

Table 2.91. Studies with information on interaction of smoking and alcohol in the causation of cancer at various sites (UADT new studies screened from 1999 until now)

Reference	Place, year	Alcohol categories	Smoking categories	Relative risk (95%CI)	Comments	
Oral cavity						
<i>Case-control studies</i>						
Znaor <i>et al.</i> (2003)	India, 1993-1999	Drinker	Smokers/Chewing			Unconditional logistic regression model. All ORs were adjusted for age, center and education. ORs corresponding to 1 habit were obtained after adjusting for the other 2 habits, and the joint effects of 2 habits were obtained after adjusting for the third habit. Likelihood ratio test for interaction models between drinking, smoking and chewing habits (drinking and smoking p=0.02; chewing and drinking p=0.15; chewing and smoking p=0.00; chewing and smoking and drinking p=0.00)
			No/No	1.00		
			No/Yes T-	3.39 (2.04-5.66)		
			No/Yes T+	9.27 (6.79-12.66)		
			Yes/No	2.45 (1.94-3.10)		
			No/No	2.56 (1.42-4.64)		
			Yes/Yes T-	4.80 (2.79-8.27)		
			Yes/Yes T+	8.53 (6.13-11.89)		
			No/Yes T-	4.36 (1.55-12.30)		
			No/Yes T+	24.28 (14.87-39.65)		
			Yes/No	4.81 (3.74-6.19)		
			Yes/Yes T-	8.10 (4.68-14.02)		
Yes/Yes T+	16.34 (12.13-22.00)					
Castellsagué <i>et al.</i> (2004)	Spain, 1996-1999	Never-drinker	Never-smoker	1.0	Unconditional logistic regression model that included an interaction term; risk estimates were adjusted for age, gender, center, years of schooling, average number of cigarettes smoked per day and average millimeters of pure ethanol consumed per day; interaction term statistically significant (p=0.008) for tobacco smoking status (ever-smoker) and alcohol drinking status (ever-drinker).	
			Ever smoker	1.57 (0.53-4.69)		
			1-10 cig/day	2.87 (0.56-14.80)		
			11-20 cig/day	1.04 (0.18-6.03)		
			21 or more cig/day	1.85 (0.31-11.13)		
			Ever-drinker	Never-smoker		1.66 (0.80-3.44)
				Ever-smoker		12.66 (5.51-29.11)
				1-10 cig/day		5.31 (2.10-13.45)
				11-20 cig/day		15.39 (6.33-37.43)
				21 or more cig/day		18.77 (7.86-44.82)
				1-2 drinks/day		Never-smoker
			Ever-smoker			7.27 (3.00-17.61)
		1-10 cig/day	4.66 (1.68-12.94)			
		11-20 cig/day	11.09 (4.02-30.56)			
		21 or more cig/day	8.20 (2.93-22.94)			
		3-5 drinks/day	Never smoker			1.07 (0.18-6.38)
			Ever smoker	21.55 (8.35-55.58)		
			1-10 cig/day	32.18 (8.14-127.10)		
			11-20 cig/day	26.55 (8.60-81.98)		
			21 or more cig/day	22.04 (7.96-61.01)		
			6 or more drinks/day	Never-smoker		6.19 (0.98-39.17)
		Ever-smoker		39.68 (15.67-100.44)		
		1-10 cig/day		2.65 (0.26-26.54)		
		11-20 cig/day		43.12 (15.02-123.80)		

