

Supplementary Table S1. Characteristics of the individual studies from the International Head and Neck Cancer Epidemiology (INHANCE) Consortium used in the current analysis. INHANCE consortium.

Study name, location	Case source	Age eligibility	Case participation rate, %	Control source	Control participation rate, %	Matched factors	Recruitment period
Milan (1984-1989), Italy	Hospital	<80	95 ^a	Hospital - unhealthy	95 ^a	--	1984-1989
Aviano, Italy	Hospital	>18	>95 ^a	Hospital - unhealthy	95 ^a	--	1987-1992
France (1987-1992), France	Hospital	NA	95 ^a	Hospital - unhealthy	95 ^a	Age, sex, hospital	1987-1992
Italy Multicenter	Hospital	18-80	>95	Hospital - unhealthy	>95	--	1990-1999
Switzerland	Hospital	<80	>95	Hospital - unhealthy	>95	--	1991-1997
New York, NY, USA (multicenter)	Hospital	21-80	91	Hospital- unhealthy	97	Age, sex, hospital, year of interview	1981-1990
Seattle (1985-1995), WA, USA	Cancer registry	18-65	54.4,63.3 ^b	Random digit dialing	63.0,60.9 ^b	Age, sex	1985-1995
Iowa, IA, USA	Hospital	>18	87	Hospital - unhealthy	92	Age, sex	1993-2006
North Carolina (1994-1997), NC, USA	Hospital	>17	88	Hospital - unhealthy	86	Age, sex	1996-1997
Tampa, FL, USA	Hospital	≥18	98	Hospital - noncancer	90	Age, sex, ethnicity	1994-2003
Los Angeles, CA, USA	Cancer registry	18-65	49	Neighborhood	68	Age, sex, neighborhood	1999-2004
Houston, TX, USA	Hospital	≥18	95	Hospital visitors	>80	Age, sex, ethnicity	2001-2006
Puerto Rico	Cancer registry	21-79	71	Residential records (healthy population)	83	Age, sex	1992-1995
Latin America	Hospital	15-79	95	Hospital - unhealthy	86	Age, sex, ethnicity, city	2000-2003
International Multicenter, IARC	Hospital	NA	88,7	Hospital/Community	87,3	Age, sex, center	1992-1997
Boston, MA, USA	Hospital	≥18	88,7	Residential records	48,7	Age, sex, neighborhood	1999-2003
Sao Paulo, Brazil	Hospital	NA		Hospital-unhealthy		age, sex, city of residence, hospital	2002-2007
New York (MSKCC), NY, USA	Hospital	NA	--	Blood donors	--	Age, sex	1992-1994
Seattle-Leo, WA, USA	Cancer registry	20-74	81	Random digit dialing	75	Age, sex	1983-1987
Western Europe (ARCAGE)	Hospital	NA	82	Hospital-unhealthy (population-based for UK centers)	68	Age, sex, ethnicity, city	2000-2005

Japan (2001-2005)	Cancer Hospital	20-79	97,00	Hospital - unhealthy	97,00	Age, sex	2001-2005
North Carolina (2002-2006), NC, USA	Cancer registry	20-80	82	DMV files	61	Age, sex, ethnicity	2002-2006
France Multicenter (2001-2007)	Cancer registry	<=75	82,5	Random digit dialing	80,6	Age, sex, region	2001-2007
Baltimore, MD, USA	Hospital	NA	100	Hospital - benign conditions	70	age, sex, HPV status	2000-2005
Beijing, China	Hospital	18-80	100	Hospital	100	Age, sex	1988-1989
Milan (2006-2009), Italy	Hospital	18-80	>95	Hospital	>95	----	2006-2009

ABBREVIATIONS: ARCAGE: Alcohol-Related Cancers And Genetic susceptibility in Europe; DMV: Department of Motor Vehicles; HPV: Human Papilloma Virus; IARC: International Agency for Research on Cancer; MSKCC: Memorial Sloan Kettering Cancer Center; NA: Not Available.

^a Participation rate was not formally assessed, estimated response rate reported.

^b Two response rates are reported because data were collected in two population-based case-control studies, the first from 1985 to 1989 among men and the second from 1990 to 1995 among men and women.

