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Alcohol Consumption and Cancer of the Oral Cavity and Pharynx from 1988 to 2009: An Update

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Abstract

The evidence for the human carcinogenic effects of alcohol drinking on the risk of cancers of the oral cavity and pharynx has been considered sufficient in the IARC Monograph 44 on alcohol and cancer in 1988. We evaluated human carcinogenic evidence related to oral and pharyngeal cancer risk based on cohort and case-control studies published from 1988 to 2009. A large body of evidence from epidemiological studies of different designs and conducted in different populations has consistently supported that alcohol consumption is strongly associated with an increase in risk of oral and pharyngeal cancer. The relative risks are 3.2–9.2 for more than 60 grams/day (or more than 4 drinks/day) when adjusted for tobacco smoking and other potential confounders. A strong dose-response relationship on intensity of alcohol use is reported in most of the studies. However, no apparent association is observed for the duration of alcohol use. Compared with current drinkers, a decreased risk is associated with alcohol cessation for about 10–15 years. Similar associations have been observed among non-smokers in over 20 studies. Generally, the dominant type of alcohol consumption in each population is associated with the greatest increases in risk. A large number of studies on joint exposure of alcohol and tobacco consumption demonstrate a more than multiplicative synergistic effect.

Keywords

Alcohol Consumption; Oral Cavity; Pharynx; Neoplasm

Introduction

The evidence for the human carcinogenic effects of alcohol drinking on the risk of cancers of the oral cavity and pharynx was considered sufficient in the IARC Monograph 44 in 1988[1].

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In this review, we evaluate human carcinogenic evidence related to oral and pharyngeal cancer based on cohort and case-control studies published since 1988. PubMed searches were conducted for period between 1988 and 2009 using the following key words in various combinations: “alcohol”, “ethanol”, “beer”, “wine”, “liquor”, “oral cancer”, “pharyngeal cancer”, “oropharyngeal cancer”. We also reviewed the references cited by each article for possible additional studies. We included all of 12 cohort studies during this time period as well as case-control studies which met the following criteria: (1) published as an original article; (2) had a total sample size (cases and controls) of at least 100; (3) reported quantitative levels of alcohol consumption or had at least three levels of alcohol consumption. When data on the study populations were published multiple times, the latest study was included. Among 44 case-control studies, 13 had data on cancer of the oral cavity, 13 on cancer of the pharynx, and 26 on cancer of the oral cavity and pharynx combined.

For comparability, one drink is equivalent to 14 grams, 18 ml, or 0.49 ounces of alcohol, which generally corresponds to 330 ml of beer, 150 ml of wine, and 36 ml of hard liquor. Cancer of the oral cavity and pharynx are predominantly squamous cell carcinomas. The composition of the tumors is given where available. Generally, studies on pharyngeal cancers are predominantly oropharyngeal and hypophyargeal cancers, rather than nasopharyngeal cancer. Two case-control studies, however, specifically concentrate on nasopharyngeal cancer.

Studies are summarized in five tables. Table 1 presents the cohort studies. Table 2 summarizes the case-control studies on cancers of the oral cavity, pharynx, and oral cavity and pharynx combined. Studies that focus on specific alcohol types are shown in Table 3. Studies on the combined or joint effects of alcohol and tobacco smoking are displayed in Table 4. The associations among non-smokers are presented in Table 5. The risks associated with duration of alcohol use and the effects of alcohol cessation are summarized across the five tables.

Cohort studies: Data in Table 1

Five cohort studies of general population have been published on the relationship between alcohol drinking and oral-pharyngeal cancer[2–6]. Four studies reported smoking-adjusted relative risks, while one did not[6]. Increases in risk with alcohol consumption are observed in all five studies with various study populations from the United States, Europe, and Asia. The adjusted relative risks (RRs) (and 95% confidence intervals [CIs]) are 9.22 (2.75–30.93) for more than 60 grams (or more than 4 drinks)/day in an European population[2]; 3.24 (1.72–6.08) for more than 4 drinks/day in the American Cancer Society (ACS) prospective study [3]; and 3.9 (2.1–7.1) for 4–7 times per week in a study in Norway[5]. A strong dose-response relationship is observed in three studies[2,5,6], while two studies found that there was a J-shaped relationship with a reverse association at low alcohol consumption level[3,4]. The increases in risk with alcohol are consistently observed in studies no matter whether smoking was adjusted for or not.

Five special population cohort studies such as alcoholics or alcohol abstainers were published during the review period[7–11]. These types of studies usually do not consider the individual exposure level. The point estimates are either the standard incidence ratios (SIR) or standard mortality ratio (SMR) without adjusting for tobacco smoking. Among cohorts of alcoholics, an increase in risk for cancers of the oral cavity and pharynx has been shown when compared either to the local population rate[7,10,11] or to a general population rate[9]. Among Swedish alcoholics, Adami *et al*.[7] found a four-fold increase in risk (95% CI: 2.9–5.6) for oral cavity and pharyngeal cancers. Tonnensen *et al*.[11] also found an over 3.5-fold increase in risk (95% CI: 3.0–4.3) among men and a 17-fold increase (95% CI: 10.8–26.0) among women. Among Danish 1-year survivors of cirrhosis, Sorensen *et al*.[10] found a 9-fold increase in risk (95% CI: 7.8–10.8) when compared to national incidence rates. Furthermore, the risk was increased

over 11-fold (95% CI: 9.6–14.0) in alcoholic cirrhosis patients, but only 4-fold (95% CI: 1.8–8.2) among hepatitis cirrhosis patients. Conversely, a cohort of members of the International Organization of Good Templars (IOGT) in Norway, where members sign a statement that they will abstain from alcohol, showed a 56% decrease in risk (SIR 95% CI: 0.09–1.27) when compared to the national rates[8].

Alcohol has also been associated with second primary cancers of the oral cavity and pharynx in two cohorts of patients with a first primary cancer[12,13]. Day *et al*.[12] and Dikshit *et al*.[13] observed an increase in risk of second primary cancers, although a dramatic increase was found among Europeans (3- to 3.5-fold increase in risk among those drinking 81+ grams/day) [13] than Americans (1.5- to 2-fold increase in risk among those drinking 30+ grams/day) [12], which may be attributed to the differences in exposure intensity.

Results from prospective cohort studies of the general population provide sufficient evidence for the important role of alcohol drinking in the development of oral and pharyngeal cancer. The strength of the association is demonstrated by significantly increased relative risks, ranging from 3 to 9. A strong dose-response relationship was observed in almost all studies. The association was observed across different geographic regions and populations, which further supports the evidence.

Case-control studies: Data in Table 2

Cancer of the oral cavity

All of the eight studies on oral cancer were hospital-based case-control studies[14–21], and all but one[18] adjusted for tobacco smoking when evaluating alcohol exposure. Studies on cancers of the entire oral cavity observed an association with a dose-response relationship between alcohol drinking and oral cancer in different geographic areas in the world[14–17, 20,21]. Among two studies of tongue cancer only[18,19], Rao *et al*.[19] observed increased risks with drinking once per day (OR = 1.5 [0.9–2.5] for anterior tongue; OR = 1.5 [1.1–2.3] for base tongue); when drinking twice a day, the increase in risk rises for the anterior tongue (OR = 3.7 [1.7–10.8]) yet drops close to baseline (OR = 1.1 [0.4–3.1] for the base tongue. No trend was found in the study of tongue cancer with a limited sample size[19].

Overall, the increase risk of oral cancer associated with alcohol consumption is substantial, even after controlling for smoking. The strength of the association was shown by elevated adjusted ORs for heavy drinking ranging from 2 to 14 and a dose-relationship was observed in most studies with multiple exposure levels. The association has been observed across different geographic regions and populations, which further supports the role of alcohol drinking in oral carcinogenesis.

Cancer of the pharynx

Among nine studies on cancer of the pharynx, three were population-based[22–24] and six hospital-based studies[15–17,21,25,26]. All studies adjusted for or stratified by tobacco smoking. All studies showed strong associations with alcohol drinking, except one study on nasopharyngeal cancer in Taiwan[24]. A possible explanation for the lack of association may be the categorization of exposure, with the highest exposure group of ≥15 g (equivalent to just over 1 drink) per day, which may be too low of a level to detect an association[24]. The other study on nasopharyngeal cancer by Nam *et al*., however, showed an increase in risk with heavy alcohol consumption (24+ drinks per week) (OR = 1.9 [1.1–3.2] for men; OR = 7.3 [2.1–32.5] for women[22].

As was the case for oral cancer, alcohol consumption was associated with an increase in risk of cancers of the oro- and hypopharynx across different geographic regions and populations

with the point estimates of adjusted ORs ranging from 3 to 12. All studies observed a strong dose-response trend between increasing alcohol consumption and risk.

Cancer of the oral cavity and pharynx combined

Nineteen studies of oral cavity and pharyngeal cancer combined were identified[27–45]. Six studies are population-based[30,34,38,40,42,43] and the rest are hospital-based studies. Increased risk of oro-pharyngeal cancer has been observed in most of the studies across different geographic regions and populations with the point estimates of adjusted ORs ranging from 2 to 20 for heavy drinking when adjusting for tobacco smoking and other confounding factors. All but two studies[37,40] observed a strong dose-response trend between alcohol consumption and oral and pharyngeal cancers. The lack of significant associations in two studies may be explained by the small sample size of cases (86 male and 36 female cases in Merletti *et al*.'s study and 65 male and 51 female cases in Llewellyn *et al*.'s study), which results in limited power to detect an association, as well as the inclusion of light drinkers in the baseline comparison group (1–20 grams/day in Merletti *et al*.'s study and within recommended level in Llewellyn *et al*.'s study).

Risk associated with type of alcoholic beverage: Data in Table 3

Assessment of different types of alcoholic beverages is a complicated task; drinkers rarely consume only one type of alcohol, and isolating the effects of a single type in the presence of the other types is difficult to accomplish. In some populations, most of the drinkers consume only one major type of alcoholic beverages, which makes it more difficult to detect any potential difference across different types[19,20,29]. Heterogeneity of effects across different populations adds more difficulty in interpreting results. Overall, among studies in the US, the ranking from highest to lowest risk alcohol type is beer, hard liquor, and wine[12,30,35,39]. In European studies among Italian and Swiss populations, the highest risk is associated with wine consumption[17,27,28], while in a Swedish population, the highest risk is associated with beer and liquor[46]. In Latin America, hard liquor is associated with the highest risk among Cuban[33] and Brazilian populations[47], and wine among Uruguayans[16,25]. In India, arrack, a popular type of hard liquor in South and Southeast Asia, is associated with the highest risk[21]. In several studies, the other types of alcoholic beverages are not controlled for which may distort the association. Generally, the dominant types of alcohol are associated with the greatest increases in risk. The hypothesis that ethanol and its metabolites as the principal carcinogenic agents in alcoholic beverages, rather than beverage-specific constituents, has also been supported by a pooling project, the International Head and Neck Cancer Epidemiology (INHANCE) Consortium with 15 case-control studies[48]. This pooled analysis included 858 cases and 986 controls of beer-only drinkers, 499 cases and 527 controls of liquor-only drinkers, 1 021 cases and 2 460 controls of wine-only drinkers, and 1 124 cases and 3 487 controls of never drinkers. Comparable results for ethanol-standardized consumption among beer-only drinkers (ORs = 1.6, 1.9, 2.2, and 5.4 for ≤5, 6–15, 16–30, and >30 drinks per week, respectively; $P_{trend} < 0.0001$), liquor-only drinkers (ORs = 1.6, 1.5, 2.3, and 3.6; $P < 0.0001$), and wine-only drinkers (ORs =1.1, 1.2, 1.9, and 6.3; $P < 0.0001$) were observed.

Studies on combined or joint effects with tobacco: Data in Table 4

The joint effects of alcohol and smoking on cancers of the oral cavity and pharynx have been evaluated extensively. These studies varied in their methods and approaches for assessing effect modification, ranging from descriptive to formal estimation of interaction terms in multivariate models.

The evidence comes almost entirely from case–control studies carried out in Asia, Australia, Europe, and the US. Three prospective cohort studies have reported joint effects between

alcohol and tobacco exposures including the European Prospective Investigation into Cancer and Nutrition (EPIC) study[2], a cohort study of Japanese men in Hawaii[4], and a nested case-control study from a cohort of male participants in a gastric mass screening survey in Japan [6]. Overall, a majority of studies on both exposure of alcohol and tobacco consumption demonstrate a joint effect[2,4,6,16,[17],[19–23],[25],[30],[31],[33–35],[39–43],45,46,49,50], including the INHANCE Consortium, which reported a greater than multiplicative joint effect between ever tobacco and alcohol use ($OR_{interaction}$ = 2.15 [1.53–3.04])[51]. The population attributable risk for tobacco and alcohol was 72% (4% due to alcohol alone, 33% due to tobacco alone, and 35% due to tobacco and alcohol combined).

Effect of alcohol in nonsmokers: Data in Table 5

Since tobacco smoking is a major risk factor for oral and pharyngeal cancer, evaluation of alcohol effect among non-smokers will avoid a strong confounding effect by tobacco smoking. An increase in risk of alcohol exposure is consistently observed among non-smokers. Fioretti *et al*.[52] reported three-fold increased risk for cancer of the oral cavity and pharynx among alcohol drinkers compared to non-drinkers in Italy. Talamini *et al*.[53] reported a significant dose-response relationship between alcohol and cancer of the oral cavity and pharynx with 27 cases and 572 controls (p=0.04) in Italy. Ng *et al*. [54] observed a strong dose-response relationship among men (p<0.001) in the US. A dose-response relationship was seen between alcohol and cancer of the oral cavity and pharynx with 60 non-smoking cases and 692 controls (p=0.01) from Italy and Switzerland[55]. The pooling project from the INHANCE Consortium [56], including 383 oral cancer, 369 oropharyngeal or hypopharyngeal cancers, 155 oral or pharyngeal (not otherwise specified) cancer cases, and 5 775 controls, observed a significant dose-response relationship for oro- and hypopharyngeal cancer and frequency of alcohol drinking (p < 0.001). The adjusted ORs were 1.66 (1.18–2.34) for 1–2 drinks/day, 2.33 (1.37–3.98) for 3–4 drinks/day, and 5.50 (2.26–13.36) for 5+ drinks/day. The association was weaker for cancer of the oral cavity.

In addition, among the studies on effect modification by tobacco listed in Table 4, the effect of alcohol consumption among non-smokers was presented in 18 studies[2,4,6,17,[19–21],[30],[31],[33–35],[40],[42],43,46,49,50]. The majority of these studies found a strong association with alcohol drinking among non-smokers with a dose-response relationship which supports evidence for the carcinogenic effects of alcohol consumption.

Risk associated with duration of alcohol use

The evaluation of risk from the duration of alcohol consumption comes entirely from case-control studies. Most of the studies found no clear trend[17–19,24,32,33] on oral cavity and pharyngeal cancer, except for one study in India[21], one study in Spain[31], and two studies in Uruguay [16,25], where dose-response relationships were observed (Table 2). In addition, no apparent association was observed for the duration of alcohol use and the risk of head and neck cancer among never tobacco users in the INHANCE study[56] (Table 5).

Risk associated alcohol cessation

Case-control studies of alcohol cessation may be affected by confounding by indication because the pre-cursors and early malignancies of the oral cavity and pharynx may lead to alcohol cessation. Nevertheless, this may result in an underestimation of the effect of alcohol cessation. The risk of oral and pharyngeal cancer has been stronger in current alcohol drinkers than in former drinkers[14,16,19,20,[25],31,33,39,47] except in one study which did not find an association with nasopharyngeal cancer[24] (Schlecht et al., 2001[47] in Table 3; the others in Table 2). For recent quitters, risk for oral and pharyngeal cancers either increases above or stays the same as current drinkers. As the number of years quit increases, however, the risk

gradually drops, below the risk of current drinkers, and near the levels of never-drinkers in three studies for over 10 years of quitting (De Stefani *et al*.)[25], after 14 years of quitting (Castellsague *et al.)*[31], and after 20 years of quitting among men (Hayes *et al*.)[34] (Table 2). However, Day *et al*.[12] and Franceschi *et al*.[32], on the other hand, observed that a reduction in risk with quitting compared to current drinkers is not attained after 5 or even 11 years of quitting, respectively (Table 1 and Table 2).