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			21 or more cig/day	50.65 (19.11–134.24)	
Muwonge <i>et al.</i> (2008)	India, 1996-2004	Only males Drinker No No No Yes Yes Yes No Yes	Only males Smoker/Chewing No/No Yes/No No/Yes No/No Yes/No No/Yes Yes/Yes Yes/Yes	1.0 1.3 (0.6–2.6) 4.8 (2.2–10.5) 1.2 (0.3–6.0) 2.6 (1.4–5.0) 6.4 (2.8–14.6) 5.5 (2.6–11.4) 4.8 (2.5–9.3)	Conditional logistic regression models, risk estimates were adjusted for education and religion. [No formal test for interaction reported]
Hashibe <i>et al.</i> (2009)	Central and Occidental Europe, Latin America, North America, 1992-2006	Drinks per day Never 1-2 3 or more	Cigarettes per day Never 1-20 >20 Never 1-20 >20 Never 1-20 >20	1.0 1.72 (1.17–2.53) 3.13 (1.14–8.59) 0.88 (0.65–1.20) 2.72 (1.47–5.04) 3.23 (1.84–5.67) 1.05 (0.62–1.77) 9.60 (5.04–18.28) 15.49 (7.24–33.14)	Unconditional logistic regression, risk estimates for age, sex, education, race/ethnicity, and study center; interaction term statistically significant (p<0.01)
<i>Cohort studies</i>					
Yen <i>et al.</i> (2008)	Taiwan 2005-2007	None Alcohol only Alcohol Alcohol Alcohol	Tobacco and betel quid None Smoking only Betel quid only Smoking Smoking + betel quid Betel quid Smoking + betel quid	1.0 4.65 (2.74–7.89) 0.95 (0.29–3.11) 10.97 (3.22–37.34) 9.03 (5.36–15.22) 21.79 (11.08–42.85) 16.08 (5.34–48.39) 39.66 (26.04–60.38)	Multivariate logistic regression models were used in the analysis. No information on variables adjusted in the models.

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Reference	Place, year	Alcohol categories	Smoking categories	Relative risk (95%CI)	Comments	
Pharynx						
<i>Case-control studies</i>						
Znaor <i>et al.</i> (2003)	India, 1993-1999	Drinker No No No No Yes No No Yes Yes Yes Yes Yes	Smoker/Chewing			Unconditional logistic regression model. All ORs were adjusted for age, center and education. ORs corresponding to 1 habit were obtained after adjusting for the other 2 habits, and the joint effects of 2 habits were obtained after adjusting for the third habit. Likelihood ratio test for interaction models between drinking, smoking and chewing habits (drinking and smoking p=0.02; chewing and drinking p=0.59; chewing and smoking p=0.01; chewing and smoking and drinking p=0.00)
			No/No	1.00		
			No/Yes T-	1.60 (0.61-4.17)		
			No/Yes T+	3.73 (2.20-6.31)		
			Yes/No	3.54 (2.54-4.94)		
			No/No	-		
			Yes/Yes T-	4.89 (2.29v10.43)		
			Yes/Yes T+	4.55 (2.74-7.56)		
			No/Yes T-	-		
			No/Yes T+	4.28 (1.72-10.62)		
			Yes/No	8.41 (5.94-11.90)		
Yes/Yes T-	10.75 (5.53-20.90)					
Yes/Yes T+	13.44 (8.90-20.29)					
Hashibe <i>et al.</i> (2009)	Central and Occidental Europe, Latin America, North America, 1992-2006	Drinks per day Never 1-2 3 or more	Cigarettes per day			Unconditional logistic regression, risk estimates for age, sex, education, race/ethnicity, and study center; interaction term statistically significant (p <0.01)
			Never	1.0		
			1-20	1.90 (1.34-2.68)		
			>20	2.83 (1.66-4.82)		
			Never	1.26 (0.92-1.73)		
			1-20	2.57 (1.72-3.83)		
			>20	4.10 (2.66-6.32)		
			Never	2.94 (1.73-5.02)		
			1-20	11.37 (6.50-19.89)		
			>20	14.29 (7.26-28.15)		