Supplementary Table S2. Distribution of cases of oral cavity, oropharyngeal, hypopharyngeal, and laryngeal cancers, and controls according to selected variables. INHANCE Consortium

	Controls		Oral cavity		Oropharynx		Hypopharynx		Larynx	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
TOTAL	24,234	(100)	4085	(100)	3359	(100)	983	(100)	3340	(100)
Sex^a										
Female	7533	(31.1)	1552	(38.0)	780	(23.2)	138	(14.0)	533	(16.0)
Male	16,701	(68.9)	2533	(62.0)	2579	(76.8)	845	(86.0)	2807	(84.0)
Age (years)^a										
<40	1720	(7.1)	284	(7.0)	124	(3.7)	7	(0.7)	68	(2.0)
40 to 44	1711	(7.1)	234	(5.7)	211	(6.3)	38	(3.9)	116	(3.5)
45 to 49	2479	(10.2)	442	(10.8)	449	(13.4)	104	(10.6)	294	(8.8)
50 to 54	3547	(14.6)	645	(15.8)	617	(18.4)	184	(18.7)	493	(14.8)
55 to 59	4217	(17.4)	743	(18.2)	727	(21.6)	211	(21.5)	682	(20.4)
60 to 64	3944	(16.3)	670	(16.4)	542	(16.1)	182	(18.5)	671	(20.1)
65 to 69	3431	(14.2)	492	(12.0)	409	(12.2)	144	(14.6)	603	(18.1)
70 to 74	2304	(9.5)	336	(8.2)	206	(6.1)	92	(9.4)	310	(9.3)
≥75	881	(3.6)	239	(5.9)	74	(2.2)	21	(2.1)	103	(3.1)
Study name										
Aviano	652	(2.7)	52	(1.3)	71	(2.1)	38	(3.9)	91	(2.7)
Baltimore	162	(0.7)	36	(0.9)	83	(2.5)	4	(0.4)	31	(0.9)
Beijing	380	(1.6)	377	(9.2)						
Boston	400	(1.7)	90	(2.2)	145	(4.3)	22	(2.2)	68	(2.0)
France (1987-1992)	194	(0.8)	41	(1.0)	50	(1.5)	27	(2.7)	127	(3.8)
France Multicenter (2001-2007)	3149	(13.0)	343	(8.4)	489	(14.6)	275	(28.0)	368	(11.0)
Houston	712	(2.9)	182	(4.5)	306	(9.1)	30	(3.1)	108	(3.2)
International Multicenter	1297	(5.4)	640	(15.7)	224	(6.7)			2	(0.1)
Iowa	550	(2.3)	173	(4.2)	97	(2.9)	7	(0.7)	60	(1.8)
Italy Multicenter	2246	(9.3)	126	(3.1)	193	(5.7)	77	(7.8)	324	(9.7)
Japan (2001-2005)	2796	(11.5)	100	(2.4)	63	(1.9)	63	(6.4)	80	(2.4)
Latin America	993	(4.1)	199	(4.9)	154	(4.6)	66	(6.7)	367	(11.0)
Los Angeles	815	(3.4)	34	(0.8)	93	(2.8)	8	(0.8)	51	(1.5)
Milan (1984-1989)	1450	(6.0)	40	(1.0)	32	(1.0)	25	(2.5)	229	(6.9)
Milan (2006-2009)	568	(2.3)	64	(1.6)	10	(0.3)	9	(0.9)	145	(4.3)
MSKCC	89	(0.4)	34	(0.8)	5	(0.1)	5	(0.5)	24	(0.7)
New York Multicenter	1098	(4.5)	303	(7.4)	286	(8.5)	17	(1.7)	123	(3.7)
North Carolina (1994-1997)	157	(0.6)	28	(0.7)	24	(0.7)	10	(1.0)	25	(0.7)
North Carolina (2002-2006)	962	(4.0)	99	(2.4)	218	(6.5)	33	(3.4)	239	(7.2)
Puerto Rico	278	(1.1)	25	(0.6)	35	(1.0)	10	(1.0)		
Sao Paulo	1145	(4.7)	347	(8.5)	111	(3.3)	52	(3.4)	224	(6.7)
Seattle (1985-1995)	502	(2.1)	160	(3.9)	113	(3.4)				
Seattle-Leo	431	(1.8)	113	(2.8)	85	(2.5)	29	(3.0)	116	(3.5)
Switzerland	823	(3.4)	109	(2.7)	110	(3.3)	72	(7.3)	111	(3.3)
Tampa	738	(3.0)	16	(0.4)	37	(1.1)	1	(0.1)	38	(1.1)
Western Europe	1647	(6.8)	354	(8.7)	325	(9.7)	103	(10.5)	389	(11.6)

