

## Tobacco and alcohol use and oral cancer in Puerto Rico<sup>†</sup>

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### Abstract

**Objectives:** To determine risk for oral cancer in Puerto Rico associated with use of alcohol and tobacco.

**Methods:** In Puerto Rico, alcohol and tobacco use were compared among nonsalivary gland cancers of the mouth and pharynx ( $n = 342$ ), cancers of major and minor salivary glands ( $n = 25$ ) and 521 population-based controls.

**Results:** Alcohol (usual use,  $P_{\text{trend}} < 0.0001$  for men and  $P_{\text{trend}} = 0.02$  for women) and tobacco (usual use,  $P_{\text{trend}} < 0.0001$ , for both men and women) were strong independent risk factors for oral cancer in Puerto Rico, with a multiplicative effect from combined exposures. Risks did not vary systematically by use of filter *vs.* nonfilter cigarettes. Risks with use of other forms of smoked tobacco were about sevenfold among both men and women. Risks decreased only gradually after cessation of tobacco and alcohol use. Tobacco use, but not alcohol, was linked to cancers of the salivary glands. The burden of oral cancer due to alcohol and tobacco use in Puerto Rico (76% for men, 52% for women) agreed closely with earlier estimates for the mainland US population, while about 72% of salivary gland cancer (men and women, combined) was due to tobacco use.

**Conclusions:** Excess risks for oral cancer in Puerto Rico are largely explained by patterns of alcohol and tobacco use. Smoking filter *vs.* nonfilter cigarettes does not alter risk, while cessation of alcohol and tobacco use appears to reduce risk only gradually.

### Introduction

Incidence of cancers of the oral cavity and pharynx (excluding lip and nasopharynx) is substantially greater among residents of Puerto Rico (men, 18.5 per 100,000; women, 4.5 per 100,000) [1] than among US Hispanics of the 50 states and District of Columbia (mainland US) (men, 8.9 per 100,000; women, 2.7 per 100,000) [2] or several other Hispanic populations in Central and South America [3]. Among men, the rates are intermediate to those for mainland US non-Hispanic Whites (15.1 per 100,000) and Blacks (20.4 per 100,000), while among women, the rates are slightly lower than those for mainland non-Hispanic Whites (6.1 per 100,000) and Blacks (5.8 per 100,000) [2].

Tobacco and alcohol are the major causes of squamous cell oral and pharyngeal cancer [4, 5], but questions remain about the effects of specific tobacco products, the interrelationship of tobacco and alcohol use as determinants of risk, and the rate of decline in risk with cessation of use. Also, little is known about their impact on cancers of the major and minor oral salivary glands. In a population-based case-control study in Puerto Rico, we evaluated the role of tobacco and alcohol in the etiology of nonsalivary gland cancers of the mouth and pharynx (hereafter referred to as oral cancer) and cancers of the major and minor salivary glands (hereafter referred to as salivary gland cancer).

### Methods

All Puerto Rican men and women, aged 21 to 79 years, diagnosed with a newly incident histologically confirmed

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cancer of the oral cavity (excluding lip and major salivary glands) and pharynx (excluding nasopharynx) (ICD-9 [6] codes 141, 143–146, 148, 149) between December 1992 and February 1995, were included for study. Beginning in February 1993, cancers of the major salivary glands (ICD-9 [6] code 142) were also included. The Central Cancer Registry of the Department of Health of Puerto Rico collects data on all malignant tumors occurring on the island through systematic searches for cases in the vital statistics office and in all hospital clinics, pathology laboratories, radiotherapy departments, and offices of private physicians throughout the island. To expedite case ascertainment for this study, patients were identified through independent contacts with island pathology laboratories as well as the Central Cancer Registry. Abstractors recorded basic demographic information and tumor characteristics. Upon review, persons with cancers of the major and minor salivary glands were designated as salivary gland cases – based upon site (ICD-9 [6] code 142) or tumor morphology (ICD-O [7] codes 8082, lymphoepithelial carcinoma; 8140, adenoma; 8200, adenoid cystic carcinoma; and 8430, mucoepidermoid carcinoma) (regardless of site of occurrence in the oral cavity). All other cases (*i.e.*, the nonsalivary cancers) were designated as the oral cancer cases. Oral cancers were further classified by site as tumors of the tongue, other mouth, or pharynx. One oral cancer of uncertain origin (mouth or pharynx) was classified to ‘other mouth’.