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Reference	Place, year	Alcohol categories	Smoking categories	Relative risk (95%CI)	Comments
<i>Cohort–studies</i>					
Friborg <i>et al.</i> (2007)	Singapore, 1993-1998	Drinks per week	Years of smoking		RR were calculated by Cox proportional hazard models, adjusted for age at interview, sex, dialect group, year of interview, education, summed intakes of protein-rich preserved foods items, summed intakes of fresh vegetables and history of familial nasopharyngeal cancer.
Oropharynx		Non-drinker	Non-smoker	1.00	
		Non-drinker	1-39	2.2 (0.8–5.9)	
			>40	2.9 (1.2–6.8)	
		1-7	1-39	4.8 (1.6–14.3)	
			>40	6.2 (2.2–17.5)	
		>7	1-39	4.9 (1.3–18.5)	
			>40	18.4 (7.5–45.1)	
Nasopharyngeal		Non-drinker	Non-smoker	1.00	
		Non-drinker	1-39	1.2 (0.7–2.1)	
			>40	2.0 (1.1–3.6)	
		1-7	1-39	0.7 (0.3–1.8)	
			>40	2.3 (0.9–5.9)	
		>7	1-39	1.2 (0.5–3.1)	
			>40	1.8 (0.5–5.9)	
Oesophagus					
<i>Case–control studies</i>					
Castellsagué <i>et al.</i> (1999)	Argentina, Brazil, Paraguay, Uruguay, 1986-1992	Men	Smoker		Odds ratios were estimated by unconditional logistic regression models, adjusted by age group, hospital and education. Interaction term non statistically significant for males (p=0.9) and for females (p=0.01)
		Drinker	Never	1.00	
		Never	Ever	4.45 (2.09–9.47)	
		Ever	Never	4.03 (1.76–9.21)	
		Ever	Ever	17.0 (8.36–34.78)	
		Women	Smoker		
		Never	Never	1.00	
		Never	Ever	1.57 (0.89–2.75)	
		Ever	Never	1.42 (0.82–2.48)	
		Ever	Ever	7.26 (3.68–14.33)	

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Znaor <i>et al.</i> (2003)	India, 1993-1999	Drinker	Smoker/Chewing		
		No	No/No	1.00	Unconditional logistic regression models were used to calculate ORs adjusted for age, center and education. ORs corresponding to 1 habit were obtained after adjusting for the other 2 habits, and the joint effects of 2 habits were obtained after adjusting for the third habit. Likelihood ratio test for interaction models between drinking, smoking and chewing habits (drinking and smoking p=0.62; chewing and drinking p=0.00; chewing and smoking p=0.00; chewing and smoking and drinking p=0.00)
		No	No/Yes T-	3.30 (1.53-7.13)	
		No	No/Yes T+	5.74 (3.50-9.42)	
		No	Yes/No	3.57 (2.51-5.06)	
		Yes	No/No	3.41 (1.46-7.99)	
		No	Yes/Yes T-	4.82 (2.23-10.44)	
		No	Yes/Yes T+	7.22 (4.47-11.64)	
		Yes	No/Yes T-	-	
		Yes	No/Yes T+	2.94 (2.94-15.32)	
		Yes	Yes/No	7.33 (5.06-10.62)	
Yes	Yes/Yes T-	9.12 (4.35-19.12)			
Yes	Yes/Yes T+	8.65 (5.50-13.62)			
Lee <i>et al.</i> (2005)	Taiwan 1996-2003	Drinker	Smoker/Chewing		Unconditional logistic regression models were used to calculate the Ors adjusted age, sex, and hospital of study, education, consumption of fruits and vegetables. The binary interaction terms calculated by multiplying the indicators for 2 explored risk factors were added to the main effect models, and their significance tested by likelihood ratio statistic based on a multiplicative model. Likelihood ratio test for interaction models between drinking, smoking and chewing habits (drinking and smoking p=0.0001; chewing and drinking p=0.248; chewing and smoking p=0.753)
		No	No/No	1.00	
		No	No/Yes	-	
		No	Yes/No	2.0 (1.2-3.3)	
		Yes	No/No	1.7 (0.8-3.6)	
		No	Yes/Yes	3.8 (1.5-9.6)	
		Yes	No/Yes	13.7 (3.8-48.8)	
		Yes	Yes/No	20.4 (12.7-32.9)	
Yes	Yes/Yes	41.2 (23.6-72.0)			
Wu <i>et al.</i> (2006)	Taiwan	Drinker	Smoker/Chewer		Unconditional logistic regression models were used. Adjusted ORs were estimated by seven dummy variables according to the exposure to alcohol, betel quid, and cigarette and adjusted for age and education.
		No	No/No	1.0	
		Yes	No/No	23.3 (4.3-142.2)	
		No	No/Yes	-	
		No	Yes/No	6.5 (1.9-29.8)	
		Yes	No/Yes	39.6 (5.4-333.2)	
		Yes	Yes/No	108.0 (35.1-478.0)	
		No	Yes/Yes	8.7 (1.5-52.2)	
Yes	Yes/Yes	195.6 (64.0-864.2)			