Continues

Supplementary Table S2. Continued

Race^a										
Asian and Pacific Islanders	3779	(15.6)	833	(20.4)	132	(3.9)	64	(6.5)	87	(2.6)
Black	631	(2.6)	149	(3.6)	108	(3.2)	30	(3.1)	109	(3.3)
Hispanic	304	(1.3)	29	(0.7)	37	(1.1)	2	(0.2)	7	(1.0)
Others and Brazilians	2267	(9.3)	564	(13.8)	301	(9.0)	121	(12.3)	598	(17.9)
White	17,253	(71.2)	2510	(61.4)	2781	(82.8)	766	(77.9)	2514	(75.3)
Education^a										
No education	980	(4.0)	472	(11.6)	55	(1.6)	32	(3.3)	94	(2.8)
≤Junior high school	8408	(34.7)	1341	(32.8)	969	(28.8)	409	(41.6)	1495	(44.8)
Some high school	4340	(17.9)	787	(19.3)	715	(21.3)	257	(26.1)	632	(18.9)
High school graduate	3097	(12.8)	567	(13.9)	510	(15.2)	121	(12.3)	458	(13.7)
Technical sch., some college	3680	(15.2)	513	(12.6)	559	(16.6)	90	(9.2)	408	(12.2)
≥College graduate	3729	(15.4)	405	(9.9)	551	(16.4)	74	(7.5)	253	(7.6)
Cigarette smoking status										
Never user	10,570	(43.6)	1263	(30.9)	660	(19.6)	72	(7.3)	223	(6.7)
Former user	7804	(32.2)	717	(17.6)	939	(28.0)	292	(29.7)	1072	(32.1)
Current user	5860	(24.2)	2105	(51.5)	1760	(52.4)	619	(63.0)	2045	(61.2)
Cigarette smoking intensity (cigarettes/day)										
≥1-10	4046	(16.7)	475	(11.6)	452	(13.5)	138	(14.0)	352	(10.5)
>10-20	5837	(24.1)	1254	(30.7)	1157	(34.4)	391	(39.8)	1366	(40.9)
>20-30	1826	(7.5)	567	(13.9)	503	(15.0)	186	(18.9)	657	(19.7)
>30-40	1301	(5.4)	373	(9.1)	412	(12.3)	149	(15.2)	503	(15.1)
>40	654	(2.7)	153	(3.7)	175	(5.2)	47	(4.8)	239	(7.2)
Cigarette smoking duration (years)										
1-10	1801	(7.4)	132	(3.2)	166	(4.9)	20	(2.0)	72	(2.2)
11-20	2696	(11.1)	228	(5.6)	220	(6.5)	56	(5.7)	169	(5.1)
21-30	3426	(14.1)	572	(14.0)	562	(16.7)	172	(17.5)	523	(15.7)
31-40	3327	(13.7)	1004	(24.6)	968	(28.8)	347	(35.3)	1084	(32.5)
>40	2414	(10.0)	886	(21.7)	783	(23.3)	316	(32.1)	1269	(38.0)
Cigar smoking status										
Never user	19,438	(80.2)	3,347	(81.9)	2991	(89.0)	853	(86.8)	3023	(90.5)
Current user	1004	(4.1)	186	(4.6)	248	(7.4)	57	(5.8)	197	(5.9)
Unknown	3792	(15.6)	552	(13.5)	120	(3.6)	73	(7.4)	120	(3.6)
Pipe smoking status										
Never user	20,269	(83.6)	3719	(91.0)	3073	(91.5)	862	(87.7)	3074	(92.0)
Current user	1125	(4.6)	242	(5.9)	205	(6.1)	52	(5.3)	164	(4.9)
Unknown	2840	(11.7)	124	(3.0)	81	(2.4)	69	(7.0)	102	(3.1)

ABBREVIATIONS: MSKCC: Memorial Sloan Kettering Cancer Center.

^a We excluded subjects with missing information on age, sex, race and cigarette smoking habits. Missing values for education were imputed according to the INHANCE protocol.