The INHANCE Consortium[57] with analysis of 13 case-control studies reported beneficial effects of alcohol cessation after quitting for 20 years or longer (OR = 0.45 [0.26–0.78] for oral cancer; OR = 0.74 [0.50–1.09] for oro- and hypopharyngeal cancer, compared to current drinkers) (Table 2).

Conclusions

The evidence for the human carcinogenic effects of alcohol drinking on the risk of cancers of the oral cavity and pharynx has been considered sufficient in the IARC Monograph 44 on alcohol and cancer in 1988 [1] as well as by a more recent IARC Monograph 96 [58]. The human carcinogenic evidence related to oral and pharyngeal cancer risk in this review is based on relevant publications after 1988.

Increases in risk with alcohol consumption are observed in all five cohort studies with study populations from the US, Europe, and Asia. Heavy drinking is associated with a significantly increased risk in all five studies, no matter whether or not cigarette smoking was controlled for. Five special population cohort studies observed a statistically significant association between alcohol consumption and oral-pharyngeal cancer. Four studies of alcoholics showed positive associations and one study in members of the IOGT in Norway (less alcohol drinking) showed a 56% decrease in risk. For case-control studies, all 6 studies of oral cancer, 8 of 9 studies of pharyngeal cancer, and 17 of 19 studies reported statistically significant associations between alcohol drinking and risk of oral-pharyngeal cancer. Almost all studies have controlled for tobacco smoking.

The independent effect of alcohol consumption on the risk of oral and pharyngeal cancer occurs across different geographic regions and populations in the world, especially among over 20 studies of non-smokers. The risk increases with increased amounts of alcohol drinking in the majority of these studies. A meta-analysis of studies published until 2000, including 7 954 cases, estimated RRs of 1.75 (1.70–1.82) for 25 g/day, 2.85 (2.70–3.04) for 50 g/day, and 6.01 (5.46–6.62) for 100 g/day[59]. An update of that work to 2009 gave RRs of 1.21 (1.10–1.33) for ≤ 1 drink/day and 5.24 (4.36–6.30) for ≥ 4 drinks/day[60].

The dominant alcohol types in specific region are associated with the greatest increased risk. A large number of studies on joint exposure of alcohol and tobacco demonstrate a synergistic effect. Most studies reported no association between duration of alcohol use and the risk of oral-pharyngeal cancer. Compared with current drinkers, reduced risk was associated with alcohol cessation for more than 10 years.

In conclusion, results from a substantial amount of epidemiological studies with different designs from different geographical regions provide sufficient evidence and confirms the 1988 IARC Working Group's conclusion that alcohol consumption is carcinogenic, can cause oral and pharyngeal cancer.

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Table 1

Cohort Studies on Alcohol and Oral Cavity and Pharyngeal Cancers

Ref No.	Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk	95% CI	Adjustment factors in study design or analysis	Comments
3	Boffetta, et al. (1990) USA	American Cancer Society Prospective Study: Cohort of 276,802 white men from over 25 states; aged 40–59 yrs; enrollment in 1959, mortality follow-up until 1971; 3% of cohort lost to follow-up	Questionnaire	Oral cavity (ICD7 140–145)	**Total alcohol** Non-drinker Occasional drinker 1 drink/day 2 3 4 5 6+ Irregular drinker	55 10 6 12 13 13 5 26 15	1 1.2 0.4 1.0 2.2 3.2 2.7 6.2 2.0	0.6–2.4 0.2–1.0 0.5–1.9 1.2–4.0 1.7–6.1 1.0–6.8 3.7–10.1 1.1–3.5	Age, smoking	
7	Adami, et al. (1992) Uppsala, Sweden	Cohort of 9,353 patients (8,340 men, 1,013 women) diagnosed with alcoholism in the Inpatient Register; incidence follow-up 1965–84	Inpatient Register records	Oral cavity and pharynx (ICD7 140–148)	**Overall** Men Women	36 33 3	**SIR** 4.1 3.9 7.0	2.9–5.6 2.7–5.5 1.4–20.3		Expected rates from local population
8	Kjaerheim, et al. (1993) Norway	Cohort of 5,332 members of the International Organization of Good Templars (IOGT) (alcohol abstainers), aged 10 + yrs; enrollment in 1980; incidence follow-up until 1989		Oral cavity and pharynx (ICD7 141–148)	**Overall** Men Women	3 2 1	**SIR** 0.44 0.11 0.36	0.09–1.27 N/A N/A		Expected rates from national incidence rates
11	Tonnensen, et al. (1994) Copenhagen, Denmark	Cohort of 18,307 (15,214 men, 3,093 women) alcoholics from a public outpatient clinic for free treatment; incidence follow-up 1954–87	Interview with a social worker and psychiatrist	Oral cavity and pharynx	Men Women	109 22	**SIR** 3.6 17.2	3.0–4.3 10.8–26.0		Cohort cancer incidence compared to total Danish population

Ref No.	Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk	95% CI	Adjustment factors in study design or analysis	Comments
12	Day, et al. (1994) USA	Nested case-control study of second primary cancers; cohort of 1, 090 first primary cancers of oral cavity and pharynx; enrollment of first primary cancers in 1984–85; follow-up until 1989; 80 (56 men, 24 women) developed second primary cancers during follow-up; 189 (132 men, 57 women) randomly selected from cohort, matched on sex, study area, that were free of second primary cancer at the end of follow-up	Interviewer-administered questionnaire	Oral cavity, pharynx, esophagus, larynx	**Total alcohol** <5 drinks/wk 5–14 15–29 ≥ 30 **Years since last drank alcohol** Current drinkers <5 ≥5	9 10 14 24 29 17 7	1 1.6 2.1 1.5 1 5.4 1.9	0.5–5.1 0.7–6.6 0.5–4.5 1.6–18.0 0.6–6.7	Age at first cancer diagnosis, stage of first cancer, lifetime smoking	Nested case-control study among cases of Blot (1988) study; Looked at type of alcohol and cessation of alcohol
4	Chyou, et al. (1995) Hawaii, USA	Hawaiian Japanese Study: Cohort of 7,995 men of Japanese ancestry identified by the Honolulu Heart Program, aged 45–68 yrs; recruitment from 1965–68, incidence follow-up until 1993; 1–2% lost to follow-up	Interviewer-administered questionnaire	Oral cavity, pharynx, esophagus, larynx (ICD8 140–150, 161)	**Total alcohol** Non-drinker <4 oz/month 4–24.9 25+ *p* for trend	16 5 18 52	1 0.57 1.74 4.67	0.21–1.57 088–3.41 2.62–8.32 <0.0001	Age, number of cigarettes/ day, years smoked	Study population from Kato (1992); Looked at type of alcohol and joint effects with smoking
9	Sigvardsson, et al. (1996) Sweden	Cohort of 15,508 alcoholic women ascertained through the Temperance Boards and 15,508 non-alcoholic women from population matched individually on region and date of birth; enrolled in 1947–1977; follow-up for incidence	Temperance Boards records	Tongue (ICD7 141), mouth (143, 144), tonsil (145), hypopharynx (147)	*Tongue* Comparisons Alcoholics *Mouth* Comparisons Alcoholics *Tonsil* Comparisons Alcoholics *Hypopharynx* Comparisons Alcoholics	2 17 1 12 1 11 1 9	1 8.5 1 12.0 1 11.0 1 9.0	2.0–37.0 1.6–92.0 1.4–85.0 1.1–71.0		

Ref No.	Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk	95% CI	Adjustment factors in study design or analysis	Comments
6	Murata, et al. (1996) Japan	Nested case-control study; cohort of 17,200 men part of a gastric mass screening survey in 1984; incidence follow-up until 1993; 2 controls per case, matched on sex, birth-year, city/ county	Self-administered questionnaire	Oral cavity, pharynx, esophagus, larynx (ICD9 140–150, 161)	**Total alcohol**[1] 0 cups/day 0.1–1.0 1.1–2.0 2.1+ χ^2 for trend	17 13 11 10	1 1.0 1.9 9.0 9.6	$p<0.01$	[1]Unit is cup of 180 ml of sake: corresponds to 27 ml of ethanol; Looked at joint effects with smoking	
5	Kjaerheim, et al. (1998) Norway	Cohort of 10,960 men born from 1893–1929 who completed 2 questionnaires sent to a probability sample of the Norwegian population; incidence follow-up 1968–1992	Mailed survey	Oral cavity, pharynx, larynx, esophagus (ICD7 141, 143–145, 147–148, 150, 161)	**Total alcohol** Never or <1 time/week Previously 1–3 times/week 4–7 *p* for trend	26 4 18 19	1 0.9 1.1 3.9	0.3–2.7 0.6–1.9 2.1–7.1 0.003	Age, smoking	Looked at type of alcohol
10	Sorensen, et al. (1998) Denmark	Cohort of 11,605 1-year survivors of cirrhosis from the Danish National Registry of Patients (NRP); recruitment from 1977–89; incidence follow-up until 1993	Admission records of Danish NRP	Oral cavity and pharynx (ICD7 and after 1978, ICDO)	*All cirrhosis* Overall Men Women *Alcoholic cirrhosis* *Chronic hepatitis cirrhosis*	143 96 47 115 8	**SIR** 9.2 8.1 12.9 11.6 4.2	7.8–10.8 $p<0.05$ $p<0.05$ 9.6–14.0 1.8–8.2		Expected rates from national incidences
2	Boeing, et al. (2002) Denmark, France, Germany, Italy, Spain, Sweden, Netherlands, UK	European Prospective Investigation into Cancer and Nutrition (EPIC): Cohort of 417,752 healthy adults; recruitment initiated in 1992, follow-up ongoing	Mailed questionnaire	Oral cavity, pharynx, esophagus (ICDO C00.0–C10.9, C13.0–13.9, C15.0–15.9)	**Lifelong alcohol** No alcohol >0–30 g/day >30–60 >60	4 83 20 17	**Hazard RR** 1.0 1.21 3.17 9.22	0.43–3.40 1.00–10.05 2.75–30.93	Follow-up time, sex, education, BMI, vegetable and fruit consumption, tobacco smoking, energy intake	Looked at joint effects with smoking
13	Dikshit, et al. (2005)	Occurrence of second primary tumors among a cohort of 876 male	Interviewer-Administered questionnaire	Oral cavity, pharynx, esophagus	**Total alcohol** 0–40 g/day 41–80 81–120	4 4 12 17	1 0.8 3.0 3.5	0.2–3.3 0.9–9.5 1.1–11.2	Age, center, occupation, smoking, site of first cancer	

Ref No.	Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk	95% CI	Adjustment factors in study design or analysis	Comments
	Switzerland, France, Italy, Spain	cases of laryngeal/ hypopharyngeal cancer from a multicentric population-based case-control study (1979–82), follow-up until 2000		(ICD9 140–150)	≥ 121					

Table 2

Alcohol and Oral Cavity and Pharyngeal Cancers

site ode)	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk	95% CI	Adjustment factors in study design or analysis	Comments
ly								
vity (ICD9 141, 143–145)	404 (248 men, 156 women) cases diagnosed at seven participating hospitals in the Beijing area; histologically confirmed; 100% response rate	404 randomly selected non-cancer hospital-based controls, individually matched on age, sex, hospital; 100% response rate	Interviewer-administered standardized questionnaire	**Total alcohol in spirit equivalent** Never Ever Ex-drinkers Current *0–26 g/day* 26–49 50–99 >99	1 1.53 1.15 1.59 1.33 1.14 1.37 2.78	1.02–2.30 0.55–2.43 1.05–2.42 0.74–2.34 0.63–2.07 0.71–2.62 1.22–6.32	Age, sex, education, smoking	Looked at type of alcohol and joint effects with smoking
	111 (65 men, 46 women) cases diagnosed at seven participating hospitals in the Beijing area; aged 20–80 yrs; histologically confirmed;	111 randomly selected non-cancer hospital-based controls, excluded patients of alcohol and tobacco-related conditions; individually matched on age, sex, hospital	Interviewer-administered standardized questionnaire	**Total alcohol in spirit equivalent** Never Ever Ex-drinkers Current 0–50 g/day 50 >50 **Years of drinking** Never drinker ≤25 years >25	1 1.17 0.94 1.20 1.20 0.69 1.63 1 1.24 1.26	0.59–2.38 0.28–3.22 0.58–2.50 0.45–3.18 0.21–2.26 0.60–4.44 0.54–2.83 0.56–2.83	Education, smoking	Part of Zheng (1990) study; Looked at type of alcohol and joint effects with smoking
-10, 141–4)	637 male cases from the hospital	635 hospital-based unmatched controls free from cancer, infectious disease, benign lesion	Interviewer-administered questionnaire before clinical examination	**Total alcohol** *Frequency* Non-user Once/day Twice **Years of drinking** Non-user 1–10 years 11–20 21–30 *31+*	Anterior/base tongue 1/1 1.5/1.5 3.7/1.1 1/1 1.2/1.5 2.0/1.6 3.3/2.0 1.3/0.5	0.9–2.5/1.1–2.3 1.7–10.8/0.4–3.1 0.6–2.6/0.9–2.5 0.9–4.4/0.9–2.9 1.4–8.9/1.0–4.6 0.3–4.8/0.2–1.4		