Population controls were selected from residents of Puerto Rico. For subjects younger than 65 years old, male-designated and female-designated households were selected from dwelling unit enumeration, within a two-stage area probability sample. Residents of the selected dwelling units were screened and study controls selected using age and gender-specific sampling rates to approximate a 1:1 ratio with the cases. Controls aged 65 years and over were selected from the rosters of the Health Care Financing Administration (HCFA) by systematic sampling, after a random start, to approximate the distribution of cases with regard to age (65–69 yrs, 70–74 yrs, 75–79 yrs) and gender. Three separate samplings from HCFA rosters were made during the course of field work, with approximately one-third of the required controls identified during each sampling.

Training sessions were carried out for household enumeration, interviewing, and biologic sample collection. Tracing activities were necessary to locate HCFA controls. Introductory letters were sent to cases (after physician consent) and to controls, followed by telephone calls to arrange personal interviews. Beginning in February 1993, cases and controls were interviewed, generally in their homes, using a structured pre-tested

questionnaire in Spanish. Detailed information was collected on tobacco use (including tobacco type, age started, age stopped, total years and amount usually used) and alcohol use (including beverage type, age started, age stopped, total years used and usual weekday and weekend consumption), demographic characteristics, medical and dental history, diet, occupation, and other selected factors. Cigarette smokers were persons who had smoked at least 100 cigarettes in their lifetime. Persons were considered to have used cigars, pipe, snuff, or chewing tobacco when these products were used for six months or more. Lifetime consumption of cigarettes was estimated from usual daily consumption of cigarettes and total years of use. Persons were considered to be alcohol drinkers if they had at least 12 drinks of any kind of alcohol in their lifetime. Lifetime alcohol consumption was estimated from usual weekly intake (combining weekday and weekend amounts) of alcoholic drinks (with each drink equivalent to 1.5 ounces of liquor, 4 ounces of wine, or 12 ounces of beer) and total years of use. Refusal conversion and re-interview procedures were implemented to ensure high response rates and to verify the quality of the interview data.

Odds ratios (OR) were estimated by unconditional logistic regression analysis [8], adjusted for age. Tobacco-specific ORs were adjusted for lifetime alcohol intake and alcohol-specific ORs were adjusted for lifetime tobacco use. In selected analyses, additional adjustment was carried out for residence (San Juan metropolitan area, other), education (> 12 years, 12 years/high school graduate, 8–11 years, < 8 years), current household income (\$20,000 or more, \$15,000–19,999, \$10,000–14,999, and < \$10,000), and consumption of raw fruits and vegetables (quartiles of consumption). To test for trend, the exposure variable was treated as continuous in the model with each level of the categorical variable represented by the median value of that category among the controls. The population attributable risk was estimated with adjustment for age and, where appropriate, for gender [9].

After exclusion of two controls with self-reported histories of oral cancer, 519 cases (429 males, 90 females) and 629 controls (503 males, 126 females) were eligible for study. Interview response rates were lower for male than female cases (69% and 77%, respectively), but were similar among male and female controls (83% and 82%, respectively). Response rates varied by tumor type from 64% for tongue cancer to 79% for other tumors of the mouth (Table 1). Cases and controls were similar with respect to place of residence, but cases reported less education and lower income than controls. Female cases tended to be older than female controls (Table 2).

Table 1. Study participation, Puerto Rico, 1992–95

Study status	Controls		All Cancer		Cancer type			
	Males	Females	Males	Females	Oral (nonsalivary gland)			Salivary gland
					Tongue	Other mouth	Pharynx	
Eligible subjects	503	126	429	90	145	153	189	32
Participants	417	104	298	69	93	121	128	25
(Percent)	(83%)	(82%)	(69%)	(77%)	(64%)	(79%)	(68%)	(78%)
Nonparticipants	86	22	131	21	52	32	61	7
Too ill/deceased	12	2	82	11	29	19	42	3
Refusal/incomplete	43	5	23	4	12	4	9	2
Untraced/moved	31	15	26	6	11	9	10	2