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Reference	Place, year	Alcohol categories	Smoking categories	Relative risk (95%CI)	Comments	
Hashibe <i>et al.</i> (2007)	Romania, Poland, Russia 2000-2002	Squamous cell carcinoma				Unconditional logistic regression was employed to estimate odds ratios, adjusted for age, sex, education, body mass index, fruit intake, vegetable intake, center. Interactions between tobacco and alcohol were assessed by comparing the fit of a regression model including terms for consumption of tobacco alone, alcohol alone, and both products, to that of a model including also an interaction term between the two habits. Interaction OR for squamous cell carcinoma of oesophagus 7.45 and interaction OR for adenocarcinoma of oesophagus 0.11. Likelihood ratio test for interaction models between drinking and smoking for squamous cell carcinoma of oesophagus ($p < 0.01$) and for adenocarcinoma of oesophagus ($p = 0.74$)
		Drinker	Tobacco			
		No	No	1.00		
		No	Yes	0.71 (0.07–7.00)		
		Yes	No	0.96 (0.28–3.28)		
		Yes	Yes	6.42 (2.03–20.30)		
		Adenocarcinoma				
		Drinker	Tobacco			
No	No	1.00				
No	Yes	4.34 (0.34–5.86)				
Yes	No	1.56 (0.16–15.38)				
Yes	Yes	4.27 (0.47–39.10)				
Lee <i>et al.</i> (2007)	Taiwan 1996-2005	Drinker	Smoker or chewer			Unconditional logistic regression models was used to estimate ORs adjusted for center, age, sex, education, consumption of vegetables and fruits. Tobacco was found to interact with light-to-moderate alcohol (0.1-3.0 grams/day) to increase the risk of oesophageal cancer in a supra-multiplicative way (OR 5.5-5.7, $P < 0.05$), whereas with heavy alcohol consumption in a simple multiplicative model (OR 1.7-2.3, $p > 0.05$)
		No	No	1.00		
		0.1-10 grams/day	No	0.6 (0.2–2.2)		
		10.1-30 grams/day	No	1.2 (0.3–4.1)		
		>30 grams/day	No	8.2 (3.8–18.0)		
		No	1-30 pack-years	2.7 (1.6–4.5)		
		0.1-10 grams/day	1-30 pack-years	8.2 (4.5–15.2)		
		10.1-30 grams/day	1-30 pack-years	13.1 (7.2–23.8)		
		>30 grams/day	1-30 pack-years	36.1 (20.2–64.6)		
		No	>30 pack-years	2.1 (1.2–3.6)		
		0.1-10 grams/day	>30 pack-years	8.6 (4.7–15.8)		
		10.1-30 grams/day	>30 pack-years	18.6 (10.3–33.8)		
>30 grams/day	>30 pack-years	41.2 (24.0–70.7)				