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site ode)	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk	95% CI	Adjustment factors in study design or analysis	Comments
vity	591 (309 men, median age 56 yrs; 282 women, median age 58) cases from 3 center in Bangalore, Madras, and Trivandrum; response rate 97%	582 (292 men, dedian age 55 yrs; 290 women, median age 52 yrs) hospital-based controls from the same hospitals as cases; frequency matched by center, age and sex; response rate 90%	Interviewer (social worker)-administered questionnaire	**Total alcohol** *Men only* Abstainers Former (abstained 12 + months) Current <3 drinks/wk 3–13 ≥ 14 *p* for trend **Years since quit drinking** Current < 10 ≥ 10 χ^2 for trend	1 1.78 2.17 2.14 1.97 1 0.94 0.62 0.36	0.97–3.28 1.00–4.69 0.89–5.19 0.85–4.57 0.01 0.43–2.09 0.19–2.05 *p*=0.55	Center, age, education, paan chewing, smoking	Looked at alcohol cessation and joint effects with paan chewing
ly								
arynx (ICD 9 148.0–48.3, 149.8)	281 male cases from Turin and Varese (Italy), Navarra and Zaragoza (Spain), Geneva (Switzerland), Calvados (France); histologically confirmed; response rate 75% (Spain and Italy) and 92% (Geneva)	3,057 male population controls stratified by age from census lists, electoral lists, or population registries; response rate 75% (64% in Geneva and 56% in Turin)	Interviewer-administered questionnaire	**Total alcohol** 0–20 g/day 21–40 41–80 81–120 *121+*	1 1.57 3.15 5.59 12.54	0.72–3.42 1.58–6.24 2.79–11.21 6.29–25.00	Age, place, age/place interaction	Looked at joint effects with smoking
arynx	204 (141 men, 63 women) whites from the National Mortality Followback Survey who died of NPC, age <65 yrs; 89% overall response rate for whole study population	408 (282 men, 126 women) randomly selected (2:1 controls:cases) whites from the same survey, matched on age and sex; died from causes unrelated to smoking or alcohol use	Questionnaire from next of kin	**Total alcohol** 0–3 drinks/week 4–23 ≥24 *p for trend*	Men/Women 1/1 1.1/1.2 1.9/7.3	0.6–1.8/0.4–3.1 1.1–3.2/2.1–32.5 0.007 / <0.001	Gender, cigarette use	Looked at joint effects with smoking

site code)	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk	95% CI	Adjustment factors in study design or analysis	Comments
rynx and hypopharynx	105 male cases from the Otorhinolaryngology-Head and Neck Surgery Dept. of the University of Heidelberg; histologically confirmed	420 outpatient males without known cancer from the same center as cases; matched (4:1 controls:cases) on age and residential area	Interviewer-administered standardized questionnaire	**Total alcohol** <25 g/day 25–50 50–75 75–100 >100 *X^2 for trend*	1 3.5 12.9 54.7 125.2 70.59	1.4–8.6 4.7–35.6 13.5–221.0 28.4–551.6 *p*=0.0001	Tobacco smoking	Beer is preferred alcoholic beverage in area
arynx	375 (260 men, 115 women) from 2 teaching hospitals in Taipei; histologically confirmed; 99% response rate	327 (223 men, 104 women) population controls with no history of NPC using the National Household Registration System, individually matched on age, sex, residence; 88% response rate	Interviewer-administered structured questionnaire	**Drinking status** Never Former Current **Total alcohol** 0 g of ethanol/day 0– <15 ≥15 *p for trend* **Years of drinking** Non-drinker <15 ≥15 *p for trend*	1 1.6 0.8 1 0.7 1.1 1 10.7 1.1	0.6–4.5 0.6–1.2 0.5–1.2 0.7–1.7 0.9 0.4–1.2 0.7–1.6 0.9	Age, sex, race, education, family history of NPC, smoking	
yranx	85 males cases identified in the four major hospitals in Montevideo; microscopically confirmed; 97.5% response rate	640 hospital-based male controls from the same hospitals as cases; excluded patients of alcohol and tobacco-related conditions with no recent changes in diet; frequency matched (2:1 controls:cases) on age and residence; 97% response rate	Interviewer-administered questionnaire	**Total alcohol** Never Former Current 1–60 ml ethanol/day 61–120 121–240 241+ *p for trend* **Years of drinking** Never 1–29 years 30–39 40–49 50+ *p for trend* **Years since quit drinking** Current 1–4 years 5–9 10+ Never	1 5.8 6.0 2.3 7.6 5.6 12.8 1 5.1 3.9 8.2 7.9 1 1.4 1.3 0.4 0.2	1.7–19.3 2.0–18.0 0.7–8.1 2.3–24.4 1.7–18.6 4.0–41.2 <0.0001 1.5–17.4 1.2–12.9 2.5–26.5 2.3–27.8 0.0005 0.6–3.2 0.4–4.3 0.1–1.5 0.1–0.5 0.0007	Age, residence, urban/rural status, education, BMI, smoking	Looked at cessation of alcohol, type of alcohol, and joint effects with smoking

site ode)	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk	95% CI	Adjustment factors in study design or analysis	Comments
				p for trend				
ngeal Cancer								
vity 40, 141, 143–145)	157 men identified from hospitals in Milan and Pordenone; below age 75 yrs; histologically confirmed; response rate 98%	1272 hospital-based non-cancer male patients from same hospitals as cases matched on age and area of residence; excluded patients of alcohol and tobacco-related conditions; response rate 97%	Interviewer-administered questionnaire	**Total alcohol** ≤ 19 drinks/wk 20–34 35–59 60+ χ^2 for trend **Years of drinking** <30 years 30–39 40+ χ^2 for trend	1 1.1 3.2 3.4 18.74 1 1.2 0.7 1.28	0.5–2.5 1.6–6.2 1.7–7.1 *p*<0.01 0.7–2.0 0.4–1.3 NS	Age, area of residence, education, occupation, smoking habits	Also looked at pharyngeal cancers; Looked at type of alcohol and joint effects with smoking
, hypopharynx/ unction included 46, 148, 161.1)	134 men, below age 75 yrs; histologically confirmed; response rate 98% overall for cases	1272 hospital-based non-cancer male patients from same hospitals as cases matched on age and area of residence; excluded patients of alcohol and tobacco-related conditions; response rate 97%	Interviewer-administered questionnaire	**Total alcohol** ≤ 19 drinks/wk 20–34 35–59 60+ χ^2 for trend **Years of drinking** <30 years 30–39 40+ χ^2 for trend	1 0.9 1.5 3.6 21.66 1 1.1 0.9 0.16	0.4–2.0 0.8–3.1 1.8–7.2 *p*<0.01 0.6–2.1 0.4–1.8 NS	Age, area of residence, education, occupation, smoking habits	Also looked at oral cancers; Looked at type of alcohol and joint effects with smoking
vity (ICDO 140, 141, 143–	157 (113 men, 44 women) cases from the Korea Cancer Center Hospital (KCCH); cytological and/or histopathological confirmation	471 (339 men, 132 women) hospital-based non-cancer controls from KCCH matched (3:1 controls: cases) on age, sex, admission date; excluded patients of alcohol and	Interviewer-administered standardized questionnaire in hospital	**Total alcohol**[1] Non-drinker <1 hop/day 1–2 hop/day 2–4 hop/day >4 hop/day	Men only 1 0.59 3.61 4.23 14.82	0.25–1.40 1.82–7.17 2.13–8.40 5.03–43.67	Smoking	Looked at pharynx also; [1] 1 hop=90 ml of soju [generally 20% alcohol, 14 g of ethanol] Soju is most frequent alcohol type

site ode)	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk	95% CI	Adjustment factors in study design or analysis	Comments
		tobacco-related conditions						
(ICDO 146–149)	152 (133 men, 19 women) cases from the Korea Cancer Center Hospital (KCCH); cytological and/or histopathological confirmation	456 (399 men, 57 women) hospital-based non-cancer controls from KCCH matched (3:1 controls: cases) on age, sex, admission date; excluded patients of alcohol and tobacco-related conditions	Interviewer-administered questionnaire	**Total alcohol**[1] Non-drinker <1 hop/day 1–2 hop/day 2–4 hop/day *>4 hop/day*	Men only 1 1.22 2.16 4.07 11.23	0.60–2.50 1.13–4.15 2.11–7.85 4.23–29.83	Smoking	Looked at oral cavity also [1] 1 hop=90 ml of soju [generally 20% alcohol, 14 g of ethanol] Soju is most frequent alcohol type
vity 140, 141, 143–5)	1563 male cases from the Cancer Institute (Chennai) and the Regional Cancer Center (Trivandrum); histologically confirmed	1,711 male patients with non-tobacco-related cancers from same centers as cases and 1927 healthy male hospital visitors from only Chennai	Interviewer-administered questionnaire	**Total alcohol** *Average amount of ethanol* Never drinker 0–<20 ml/day 20–50 >50 **Years of drinking** Never drinker <20 years 20–29 30–39 ≥40	1 1.23 2.40 2.98 1 1.79 2.06 2.20 2.51	0.98–1.54 1.87–3.06 2.34–3.80 1.44–2.21 1.62–2.62 1.62–3.00 1.51–4.16	Age, center, education, smoking	Looked at pharynx also; Looked at type of alcohol and joint effects with smoking and chewing
146, 148, 149)	636 male cases from the Cancer Institute (Chennai) and the Regional Cancer Center (Trivandrum); histologically confirmed	1,711 male patients with non-tobacco-related cancers from same centers as cases and 1927 healthy male hospital visitors from only Chennai	Interviewer-administered questionnaire	**Total alcohol** *Average amount of ethanol* Never drinker 0–<20 ml/day 20–50 >50 **Years of drinking** Never drinker <20 years 20–29 30–39 ≥40	1 1.09 2.34 3.60 1 1.36 2.46 2.95 3.06	0.80–1.49 1.71–3.21 2.70–4.82 1.01–1.83 1.83–3.30 2.06–4.21 1.72–5.45	Age, center, education, smoking	Looked at oral cavity; Looked at type of alcohol and joint effects with smoking and chewing
vity (excluding lip)	335 males cases identified in the four major hospitals in Montevideo;	1501 hospital-based non-cancer male controls;	Interviewer-administered questionnaire in hospital	**Total alcohol** Never Ever Former	1 3.3 3.0 3.4 1.2 4.3 4.9 7.0 1 2.5 3.9 3.4 3.3	2.2–4.8 1.9–4.7 2.3–5.2 0.8–2.0 2.7–6.8 3.1–7.9 4.2–11.5 <0.0001 1.5–4.2 2.5–6.2 2.1–5.4 2.0–5.5 <0.0001	Age, residence, urban/ rural status, hospital, year of diagnosis, education, family	Looked at pharynx also; Looked at type of alcohol and

site ode)	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk	95% CI	Adjustment factors in study design or analysis	Comments
	microscopically confirmed; 97% response rate	excluded patients of alcohol and tobacco-related conditions with no recent changes in diet; 97% response rate		Current 1–60 ml ethanol/day 61–120 121–240 241+ *p* for trend **Years of drinking** Never 1–29 years 30–39 40–49 50+ *p for trend*			history of cancer, occupation, vegetable and fruit consumption, mate, smoking	joint effects with smoking
t (excluding nasopharynx)	441 males cases identified in the four major hospitals in Montevideo; microscopically confirmed; 97% response rate	1501 hospital-based non-cancer male controls; excluded patients of alcohol and tobacco-related conditions with no recent changes in diet; 97% response rate	Interviewer-administered questionnaire	**Total alcohol** Never Ever Former Current 1–60 ml ethanol/day 61–120 121–240 241+ *p for trend* **Years of drinking** Never 1–29 years 30–39 40–49 50+ *p* for trend	1 4.3 3.9 4.5 1.4 4.4 7.9 11.7 1 3.3 4.8 4.6 4.7	2.9–6.4 2.5–6.1 3.0–6.8 0.9–2.2 2.8–7.0 5.0–12.3 7.2–18.9 <0.0001 2.0–5.3 3.0–7.5 2.9–7.1 2.9–7.6 <0.0001	Age, residence, urban/ rural status, hospital, year of diagnosis, education, family history of cancer, occupation, vegetable and fruit consumption, mate, smoking	Looked at oral cavity also; Looked at type of alcohol and joint effects with smoking
vity 140, 141, 143–5) rynx/ Hypo-pharynx 146, 148)	3,390 cases 3,875 cases	12,593 controls 12,593 controls	Interview or self-administrated questionnaire	**Years since quit drinking** Current >1–4 years 5–9 10–19 20+ Never *p* for trend **Years since quit drinking** Current >1–4 years 5–9 10–19 20+ Never *p* for trend	1 0.81 0.77 0.66 0.45 0.65 1 1.04 0.95 1.15 0.74 0.65	0.61–1.07 0.52–1.15 0.47–0.92 0.26–0.78 0.36–1.16 0.05 0.73–1.48 0.61–1.49 0.92–1.43 0.50–1.09 0.42–1.02 0.18	Age, sex, race/ ethnicity, education, study center, tobacco pack-years, alcohol drinking frequency	Looked at alcohol cessation only.

site ode)	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk	95% CI	Adjustment factors in study design or analysis	Comments
ngeal Cancer Combined								
vity and pharynx (ICD9 3–146, 148, 149), ng salivary gland and rynx	1,114 (762 men, 352 women) cases identified from the population-based registries covering metropolitan Atlanta (Georgia), Los Angeles and Santa Clara and San Mateo counties (California), New Jersey; aged 18–79; pathologically confirmed; 75% response rate	1,268 population controls from random-digit-dialing, aged 18–64, frequency matched on age, sex, race (black, white), 79% (under 65 yrs) and 76% (65+ yrs) response rate.	Interviewer-administered structured questionnaire	**Total alcohol** <1 drink/wk 1–4 5–14 15–29 30+	Men/Women 1/1 1.2/1.2 1.7/1.3 3.3/2.3 8.8/9.1	Men/Women 0.7–2.0/0.7–1.9 1.0–2.7/0.8–2.1 2.0–5.4/1.2–4.5 5.4–14.3/3.9–21	Age, race, study location, smoking, respondent status (self vs. proxy)	Looked at type of alcohol, controlling for other types, and joint effects with smoking; Association and trend similar for all oral cavity and pharynx
vity and oropharynx 140.3–140.5, 141, 143–	122 (86 men, 36 women); histologically confirmed; 85% response rate	606 (385 men, 221 women) population-based controls randomly selected from files of residents, stratified by age and sex; 55% response rate	Interviewer-administered standardized questionnaire	*Men* **Total alcohol** 1–20 g/day 21–40 41–80 81–120 >120 *Women* **Total alcohol** 1–20 g/day 21–40 *>40*	1 0.7 1.3 0.6 2.1 1 3.0 3.4	0.2–2.6 0.4–3.8 0.2–2.1 0.6–6.8 0.9–10.5 0.9–12.9	Age, education, area of birth, smoking habits	Looked at type of alcohol and joint effects with smoking
vity and pharynx	305 male cases from hospitals in Pordenone and Milan; median age=58 yrs, histologically confirmed; 2% refusal rate	1621 male hospital-based non-cancer controls, median age=57 yrs, matched by area of residence and age; excluded patients of alcohol and tobacco-related conditions; 3% refusal rate	Interviewer-administered questionnaire in hospital	**Total alcohol** ≤ 20 wine/wk 22–55 drinks/wk 56–83 *≥84*	1 0.8 1.8 4.1	0.3–2.3 0.8–4.4 2.0–8.2	Age, area of residence, occupation, smoking and drinking habits	Includes study population from Franceschi (1990); Looked at types of alcohol

site ode)	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk	95% CI	Adjustment factors in study design or analysis	Comments
vity and pharynx	272 (236 men, 36 women) cases from hospitals in Pordenone, median age=60 yrs, histologically confirmed; 3% refusal rate	1,884 (1122 men, 762 women) non-cancer, hospital-based controls, median age=58 yrs, matched by area of residence and age; excluded patients of alcohol and tobacco-related conditions; 3% refusal rate	Interviewer- administered questionnaire in hospital	**Total alcohol** ≤ 20 drinks/wk 21–34 35–55 56–83 ≥ 84 *p for trend*	Non-cancer controls 1 2.2 2.4 6.6 11.4	1.2–4.0 1.2–4.7 3.5–12.5 6.0–21.4 <0.01	Age, sex, education, occupation, tobacco	Includes study population from Barra (1990) study; Also compared results to cancer control group with similar results; Looked at types of alcohol
vity, pharynx, larynx	200 male cases from the departments of ENT of the Universities of Heidelberg and Giessen; histologically confirmed	800 outpatient males without known cancer matched on age and residential area (4:1 controls:cases)	Interviewer-administered questionnaire	**Total alcohol** <25 g/day 25–50 50–75 75–100 *>100*	1 1.7 6.7 16.2 21.4	1.0–2.7 3.9–11.3 7.1–36.8 11.2–40.6	Tobacco smoking	Beer is preferred alcoholic beverage in area; Looked at joint effects with smoking
vity and pharynx	290 (201 men, 89 women) cases identified from pathology records of 20 major hospitals in Erie, Niagara, Monroe (New York); aged 45 yrs or younger; pathologically confirmed; response rate of those contacted 60%	290 (201 men, 89 women) population controls individually matched on age, sex, neighborhood; response rate 41%	Interviewer-administered standardized questionnaire	**Quantity-frequency-duration derived quintiles** 1 2 3 4 5 *p* for trend	1 2.4 2.7 3.4 *14.8*	1.1–5.2 1.2–6.1 1.6–7.4 6.8–32.3 <0.0001		Excluded black cases from analysis
vity and oropharynx	359 white and black male veterans with invasive cancer and in situ carcinoma identified in the Department of Veterans Affairs Medical Center; median age: 57 yrs;	2,280 white or black male patients from the same center as cases of the same age range as cases (37–80 yrs); median age:58 yrs; excluding	Interviewer-administered standardized questionnaire	**Total alcohol (in whiskey equiv./ day)[1]** Minimal 2–5 WE/day 6–10 11–21 22+ Ex-drinker (abstained 2+ yrs)	1 2.6 6.4 7.9 7.1 1.9	1.4–4.7 3.7–11.0 4.6–13.4 4.1–12.2 0.6–5.7	Age, race, tobacco smoking	Looked at type of alcohol and joint effects with smoking [1]1 whiskey equivalent is 10.2 g of alcohol