Table 2. Selected characteristics of study participants, Puerto Rico, 1992–95

Characteristic	Males		Females	
	All cases	Controls	All cases	Controls
Study participants	298	417	69	104
Age				
< 55	21%	25%	15%	34%
55-69	51%	50%	42%	36%
70 +	28%	25%	43%	30%
Residence				
Metro San Juan	27%	26%	23%	24%
Other	73%	74%	77%	76%
Education				
> 12 years	10%	21%	10%	25%
12 years/ high school	18%	20%	6%	15%
8-11 years	24%	17%	19%	12%
< 8 years	48%	42%	65%	47%
Unknown	0%	0%	0%	1%
Income				
\$20,000 +	5%	15%	7%	11%
\$15,000–19,999	7%	13%	3%	12%
\$10,000–14,999	27%	27%	22%	13%
< \$10,000	60%	41%	68%	61%
Unknown	1%	4%	0%	3%

**Results**

*Oral cancer*

Any cigarette use was associated with an increased risk for oral cancer among men (OR = 3.9) and women (OR = 4.9). Risks increased with increasing cigarette use, whether estimated by usual daily amount ( $P_{\text{trend}} < 0.0001$ , for both men and women) (Table 3) or by cumulative lifetime consumption ( $P_{\text{trend}} < 0.0001$ , for both men and women) (data not shown). Risks were elevated for cancer of the tongue (for men: OR = 2.3, 95% confidence interval [CI] = 0.9–5.9 and for women: OR = 3.7, CI = 1.1–12.4), other mouth (for men:

OR = 5.4, CI = 1.8–15.9 and for women: OR = 4.2, CI = 1.2–14.8), and pharynx (for men: OR = 4.8, CI = 1.9–12.2 and for women: OR = 7.2, CI = 1.7–31.2). The level of risk, for a given amount of cigarette consumption, tended to be greater for women than for men. Further statistical adjustment for residence, education, income, and consumption of raw fruits and vegetables did not substantially alter the findings (data not shown).

Risks were greatest for recent cigarette smokers (ORs = 7.5 for men, 14.1 for women). After smoking cessation, the risks decreased gradually but remained elevated up to 19 years later. These estimates were not changed substantially by excluding from analysis the users of other types of tobacco (pipes, cigars, and chewing tobacco) (data not shown). Even among long-term quitters (20+ years), the risks tended to increase with amount of former use ( $P_{\text{trend}} = 0.01$ ), with a threefold excess risk (OR = 3.1, CI = 1.2–8.1) among those who formerly OK smoked 20+ cigarettes per day (data not shown). Men who smoked mostly nonfilter cigarettes had marginally lower risks of oral cancer (after adjustment for age and lifetime alcohol and cigarette use) than men who smoked both filter and nonfilter cigarettes (OR = 1.9; 78 cases, CI = 0.8–4.5) or mostly filter cigarettes (OR = 1.3; 125 cases, CI = 0.5–3.0).

Use of other forms of tobacco was associated with an approximately sevenfold increased risk for oral cancer (all sites), among both men and women (Table 3), with excess risks for pipe (10 cases, OR = 133, CI = 7.4–2380) and cigar use (10 cases, OR = 8.9, CI = 2.0–38.9) among men, and for cigar use (six cases, OR = 28.8, CI = 3.1–1418, exact method) among women. Only one person, a male oral cancer case, used smokeless tobacco.

A history of alcohol use was associated with an increased risk for oral cancer among men (OR = 2.5), but not among women (OR = 1.1). Among men, risks increased with increasing average use ( $P_{\text{trend}} < 0.0001$ ) (Table 3) and total lifetime consumption ( $P_{\text{trend}} < 0.0001$ ) (data not shown). Risks were elevated, parti-

Table 3. Risk for oral cancer (except salivary gland), by tobacco and alcohol use