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Pandeya <i>et al.</i> (2009)	Australia 2002-2005	Drinker	Tobacco		Unconditional logistic regression models was used to estimate the ORs, adjusted by age, sex, body mass index 1 year ago, frequency of heartburn or acid reflux, education, and frequency of aspirin use in the past 5 years.
		Adenocarcinoma of oesophagus			
		Never-drinker	Never-smoker	1.0	
		<10 g		0.25 (0.05–1.25)	
		10-69.9 g		0.76 (0.37–1.59)	
		70.0-209.9 g		0.84 (0.39–1.83)	
		210-419.9 g		0.41 (0.15–1.15)	
		420 g or more		0.87 (0.23–3.27)	
		Never-drinker	Former smoker	1.0	
		<10 g		0.96 (0.23–3.99)	
		10-69.9 g		0.57 (0.19–1.74)	
		70.0-209.9 g		0.53 (0.18–1.59)	
		210-419.9 g		0.65 (0.21–1.99)	
		420 g or more		0.51 (0.13–2.00)	
		Never-drinker	Current smoker	1.0	
		<10 g		2.25 (0.22–23.37)	
		10-69.9 g		1.05 (0.18–23.37)	
		70.0-209.9 g		1.10 (0.19–6.35)	
		210-419.9 g		0.69 (0.11–4.42)	
		420 g or more		2.14 (0.30–14.99)	
		Esophagogastric junction adenocarcinoma			
		Never-drinker	Never-smoker	1.0	
		<10 g		0.58 (0.19–1.77)	
		10-69.9 g		0.85 (0.43–1.71)	
70.0-209.9 g		0.86 (0.40–1.84)			
210-419.9 g		0.98 (0.40–2.43)			
420 g or more		1.02 (0.24–4.34)			
Never-drinker	Former smoker	1.0			
<10 g		0.73 (0.20–2.61)			
10-69.9 g		0.70 (0.27–1.80)			
70.0-209.9 g		0.51 (0.20–1.31)			
210-419.9 g		0.51 (0.19–1.34)			
420 g or more		0.73 (0.23–2.27)			
Never-drinker	Current smoker	1.0			
<10 g		1.27 (0.19–8.45)			
10-69.9 g		0.68 (0.18–2.51)			
70.0-209.9 g		0.65 (0.17–2.44)			
210-419.9 g		0.49 (0.12–2.05)			
420 g or more		0.49 (0.09–2.62)			

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Reference	Place, year	Alcohol categories	Smoking categories	Relative risk (95%CI)	Comments	
Pandeya <i>et al.</i> (contd)	Australia 2002-2005	Squamous cell carcinoma of esophagus				Unconditional logistic regression models was used to estimate the ORs, adjusted by age, sex, body mass index 1 year ago, frequency of heartburn or acid reflux, education, and frequency of aspirin use in the past 5 years
		Never-drinker <10 g 10-69.9 g 70.0-209.9 g 210-419.9 g 420 g or more	Never-smoker	1.0		
				0.50 (0.18–1.39)		
				0.46 (0.23–0.95)		
				0.78 (0.32–1.92)		
				2.88 (1.04–7.97)		
		Never drinkers <10 g 10-69.9 g 70.0-209.9 g 210-419.9 g 420 g or more	Former smoker	1.86 (0.19–18.11)		
				1.0		
				4.13 (0.76–22.41)		
				2.30 (0.49–10.80)		
				1.41 (0.30–6.74)		
		Never-drinker <10 g 10-69.9 g 70.0-209.9 g 210-419.9 g 420 g or more	Current smoker	1.41 (0.30–6.74)		
				3.69 (0.77–17.66)		
				8.43 (1.59–44.80)		
1.0						
0.35 (0.03–4.28)						
		0.48 (0.11–2.09)				
		2.00 (0.50–7.98)				
		4.95 (1.08–22.66)				
		21.87 (3.90–122.49)				
<i>Cohort Studies</i>						
Fan <i>et al.</i> (2008)	Shanghai, People's Republic of China 1986-2006	Drinks per day Non-drinker	Years of smoking Non-smoker <40 40 or more	1.0	Hazard ratios were calculated using Cox proportional hazards regression models, which included covariates for age at interview, year of interview, neighborhood of residence at recruitment, body mass index, level of education, and summed intakes of preserved food items (in tertiles) and fresh vegetables (in tertiles)	
				1.26 (0.58–2.73)		
		<4	Non-smoker <40 40 or more	2.18 (0.80–5.92)		
				1.75 (0.75–4.11)		
		4 or more	Non-smoker <40 40 or more	2.01 (1.00–4.01)		
				4.13 (1.85–9.25)		
				3.86 (0.86–17.26)		
				4.55 (2.03–10.18)		
		40 or more	8.00 (3.36–19.05)			
Ishiguro <i>et al.</i> (2009)	Japan 1993-2004	Light	Light	1.0	HRs were adjusted for age (years) at baseline, study area, body mass index, preference for hot foods and drinks, and Flushing response; p value for interaction =0.70	
		Light	Heavy	2.31 (1.58–3.38)		
		Heavy	Light	2.96 (2.01–4.34)		
		Heavy	Heavy	6.12 (4.13–9.05)		

