41	22	
HR[†]		1.00	0.70	0.66	0.85	0.55
95%CI[†]			0.41, 1.18	0.39, 1.11	0.46, 1.56	
Esophagus (EADC[‡])						
No.	305	24	103	135	43	
HR[†]		1.00	1.52	1.36	1.11	0.73
95%CI[†]			0.97, 2.38	0.88, 2.12	0.66, 1.85	
Gastric Cardia						
No.	231	29	65	93	44	
HR[†]		1.00	0.80	0.78	0.89	0.75
95%CI[†]			0.51, 1.24	0.51, 1.20	0.55, 1.45	
Gastric noncardia						

Sites[†]	Total	None	≤1 can/ week	2–6 cans/week	≥1 can/day	*P* for trend[§]
No.	224	33	70	89	32	
HR[†]		1.00	0.82	0.80	0.75	0.30
95%CI[†]			0.54, 1.25	0.53, 1.21	0.45, 1.24	

[†]Hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated in Cox proportional hazards models adjusted for age, sex, tobacco smoking, alcohol drinking, BMI, education, ethnicity, usual physical activity throughout the day, vigorous physical activity, and the daily intake of fruit, vegetables, red meat, white meat, and calories.

[‡]ESCC = Esophageal Squamous Cell Carcinoma, EADC = Esophageal Adenocarcinoma

[§]*P* values for trend were calculated by representing intake as an ordinal variable for each category in the adjusted models described above.