Consumption pattern	Men				Women			
	Cases	Controls	OR <sup>a</sup>	(CI) <sup>b</sup>	Cases	Controls	OR <sup>a</sup>	(CI) <sup>b</sup>
<i>Tobacco use<sup>c</sup></i>								
Nonsmoker (referent)	16	140	1.0 <sup>c</sup>		14	71	1.0 <sup>c</sup>	
Cigarette smoker (any)	259	270	3.9	(2.1–7.1)	36	30	4.9	(2.0–11.6)
Used other tobacco only	11	7	7.6	(2.1–27.7)	6	3	7.1	(1.4–34.6)
Usual use (cigarettes per day)								
1–9	9	61	0.9	(0.4–2.4)	5	9	2.2	(0.6–8.4)
10–19	30	53	2.8	(1.3–6.0)	6	7	4.3	(1.1–16.1)
20–39	118	89	6.0	(3.1–11.4)	19	12	6.4	(2.1–19.6)
40+	101	65	4.9	(2.5–9.7)	6	2	28.2	(3.7–216.0)
<i>P</i> <sub>trend</sub>			<0.0001				0.0001	
Years since last smoked cigarettes								
Recent use <sup>f</sup>	183	103	7.5	(3.9–14.4)	23	10	14.1	(4.2–47.2)
Quit 2–9 years	37	38	4.1	(1.8–8.9)	8	5	8.7	(2.2–35.2)
Quit 10–19 years	20	56	2.0	(0.9–4.5)	2	4	2.1	(0.3–13.9)
Quit 20+ years	18	73	1.2	(0.5–2.7)	2	10	0.8	(0.1–4.2)
<i>Alcohol use<sup>d</sup></i>								
Nondrinker (referent)	9	67	1.0 <sup>d</sup>		26	70	1.0 <sup>d</sup>	
Alcohol drinker	277	350	2.5	(1.1–5.5)	30	34	1.1	(0.4–2.7)
Usual use (drinks per week)								
1–7	19	117	0.8	(0.3–2.1)	13	30	0.8	(0.3–2.1)
8–21	28	87	1.4	(0.6–3.4)	1	1	0.9	(0.0–17.0)
22–42	49	55	3.3	(1.4–8.0)	12	1 <sup>e</sup>	9.1	(0.9–94.2)
>42	164	58	7.7	(3.3–17.9)				
<i>P</i> <sub>trend</sub>			<0.0001				0.02	
Years since last drank alcohol								
Recent use <sup>f</sup>	163	216	2.4	(1.0–5.4)	15	22	1.2	(0.4–3.4)
Quit 2–9 years	60	47	3.6	(1.5–9.0)	6	4	1.0	(0.2–5.4)
Quit 10–19 years	34	40	2.7	(1.0–7.0)	5	4	1.1	(0.2–6.4)
Quit 20+ years	20	46	1.3	(0.5–3.6)	4	4	0.9	(0.2–4.8)

<sup>a</sup> OR = Odds ratio.

<sup>b</sup> CI = 95% confidence interval.

<sup>c</sup> Odds ratio, adjusted for age and alcohol use.

<sup>d</sup> Odds ratio, adjusted for age and tobacco use.

<sup>e</sup> For women, 22+ drinks per week.

<sup>f</sup> Recent use: up to two years prior to interview.

cularly among men, for cancer of the tongue (men: OR = 3.8, CI = 0.8–17.0; women: OR = 1.0, CI = 0.3–3.4), other mouth (men: OR = 2.7, CI = 0.8–10.0; women: OR = 1.9, CI = 0.6–6.1), and pharynx (men: OR = 2.5, CI = 0.8–7.6; women: OR = 1.4, CI = 0.3–6.3). Risks were similar for men who were recent users of alcohol (OR = 2.4) and those who had quit two to nine (OR = 3.6) or 10–19 years prior to interview (OR = 2.7), but only a slight excess was seen for those who had quit for 20 or more years (OR = 1.3). Few women drank more than 21 drinks per week, but risk in this group (OR = 9.1) was similar to that observed among men who consumed similar quantities.

Among men, nonsmokers who drank heavily (>42 drinks per week) had about a sixfold increased risk for

oral cancer, while nondrinkers and light drinkers (1–7 drinks per week) who smoked 20 or more cigarettes per day showed excesses of two- to fourfold (Table 4). Joint exposure to alcohol and tobacco resulted in risks consistent with independent effects, on a multiplicative scale, with excesses of 40- to 50-fold among heavy users of both products. Among women (data not shown), risks were not elevated among those who smoked and drank lightly (<20 cigarettes per day, 1–7 drinks per week) (10 cases, OR = 1.2, CI = 0.5–3.2), but were increased among heavy smokers and light drinkers (20+ cigarettes per day, 1–7 drinks per week) (10 cases, OR = 4.4, CI = 1.4–13.7), and among heavy smokers and drinkers (20+ cigarettes per day, 8+ drinks per week) (12 cases, OR = ∞, CI = 9.0–∞, exact method).