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Larynx					
Talamini <i>et al.</i> (2002)	Italy and Switzerland, 1992-2000	Drinks per week Never and <14	Cigarettes per day Never	1.00	Odds ratios were estimated using multiple logistic regression models, adjusted on quinquennia of age, sex, and area of residence, and adjusted for years of education. [No formal test for interaction reported]
			1-14	9.7 (3.56–26.13)	
			15-24	27.6 (10.19–74.73)	
			25 or more	18.9 (5.69–62.70)	
		14-27	Never	0.8 (0.19–2.95)	
			1-14	8.0 (2.82–22.80)	
			15-24	31.5 (11.96–82.94)	
			25 or more	52.5 (18.28–150.62)	
		28-55	Never	1.7 (0.42–7.01)	
			1-14	18.7 (6.99–50.22)	
			15-24	66.5 (26.83–165.03)	
			25 or more	83.9 (30.92–227.52)	
		56 or more	Never	8.5 (2.39–30.17)	
			1-14	63.7 (20.97–193.42)	
			15-24	139.9 (54.73–357.86)	
			25 or more	177.2 (64.99–483.28)	
Ramroth <i>et al.</i> (2004)	South-West Germany 1998-2000	Grams ethanol/day 25 or less	Pack years 0	1.0	
		>25-50	>0-10	-	
		>50-75	>10-20	-	
		>75-100	>20-40	-	
		>100-150	>40-80	-	
		>150	>80	52.6 (17.9–154.6)	
Hashibe <i>et al.</i> (2009)	Central and Occidental Europe, Latin America, North America, 1992-2006	Drinks per day Never	Cigarettes per day Never	1.0	Unconditional logistic regression, risk estimates for age, sex, education, race/ethnicity, and study center; interaction term non statistically significant (p <0.63)
			1-20	6.06 (4.03–9.11)	
			>20	12.83 (7.95–20.71)	
		1-2	Never	1.20 (0.72–2.02)	
			1-20	8.33 (5.07–13.69)	
			>20	16.91 (9.66–29.61)	
		3 or more	Never	3.16 (1.23–8.16)	
			1-20	18.94 (10.64–33.71)	
			>20	36.87 (16.60–81.90)	

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Mixed upper aerodigestive tract (UADT)					
<i>Case-control studies</i>					
Hayes <i>et al.</i> (1999)	Puerto Rico, 1992-1995	Men Drinks/week None	Tobacco None	1.0	Analysis of joint effect of tobacco smoking and alcohol consumption only for men. Odds ratios were estimated by unconditional logistic regression analysis, adjusted for age. [No formal test for interaction reported]
			Low	-	
			10-19 cigarettes/day	11.3 (0.6-213.0)	
			20-39 cigarettes/day	1.8 (0.2-19.0)	
			40 e + cigarettes/day	2.4 (0.2-27.6)	
		1-7	None	0.2 (0.0-1.5)	
			Low	1.6 (0.5-4.8)	
			10-19 cigarettes/day	1.3 (0.2-7.2)	
			20-39 cigarettes/day	3.8 (1.2-12.0)	
			40 e + cigarettes/day	4.3 (1.1-16.7)	
		8-21	None	0.6 (0.1-3.5)	
			Low	1.3 (0.3-5.7)	
			10-19 cigarettes/day	1.8 (0.4-8.3)	
			20-39 cigarettes/day	6.2 (2.0-19.3)	
			40 e + cigarettes/day	4.1 (0.9-18.7)	
		22-42	None	1.6 (0.3-9.6)	
			Low	3.7 (0.8-16.4)	
			10-19 cigarettes/day	18.6 (4.1-84.0)	
			20-39 cigarettes/day	11.3 (3.7-34.5)	
			40 e + cigarettes/day	10.5 (2.9-37.9)	
		more than 42	None	6.4 (1.3-31.9)	
			Low	5.5 (1.6-19.0)	
			10-19 cigarettes/day	12.2 (3.3-45.6)	
			20-39 cigarettes/day	50.2 (16.6-152.0)	
			40 e + cigarettes/day	38.7 (13.6-110.0)	

