CC/2015/03

COMMITTEE ON CARCINOGENICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

Consumption of Alcohol and Laryngeal Cancer Risk

1. As part of the strategy proposed to consider the role of alcohol consumption and cancer risk, it was suggested that the COC review the epidemiological data on alcohol consumption and cancer. In 2007 (published IARC 2010), IARC reviewed the epidemiological evidence on the possible association between alcoholic beverage consumption and cancer at 27 anatomical sites (cancers of the oral cavity and the pharynx, larynx, oesophagus, liver, breast stomach, colon and/or rectum, pancreas, lung, urinary bladder, endometrium, ovary, uterine cervix, prostate, kidney, lymphatic and haematopoietic system, testis, brain, thyroid, melanoma and other female cancers (vulva and vagina)). They re-affirmed their previous conclusion (IARC, 1988) that cancers of the upper digestive tract (oral cavity, pharynx, larynx, and oesophagus) and the liver are causally related to the consumption of alcoholic beverages. In addition, IARC considered that there was now sufficient evidence to conclude that cancer of the colo-rectum and female breast are causally related to the consumption of alcoholic beverages (IARC, 2010). Following another IARC review in 2009 (IARC 2012), IARC reaffirmed their position for the aforementioned cancers and also reported an association between alcohol consumption and cancer of the pancreas, although they were unable to reach a conclusion on whether this was causal.

Laryngeal Cancer Statistics for the UK

2. In 2011, laryngeal cancer accounted for 1% of all new cases of cancer in males, and 0.3% in females. There were 2,360 new cases of laryngeal cancer in the UK, 1,932 (82%) of these were in men and 428 (18%) in women. The crude incidence rate showed that there were 6 new laryngeal cancer cases for every 100,000 males in the UK, and 1 for every 100,000 females in 2011. Laryngeal cancer incidence is related to age, with the highest incidence rates being in older men and women. In the UK between 2009 and 2011, almost three-quarters (74%) were diagnosed in those aged 60 and over. Laryngeal cancer accounted for 0.5% of deaths from cancer in the UK (2012). Laryngeal cancer was the 18th most common cause of cancer death among men in the UK (2012), accounting for 0.7% of all male deaths from cancer. Laryngeal cancer accounted for 0.2% of all female cancer deaths in the UK (2012). Around 780 people in the UK died from laryngeal cancer in 2012, with 8 in 10 laryngeal cancer deaths occurring in men.

Laryngeal Cancer Risk Factors

3. Risk factors for laryngeal cancer include tobacco and alcohol, diet, infections, medical conditions, previous cancers, family history, occupational exposures and indoor air pollution. A study published by Parkin et al. (2011) estimated that, in the

UK, more than 90% of laryngeal cancers were linked to lifestyle and environmental factors. Parkin et al. (2011) estimated that around 79% of laryngeal cancers in the UK in 2010 were caused by smoking, and 25% were linked to alcohol. The combined effect of smoking and alcohol consumption has been estimated to account for 89% of laryngeal cancers, with smoking having a stronger effect than alcohol on risk of laryngeal cancer.

Updated review of Alcohol consumption and Laryngeal Cancer

4. In the evaluation of the carcinogenicity of alcohol (IARC monograph 96, 2010 (Annex A) and IARC monograph 100e, 2012 (Annex B)), IARC state that alcohol causes laryngeal cancer and classifies it as a group 1 definite carcinogen. Literature for the current review was obtained following a PubMed search and the search terms included alcohol, ethanol, drinking, consumption and laryngeal cancer. Studies published since January 2008 to December 2014 were included in the retrieval to ensure all studies published on this topic since the last IARC review to date were considered.