site ode)	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk	95% CI	Adjustment factors in study design or analysis	Comments
	histologically confirmed	patients with cancer or dysplasia of the pharynx, larynx, lung, esophagus						
vity and pharynx ng nasopharynx)	1,560 (1,097 men, 463 women) cases enrolled in 28 hospitals in 8 US cities	2,948 (2,075 men, 873 women) hospital-based controls matched on age, sex, race, hospital, date of interview	Interviewer-administered questionnaire	**Total alcohol** (whiskey equiv.) Non-drinker Occasional 1–3.9 oz/day 4–6.9 7+	Men/Women 1/1 1.4/1.2 2.9/1.8 4.7/4.8 7.3/--	Men/Women 0.9–2.0/0.9–1.6 2.0–4.2/1.3–2.6 3.2–7.1/2.9–7.8 5.1–10.7/---	Age, education, smoking, race, time period, type of hospital	Looked at type of alcohol and joint effects with smoking 1 oz WE=10.2 g of alcohol
vity and oropharynx ng salivary glands and l	303 women aged ≥40 yrs from the University Hospital's Head Cancer Center	1779 women controls from a national survey by National Central Bureau of Statistics matched on age	Hospital records (cases) and national survey (controls)	**Total alcohol** Non-drinker 1–5 units[1]/day >5	1 3.5 20.8	2.5–4.8 11.4–37.8	Age, tobacco smoking	Looked at joint effects with smoking [1]1 alcohol unit = 330 ml beer, 150 ml wine or 30 ml spirit
vity and pharynx ng lip, salivary glands, rynx) (ICD9 141–143– 8, 149)	342 (286 men, 56 women) identified through pathology laboratories and Central Cancer Registry, aged 21–79 yrs; histologically confirmed; 70% response rate	521 (417 men, 104 women) population-based controls frequency matched by age and gender; 83% response rate	Interviewer-administered questionnaire	**Total alcohol** Non-drinker 1–7 drinks/week 8–21 22–42 >42 *p* for trend **Years since last drank alcohol** Non-drinker Recent use (<2 yr) Quit 2–9 yr Quit 10–19 yr Quit 20+ yr	Men/Women 1/1 0.8/0.8 1.4/0.9 3.3/9.1 7.7/-- Men/Women 1/1 2.4/1.2 3.6/1.0 2.7/1.1 1.3/0.9	0.3–2.1/0.3–2.1 0.6–3.4/0.0–17.0 1.4–8.0/0.9–94.2 3.3–17.9/--- <0.0001/0.02 1.0–5.4/0.4–3.4 1.5–9.0/0.2–5.4 1.0–7.0/0.2–6.4 0.5–3.6/0.2–4.8	Age, tobacco use	Looked at cessation of alcohol and joint effects with smoking
vity and pharynx ng lip, salivary glands, rynx)	754 (638 men, 116 women) cases from major teaching and general hospitals in Pordenone, Rome, Latina (Italy) and Vaud (Switzerland); aged 22–77, 95% response rate,	1,775 (1,254 men, 521 women) hospital-based non-cancer controls from the same network of hospitals as cases; excluded tobacco and	Interviewer-administered questionnaire	**Total alcohol** Never 1–20 drinks/wk 21–62 63–90 ≥ 91 X^2 *for trend* **Years of drinking** ≤ 27 years 28–35 36–44	1 0.7 2.4 8.0 11.6 167.4 1 1.0 1.1 0.9 0.15 1 1.2 1.8 3.3 1.9 1.6	0.4–1.1 1.5–3.9 4.6–14.2 6.3–21.5 *p*<0.001 0.7–1.5 0.7–1.7 0.5–1.5 *p*=0.70 0.6–2.4 1.0–3.5 1.5–7.3 1.0–3.8 *p*=0.21	Age, sex, study center, education, interviewer, tobacco smoking	Study population from Franceschi (1999); Looked at alcohol cessation

site code)	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk	95% CI	Adjustment factors in study design or analysis	Comments
	histologically confirmed	alcohol-related conditions; frequency matched (5:1 for women, 2:1 for men controls:cases) on age, sex, area of residence; response rate 95%		≥ 45 *X^2 for trend* **Years since quit drinking** Current 1–3 years 4–6 7–10 ≥ 11 χ^2 for trend				
vity and oropharynx	200 (143 men, 57 women) cases identified in the Instituto Nacional de Oncologia y Radiobiologia (INOR) of Havana; median age 64 yrs; 88% response rate	200 (136 men, 64 women) hospital-based controls admitted to INOR and 3 other major hospitals in Havana; excluded patients of alcohol and tobacco-related conditions; frequency matched on age and sex; median age 62 yrs; 79% response rate	Interviewer (dentist)-administered questionnaire	**Total alcohol** Abstainers Former (abstained 12 + months) Current <7 drinks/week 7–20 21–69 70+ *X^2* for trend **Years of drinking** <33 years 33–44 ≥45 χ^2 for trend	1 1.04 1.09 1.60 2.20 5.73 8.75 1 1.98 1.81 0.56	0.52–2.06 0.46–2.57 0.70–3.67 0.89–5.45 1.77–18.52 *p*<0.01 0.93–4.22 0.85–3.87 *p*=0.46	Age, sex, area of residence, education, smoking	Looked at cessation of alcohol, type of alcohol, and joint effects with smoking
vity and oropharynx ng lip)	333 (237 men, 96 women) cases of in situ and invasive cancers ascertained through the population-based Cancer Surveillance System (participant of SEER), aged 18–65 from two original studies; response rate 54% and 63%	541 (387 men, 154 women) population-based controls frequency matched on age and sex; response rate 63% and 61%	Interviewer-administered structured questionnaire	**Total alcohol** <1 drink/week 1–7 8–14 15–42 ≥43	1 1.0 1.7 2.8 4.7	0.6–1.5 1.0–2.9 1.7–4.8 2.4–9.4	Age, sex, race, smoking	Looked at joint effects with smoking and *ADH3*

site ode)	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk	95% CI	Adjustment factors in study design or analysis	Comments
vity and pharynx	749 (634 men, 115 women) cases from Pordenone, Rome, Latina (Italy) and Vaud (Switzerland) admitted to major teaching and general hospitals in area under surveillance; aged 22–77; histologically confirmed	1,772 (1,252 men, 520 women) hospital-controls from the same network of hospitals as cases; aged 20–78 yrs; excluded patients of alcohol and tobacco-related conditions	Interview-administered structured questionnaire	**Total alcohol** 1–2 drinks/day 3–4 5–7 8–11 ≥12 X^2 for trend	1 2.1 5.0 12.2 21.1 272.07	1.5–2.9 3.5–7.1 8.4–17.6 14.0–31.8 p<0.0001	Age, sex, study center, education, smoking habit	Looked at type of alcohol
vity and oropharynx C1–C10)	375 (304 men, 71 women) cases identified from hospitals in Granada (1), Sevilla (1), Barcelona (2); mean age 60 yrs; histologically confirmed; 76.5% response rate	375 (304 men, 71 women) non-cancer hospital-controls from same hospitals as cases, frequency matched on age and sex, mean age 60 yrs; excluded patients with alcohol and tobacco-related diagnoses; 91% response rate	Interviewer-administered standardized questionnaire in hospital	**Total alcohol** Never drinker Ever Ex-drinker Current 1 drink/day 2 3–4 5–6 7–10 ≥ 11 *p for trend* **Years of drinking** Never drinker 1–20 years 21–30 31–40 41–50 ≥ 51 *p for trend* **Years since quit drinking** Never drinker Current 1–2 3–7 8–13 ≥ 14 *p* for trend	1 2.86 2.12 3.46 2.00 3.74 6.22 10.58 10.29 13.66 1 1.37 2.49 3.18 4.00 5.13 1 3.5 3.9 1.7 2.3 1.5	1.59–5.15 1.13–3.99 1.88–6.35 1.06–3.77 1.62–8.63 2.82–13.71 4.57–24.46 4.57–23.17 6.02–31.96 <0.0001 0.65–2.91 1.22–5.09 1.61–6.29 1.99–8.02 2.45–10.72 <0.0001 1.9–6.5 1.7–9.1 0.8–3.9 1.0–5.3 0.7–3.3 0.003	Age group, sex, education, tobacco smoking, center	Looked at type of alcohol, joint effects with smoking, and alcohol cessation
vity and oropharynx ng salivary glands, rynx, hypopharynx) C00-C06, C09, C10)	116 (65 men, 51 women) cases identified by the Thames Cancer Registry; aged ≤45	207 (112 men, 95 women) non-cancer patient controls matched (2:1	Self-completed questionnaire	**Total alcohol** Within recommended levels[1]	Men/Women 1/1 1.6/1.6	Men/Women 0.8–3.1/0.6–4.2	Social class, race, ever smoking, (matching variables: age, sex, area of residence)	[1]Recommended levels for men: ≤ 21 units/wk, for women: ≤14 units/wk

site ode)	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk	95% CI	Adjustment factors in study design or analysis	Comments
	yrs; 59% response rate	controls:cases when feasible) on age, sex, area of residence		Over recommended levels				
vity and oropharynx C00-C06, C09, C10)	53 (28 men, 25 women) cases from 14 participating hospitals in the southeast of England; aged ≤45 yrs; 80% response rate	91 (45 men, 46 women) non-cancer patient controls matched (2:1 controls:cases when feasible) on age, sex, area of residence	Interviewer-administered standardized questionnaire and self-completed questionnaire	**Total alcohol** Within recommended levels[1] Over recommended levels	Men/Women 1/1 8.1/3.8	Men/Women 1.6–40.1/0.7–20.7	Social class, race, ever smoking (matching variables: age, sex, area of residence)	[1]Recommended levels for men: ≤ 21 units/wk, for women: ≤14 units/wk
vity and pharynx	137 (113 men, 24 women) from Milan and Pordenone, Italy (1984–93) and Vaud, Switzerland (1992–1997), below age 46 yrs; histologically confirmed; 95% response rate	298 (226 men, 72 women) non-cancer hospital-based controls, matched 2:1 (control:case) for men and 3:1 for women on age, sex, study center, below age 46 yrs; excluded patients of alcohol and tobacco-related conditions; response rate 95%	Interviewer-administered questionnaire	**Total alcohol** Non-drinkers <3 drinks/day 3-<6 6-<10 ≥ 10 *X^2 for trend*	1 0.70 0.99 3.69 4.94 17.53	0.27–1.78 0.35–2.81 1.23–11.08 1.62–15.10 *p*<0.0001	Age, sex, study center, education, marital status, BMI, tobacco, coffee consumption	Study populations from Franceschi (1990) and Franceschi (2000) Looked at joint effects with smoking
vity and pharynx 40–149, excludes 142 and	74 (71 men, 3 women) randomly selected from 1,688 cancers identified at a medical center; 74% response rate	187 patients with periodontal disease free of leukoplakia and oral cancer, randomly selected from 25,882 patients; 94% response rate 164 leukoplakia patients free of oral cancer, randomly selected from 435 identified at	Interviewer-administered questionnaire	*Leukoplakia vs. normal* **Total alcohol** No Yes *Oral cancer vs. leukoplakia* **Total alcohol** No Yes	1 0.76 1 2.37	0.40–1.43 1.47–3.82	Smoking, betel quid chewing	

Site (code)	Characteristics of cases	Characteristics of controls	Exposure assessment		Exposure categories	Relative risk	95% CI	Adjustment factors in study design or analysis	Comments
		the same medical center; 82% response rate							

Table 3

Risk from Different Types of Alcohol on Oral Cavity and Pharyngeal Cancers

Ref No.	Reference, study location and period	Organ site (ICD code)	Characteristics of study population	Exposure assessment	Exposure categories	Relative risk	95% CI	Adjustment factors in study design or analysis	Comments
30	Blot, et al. (1988) USA, 1984–85	Oral cavity and pharynx (ICD9 141, 143–146, 148, 149), excluding salivary gland and nasopharynx	1,114 (762 men, 352 women) cases identified from the population-based registries covering metropolitan Atlanta (Georgia), Los Angeles and Santa Clara and San Mateo counties (California), New Jersey; aged 18–79; pathologically confirmed; 75% response rate. 1,268 population controls from random-digit-dialing, aged 18–64, frequency matched on age, sex, race (black, white), 79% (under 65 yrs) and 76% (65+ yrs) response rate.	Interviewer-administered standardized questionnaire	**Hard liquor** < 1 drink/wk 1–4 5–14 15–29 30+ **Beer** < 1 drink/wk 1–4 5–14 15–29 30+ **Wine** < 1 drink/wk 1–4 5–14 15–29 30+	Men/Women 1/1 1.0/1.3 1.3/1.5 2.6/4.9 5.5/7.8 1/1 1.2/2.2 1.7/2.9 3.4/2.3 4.7/18.0 1/1 0.7/0.6 0.7/0.8 0.9/0.5 2.5/1.6	Men/ Women 0.7–1.3 / 0.9–2.1 0.9–1.8 / 0.9–2.5 1.7–3.9 / 1.6–14.3 3.4–9.1 / 2.1–29.2 0.8–1.7 / 1.4–3.6 1.2–2.4 / 1.5–5.6 2.7–5.1 / 0.9–6.5 3.0–7.3 / 2.1–159.0 0.5–1.0 / 0.4–1.0 0.4–1.0 / 0.4–1.4 0.5–1.8 / 0.1–2.3 0.9–6.5 / 0.2–13.6	Age, race, study location, respondent status (self vs. proxy), smoking, other two types of alcoholic beverages;	
40	Merletti, et al. (1989) Torino, Italy, 1982–84	Oral cavity and oropharynx (ICD9 140.3–140.5, 141, 143–146)	122 (86 men, 36 women) cases; histologically confirmed; 85% response rate. 606 (385 men, 221 women) population-based controls randomly selected from files of residents, stratified by age and sex; 55% response rate.	Interviewer-administered questionnaire	**Type of alcohol** Wine only Beer Aperitifs Liquo	Men/Women 1/1 2.1/6.1 1.4/0.4 0.7/0.8	Men/ Women 1.1–4.0 / 1.4–26.5 0.7–2.6 / 0.1–1.7 0.4–1.4 / 0.3–2.3	Age, education, area of birth, smoking habits, alcohol consumption	