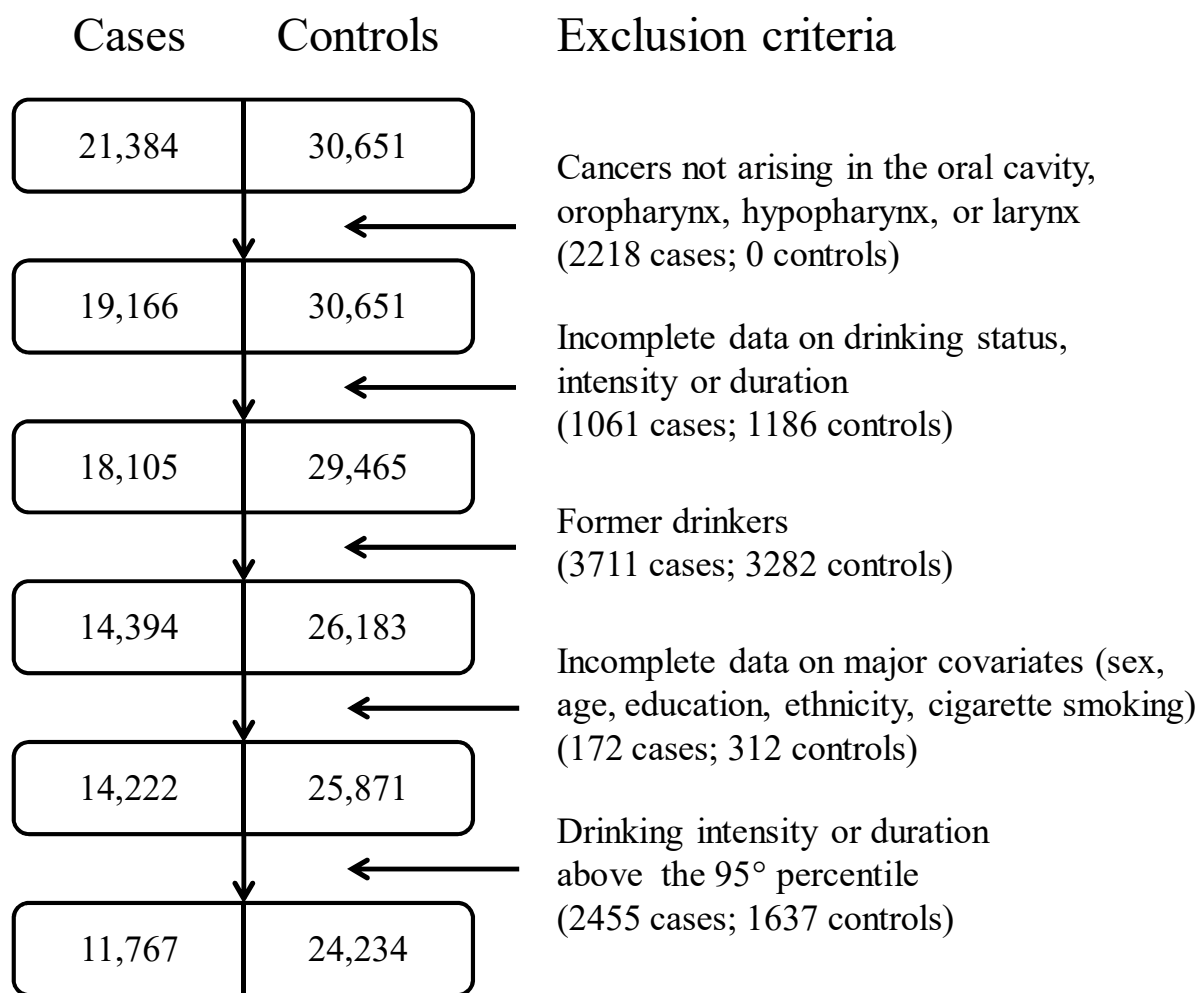
Supplementary Table S3. Odds Ratio (OR) and 95% Credible Intervals (CI) of cases of oral cavity, oropharyngeal, hypopharyngeal, and laryngeal cancers, for selected levels of alcohol intensity and duration.
INHANCE Consortium