5. Each cohort and case-control study was assessed for quality using a modified scoring scheme similar to the Newcastle-Ottawa star scoring scheme. Pooled or meta-analyses were not scored. Information on alcohol consumption was extracted from all the relevant studies. Alcohol consumption categories varied between studies. For comparative purposes and to obtain a uniform variable for alcohol consumption, where possible, we calculated alcohol intake in terms of grams of ethanol/day. Information on adjustment factors used in the individual studies e.g. smoking, body mass index (BMI), obesity and caffeine intake were also extracted from the papers.

Meta- and combined analyses of alcohol consumption and Laryngeal cancer risk and mortality and secondary events (Table 1)

6. Three meta-analyses and 3 pooled analyses have been performed since the last IARC review. The papers are presented in the following order: analysis considering European/North American populations first followed by worldwide pooled analysis/meta-analysis.

7. Hashibe et al. (2009) conducted a pooled analysis with 18 European and American case-control studies participating in the International Head and Neck Cancer Epidemiology (INHANCE) consortium. They examined the effect of alcohol alone, tobacco alone and the interaction of both alcohol and tobacco on the risk of head and neck cancers including laryngeal cancer. They also estimated the Population Attributable Risk (PAR) for each cancer sub-site. There were 2,959 laryngeal cancer cases and 13,130 controls included in the analysis. In the exposure assessment, information was obtained on drinking status, frequency of consumption, duration of consumption and types of alcoholic beverages consumed. Odds ratios (OR) and 95% CI were estimated using unconditional logistic regression models and were adjusted for age, sex, education, race/ethnicity and study centre. In their analysis, they reported an OR of 1.21 (95% CI 0.77 – 1.92) for alcohol alone, an OR of 6.76 (95% CI 4.58 – 9.96) for tobacco alone and an OR of 14.22 (95% CI 8.26 - 24.46) for both alcohol and tobacco combined. For laryngeal cancer, they observed that the multiplicative interaction parameter (ψ) was consistent with an interaction

that was greater than multiplicative but the confidence interval included the null value (ψ=1.62, 95% CI=0.85 – 3.09). The PAR for tobacco and alcohol, alone and overlapped was 88.5% (95%CI 82.1 – 92.4) for laryngeal cancer, of which 2.9% (95% CI -0.3 – 4.4) was for alcohol alone, 52.2% (95% CI 77.8 – 36.0) was for tobacco alone and 33.4% (95% CI 4.5 -52.1) was the overlap between tobacco and alcohol.

8. Lubin et al (2010) also conducted a pooled analysis using data from the INHANCE consortium (European and American populations) on the effects of alcohol consumption, tobacco smoking and body mass index (BMI) on head and neck cancers including laryngeal cancer. The analysis was performed using data from 15 of the 17 case-control studies outlined in Hashibe et al. (2007). Two of the studies (North American Iowa population , Wang et al., (2005), (did not collect data on BMI)) and the French population of Benhamou et al. (2004), previously included in the study by Gaudet et al. (did not enrol never smokers)) were excluded from the analysis, but data were added from the INHANCE US multicentre study (Blot et al., 1988). For the exposure assessment, the following equivalent g ethanol/day were calculated: <12.5 g ethanol/day = < 1 drink, 12.5 – 36.0 g ethanol/day = 1 – 2.9 drinks/day), 37.5g – 61.0g ethanol/day = 3.0 – 4.9 drinks/day and 62.5 g ethanol - 125 g ethanol/day = 5- 10 drinks/day. Linear exponential models were fitted for the excess odds ratio (EOR) for laryngeal cancer in total drink-years and drinks/day. For analysis of alcohol consumption, results were adjusted for sex, education, BMI, smoking and use of other tobacco products. They observed increased risk in laryngeal cancer with increasing drink-years compared to the reference category of never drinker (OR = 0.98 (95% CI 0.8 - 1.2) for 1-49 drink-years; 0.94 (95% CI 0.6 - 1.4) for 50-99 drink-years; 1.20 (95% CI 0.8 - 1.8) for 100-149 drink-years; 1.35 (95% CI 0.8 - 2.2) for 150-199 drink-years and 1.80 (95% CI 1.1 - 3.1) for ≥200 drink-years). Adjusting additionally for drink-years, they also observed an increase in risk of laryngeal cancer with increasing drinks/day compared to the reference category of < 1 drink/day (OR = 1.05 (95% CI 0.8 - 1.4) for 1-2.9 drinks/day; 1.08 (95% CI 0.7 - 1.6) for 3.0-4.9 drinks/day and 1.64 (95% CI 1.0 - 2.6) for 5-10 drinks/day). They also reported that ORs for laryngeal cancer by drink-years and drinks/day were similar and not modified by BMI categories of < 18.5, 18.5-24.9, 25.0 – 29.9 and ≥ 30.