Ref No.	Reference, study location and period	Organ site (ICD code)	Characteristics of study population	Exposure assessment	Exposure categories	Relative risk	95% CI	Adjustment factors in study design or analysis	Comments
29	Barra, et al. (1990) Milan & Pordenone, Italy 1986–90	Oral cavity and pharynx	305 (all men), median age=58 yrs, histologically confirmed; 2% refusal rate 1621 (all men) hospital-based controls, median age=57 yrs, matched by area of residence and age; excluded patients of alcohol and tobacco-related conditions; 3% refusal rate.	Interviewer-administered standardized questionnaire	**Wine only** ≤20 glass wine/wk 21–55 drinks/wk 56–83 ≥84 **Wine and beer** ≤20 glass wine/wk 21–55 drinks/wk 56–83 ≥84 **Wine and spirits** ≤20 glass wine/wk 21–55 drinks/wk 56–83 ≥84	1 1.9 7.3 11.2 1 0.7 3.9 7.4 1 1.1 3.5 9.9	1.0–3.4 3.8–14.1 3.8–33.1 0.2–2.5 1.6–9.6 3.2–17.3 0.5–2.4 1.7–6.9 4.3–22.7	Age, area of residence, occupation, smoking and drinking habits	
17	Franceschi, et al. (1990) Milan & Pordenone, Italy, 1986–89	Oral cavity (ICD9 140, 141, 143–145) Pharynx, hypopharynx/ larynx junction included (ICD9 146, 148, 161.1)	157 male controls, below age 75 yrs; histologically confirmed; response rate 98% overall for cases. 1272 hospital-based non-cancer male controls from same hospitals as cases matched on age and area of residence; excluded patients of alcohol and tobacco-related conditions; response rate 97%. 134 male cases, below age 75 yrs; histologically confirmed; response rate 98% overall for cases.	Interviewer-administered questionnaire	**Wine** 0–20 glasses/week 21–34 35–55 56–83 84+ χ^2 for trend **Beer** 0 glasses/week 1–13 14+ χ^2 for trend **Hard liquor** 0 glasses/week 1–6 7+ χ^2 for trend **Wine** 0–20 glasses/week 21–34 35–55 56–83 84+ χ^2 for trend **Beer** 0 glasses/week 1–13 14+ χ^2 for trend **Hard liquor** 0 glasses/week 1–6 7+ χ^2 for trend	1 1.1 1.9 4.9 8.5 47.68 1 1.0 0.8 0.30 1 0.7 0.9 0.66 1 0.7 1.9 3.1 10.9 46.44 1 0.5 0.9 0.47 1 0.4 1.2 0.24	0.5–2.3 0.9–3.7 2.6–9.5 3.6–20.2 $p<0.01$ 0.6–1.8 0.5–1.4 NS 0.4–1.3 0.6–1.3 NS 0.3–1.6 0.9–3.7 1.6–6.1 4.7–25.3 $p<0.01$ 0.3–1.0 0.5–1.5 NS 0.2–0.9 0.8–1.8 NS	Age, area of residence, education, occupation, smoking habits	

Ref No.	Reference, study location and period	Organ site (ICD code)	Characteristics of study population	Exposure assessment	Exposure categories	Relative risk	95% CI	Adjustment factors in study design or analysis	Comments
20	Zheng, et al. (1990) Beijing, China (PRC), 1988–89	Oral cavity (ICD9 141, 143–145)	404 (248 men, 156 women) cases diagnosed at seven participating hospitals in the Beijing area; histologically confirmed; 100% response rate. 404 randomly selected non-cancer hospital-based controls, individually matched on age, sex, hospital; 100% response rate.	Interviewer-administered questionnaire	**Type of alcohol** Never drinker Spirits only Beer/wine only Mixed	1 1.46 1.00 1.13	0.93–2.28 0.33–3.08 0.45–2.80	Age, sex, education, smoking	
28	Barra, et al. (1991) Pordenone, Italy, 1985–90	Oral cavity and pharynx	272 (236 men, 36 women) cases, median age=60 yrs, histologically confirmed; 3% refusal rate. 1,884 (1122 men, 762 women) non-cancer, hospital-based controls, median age=58 yrs, matched by area of residence and age; excluded patients of alcohol and tobacco-related conditions; 3% refusal rate for each group.	Interviewer-administered standardized questionnaire	**Wine** ≤20 drinks/wk 21–34 35–55 56–83 ≥84 χ^2 for trend **Beer** 0 drinks/wk 1–13 ≥14 χ^2 for trend **Spirits** 0 drinks/wk 1–13 ≥14 *χ^2 for trend*	1 1.7 3.3 6.8 15.6 107.9 1 0.7 1.4 1.5 1 0.8 1.6 1.1	1.0–3.1 1.8–5.9 3.9–12.1 8.2–29.7 p<0.01 0.4–1.0 1.0–1.9 NS 0.6–1.1 1.1–2.3 NS	Age, sex, education, occupation, tobacco	
39	Mashberg, et al. (1993) New Jersey, USA, 1972–83	Oral cavity and oropharynx	359 white and black male veterans with invasive cancer and in situ carcinoma identified in the Department of Veterans Affairs Medical Center; median age: 57 yrs; histologically confirmed	Interviewer-administered questionnaire	**Type of alcohol** Minimal drinking Mixed consumption Whiskey only Whiskey predominantly Beer only Beer predominantly	1 8.3 3.8 5.3 2.6 8.3	4.7–14.8 1.8–8.1 1.1–26.3 1.3–5.2 3.4–20.2	Age, race, tobacco smoking, average total alcohol consumption	

Ref No.	Reference, study location and period	Organ site (ICD code)	Characteristics of study population	Exposure assessment	Exposure categories	Relative risk	95% CI	Adjustment factors in study design or analysis	Comments
			2,280 white or black male patients from the same center as cases of the same age range as cases (37–80 yrs); median age: 58 yrs; excluding patients with cancer or dysplasia of the pharynx, larynx, lung, esophagus						
53	Ng, et al. (1993) USA, 1977–91	Oral cavity and pharynx (ICD9 141, 143–146, 148, 149)	173 (73 men, 100 women) white non-smoking cases in 8 US cities; histologically confirmed 613 (254 men, 359 women) hospital-based controls matched (up to 4:1 control:case) on age, sex, date of interview; excluded patients with tobacco related conditions		*Men* **Beer** Non-drinker <1 OWE[1]/day 1–2.9 3+ χ^2 *for trend* **Wine** Non-drinker <1 OWE[1]/day 1–2.9 3+ χ^2 *for trend* **Liquor** Non-drinker <1 OWE[1]/day 1–2.9 3+ χ^2 for trend *Women* **Beer** Non-drinker <1 OWE[1]/day 1+ χ^2 *for trend* **Wine** Non-drinker <1 OWE[1]/day 1+ χ^2 *for trend* **Liquor** Non-drinker <1 OWE[1]/day 1+ χ^2 for trend	1 1.9 2.6 5.1 13.6 1 0.9 1.5 1.6 0.01 1 1.1 2.0 0.4 0.25 1 0.68 0.78 0.96 1 0.71 0.98 0.23 1 2.87 1.13 1.93	0.9–3.8 1.1–5.9 1.8–14.2 $p<0.001$ 0.5–1.8 0.5–4.9 0.0–29.7 NS 0.6–2.2 0.7–5.3 0.0–7.1 NS 0.10–4.93 0.35–1.75 NS 0.14–3.59 0.54–1.77 NS 0.90–9.18 0.60–2.13 NS		[1]OWE: ounces of whiskey equivalent

Ref No.	Reference, study location and period	Organ site (ICD code)	Characteristics of study population	Exposure assessment	Exposure categories	Relative risk	95% CI	Adjustment factors in study design or analysis	Comments
12	Day, et al. (1994) USA, 1984–85	Oral cavity, pharynx, esophagus, larynx	80 (56 men, 24 women) with second primary cancers from cohort of 1, 090 first primary cancers). 189 (132 men, 57 women) randomly selected from cohort that were free of second primary cancer at the end of follow-up (1989).	Interviewer-administered standardized questionnaire	**Beer** < 1 drink/wk 1–14 ≥15 **Liquor** < 1 drink/wk 1–14 ≥15 **Wine** < 1 drink/ wk ≥ 1	1 2.4 3.8 1 1.2 0.4 1 0.6	0.8–7.1 1.2–12.0 0.5–2.9 0.1–1.1 0.2–1.3	Age at first cancer diagnosis, stage of first cancer, lifetime smoking, other two types of alcoholic beverages	
35	Kabat, et al. (1994) USA, 1977–90	Oral cavity and pharynx (excluding nasopharynx)	1,560 (1,097 men, 463 women) cases enrolled in 28 hospitals in 8 US cities. 2,948 (2,075 men, 873 women) hospital-based controls matched on age, sex, race, hospital, date of interview.	Interviewer-administered standardized questionnaire	*(In oz. of whiskey equivalents/day)* **Beer** Non-drinker Occasional 1–2.9 oz/day 4–6.9 7+ **Wine** Non-drinker Occasional 1–2.9 oz/day 4–6.9 7+ **Hard liquor** Non-drinker Occasional 1–2.9 oz/day 4–6.9 7+	Men/Women 1/1 1.5/1.3 2.5/1.9 4.1/3.6 5.3/-- 1/1 0.8/0.8 1.3/0.8 1.0/2.7 2.7/-- 1/1 1.0/1.1 1.7/1.9 2.6/7.6 3.1/--	Men/ Women 1.2–1.9 / 1.0–1.9 2.0–3.3 / 1.1–3.1 2.9–5.7 / 1.7–7.5 4.0–7.0 / --- 0.7–1.0 / 0.6–1.1 0.9–1.7 / 0.5–1.4 0.5–2.3 / 1.0–7.7 1.6–4.6 / --- 0.8–1.3 / 0.8–1.5 1.4–2.3 / 1.2–2.9 1.8–3.7 / 3.9–14.8 2.4–4.1 / ---	Age, education, smoking, race, time period, type of hospital	1 oz WE =10.2 g of alcohol

Ref No.	Reference, study location and period	Organ site (ICD code)	Characteristics of study population	Exposure assessment	Exposure categories	Relative risk	95% CI	Adjustment factors in study design or analysis	Comments
4	Chyou, et al. (1995) Hawaii, USA	Oral cavity, pharynx, esophagus, larynx (ICD8 140–150, 161)	Cohort of 7,995 men of Japanese ancestry, aged 45–68 yrs; recruitment from 1965–68, incidence follow-up until 1993; 1–2% lost to follow-up.	Interviewer-administered questionnaire	**Beer** Alcohol non-drinker <49 oz/month 49–360 361+ *p* for trend **Wine** Alcohol non-drinker ≤4 oz/month >4 *p* for trend **Spirits** Alcohol non-drinker ≤4 oz/month >4 *p* for trend	1 0.67 1.91 3.66 1 2.54 3.80 1 1.59 3.61	 0.25–1.82 0.97–3.75 2.01–6.69 <0.0001 1.15–5.60 1.76–8.18 0.0001 0.80–3.15 1.98–6.58 <0.0001	Age, number of cigarettes/day, years smoked	
19	Zheng, et al. (1997) Beijing, China (PRC), 1988–89	Tongue	111 (65 men, 46 women) cases diagnosed at seven participating hospitals in the Beijing area; aged 20–80 yrs; histologically confirmed. 111 randomly selected non-cancer hospital-based controls, individually matched on age, sex, hospital	Interviewer-administered questionnaire	**Type of alcohol** None Spirits only Beer/Wine	1 1.15 1.17	 0.28–4.02 0.56–2.42	Education, smoking (age and sex matched on)	
5	Kjaerheim, et al. (1998) Norway	Oral cavity, pharynx, larynx, esophagus (ICD7 141, 143–145, 147–148, 150, 161)	Cohort of 10,960 men born from 1893–1929 who completed 2 questionnaires sent to a probability sample of the Norwegian population; incidence follow-up 1968–1992	Mailed survey	**Beer** Never or <1 time/week Previously 1–3 times/week 4–7 *p* for trend **Spirits** Never or <1 time/week Previously 1–3 times/week 4–7 *p* for trend	1 1.0 1.4 4.4 1 1.3 1.4 2.7	 0.5–1.9 0.7–3.1 2.4–8.3 <0.001 0.7–2.3 0.6–3.6 1.1–7.0 0.06	Age, smoking	

Ref No.	Reference, study location and period	Organ site (ICD code)	Characteristics of study population	Exposure assessment	Exposure categories	Relative risk	95% CI	Adjustment factors in study design or analysis	Comments
46	Schildt, et al. (1998) Sweden, 1980–89	Oral cavity (ICD7 140, 141, 143–145)	354 (237 men, 117 women) cases from 4 most northen counties in Sweden (Norrbotten, Vasterbotten, Jamtland, Vasternorrland) reported to the Cancer Registry (175 living, 235 deceased); histologically confirmed; 96% response rate. 354 (237 men, 117 women) population controls from the National Population Registry individually matched on age, sex, county; 91% response rate.	Self-completed questionnaire	**Type of alcohol**[1] Light beer Beer Wine Liquor *Amount*frequency score*- **Wine** Low Medium High **Liquor** Low Medium High	1.2 1.5 1.0 1.5 1.3 0.9 8.6 1.3 1.6 3.6	0.7–1.7 0.7–3.2 0.6–1.5 0.9–2.3 0.9–1.8 0.5–1.8 1.0–70.0 0.9–2.0 1.0–2.7 1.8–7.2	[1]Snuff and smoking in addition to types of alcohol listed	
33	Garrote, et al. (2001) Havana, Cuba, 1996–99	Oral cavity and oropharynx	200 (143 men, 57 women) cases identified in the Instituto Nacional de Oncologia y Radiobiologia (INOR) of Havana; median age 64 yrs; 88% response rate. 200 (136 men, 64 women) hospital-based controls admitted to INOR and 3 other major hospitals in Havana; excluded patients of alcohol and tobacco-related conditions; frequency matched on age and sex; median age 62 yrs; 79% response rate.	Interviewer (dentist)-administered questionnaire	**Hard liquor** 0 drinks/week 1–7 8–20 21–69 ≥70 χ^2 for trend **Beer** 0 drinks/week <7 ≥7 χ^2 for trend **Wine** 0 drinks/week <2 ≥2 χ^2 for trend	1 1.3 1.0 4.2 5.1 4.58 1 1.5 1.5 0.85 1 1.0 0.8 0.15	0.5–3.3 0.4–2.4 1.1–16.5 1.1–23.3 p<0.05 0.6–3.9 0.5–4.6 p=0.36 0.4–2.4 0.2–3.2 p=0.70	Age, sex, area of residence, education, smoking, other two types of alcohol	

Ref No.	Reference, study location and period	Organ site (ICD code)	Characteristics of study population	Exposure assessment	Exposure categories	Relative risk	95% CI	Adjustment factors in study design or analysis	Comments
47	Schlecht, et al. (2001) Brazil, 1986–89	Oral cavity excluding salivary gland (ICD9 140–141, 143–145) Pharynx excluding nasopharynx (ICD9 146, 148–149)	373 cases selected from hospitals in Sao Paulo, Curitiba, Goiania; histopathologically confirmed. 1578 hospital-based non-cancer controls matched (2:1 controls:case) on age, sex, hospital area, admission period. 217 cases selected from hospitals in Sao Paulo, Curitiba, Goiania; histopathologically confirmed. 1578 hospital-based non-cancer controls matched (2:1 controls:case) on age, sex, hospital area, admission period.	Interviewer-administered questionnaire	**Beer** Non-drinker 1–10 kg 11–100 >100 Other than beer **Wine** Non-drinker 1–10 kg 11–100 >100 Other than wine **Hard liquor** Non-drinker 1–10 kg 11–100 >100 Other than hard liquor **Cachaca** Non-drinker 1–10 g 11–100 101–500 501–1000 1001–2000 >2000 Other than cachaca **Beer** Non-drinker 1–10 g 11–100 >100 Other than beer **Wine** Non-drinker 1–10 g 11–100 >100 Other than wine **Hard liquor** Non-drinker 1–10 g 11–100 >100 Other than hard liquor **Cachaca** Non-drinker 1–10 g 11–100	1 3.6 2.8 3.7 3.1 1 3.4 4.3 3.0 2.9 1 3.3 3.1 6.9 3.2 1 1.4 2.0 4.5 7.2 8.7 9.9 3.7 1 3.2 3.4 1.1 3.1 1 3.1 2.8 3.0 3.6 1 4.1 4.6 2.5 3.1 1 2.8 2.9 5.4 9.2 14.3 12.5 2.1	1.9–7.0 1.4–5.6 1.4–10.3 1.6–5.8 1.8–6.5 1.9–10.1 1.2–7.3 1.6–5.5 1.3–8.2 1.5–6.6 2.8–17.1 1.7–5.8 0.4–5.4 1.0–4.2 2.2–9.2 3.5–14.7 4.3–17.6 3.8–25.5 1.8–7.8 1.1–9.2 1.1–10.4 0.3–4.1 1.0–9.2 1.0–9.2 0.8–9.4 0.8–11.1 1.3–10.5 1.0–17.7 1.5–14.1 0.7–9.8 1.1–8.8 0.4–19.6 0.9–9.1 1.7–17.5 2.9–29.3 4.4–45.8 2.9–53.7 0.6–7.8	Tobacco smoking, remaining alcohol consumption, income, education, race, beverage temperature, religion, wood stove use, spicy food (matched variables: age, sex, study location, admission period)	