		Oral cavity		Oropharynx		Hypopharynx		Larynx	
		OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
1	5	1.40	1.30-1.51	1.25	1.14-1.36	1.84	1.58-2.20	1.14	1.08-1.20
	10	1.38	1.29-1.48	1.38	1.26-1.52	1.81	1.55-2.17	1.12	1.06-1.19
	20	1.35	1.25-1.45	1.67	1.46-1.99	1.76	1.48-2.13	1.09	1.01-1.17
	40	1.28	1.14-1.44	1.56	1.16-2.73	1.67	1.28-2.21	1.03	0.90-1.16
2	5	1.97	1.72-2.29	1.44	1.19-1.70	3.35	2.52-4.83	1.32	1.20-1.46
	10	1.94	1.71-2.21	1.61	1.39-1.86	3.25	2.49-4.55	1.31	1.20-1.44
	20	1.86	1.68-2.08	2.01	1.74-2.40	3.07	2.42-4.14	1.29	1.18-1.41
	40	1.73	1.54-1.94	1.97	1.45-2.73	2.73	2.10-3.64	1.25	1.10-1.40
5	5	5.52	3.92-7.97	2.19	1.35-3.32	11.95	6.94-25.47	2.07	1.63-2.65
	10	5.32	3.96-7.32	2.56	1.81-3.53	11.41	6.93-23.31	2.09	1.70-2.60
	20	4.95	3.95-6.27	3.49	2.88-4.38	10.38	6.85-19.58	2.14	1.83-2.52
	40	4.29	3.59-5.16	3.93	2.92-6.03	8.58	6.06-15.20	2.23	1.96-2.52
10	5	6.07	1.99-13.49	4.43	1.64-10.13	21.62	4.45-82.86	4.37	2.71-7.15
	10	6.23	2.32-12.67	5.55	2.74-10.53	21.65	5.31-75.35	4.56	3.01-6.98
	20	6.54	3.19-11.13	8.79	6.16-12.65	21.91	7.43-65.55	4.95	3.66-6.77
	40	7.32	4.75-10.31	12.48	8.89-22.72	23.29	11.85-51.70	5.88	4.83-7.16

Legends to supplementary figures

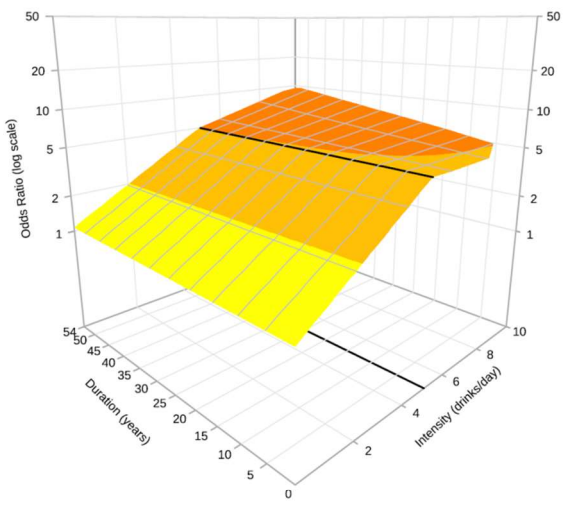
Supplementary Figure S1. Flow-chart of subjects' selection process. INHANCE Consortium.

Supplementary Figure S2. Bivariate spline models estimates of odds ratios of oral cavity, oropharyngeal, and laryngeal cancers in current drinkers for the joint effect of intensity and duration of alcohol consumption, in strata of gender. On the grid, black thicker lines represent knot locations, at 5 drinks/day for oral cavity in men, and at 30 years for oropharyngeal cancer in men. INHANCE Consortium.