Table 2.91. Studies with information on interaction of smoking and alcohol in the causation of cancer at various sites (UADT new studies screened from 1999 until now)

Reference	Place, year	Alcohol categories	Smoking categories	Relative risk (95%CI)	Comments		
Peters <i>et al.</i> (2005)	USA, 1999-2003	Drinks/week	0	0	1.0	Unconditional logistic regression model that included an interaction term; risk estimates were adjusted for age, gender and race; interaction estimated for heavy smokers (>35 pack-years) and heavy alcohol use (>30 drinks per week) for oral cavity (p=0.004), pharynx (p=0.048) and larynx cancer (p=0.6)	
			>0-6	>0-15	1.2 (0.8–1.7)		
				>15-35	1.4 (1.0–2.1)		
				>35-58	1.7 (1.1–2.6)		
				>58	3.5 (2.2–5.5)		
				0	0.7 (0.5–1.0)		
				>0-15	0.8 (0.5–1.3)		
				>15-35	1.0 (0.6–1.7)		
				>35-58	1.1 (0.6–2.0)		
				>58	2.3 (1.3–4.2)		
				0	0.9 (0.6–1.4)		
				>6-11	>0-15		1.1 (0.6–1.9)
				>15-35	1.3 (0.8–2.4)		
				>35-58	1.6 (0.9–2.9)		
				>58	3.2 (1.8–5.9)		
			>11-26	0	1.4 (0.9–2.1)		
				>0-15	1.6 (0.9–2.8)		
				>15-35	2.0 (1.2–3.4)		
				>35-58	2.4 (1.4–4.2)		
				>58	4.9 (2.7–8.8)		
			>26	0	1.8 (1.1–3.1)		
				>0-15	2.1 (1.1–4.0)		
				>15-35	2.6 (1.4–4.8)		
				>35-58	6.5 (3.2–13.0)		
				>58	17.3 (7.8–38.3)		
			Drinks weekly	Pack-years			
			<10	Equal or <1	1.0		
				>1 to <25	1.44 (1.00–2.07)		
		Equal or 25 to <45	1.61 (1.05–2.48)				
		Equal or >45	2.99 (1.94–4.62)				
	10 or more to <20	Equal or <1	1.10 (0.55–2.22)				
		>1 to <25	1.97 (1.10–3.53)				
		Equal or 25 to <45	2.10 (1.06–4.15)				
		Equal or >45	5.92 (3.04–11.55)				
	20 or more to <40	Equal or <1	2.50 (1.21–5.16)				
		>1 to <25	2.90 (1.58–5.33)				
		Equal or 25 to <45	6.43 (3.49–11.84)				
		Equal or >45	8.42 (4.99–14.22)				
	40 or more	Equal or <1	4.61 (1.45–14.66)				
		>1 to <25	3.96 (1.90–8.25)				

Table 2.91. Studies with information on interaction of smoking and alcohol in the causation of cancer at various sites (UADT new studies screened from 1999 until now)