Ref No.	Reference, study location and period	Organ site (ICD code)	Characteristics of study population	Exposure assessment	Exposure categories	Relative risk	95% CI	Adjustment factors in study design or analysis	Comments
					101–500 501–1000 1001–2000 >2000 Other than cachaca				
		Oral cavity and pharynx	395 cases/391 controls restricted to smokers only.		**Drinking status** Current drinkers Former drinkers Never drinkers	1 0.77 0.37	0.3–2.0 0.1–0.9		
21	Znaor, et al. (2003) Chennai & Trivandrum, India, 1993–99	Oral cavity (ICD9 140, 141, 143–5) Pharynx (ICD9 146, 148, 149)	1563 male cases from the Cancer Institute (Chennai) and the Regional Cancer Center (Trivandrum); histologically confirmed 1,711 male patients with non-tobacco-related cancers from same centers as cases and 1927 healthy male hospital visitors from only Chennai 636 male cases from the Cancer Institute (Chennai) and the Regional Cancer Center (Trivandrum); histologically confirmed.	Interviewer-administered questionnaire	**Type of alcohol** Never drinkers Arrack only Country liquor only Spirits only Cliq/arrac+spirits only Cliq/arrac+spirits +toddy only **Type of alcohol** Never drinkers Arrack only Country liquor only Spirits only Cliq/arrac+spirits only Cliq/arrac+spirits +toddy only	1 7.19 1.73 1.04 2.12 1.80 1 3.91 2.53 1.14 2.42 2.89	5.11–10.12 1.30–2.32 0.78–1.38 1.33–3.40 1.32–2.46 2.49–6.16 1.78–3.60 0.79–1.65 1.37–4.26 2.00–4.17	Age, center, education, smoking, and alcohol consumption	
27	Altieri, et al. (2004) Itlay and Switzerland, 1992–97	Oral cavity and pharynx	749 (634 men, 115 women) cases from Pordenone, Rome, Latina (Italy) and Vaud (Switzerland) admitted to major teaching and general hospitals in area under surveillance; aged 22–77; histologically confirmed. 1,772 (1,252 men, 520 women)	Interview-administered structured questionnaire	**Wine** Non-wine drinkers 1–2 drinks/day 3–4 5–7 8–11 12+ χ^2 for trend **Beer** Non-beer drinkers 1–2 3+ χ^2 for trend **Spirits** Non-spirit drinkers	1 2.2 7.1 11.8 16.1 221.83 1 1.2 2.3 9.86 1 1.0 1.9 1.14	1.6–3.0 5.0–10.1 8.1–17.2 10.2–25.3 $p<0.0001$ 1.0–1.5 1.4–3.7 0.02 0.8–1.2 1.1–3.3 0.29	Age, sex, study center, education, smoking habit, and other types of alcohol	

Ref No.	Reference, study location and period	Organ site (ICD code)	Characteristics of study population	Exposure assessment	Exposure categories	Relative risk	95% CI	Adjustment factors in study design or analysis	Comments
			hospital-controls from the same network of hospitals as cases; aged 20–78 yrs; excluded patients of alcohol and tobacco-related conditions		1–2 3+ χ^2 for trend				
31	Castellsague, et al. (2004) Spain, 1996–99	Oral cavity and oropharynx (ICDO C1–C10)	375 (304 men, 71 women) cases identified from hospitals in Granada (1), Sevilla (1), Barcelona (2); mean age 60 yrs; histologically confirmed; 76.5% response rate. 375 (304 men, 71 women) non-cancer hospital-controls from same hospitals as cases, frequency matched on age and sex, mean age 60 yrs; excluded patients with alcohol and tobacco-related diagnoses; 91% response rate	Interviewer-administered standardized questionnaire in hospital	**Type of alcohol** Never drinkers Only beer Only wine and beer Only wine Spirits w/t wine or beer *p* for trend	1 1.16 1.96 2.71 7.28	0.47–2.82 0.96–3.99 1.31–5.60 3.65–14.52 <0.0001	Age group, sex, education, tobacco smoking, center, and daily consumption of pure ethanol	
25	De Stefani, et al. (2004) Montevideo, Uruguay, 1997–2003	Hypophyranx	85 males cases identified in the four major hospitals in Montevideo; microscopically confirmed; 97.5% response rate. 640 hospital-based male controls from the same hospitals as cases; excluded patients of alcohol and tobacco-related conditions with no recent changes in diet;	Interviewer-administered questionnaire	**Beer** Beer abstainers 1–60 ml ethanol/day 61+ *p* for trend **Red wine** Wine abstainers 1–60 61–120 121+ *p* for trend **Hard liquor** Liquor abstainers 1–60 61–120 121+ *p* for trend	1 0.8 0.2 1 2.3 5.2 4.5 1 0.9 2.2 3.3	0.3–1.9 0.1–1.1 0.08 0.9–5.5 2.2–12.4 1.9–10.8 0.0001 0.4–1.9 0.9–5.2 1.6–6.8 0.0008	Age, residence, urban/rural status, education, BMI, smoking, and other two type of alcohols	

Ref No.	Reference, study location and period	Organ site (ICD code)	Characteristics of study population	Exposure assessment	Exposure categories	Relative risk	95% CI	Adjustment factors in study design or analysis	Comments
			frequency matched (2:1 controls:cases) on age and residence; 97% response rate						
16	De Stefani, et al. (2007) Montevideo, Uruguay, 1988–2000	Oral cavity (excluding lip) Pharynx (excluding nasopharynx	335 males cases identified in the four major hospitals in Montevideo; microscopically confirmed; 97% response rate. 1501 hospital-based non-cancer male controls; excluded patients of alcohol and tobacco-related conditions with no recent changes in diet; 97% response rate. 441 males cases identified in the four major hospitals in Montevideo; microscopically confirmed; 97% response rate.	Interviewer-administered questionnaire	**Beer** Beer abstainers 1–22 ml ethanol/day 23+ *p* for trend **Wine** Wine abstainers 1–60 61–120 121+ *p* for trend **Hard liquor** Liquor abstainer 1–60 61–120 121+ *p* for trend **Beer** Beer abstainers 1–22 ml ethanol 23+ *p* for trend **Wine** Wine abstainers 1–60 61–120 121+ *p* for trend **Hard liquor** Liquor abstainer 1–60 61–120 121+ *p* for trend	1 0.5 0.4 1 0.8 1.5 1.4 1 0.8 1.8 1.4 1 0.8 0.3 1 1.1 2.7 2.5 1 0.9 1.6 0.9	0.3–0.9 0.2–0.9 0.004 0.6–1.2 1.0–2.1 0.9–2.4 0.03 0.6–1.2 1.2–2.7 0.8–2.2 0.03 0.4–1.3 0.2–0.7 0.001 0.8–1.5 1.9–3.8 1.6–3.9 <0.0001 0.7–1.3 1.1–2.3 0.5–1.4 0.5	Age, residence, urban/rural status, hospital, year of diagnosis, education, family history of cancer, occupation, vegetable and fruit consumption, mate, smoking, total alcohol intake	

Ref No.	Reference, study location and period	Organ site (ICD code)	Characteristics of study population	Exposure assessment	Exposure categories	Relative risk	95% CI	Adjustment factors in study design or analysis	Comments
48	Purdue, et al. (2009) International Consortium of Head and Neck Cancer. Combined analysis of 15 studies from US, South and Central American, European countries	Oral cavity, pharynx, oro-pharynx, hypo-pharynx oral cavity or pharynx not otherwise specified, larynx, and head and neck cancer unspecified (excluding salivary gland)	858 cases and 986 controls of beer-only drinkers. 1124 cases and 3487 controls of never drinkers 499 cases and 527 controls of liquor-only drinkers. 1021 cases and 2460 controls of wine-only drinkers.	Interview or self-administrated questionnaire	**Beer-only drinkers** Never drinkers ≤5 drinks[1]/week 6–15 16–30 30+ *p* for trend **Liquor-only drinkers** Never drinkers ≤5 drinks[1]/week 6–15 16–30 30+ *p* for trend **Wine-only drinkers** Never drinkers ≤5 drinks[1]/week 6–15 16–30 30+ *p* for trend	1 1.6 1.9 2.2 5.4 1 1.6 1.5 2.3 3.6 1 1.1 1.2 1.9 6.3	1.3–2.1 1.4–2.7 1.3–3.5 3.1–9.2 <0.0001 1.0–2.6 1.0–2.4 1.4–4.0 2.2–5.8 <0.0001 0.8–1.6 0.8–1.9 0.9–3.9 2.2–18.6 <0.0001	Age, sex, race/ ethnicity, education, study center, smoking pack-years, years of cigar smoking, years of pipe smoking	[1]ethanol-standardized drinks

Table 4

Joint Effects of Alcohol and Tobacco on Oral Cavity and Pharyngeal Cancers

Ref No.	Reference, study location and period	Organ site (ICD code)	Characteristics of study population	Tobacco	Alcohol					Comments/ Adjustment factors in study design or analysis
30	Blot, et al. (1988) USA, 1984–85	Oral cavity and pharynx (ICD9 141, 143–146, 148, 149), excluding salivary gland and nasopharynx	1,114 (762 men, 352 women) cases; 1,268 population controls	*Males* No. Cases/Controls OR	Alcohol (drinks/week)					[1]Quit for 10+ yrs or smoked for >20 yrs; Adjusted for age, race, study location, respondent status (self vs. next-of-kin)
					<1	1–4	5–14	15–29	30+	
				Non-smoker	12/66 1	12/52 1.3	15/39 1.6	5/21 1.4	6/7 5.8	
				Short duration/former[1]	8/42 0.7	24/61 2.2	21/90 1.4	25/49 3.2	43/37 6.4	
				1–19/day for 20+ yrs	2/6 1.7	7/21 1.5	8/18 2.7	16/18 5.4	22/14 7.9	
				20–39/day for 20+ yrs	8/17 1.9	17/34 2.4	28/40 4.4	52/42 7.2	145/33 23.8	
				40+ /day for 20+ yrs	9/4 7.4	6/14 0.7	19/19 4.4	43/11 20.2	148/21 37.7	
				Pipe/cigar only	1/4 0.6	5/24 1.0	8/13 3.7	13/9 4.7	25/6 23.0	
				Females No. Cases/Controls OR	Alcohol (drinks/week)					
					<1	1–4	5–14	15–29	30+	
				Non-smoker	36/112 1	11/62 0.7	7/23 1.3	0/3 0.0	0/2 0.0	
				Short duration/former[1]	7/27 1.0	8/21 1.6	4/30 0.4	3/10 1.1	3/0 ~	
				1–19/day for 20+ yrs	4/13 0.9	22/15 5.1	11/15 2.8	3/3 4.6	9/3 11.0	
				20–39/day for 20+ yrs	12/19 2.2	20/25 2.7	35/18 6.9	31/9 12.4	38/3 46.0	
				40+ /day for 20+ yrs	4/0 ~	14/6 9.3	15/7 7.8	18/4 18.0	37/1 107.9	
23	Tuyns, et al. (1988)	Hypopharynx	281 male cases; 3,057 male	No. of cases OR	Alcohol (g/day)					Adjusted for age, place, age/ place interaction

Ref No.	Reference, study location and period	Organ site (ICD code)	Characteristics of study population	Tobacco	Alcohol	Comments/ Adjustment factors in study design or analysis
	Italy, Spain, Switzerland, France 1980–83		population controls	0–40 / 41–80 / 81–120 / 121+ 0–7 cigarettes/day: 4 / 10 / 7 / 11 1 / 3.0 / 5.5 / 15.0 8–15 cigarettes/day: 9 / 32 / 28 / 39 4.7 / 14.6 / 27.5 / 71.6 16–25 cigarette/day: 27 / 42 / 52 / 56 13.9 / 19.5 / 48.3 / 67.8 26+ cigarettes/day: 5 / 15 / 22 / 50 4.9 / 18.4 / 37.6 / 135.5		
40	Merletti, et al. (1989) Torino, Italy, 1982–84	Oral cavity and oropharynx (ICD9 140.3–140.5, 141, 143–146)	122 (86 men, 36 women); 606 (385 men, 221 women) population-based controls	*Men* No. Cases/Controls OR (95% CI) Alcohol (g/day): 0–40 / 41–120 / >120 0–7 tobacco g/day: 4/61, 1 / 4/82 (categories combined), 0.6 (0.2–2.0) 8–15 g/day: 7/31, 3.3 (0.9–12.4) / 15/50, 3.6 (1.1–12.0) / 5/10, 8.6 (1.9–39.0) >16: 10/57, 2.5 (0.7–8.5) / 25/82, 3.6 (1.2–11.3) / 16/12, 21.4 (5.9–77.7) *Women* No. Cases/Controls OR (95% CI) Alcohol (g/day): 0–20 / 21–40 / >40 0 tobacco g/day: 6/66, 1 / 5/46, 1.1 (0.3–4.1) / 2/25, 0.8 (0.1–4.2) 1+ g/day: 5/46, 2.8 (0.7–11.1) / 8/27, 6.5 (1.7–24.5) / 10/11, 21.3 (5.1–88.6)		Adjusted for age, education, area of birth,
17	Franceschi, et al. (1990) Milan & Pordenone, Italy, 1986–89	Oral cavity (ICD9 140, 141, 143–145), Pharynx (ICD9 146, 148, 161.1)	157 male cases; 1272 hospital-based non-cancer male controls	No. Cases/Controls OR Alcohol (drinks/week): <35 / 35–59 / 60+ Non-smoker: 3/185, 1 / 2/81, 1.6 / 1/23, 2.3 Light: 7/162, 3.1 / 7/70, 5.4 / 12/49, 10.9		Adjusted for age, area of residence, education, occupation

Ref No.	Reference, study location and period	Organ site (ICD code)	Characteristics of study population	Tobacco	Alcohol	Comments/ Adjustment factors in study design or analysis
				Intermediate	39/296 10.9 / 79/192 26.6 / 102/126 36.4	
				Heavy	7/37 17.6 / 8/19 40.2 / 19/13 79.6	
20	Zheng, et al. (1990) Beijing, China (PRC), 1988–89	Oral cavity (ICD9 141, 143–145)	404 (248 men, 156 women) cases; 404 randomly selected non-cancer hospital-based controls	No. cases/controls OR	Alcohol (lifetime consumption of spirit equivalents in kg): 0 kg / <217 kg / 217–801 kg / >801 kg	Adjusted for age, education
				0 pack-years	20/51 1 / 9/18 1.2 / 4/11 0.8 / 4/7 2.4	
				1–18 pack-years	15/25 1.4 / 15/15 2.8 / 13/6 5.6 / 4/1 15.2	
				19–32 pack-years	12/11 2.1 / 14/8 4.9 / 9/14 1.7 / 19/5 10.1	
				>32 pack-years	13/9 2.5 / 2/1 5.9 / 14/7 5.9 / 31/9 17.4	
45	Maier, et al. (1992) Heidelberg & Giessen, Germany, 1987–88	Oral cavity, pharynx, larynx	200 male cases; 800 outpatient male controls	No. Cases/Controls OR (95% CI)	Alcohol (g/day): <25 / 25–75 / >75	
				<5 tobacco-years	5/178 1 / 5/97 2.3 (0.6–8.8) / 3/10 10.3 (1.9–55.8)	
				5–50 tobacco-years	27/246 5.7 (1.9–17.3) / 50/180 14.6 (4.8–43.9) / 44/19 153.2 (44.1–532)	
				>50 tobacco-years	14/33 23.3 (6.6–82.5) / 27/28 52.8 (15.8–176.6) / 25/9 146.2 (37.7–566)	
22	Nam, et al. (1992) USA, 1986	Nasopharynx	204 (141 men, 63 women) white cases; 408 (282 men, 126 women) controls	OR (p-value if given)	Alcohol (drinks/week): 0–3 / 4–23 / 24+	Adjusted for sex
				≤30 pack-years	1 / 0.6 / 1.4	
				31–59 pack-years	1.5 / 2.3 (<0.05) / 2.6 (<0.01)	
				≥60 pack-years	2.2 (<0.05) / 2.3 (<0.05) / 5.2 (<0.01)	
39	Mashberg, et al. (1993)	Oral cavity and oropharynx	359 white and black male cases; 2,280	No. Cases/Controls OR	Alcohol (whiskey equivalent/day)	Adjusted for age, race