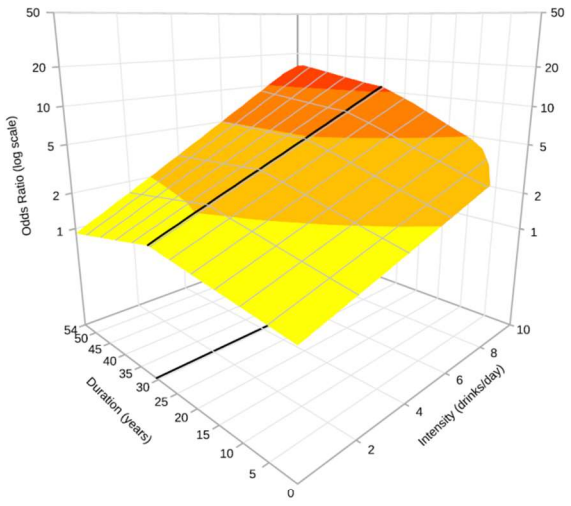


Men

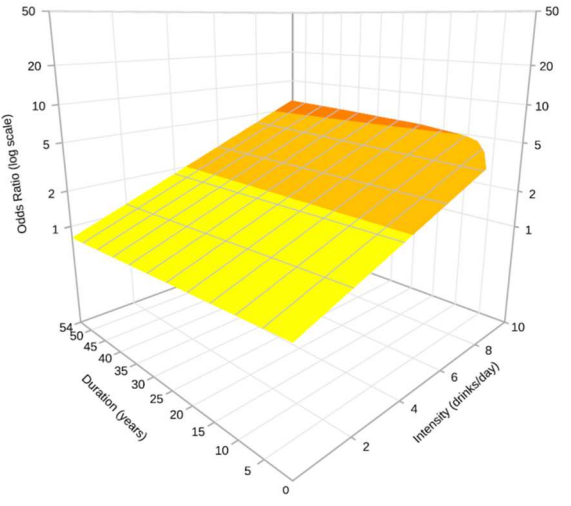
Oral cavity



Oropharynx

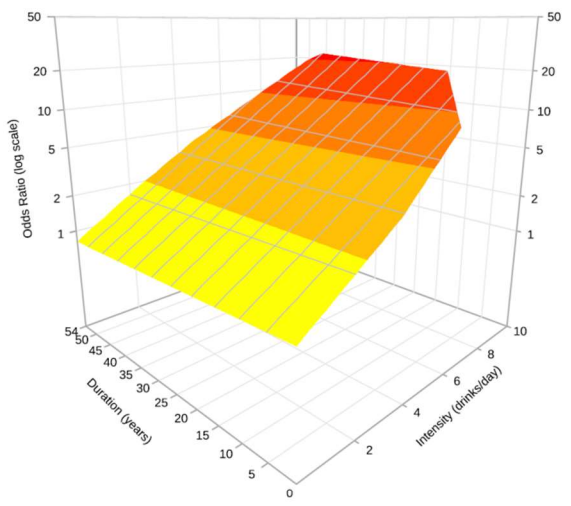


Larynx

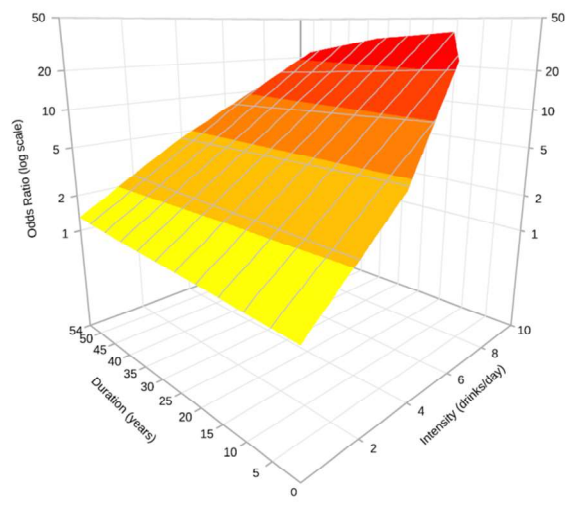


Women

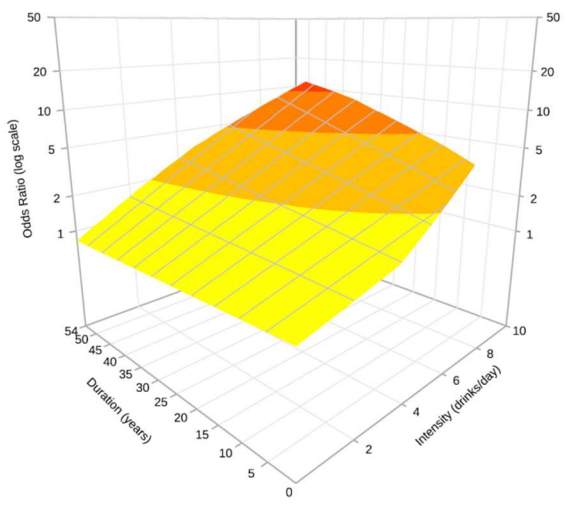
Oral cavity



Oropharynx



Larynx



Odds ratio: ■ <2 ■ 2 to <5 ■ 5 to <10 ■ 10 to <20 ■ ≥20