Table 4. Risk for oral cancer (except salivary gland) among men, by alcohol and cigarette use

Cigarette use	Alcohol use (drinks per wk)				
	None	1-7	8-21	22-42	42+
None					
OR <sup>a</sup>	1.0 <sup>b</sup>	0.2	0.6	1.6	6.4
(CI) <sup>c</sup>		(0.0-1.5)	(0.1-3.5)	(0.3-9.6)	(1.3-31.9)
Cases/controls	6/44	1/49	2/24	2/10	4/5
Low					
OR <sup>a</sup>	-	1.6	1.3	3.7	5.5
(CI) <sup>c</sup>		(0.5-4.8)	(0.3-5.7)	(0.8-16.4)	(1.6-19.0)
Cases/controls	0/13	10/47	3/16	11/7	9/12
10-19 cigarettes per day					
OR <sup>a</sup>	11.3	1.3	1.8	18.6	12.2
(CI) <sup>c</sup>	(0.6-213.0)	(0.2-7.2)	(0.4-8.3)	(4.1-84.0)	(3.3-45.6)
Cases/controls	1/1	2/12	3/13	8/4	10/7
20-39 cigarettes per day					
OR <sup>a</sup>	1.8	3.8	6.2	11.3	50.2
(CI) <sup>c</sup>	(0.2-19.0)	(1.2-12.0)	(2.0-19.3)	(3.7-34.5)	(16.6-152.0)
Cases/controls	1/5	10/21	13/17	19/14	60/10
40+ cigarettes per day					
OR <sup>a</sup>	2.4	4.3	4.1	10.5	38.7
(CI) <sup>c</sup>	(0.2-27.6)	(1.1-16.7)	(0.9-18.7)	(2.9-37.9)	(13.6-110.0)
Cases/controls	1/3	6/10	4/7	10/8	67/15

<sup>a</sup> OR = Odds ratio, adjusted for age.

<sup>b</sup> Referent.

<sup>c</sup> CI = 95% confidence interval.

### Salivary gland cancer

Salivary gland cancer was associated with cigarette use among men (OR = 9.0) and women (OR = 4.2) (Table 5). Risks increased by average number of cigarettes smoked daily (for men,  $P_{\text{trend}} < 0.01$  and for women,  $P_{\text{trend}} = 0.07$ ) and by cumulative lifetime exposure (for men,  $P_{\text{trend}} < 0.02$  and for women,  $P_{\text{trend}} = 0.03$ ). Alcohol consumption was not associated with salivary gland cancer.

### Attributable risks

The attributable risk for oral cancer associated with alcohol and/or tobacco use was 76% (CI = 65-87%) among men and 52% (CI = 28-75%) among women. The attributable risk for salivary gland cancer (men and women, combined) due to tobacco use was 72% (CI = 35-93%).

### Discussion

This population-based case-control study in Puerto Rico confirmed the link between oral cancer and use of tobacco and alcohol. Risks increased with increasing exposure to tobacco and alcohol independently, with multiplicative effects following joint exposure to these

products. The burden of oral cancer due to these behaviors in Puerto Rico (76% for men, 52% for women) is consistent with earlier estimates for the mainland US population (80% for men, 61% for women) [10], which probably accounts for the similar oral cancer incidence in Puerto Rico and among mainland US non-Hispanics [2]. The higher risks associated with tobacco use among women than among men has also been previously observed [4, 11].

In our study, risks did not vary substantially by use of filter vs. nonfilter cigarettes, in agreement with several other studies of oral cancer [11-13], suggesting a role for gas phase constituents of tobacco combustion, which are not effectively trapped by cigarette filters. Although attention has been given to particulate phase carcinogens associated with tobacco combustion [4], recent studies have shown gas phase-derived acrolein and crotonaldehyde-DNA adducts in the oral mucosa of smokers [14]. Tobacco may also have other effects contributing to carcinogenic risks in the oral cavity, as illustrated by reduction in antioxidant folate levels in buccal cells of smokers [15].