Ref No.	Reference, study location and period	Organ site (ICD code)	Characteristics of study population	Tobacco	Alcohol	Comments/ Adjustment factors in study design or analysis
	New Jersey, USA, 1972–83		white or black male controls			

	Minimal drinkers	2–5 WE/day	6–10 WE/day	11–21 WE/day	22+ WE/day
Minimal smokers	1/16 1	1/56 2.7	2/27 11.9	3/35 12.5	2/28 8.3
Cigar/Pipe	6/69 20.5	6/62 17.0	13/39 53.4	6/44 27.3	5/35 23.1
6–15 cigarettes/day	3/62 10.8	7/56 24.2	17/55 50.9	8/52 30.9	6/31 27.5
16–25 cigarettes/day	4/106 7.6	16/103 29.7	23/108 28.9	34/125 44.8	31/85 61.7
26–35 cigarettes/day	0/43 --	2/48 5.3	18/39 61.9	18/40 79.5	22/38 70.3
36+ cigarettes/day	1/61 3.2	4/50 10.2	17/74 26.8	40/65 98.4	30/126 32.0

35	Kabat, et al. (1994) USA, 1977–90	Oral cavity and pharynx (excluding nasopharynx)	1,560 (1,097 men, 463 women) cases; 2,948 (2,075 men, 873 women) hospital-based controls			Adjusted for age, education, race, time period, type of hospital

Males OR (95% CI)	Alcohol (oz/day) 1–3.9 oz/day	4–6.9 oz/day	7+ oz/day
Never	1	1.2 (0.4–3.7)	2.9 (1.1–8.1)
Ex-smoker (abstained for 12+ months)	1.0 (0.7–1.6)	1.7 (1.1–2.6)	5.1 (3.3–7.8)
1–20 cigarettes/day	1.5 (0.9–2.5)	5.8 (3.7–9.1)	11.9 (7.7–18.4)
21–30 cigarettes/day	2.2 (1.1–4.3)	6.8 (3.6–12.7)	13.5 (7.9–23.2)
31+ cigarettes/day	2.0 (1.1–3.7)	6.9 (3.9–12.4)	20.1 (12.9–31.5)

Females OR (95% CI)	Alcohol (oz/day) 1–3.9 oz/day	4+ oz/day
Never	1	3.5 (0.9–13.4)
Ex-smoker (abstained for 12+ months)	1.3 (0.9–2.0)	2.7 (1.0–7.9)
1–20 cigarettes/day	2.9 (1.9–4.3)	17.6 (8.1–37.5)
21+ cigarettes/day	3.8 (2.3–6.2)	26.7 (12.3–58.5)

4	Chyou, et al. (1995) Hawaii, USA	Oral cavity, pharynx, esophagus, larynx (ICD8 140–150, 161)	Cohort of 7,995 men of Japanese ancestry	No. cases/controls OR (95% CI) Alcohol (oz/month)	Study population from Kato (1992); Adjusted for age

Ref No.	Reference, study location and period	Organ site (ICD code)	Characteristics of study population	Tobacco	Alcohol	Comments/ Adjustment factors in study design or analysis
					0 oz/month / >0–<14 oz/month / 14+ oz/month	
				0 cigs/day	3/1134 1 / 3/888 1.3 (0.3–6.3) / 6/346 6.5 (1.6–26.0)	
				>0–20 cigs/day	8/1093 3.0 (0.8–11.3) / 6/1248 1.9 (0.5–7.7) / 24/916 10.7 (3.2–35.4)	
				>20 cigs/day	5/685 3.2 (0.8–13.4) / 7/620 4.6 (1.2–17.7) / 28/819 14.4 (4.4–47.4)	
6	Murata, et al. (1996) Japan	Oral cavity, pharynx, esophagus, larynx (ICD9 140–150, 161)	Nested case-control study; cohort of 17,200 men; 51 cases; 102 controls	No. cases/controls OR (p-value if given)	Alcohol (cups/day)[1]: 0 / 0.1–1.0 / 1.1+	[1]In sake-equivalents (180ml sake contains ~27ml ethanol)
				Non-smoker	7/26 1 / 6/18 1.2 / 5/9 2.1	
				Smoker	10/20 1.9 / 7/19 1.4 / 16/10 5.9 (<0.01)	
42	Sanderson, et al. (1997) Netherlands, 1980–90	Oral cavity and oropharynx (excluding salivary glands and lip)	303 women; 1779 women controls	No. Cases/Controls OR (95% CI)	Alcohol (units/day): Non-drinker / 1–5 units/day / >5 units/day	
				Non-smoker	125/976 1 / 39/205 2.4 (1.6–3.6)	
				Smoker	28/367 1.0 (0.6–1.5) / 65/199 6.5 (4.4–9.7)	
				Non-smoker & Smoker	46/32 32.9 (18.3–59.2)	
19	Zheng, et al. (1997) Beijing, China (PRC), 1988–89	Tongue	111 (65 men, 46 women) cases; 111 randomly selected non-cancer hospital-based controls	No. cases/controls OR (p-value if given)	Alcohol (lifetime intake, spirit equivalents in kg): Never / ≤255 kg / >255 kg	Adjusted for education (Matching variables: age, sex)
				Never	39/54 1 / 6/10 1.9 / 3/4 2.4	
				≤20 pack-years	10/11 1.2 / 9/9 1.6 / 4/3 3.0	

Ref No.	Reference, study location and period	Organ site (ICD code)	Characteristics of study population	Tobacco	Alcohol	Comments/ Adjustment factors in study design or analysis
				>20	15/7 7.6 (<0.05) 8/1 23.3 (<0.05) 17/12 4.1	
46	Schildt, et al. (1998) Sweden, 1980–89	Oral cavity (ICD7 140, 141, 143–145)	354 (237 men, 117 women); 354 (237 men, 117 women) population control	No. Cases/Controls OR (95 %CI)	Liquor (based on amount and frequency scoring) Never liquor / Low intake / Medium intake / High intake	
				Never smokers	80/100 1 50/45 1.2 (0.8–1.9) 7/11 1.4 (0.8–2.6) 4/2 4.2 (1.8–9.4)	
				Low intake Life: ≤124.8 kg of tobacco	15/22 1.0 (0.6–1.6) 26/31 1.2 (0.6–2.1) 19/17 1.4 (0.7–2.7) 4/4 4.0 (1.6–9.8)	
				High intake Life: >124.8 kg of tobacco	8/9 1.4 (0.8–2.3) 30/31 1.6 (0.9–2.9) 27/21 2.0 (1.0–3.6) 30/7 5.7 (2.4–14)	
49	Franceschi, et al. (1999) Italy & Switzerland, 1992–97	Oral cavity and pharynx (excluding lip, salivary gland, nasopharynx)	749 (634 men, 115 women) cases; 1,772 (1,252 men, 520 women) hospital-based controls	*Oral cavity* No. Cases/Controls OR (95% CI)	Alcohol (drinks/week) 0–20 / 21–48 / 49–76 / ≥77	*Study population from Franceschi (2000); Adjusted for age, area of residence, interviewer, education, vegetable and fruit intake, total energy intake*
				Never smoker	3/193 1 5/119 2.7 (0.6–11.6) 3/34 (categories combined) 4.5 (0.8–24.2)	
				1–14 cigarettes/day	2/62 2.2 (0.4–13.5) 6/49 5.9 (1.4–25.1) 11/16 30.6 (7.3–128.2) 8/6 52.4 (10.4–264.2)	
				15–24 cigarette/day	4/78 3.0 (0.6–13.8) 28/65 22.9 (6.6–79.4) 35/28 62.5 (17.4–224.2) 31/15 110.3 (29.1–418.1)	
				≥25 cigarettes/cay	4/41 5.6 (1.2–26.3) 12/27 22.7 (5.9–86.9) 25/11 103.1 (26.4–402.7) 31/7 227.8 (54.6–950.7)	
				Ex-smoker (abstained 12+ mo)	12/187 3.9 (1.1–14.1) 20/212 6.0 (1.7–21.0) 17/71 10.5 (2.9–38.6) 17/33 25.4 (6.7–96.0)	
				Pharynx No. Cases/Controls OR (95% CI)	Alcohol (drinks/week) 0–20 / 21–48 / 49–76 / ≥77	
				Never smoker	6/193 1 2/119 0.4 (0.1–2.3) 1/34 (categories combined) 0.5 (0.1–4.3)	
				1–14 cigarettes/day	4/62 2.3 (0.6–8.4) 11/49 4.5 (1.5–13.4) 17/16 16.3 (5.3–50.5) 13/6 27.5 (7.2–105.1)	
				15–24 cigarette/day	12/78 4.4 (1.6–12.5) 32/65 11.7 (4.6–30.2) 40/28 26.9 (10.0–72.3) 48/15 58.3 (20.3–167.3)	

Ref No.	Reference, study location and period	Organ site (ICD code)	Characteristics of study population	Tobacco	Alcohol	Comments/ Adjustment factors in study design or analysis
				≥25 cigarettes/cay	7/41 5.5 (1.7–17.8) / 22/27 18.6 (6.8–51.3) / 18/11 32.2 (10.3–100.4) / 36/7 100.4 (30.8–327.7)	
				Ex-smoker (abstained 12+ mo)	11/187 1.7 (0.6–4.9) / 22/212 2.7 (1.3–3.7) / 31/71 6.8 (2.6–17.8) / 31/33 14.8 (5.4–40.9)	
34	Hayes, et al. (1999) Puerto Rico, 1992–95	Oral cavity and pharynx (ICD9 141–143–146, 148, 149)	342 (286 men, 56 women) cases; 521 (417 men, 104 women) population-based controls	*Men* No. cases/controls OR (95% CI)	Alcohol (drinks/week): None / 1–7 drinks/week / 8–21 drinks/week / 22–42 drinks/week / 42+ drinks/week	Adjusted for age
				None	6/44 1 / 1/49 0.2 (0.0–1.5) / 2/24 0.6 (0.1–3.5) / 2/10 1.6 (0.3–.6) / 4/5 6.4 (1.3–31.9)	
				Low	0/13 -- / 10/47 1.6 (0.5–4.8) / 3/16 1.3 (0.3–5.7) / 11/7 3.7 (0.8–16.4) / 9/12 5.5 (1.6–19.0)	
				10–19 cigarettes/day	1/1 11.3 (0.6–213.0) / 2/12 1.3 (0.2–7.2) / 3/13 1.8 (0.4–8.3) / 8/4 18.6 (4.1–84.0) / 10/7 12.2 (3.3–45.6)	
				20–39 cigs/day	1/5 1.8 (0.2–19.0) / 10/21 3.8 (1.2–12.0) / 13/17 6.2 (2.0–19.3) / 19/14 11.3 (3.7–34.5) / 60/10 50.2 (16.6–152.0)	
				40+ cigs/day	1/3 2.4 (0.2–27.6) / 6/10 4.3 (1.1–16.7) / 4/7 4.1 (0.9–18.7) / 10/8 10.5 (2.9–37.9) / 67/15 38.7 (13.6–110.0)	
50	Schlecht, et al. (1999) Brazil, 1986–89	Oral cavity, pharynx, larynx (ICD9 140–149, 161; excluding 142 and 147)	784 cases; 1578 hospital-based controls	*Oral cavity* OR (95% CI)	Alcohol (lifetime consumption in kg): 0–10 kg / 11–530 kg / >530 kg	Same study population as Schlecht (2001); Adjusted for race, beverage temperature, religion, wood stove use, spicy food intake (matching variables: age, sex, study location, admission period)
				0–5 pack-years	1 / 1.2 (0.4–3.4) / 2.3 (0.6–9.1)	
				6–42 pack-years	2.9 (1.2–6.8) / 6.2 (2.7–14.1) / 19.5 (2.6–147)	
				>42 pack-years	7.8 (2.9–21.0) / 11.2 (4.8–26.3) / 20.3 (9.0–45.3)	
				Pharynx OR (95% CI)	Alcohol (lifetime consumption in kg): 0–10 kg / 11–530 kg / >530 kg	
				0–5 pack-years	1 / 6.2 (0.7–56.6) / 22.3 (2.1–238)	
				6–42 pack-years	2.4 (0.2–24.0) / 21.7 (2.6–180) / 66.3 (1.7–2,556)	

Ref No.	Reference, study location and period	Organ site (ICD code)	Characteristics of study population	Tobacco	Alcohol			Comments/ Adjustment factors in study design or analysis
				>42 pack-years	69.4 (6.9–694)	43.0 (4.9–340)	77.3 (9.2–625)	
33	Garrote, et al. (2001) Havana, Cuba, 1996–99	Oral cavity and oropharynx	200 (143 men, 57 women) cases; 200 (136 men, 64 women) hospital-based controls	No. cases/controls OR (95% CI)	Alcohol (drinks/week)			Adjusted for age, sex, area of residence, education; also smoking (former smokers only)
					0 drinks/week	<21 drinks/week	21+ drinks/week	
				Never smokers	14/58 1	1/14 (categories combined) 0.5 (0.1–4.7)		
				1–29 cigs/day	35/27 6.6 (2.8–15.7)	17/18 11.0 (3.7–32.8)	15/7 26.7 (7.2–100.0)	
				30+ cigs/day	15/5 10.5 (2.9–38.2)	15/3 42.3 (8.4–212.3)	21/3 111.2 (22.7–543.7)	
43	Schwartz, et al. (2001) Washington, USA, 1985–95	Oral cavity and oropharynx (excluding lip)	333 (237 men, 96 women) cases of in situ and invasive cancers; 541 (387 men, 154 women) population-based controls	No. cases/controls OR (95% CI)	Alcohol (drinks/week)			Adjusted for age, sex, race
					<1 drink/week	1–14 drinks/week	≥15 drinks/week	
				Never	26/80 1	19/90 0.8 (0.4–1.5)	5/18 1.2 (0.4–3.6)	
				1–20 pack-years	9/41 0.8 (0.31.8)	27/112 0.9 (0.5–1.6)	13/14 3.8 (1.5–9.4)	
				≥20 pack-years	10/20 1.8 (0.7–4.5)	94/110 3.3 (1.9–5.7)	130/56 9.9 (5.5–17.9)	
14	Balaram, et al. (2002) Southern, India, 1996–99	Oral cavity	591 (309 men, 282 women) cases; 582 (292 men, 290 women) hospital-based controls	*Paan chewing* No. cases/controls OR (95% CI)	Alcohol			Adjusted for age, center, education, oral hygiene, smoking
					Never drinker	Current drinker		
				Never chewer	64/174 1	48/38 2.8 (1.6–5.1)		
				Current chewer	48/18 7.3 (3.8–14.1)	46/13 8.6 (4.1–18.1)		
2	Boeing, et al. (2002) Denmark, France, Germany,	Oral cavity, pharynx, esophagus	European Prospective Investigation into Cancer and Nutrition	No. Cases Hazard RR (95% CI)	Alcohol (g/day)			Adjusted for sex, follow-up time, education, BMI, vegetable and
					0–30	>30–60	>60	