Reference	Place, year	Alcohol categories	Smoking categories	Relative risk (95%CI)	Comments
			Equal or <25 to <45	7.29 (3.73–14.27)	
			Equal or >45	13.93 (7.75–25.02)	
Applebaum <i>et al.</i> (2007)	USA, 1999-2003	Drinks weekly <3	Pack-years None	1.0	Unconditional logistic regression, risk estimates for age, sex and town of residence [No formal test for interaction reported]
			>0 to <20	1.1 (0.5–2.6)	
			20 to <45	2.3 (0.9–5.9)	
			45 or more	1.8 (0.7–4.8)	
		3 to <8	None	0.8 (0.4–1.8)	
			>0 to <20	1.4 (0.7–2.9)	
			20 to <45	1.6 (0.7–3.7)	
			45 or more	4.5 (1.9–10.8)	
		8 to <25	None	1.3 (0.5–3.2)	
			>0 to <20	1.8 (0.8–4.3)	
			20 to <45	2.5 (1.2–5.4)	
			45 or more	9.6 (4.4–21.2)	
		25 or more	None	3.5 (1.0–12.2)	
			>0 to <20	3.0 (1.1–8.4)	
			20 to <45	9.3 (4.4–19.9)	
			45 or more	14.8 (7.1–30.8)	
Hashibe <i>et al.</i> (2009)	Central and Occidental Europe, Latin America, North America, 1992-2006	Drinks per day Never	Cigarettes per day Never	1.0	Unconditional logistic regression, risk estimates for age, sex, education, race/ethnicity, and study center; interaction term statistically significant (p <0.01)
			1-20	2.20 (1.57–3.09)	
			>20	4.15 (2.44–7.07)	
		1-2	Never	1.03 (0.84–1.25)	
			1-20	3.09 (2.13–4.50)	
			>20	4.81 (3.21–7.20)	
		3 or more	Never	1.91 (1.27–2.87)	
			1-20	9.92 (6.36–15.46)	
			>20	14.23 (8.30–24.40)	
<i>Cohort studies</i>					
Ide <i>et al.</i> (2008)	Japan, baseline registration from 1988 to 1990, mean follow up period 12.5 years	Non-drinker	Non-smoker	1.0	Risk estimates adjusted for age, consumption of green tea, preference for salty foods, consumption of green-yellow vegetables; p value for interaction =0.19
			Smoker	1.1 (0.2–4.9)	
		Drinker	Non-smoker	1.0 (0.3–3.3)	
			Smoker	3.3 (1.1–9.6)	

Table 2.91. Studies with information on interaction of smoking and alcohol in the causation of cancer at various sites (UADT new studies screened from 1999 until now)

Reference	Place, year	Alcohol categories	Smoking categories	Relative risk (95%CI)	Comments	
Weikert <i>et al.</i> (2009)	Six countries in Europe: Denmark, Germany, Italy, the Netherlands, Spain, United Kingdom	Men Lifetime alcohol intake (g/d) 0.1-30	Men			Cox regression models were stratified by center and age at recruitment and adjusted for education, fruit and vegetable intake, and body-mass-index. Interaction between smoking status and alcohol consumption was tested by using the likelihood ratio test for models with and without the respective interaction term (for men: p=0.27; for women: p=0.49)
			Never-smoker	1.0		
			Ex-smoker	1.50 (0.83–2.71)		
			Current smoker (<15 cig/d)	2.33 (1.16–4.68)		
			Current smoker (15 or more cig/d)	5.76 (3.20–10.36)		
			Never-smoker	0.90 (0.26–3.10)		
		Ex-smoker	3.23 (1.66–6.30)			
		Current smoker (<15 cig/d)	3.55 (1.50–8.37)			
		Current smoker (15 or more cig/d)	11.75 (6.44–21.43)			
		>60	Never-smoker	1.71 (0.38–7.67)		
			Ex-smoker	4.24 (1.78–10.12)		
			Current smoker (<15 cig/d)	11.02 (5.17–23.52)		
			Current smoker (15 or more cig/d)	22.86 (12.27–42.60)		
			Women Lifetime alcohol intake (g/d) 0.1-18	Women		
				Never-smoker	1.0	
		Ex-smoker		1.71 (0.94–3.12)		
		Current smoker (<15 cig/d)		1.43 (0.57–3.57)		
		Current smoker (15 or more cig/d)		6.04 (3.20–11.40)		
>18	Never-smoker	1.94 (0.58–6.54)				
	Ex-smoker	0.59 (0.08–4.37)				
	Current smoker (<15 cig/d)	7.00 (2.34–20.90)				
	Current smoker (15 or more cig/d)	17.28 (8.39–35.60)				