9. In a further publication, Lubin et al. (2011) examined whether sex modified the ORs for head and neck cancers including laryngeal cancer by BMI, smoking and alcohol consumption. Using the same data-set as previously described above, ORs were estimated and adjusted for study, age, education, BMI, cigarette per day, years since smoking cessation, use of other tobacco products, drinks per day in the drink-year analysis and drink-years in the drinks per day analysis. In both males (n=1,503 laryngeal cancer cases) and females (n=237 laryngeal cancer cases), they observed increased risk of laryngeal cancer with increasing drink-years compared to the reference category of never drinker (OR = 0.91 (95% CI 0.7 – 1.2) for 1-49 drink-years; 0.78 (95% CI 0.5 -1.2) for 50–99 drink-years; 0.99 (95% CI 0.6 - 1.6) for 100–149 drink-years; 1.13 (95% CI 0.7 – 1.9) for 150–199 drink years and 1.51 (95% CI 0.9 – 2.7) for ≥200 drink years for males and OR = 1.14 (95% CI 0.8 – 1.7) for 1-49 drink-years; 2.68 (95% CI 1.0 – 7.1) for 50–99 drink-years; 3.18 (95% CI 1.0 – 11.0) for 100–149 drink-years; 3.84 (95% CI 0.8 – 19.0) for 150–199 drink years and 3.79 (95% CI 0.6 – 26.0) for ≥200 drink years) for females. They also observed an increase in risk of laryngeal cancer with increasing drinks/day compared to the

reference category of < 1 drink/day in males (OR = 1.20 (95% CI 0.9 - 1.6) for 1–2.9 drinks/day; 1.20 (95% CI 0.8 - 1.9) for 3.0-4.9 drinks/day and 1.89 (95% CI 1.1 – 3.1) for 5-10 drinks/day; P-trend <0.01) but not females (OR = 0.45 (95% CI 0.2 -1.0) for 1–2.9 drinks/day; 0.67 (95% CI 0.2 – 2.3) for 3.0-4.9 drinks/day and 0.52 (95% CI 0.1-2.7) for 5-10 drinks/day; P-trend = 0.88). When they examined whether sex modified the ORs for laryngeal cancer risk, they found the ORs were similar for laryngeal cancer risk.