Ref No.	Reference, study location and period	Organ site (ICD code)	Characteristics of study population	Tobacco	Alcohol			Comments/ Adjustment factors in study design or analysis
	Greece, Italy, Norway, Spain, Sweden, Netherlands, UK		(EPIC): Cohort of 417,752 healthy adults	Non-smoker	58 1	7 2.6 (1.1–6.0)	4 6.9 (2.3–2.7)	fruit intake, energy intake
				1–20 cigs/day	22 2.0 (1.2–3.5)	6 5.1 (2.1–12.7)	6 22.0 (8.3–58.1)	
				>20 cigs/day	7 6.8 (3.0–15.5)	7 20.7 (8.7–49.0)	7 48.7 (20.0–118.9)	
21	Znaor, et al. (2003) Chennai & Trivandrum, India, 1993–99	Oral cavity (ICD9 140, 141, 143–5) and	1563 male cases from the Cancer Institute (Chennai) and the Regional Cancer Center (Trivandrum); histologically confirmed	Chewing / Smoke / Alcohol / No. Cases/Controls / OR (95% CI)				Adjusted for age, center, and education level; T+: with tobacco; T−: without tobacco
				No / No / No	122/1471	1		
				No / No / Yes	16/75	2.56 (1.42–4.64)		
				No / Yes / No	268/1084	2.45 (1.94–3.10)		
				No / Yes / Yes	287/449	4.81 (3.74–6.19)		
				Yes-T− / No / No	24/83	3.39 (2.04–5.06)		
				Yes-T− / No / Yes	6/15	4.36 (1.55–12.30)		
				Yes-T− / Yes / No	25/49	4.80 (2.79–8.27)		
				Yes-T− / Yes / Yes	33/34	8.10 (4.68–14.02)		
				Yes-T+ / No / No	159/127	9.27 (6.79–12.66)		
				Yes-T+ / No / Yes	95/26	24.28 (14.87–39.65)		
				Yes-T+ / Yes / No	161/102	8.53 (6.13–11.89)		
				Yes-T+ / Yes / Yes	342/119	16.34 (12.13–22.00)		
		Pharynx (ICD9 146, 148, 149)	636 male cases from the Cancer Institute (Chennai) and the Regional Cancer Center (Trivandrum); histologically confirmed	Chewing / Smoke / Alcohol / No. Cases/Controls / OR (95% CI)				
				No / No / No	50/1471	1		
				No / No / Yes	0/75	-		
				No / Yes / No	175/1084	3.54 (2.54–4.94)		
				No / Yes / Yes	199/449	8.41 (5.94–11.90)		
				Yes-T− / No / No	5/83	1.60 (0.61–4.17)		
				Yes-T− / No / Yes	0/15	-		
				Yes-T− / Yes / No	10/49	4.89 (2.29–10.43)		
				Yes-T− / Yes / Yes	19/34	10.75 (5.53–20.90)		

Ref No.	Reference, study location and period	Organ site (ICD code)	Characteristics of study population	Tobacco		Alcohol			Comments/ Adjustment factors in study design or analysis
				Yes-T+	No	No	25/127	3.73 (2.20–6.31)	
				Yes-T+	No	Yes	7/26	4.28 (1.72–10.62)	
				Yes-T+	Yes	No	32/102	4.55 (2.74–7.56)	
				Yes-T+	Yes	Yes	114/119	13.44 (8.90–20.29)	

31 — Castellsague, et al. (2004) Spain, 1996–99 — Oral cavity and oropharynx (ICDO C1–C10) — 375 (304 men, 71 women); 375 (304 men, 71 women) non-cancer hospital-controls — Adjusted for age, sex, center, education

No. Cases/Controls OR (95% CI)	Alcohol (drinks/day)			
	Never drinker	1–2	3–5	6+
Never smoker	28/53 1	23/45 2.0 (0.9–4.4)	2/8 1.1 (0.2–6.4)	2/6 6.2 (1.0–39.2)
1–10 cigs/day	3/6 2.9 (0.6–14.8)	14/31 4.7 (1.7–12.9)	10/6 32.2 (8.1–127.1)	1/7 2.7 (0.3–26.5)
11–20 cigs/day	2/8 1.0 (0.2–6.0)	27/36 11.1 (4.0–30.6)	22/15 26.6 (8.6–82.0)	46/21 43.1 (15.0–123.8)
21+ cigs/day	2/8 1.9 (0.3–11.1)	22/43 8.2 (2.9–22.9)	40/31 22.0 (8.0–61.0)	131/49 50.7 (19.1–134.2)

25 — De Stefani, et al. (2004) Montevideo, Uruguay, 1997–2003 — Hypopharynx — 85 males cases; 640 hospital-based male controls — Adjusted for age, residence, urban/rural status, education, BMI

OR (95% CI	Alcohol (ml ethanol/day)		
	0–60 ml/day	61–120 ml/day	121+ ml/day
0–14 cigs/day	1	5.1 (1.1–23.3)	4.6 (0.8–25.6)
15–24 cigs/day	1.9 (0.3–12.8)	16.3 (4.2–62.9)	22.3 (5.8–86.3)
25+ cigs/day	4.3 (0.8–23.5)	5.6 (2.4–13.1)	9.4 (4.1–21.6)

41 — Rodriguez, et al. (2004) Italy and Switzerland, 1984–93, 1992–97 — Oral cavity and pharynx — 137 (113 men, 24 women) cases; 298 (226 men, 72 women) non-cancer hospital-based controls — Study populations from Franceschi (1990) and Franceschi (1999); Adjusted for education, marital status, BMI, coffee consumption (Matched variables: age, sex, study center)

No. Cases/Controls OR (95% CI)	Alcohol (drinks/day)		
	<6	6–<10	≥10
Never/ex-smokers (abstained 12+ mo)	22/157 1	4/26 1.9 (0.5–7.1)	5/8 15.7 (3.6–67.9)
1–15 cigarettes/day	9/31 2.4 (0.9–6.4)	9/4 21.2 (5.2–87.7)	2/3 8.1 (1.0–64.8)
≥15 cigarettes/day	20/43 8.3 (3.3–20.6)	24/10 44.2 (14.9–131.2)	39/16 48.1 (17.6–131.0)

Ref No.	Reference, study location and period	Organ site (ICD code)	Characteristics of study population	Tobacco	Alcohol	Comments/ Adjustment factors in study design or analysis
16	De Stefani, et al. (2007) Montevideo, Uruguay, 1988–2000	Oral cavity (excluding lip)	335 males cases; 1501 hospital-based non-cancer male controls			Adjusted for age, residence, urban/rural status, hospital, year at diagnosis, education, family history of cancer, occupation, vegetable and fruit intake, mate intake
					Oral cavity OR (95% CI) — Alcohol (ml ethanol/day): 0–60 ml/day; 61–120 ml/day; 121–240 ml/day; 241+ ml/day	
					0–9 cigs/day: 1; 3.5 (1.2–10.5); 2.9 (0.8–11.2); 1.9 (0.2–15.9)	
					10–19 cigs/day: 4.4 (2.1–9.4); 8.9 (3.9–20.4); 14.5 (6.1–34.2); 24.5 (8.3–72.1)	
					20–29 cigs/day: 4.8 (2.3–10.2); 24.1 (11.5–50); 21.2 (9.6–46.8); 50.5 (21–119)	
					30+ cigs/day: 6.5 (3.1–13.8); 29.6 (13.7–64); 42.5 (19.9–90); 33.4 (15.8–70)	
		Pharynx (excluding nasopharynx	441 males cases; 1501 hospital-based non-cancer male controls			
					Pharynx OR (95% CI) — Alcohol (ml ethanol/day): 0–60 ml/day; 61–120 ml/day; 121–240 ml/day; 241+ ml/day	
					0–9 cigs/day: 1; 0.9 (0.2–4.4); 2.5 (0.8–8.2); 9.8 (3.7–26.3)	
					10–19 cigs/day: 2.8 (1.4–5.6); 8.8 (4.3–17.9); 18.6 (9.1–38.0); 12.4 (4.0–38.7)	
					20–29 cigs/day: 3.7 (1.9–7.1); 16.8 (8.6–33.0); 31.4 (16.0–62); 53.2 (25–114)	
					30+ cigs/day: 4.7 (2.4–9.2); 24.0 (12.8–48); 36.4 (18.7–71); 43.8 (23.0–84)	
51	Hashibe, et al. (2009) International Consortium of Head and Neck Cancer. Combined analysis of 17 studies from US, South and Central American, European countries	Oral cavity (ICD9 140, 141, 143–5) Oro-pharynx/	2,993 cases; 15,751 controls			Adjusted for age, sex, education, race/ ethnicity, and study center
					Oral cavity OR (95% CI) — Alcohol (drinks/day): Never; 1–2 drinks/day; 3+ drinks/day	
					Never: 1; 0.88 (0.65–1.20); 1.05 (0.62–1.77)	
					1–20 cigs/day: 1.72 (1.17–2.53); 2.72 (1.47–5.04); 9.60 (5.04–18.28)	
					>20 cigs/day: 3.13 (1.14–8.59); 3.23 (1.84–5.67); 15.49 (7.24–33.14)	
		Hypo-pharynx (ICD9 146, 148)	4,040 cases; 15,751 controls			
					Pharynx OR (95% CI) — Alcohol (drinks/day): Never; 1–2 drinks/day; 3+ drinks/day	
					Never: 1; 1.26 (0.92–1.73); 2.94 (1.73–5.02)	

Ref No.	Reference, study location and period	Organ site (ICD code)	Characteristics of study population	Tobacco		Alcohol		Comments/ Adjustment factors in study design or analysis
				1–20 cigs/day	1.90 (1.34–2.68)	2.57 (1.72–3.83)	11.37 (6.50–19.89)	
				>20 cigs/day	2.83 (1.66–4.82)	4.10 (2.66–6.32)	14.29 (7.26–28.15)	

Table 5

Alcohol Risk among Non-Smokers on Oral Cavity and Pharyngeal Cancers

Ref No.	Reference, study location and period	Organ site (ICD code)	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk	95% CI	Adjustment factors in study design or analysis	Comments
53	Talamini, et al. (1990) Milan & Pordenone, Italy, 1986–89	Oral cavity and pharynx	27 (6 men, 21 women)	572 (288 men, 284 women) hospital-based controls matched on age and area of residence	Interviewer-administered questionnaire	**Total alcohol** <14 drinks/ week 14–55 >55 χ^2 for trend	1 1.5 2.2 4.08	0.6–3.7 0.2–27.9 0.04	Age, sex	Includes study population from Franceschi (1990)
54	Ng, et al. (1993) USA, 1977–91	Oral cavity and pharynx (ICD9 141, 143–146, 148, 149)	173 (73 men, 100 women) white cases in 8 US cities; histologically confirmed	613 (254 men, 359 women) hospital-based controls matched (up to 4:1 controls:cases) on age, sex, date of interview; excluded patients with tobacco related conditions	Interviewer-administered questionnaire	**Total alcohol** Non-drinker <1 OWE[1]/ day 1–2.9 3–6.9 7+ χ^2 for trend	Men/Women 1/1 1.3/0.9 2.4/0.9 2.9/0.4 4.4/2.6 11.7/0.00	Men/Women 0.6–3.1/0.5–1.6 1.0–5.6/0.3–2.6 1.1–7.6/0.0–7.1 1.4–13.7/0.5–13.3 p<0.001/NS		Non-smokers of study from Kabat (1994) [1]OWE: ounces of whiskey equivalent
55	Talamini, et al. (1998) Italy & Switzerland, 1992–97	Oral cavity and pharynx	60 (20 men, 40 women) cases from Pordenone, Rome, Latina (Italy) and Vaud (Switzerland); aged 22–77, 95% response rate, histologically confirmed	692 (346 men, 346 women) hospital-based controls, response rate 95%	Interviewer-administered questionnaire	**Total alcohol** Never drinkers <21 drinks/ week 21–34 35–55 ≥ 56 χ^2 for trend Ex-drinkers (abstain ≥ 1 yr)	1 0.8 0.8 5.0 5.3 6.2 2.0	0.4–1.6 0.2–2.7 1.5–16.1 1.1–24.8 p = 0.01 0.7–5.4	Age, sex, education, study center	Study population from Franceschi (2000)
52	Fioretti, et al. (1999) Milan & Pordenone, Italy, 1984–93	Oral cavity and pharynx	42 (10 men, 32 women) lifelong non-smoking cases from a network of general and teaching hospitals in	864 (442 men, 422 women) hospital-based lifelong non-smoking non-cancer controls matched on age and area of	Interviewer-administered questionnaire	**Total alcohol** Non-drinkers >0–<3 drinks/day ≥3	1 3.4 2.6 3.3 3.3 1.0	1.1–10.1 0.7–9.3 1.1–9.6 0.7–16.4 0.2–6.1	Age, sex, education, study center	Study population from Franceschi (1990)

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			Milan and Pordenone; histologically confirmed	residence; excluded patients with tobacco related conditions		Wine drinkers Beer drinkers Spirit drinkers				
56	Hashibe, et al. (2007) International Consortium of Head and Neck Cancer. Combined analysis of 15 studies from US, South and Central American, European countries	Oral cavity (ICD9 140, 141, 143–5)	383 cases who never used tobacco	5,775 controls who never used tobacco	Interview or self-administrated questionnaire	**Total alcohol** Never Ever <1 drink/day 1–2 drinks/day 3–4 drinks/day >=5 drinks/day *p* for trend **Years of drinking** Never 1–10 years 11–20 years 21–30 years 31–40 years >40 years	1.00 1.17 1.14 1.64 1.11 1.23 1.00 2.36 1.09 0.81 1.29 1.15	0.92–1.48 0.8–1.63 1.19–2.25 0.57–2.15 0.59–2.57 0.032 1.43–3.88 0.65–1.85 0.49–1.33 0.88–1.9 0.77–1.73	Age, sex, race/ethnicity, education, study center	
		Oro-pharynx/ Hypo-pharynx (ICD9 146, 148)	369 cases who never used tobacco	5,775 controls who never used tobacco		**Total alcohol** Never Ever <1 drink/day 1–2 drinks/day 3–4 drinks/day >=5 drinks/day *p* for trend **Years of drinking** Never 1–10 years 11–20 years 21–30 years 31–40 years >40 years	1.00 1.38 1.39 1.66 2.33 5.50 1.00 1.76 1.34 1.95 1.44 1.51	0.99–1.94 0.99–1.96 1.18–2.34 1.37–3.98 2.26–13.4 <0.001 0.99–3.14 0.81–2.11 1.37–2.77 0.78–2.66 0.68–3.37		
		Oral cavity or	155 cases who never used tobacco	4983 controls who never used tobacco		**Total alcohol** Never	1.00 1.09 1.08 1.24 2.32 0.77 1.00 2.59 1.09 1.26 0.86 0.92	0.77–1.54 0.67–1.75 0.77–1.99 1.24–4.34 0.27–2.18 0.891 1.38–4.86 0.56–2.11 0.73–2.17 0.47–1.57 0.49–1.71		

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		pharynx NOS (ICD9				Ever <1 drink/day 1–2 drinks/ day 3–4 drinks/ day >=5 drinks/ day *p* for trend **Years of drinking** Never 1–10 years 11–20 years 21–30 years 31–40 years >40 years				