The declining risks we observed after smoking cessation have been noted in previous studies of oral cancer [10, 16, 17] and dysplasia [18]. In a large mainland US investigation, risks were clearly excessive only among current smokers [10], while in Brazil [13] the risks decreased mainly among users of hand-rolled cigarettes,

Table 5. Risk for salivary gland cancer, by tobacco and alcohol use

Consumption pattern	Men				Women			
	Cases	Controls	OR <sup>a</sup>	(CI) <sup>b</sup>	Cases	Controls	OR <sup>a</sup>	(CI) <sup>b</sup>
Tobacco use								
Nonsmoker (referent)	1	140	1.0 <sup>c</sup>		4	71	1.0 <sup>c</sup>	
Cigarette smoker	11	270	9.0	(1.0–77.3)	8	30	4.2	(1.1–17.0)
Other tobacco only	0	7	0.0 <sup>c</sup>	(0.0–785.6)	1	3	3.8	(0.2–61.3)
Usual use (cigarettes per day)								
1–9	1	61	3.7	(0.2–63.5)	2	9	3.6	(0.5–23.7)
10–19	2	53	9.0	(0.7–114.0)	2	7	4.1	(0.6–31.0)
20–39	4	89	10.0	(1.0–103.0)	3	12	3.8	(0.6–22.0)
40+	4	65	14.6	(1.4–152.0)	1	2	9.7	(0.7–143.0)
<i>P</i> <sub>trend</sub>			0.02				0.07	
Cumulative lifetime consumption (packs of cigarettes)								
1–4,999	2	83	5.1	(0.4–61.0)	2	13	2.6	(0.4–17.0)
5,000–9,999	2	49	10.6	(0.8–141.0)	2	5	6.4	(0.8–51.8)
10,000+	7	135	12.3	(1.3–115.0)	4	11	6.1	(1.2–30.6)
<i>P</i> <sub>trend</sub>			0.02				0.03	
Alcohol use								
Nondrinker (referent)	3	67	1.0 <sup>d</sup>		6	70	1.0 <sup>d</sup>	
Alcohol drinker	9	350	0.3	(0.1–1.2)	7	34	1.6	(0.4–6.2)
Lifetime consumption (drinks)								
< 5000	1	77	0.2	(0.0–1.8)	5	23	1.8	(0.4–7.9)
> 5000	8	236	0.4	(0.1–1.6)	1	9	1.0	(0.1–10.5)

<sup>a</sup> OR = Odds ratio.

<sup>b</sup> CI = 95% confidence interval.

<sup>c</sup> Odds ratio, adjusted for age and alcohol use.

<sup>d</sup> Odds ratio, adjusted for age and tobacco use.

and in Italy [19], mainly for cases of pharyngeal origin. In our study, a residual excess risk was seen up to 20 years after cessation of tobacco use and for longer periods among former heavy smokers.

Although the effects of quitting or reducing alcohol use are not well-documented in previous studies [5, 20], the temporal pattern of risk in our study resembled that for smoking cessation, with risks remaining elevated for up to 20 years. As moderation or cessation of tobacco and alcohol use are key elements in oral cancer prevention [21], more detailed information on the time-specific risks after cessation of smoking and drinking would help to appropriately tailor prevention programs.

Occurrence of salivary gland tumors has been increasing in the US, but the reasons for this are unclear [22]. Benign cystadenolymphoma of the parotid gland (Warthin's tumor) has been linked to tobacco use [23–25], with one study [25] reporting eightfold and 17-fold tobacco-associated risks for men and women, respectively. While early studies have suggested an increased risk of salivary gland malignancies associated with tobacco use [26, 27], a recent population-based study in northern California including 150 cases [28] found that current smoking (OR = 2.1) and heavy alcohol consumption (OR = 2.5) were associated with excess risks in men, but

not in women. We found tobacco-related risks for cancers of the major and minor salivary glands (combined) among both men and women, but no association with intake of alcohol. Larger studies of salivary gland cancer may be needed to clarify these results.

In summary, our case-control study revealed that alcohol and tobacco were strong independent risk factors for oral cancer in Puerto Rico, with a multiplicative effect from combined exposures. Alcohol and tobacco use contributed to about half of the oral cancer cases among women and about three-quarters of the cases among men. Smoking filter and nonfilter cigarettes elevated risk to a similar extent, and cigar and pipe use also increased risk. We also found that cessation of tobacco and alcohol use only gradually lowered the risks for oral cancer. In a small group of salivary gland cancers, tobacco use increased risk, while no effect was seen for alcohol.

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