10. Ismali et al. (2010) performed a meta-analysis of alcohol consumption (light, moderate and heavy drinking) and laryngeal cancer risk from studies published worldwide. The analysis of alcohol consumption and laryngeal cancer included risk estimates from 40 studies (38 case-controls and 2 cohort studies). The reference category for the meta-analysis included both non-drinkers and occasional drinkers. The daily drinking categories were light drinking (≤12.5 g ethanol = ≤ 1 drink), moderate drinking (> 12.5 - <50g ethanol = > 1 drink - <4 drinks) and heavy drinking (≥ 50g ethanol = ≥4 drinks). Data for light drinking were provided in 12 studies, for moderate drinking in 35 studies and for heavy drinking in 33 studies. Relative Risks (RR) and 95% CIs were calculated using random effects models along with sub-group analyses: 1) population based controls studies, 2) using exclusively non-drinkers as reference category (not occasional drinkers) and 3) presenting RRs adjusted for the main potential confounding factors (age, sex and tobacco use). Heterogeneity among studies was also estimated using the I^2 statistic. They also performed a dose-response analysis using random-effects meta-regression model in a non-linear dose-risk framework. Overall, they reported an approximately 2-fold increase in risk of laryngeal cancer among alcohol drinkers (RR = 1.90, 95% CI 1.59 – 2.28) compared with non-drinkers/occasional drinkers. They did not find a significant association between light drinking and laryngeal cancer risk but did report an increased risk of laryngeal cancer with increasing intake at moderate and heavy consumption compared to the reference category (RR = 0.88; 95% CI 0.71–1.08 for light drinking, RR = 1.47; 95% CI 1.25–1.72 for moderate drinking and an RR = 2.62; 95% CI 2.13–3.23 for heavy drinking). Subgroup analyses provided RRs of 1.87 (95% CI 1.32–2.65) for studies with population-based controls only, 1.62 (95% CI 1.27–2.08) for studies with only non-drinkers in the reference group, and 1.84 (95% CI 1.50–2.26) for results adjusted for confounding factors. Similar results were observed in the subgroup analyses of each drinking category. For all studies combined, significant heterogeneity was observed in both the overall analysis and various subgroup analyses, excluding studies that did not report 95% CIs, those with partial overlap, and including only more precise risk estimates (standard error <0.5 in logarithmic scale). In the analysis of light drinking, low heterogeneity was observed in both the overall and subgroup analyses. However, results indicated high heterogeneity among studies reporting moderate or heavy alcohol drinking. In relation to this finding, the authors commented that the analysis had included only 2 cohort studies, one of which did not show any consistent association between alcohol drinking and laryngeal cancer, and one that showed similar results to the case-control studies for light and moderate drinking but did not present results for heavy drinking because the study included only women, few of whom were heavy drinkers. They also noted that the high level of heterogeneity was related to the magnitude, rather than direction, of the effect in moderate and heavy drinkers, which may be explained by variation in study design, quality of exposure assessment and difference in alcohol drinking patterns within strata. In their dose-response analysis,

they reported increasing RR with increasing intake of g of ethanol per day (RR = 1.20 (95% CI 1.15–1.25) for 12.5 g ethanol/day, RR = 1.45 (95% CI 1.33–1.57) for 25 g ethanol/day, RR = 1.72 (95% CI 1.52–1.90) for 37.5 g ethanol/day, RR = 2.04 (1.76–2.36) for 50 g ethanol/day, and 3.77 (2.93–4.86) for 100 g ethanol/day).

11. Bagnardi et al (2013) carried out a meta-analysis of light alcohol drinking and cancer risk from European, North American and Asian studies, including laryngeal cancer. They included 222 unique papers published before December 2010, 13 of which reported estimates for laryngeal cancer (3 cohort studies and 10 were case-control studies). Since the included studies usually reported alcohol exposure in intervals, the authors considered as light every interval whose midpoint was <12.5 g/day (1 drink/d) of alcohol. Where studies reported two or more adjusted risk estimates for light drinking, they combined them into a single estimate. The reference category was non-drinkers or occasional drinkers. The reference category contained 504 cases while the light drinker category contained 846 cases. The site-specific pooled estimates for light drinkers vs. non-drinkers indicated that no significant association was found for laryngeal cancer (overall RR = 0.90, 95% CI 0.73 – 1.10); 0.89 (95% CI 0.67 - 1.16) for men and 0.93 (95% CI 0.71 - 1.22) for women). They stratified their results by study type and reported an RR of 0.96 (95% CI 0.71 - 1.30) for cohort studies and an RR of 0.83 (95% CI 0.63 - 1.09) for case-control studies. Their data stratified by geographical area gave RRs of 0.84 (95% CI 0.43 - 1.62), 0.89 (95% CI 0.66 - 1.20), 0.91 (95% CI 0.60 - 1.37) for European, North American and Asian populations, respectively.

12. Bagnardi et al. (2015) performed their meta-analysis of data on alcohol drinking (light, moderate and heavy drinking) and cancer risk using data from 572 studies published between 1956 and 2012 including laryngeal cancer (41 studies in total (3 cohort and 38 case-control studies from European, North American and Asian populations)). Criteria set for inclusion in the meta-analysis were a) case-control studies, nested case-control studies or cohort studies published as original articles; b) studies that reported findings as odds ratios (ORs), relative risks (RRs) or hazard ratio (HRs) for at least two levels of alcohol consumption versus non-drinkers or occasional drinkers; c) studies that reported confidence intervals (CI) or standard errors of the risk estimates or sufficient data to calculate them. Criteria set for exclusion from the meta-analysis were studies reporting on specific alcohol beverage only as the non-drinkers in those studies could be drinkers of another alcoholic beverage type. For the purposes of the analysis and to have unity in the expression of consumption, they used g per day as a standard measure of ethanol intake using the following 0.8g/ml, 28g/ounce and 12.5 g/drink. For studies where the levels of consumption were reported in a range, the exposure was assigned as the midpoint of the range for the reported categories of alcohol intake. They considered as light, moderate and heavy drinking every interval whose midpoint was ≤12.5, ≤50 and > 50g per day of alcohol. The reference category included both non-drinkers and occasional drinkers. Where available, adjusted RRs were used, otherwise unadjusted RRs were calculated using the raw data presented in the paper. A meta-RR was estimated for laryngeal cancer for light drinkers versus non-drinkers, moderate drinkers versus non-drinkers and heavy drinkers versus non-drinkers using random-effects models. Statistical heterogeneity among studies was assessed using I^2. Potential sources of heterogeneity analysed were study design, gender, geographic area and publication year. Subgroup analyses were also performed on

cancer sites where 10 or more studies were available and considered study design, gender and geographical area. Bagnardi et al. (2015) reported that moderate and heavy drinking but not light drinking was associated with an increased risk of laryngeal cancer (RR = 0.87 (95% CI 0.68−1.11) I^2 = 39% for light drinkers; RR = 1.44 (95% CI 1.25−1.66), I^2 = 61% for moderate drinkers and RR = 2.65 (95% CI 2.19−3.19), I^2 = 77% for heavy drinkers. The association was slightly stronger in case-control studies than cohort studies. Analyses for potential sources of heterogeneity (study type, sex, geographical population) are shown in table A below.

Table A: Extract from Bagnardi et al (2015) of the laryngeal cancer data by study type, sex and geographical population

Alcohol intake	All		Study Type			Sex			Population groups		
	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)	N	RR (95%CI)	I^2 (%)
	All			Cohort			Men			European	
Light	0.87 (0.68-1.11)	39	3	0.81 (0.61-1.07)	21	8	0.85 (0.61-1.19)	51	4	0.83 (0.41-1.67)	54
Moderate	1.44 (1.25-1.66)	61	3	1.09 (0.70-1.72)	46	21	1.50 (1.23-1.83)	66	16	1.36 (1.12-1.65)	64
Heavy	2.65 (2.19-3.19)	77	3	1.12 (0.75-1.67)	0	22	2.77 (2.15-3.57)	83	18	2.71 (2.02-3.63)	82
				Case-Control			Women			North-American	
Light			11	0.88 (0.61-1.27)	45	3	0.89 (0.62-1.29)	0	7	0.90 (0.67-1.21)	37
Moderate			34	1.48 (1.28-1.73)	62	3	1.59 (1.06-2.38)	0	15	1.54 (1.20-1.98)	57
Heavy			33	2.81 (2.33-3.39)	76	1	1.55 (0.45-5.34)	0	13	2.74 (2.15-3.48)	60
										Asian	
Light									4	0.72 (0.34-1.50)	52
Moderate									4	1.57 (0.78-3.16)	69
Heavy									3	1.63 (0.70-3.79)	81
P (hetero-geneity test)				0.216			0.935			0.291	

Cessation effect (previously discussed at COC (CC/2014/04), included for completeness)

13. Using eight case–control studies from the International Head and Neck Cancer Epidemiology (INHANCE) consortium, Marron et al. (2010) estimated the number of years of quitting required to observe a reduced risk of head and neck cancers including laryngeal cancer and determined whether the risk declines to the level of never drinkers. They calculated odds ratios (ORs) and 95% confidence intervals (CIs) using unconditional logistic regression models for each case–control study. Overall, after ≥20 years of cessation, they found a 30% decreased risk of laryngeal cancer (OR 0.69 (0.52–0.91) compared with current drinkers. They observed that for

subjects consuming one or more drinks per day, the overall risk of laryngeal cancer initially increased in those who quit drinking 1–4 years ago but then they observed decreased risk with longer periods of time since quitting (OR for quitting drinking were 1.16 (95% CI 0.82–1.63) for 1–4 years, 0.88 (95% CI 0.65–1.19) for quitting drinking 5–9 years, 0.93 (95% CI 0.64–1.36) for quitting drinking 10–19 years, 0.69 (95% CI 0.52–0.91) for quitting drinking ≥20 years and 0.69 (95% CI 0.43–1.09) for never drinking compared with current drinking). They also observed that the ORs after quitting drinking ≥20 years appeared to decrease with increasing frequency of alcohol drinking for laryngeal cancer (<1 drink/day: OR = 0.99, 95% CI 0.56 – 1.74; 1–2 drinks/day: OR = 0.78, 95% CI 039 – 1.55; ≥3 drinks/day: OR = 0.28, 95% CI 0.09 – 0.86).

14. Ahmad-Kiadaliri et al. (2013) performed a meta-analysis on 4 case-control studies (Altieri et al., 2002; De Stefani et al., 2004; Marron et al., 2010 and Szymanska et al., 2011) to estimate the effect of alcohol cessation on the risk of developing laryngeal cancer. The generalized least square (GLS) technique developed by Greenland et al. (1992) was used to model the dose-response relationship between years since drinking cessation and the risk of disease. For laryngeal cancer, overall they found an increased risk over the initial years after quitting drinking but this was followed by a decreasing risk in subsequent years. They found that the risk of developing laryngeal cancer fell by 2% on average per year of cessation and stated that subjects who quit drinking alcohol ten years earlier had 82% of the risk of a current drinker. They reported that the risk of developing laryngeal cancer was 47% (OR 0.53, 95% CI 0.37–0.75) lower for never drinkers than for current drinkers and the time period required for the risk of laryngeal cancer following cessation to equal that of never drinkers was 36 years (95% CI 11 years – 106 years).

Summary of meta-analysis and combined analysis studies

15. In summary, the meta-analysis of Bagnardi et al. (2015), Ismali et al. (2010) and the pooled analysis of Lubin et al. (2010 and 2011) add further weight to the IARC evaluation that there is a causal association between alcohol consumption and laryngeal cancer. Both Bagnardi et al. (2015) and Islami et al. (2010) reported increased risk of laryngeal cancer among moderate and heavy drinkers but did not observe an association with light drinking. However, significant heterogeneity was observed between the studies included.

Cohort studies (Table 2)

16. The cohort studies have been divided into two categories: a) those examining laryngeal cancer incidence (3 studies) and b) those examining laryngeal cancer mortality (1 study). Within each section, the studies are reported by geographically region (UK, European, US and others regions) and within each region in order of their Newcastle-Ottawa (NO) score, beginning with the highest scoring studies.

Cohort studies examining alcohol consumption and laryngeal cancer risk

17. Maasland et al. (2014) investigated the effects of alcohol and tobacco consumption, both independently and jointly on the risk of head and neck cancer risk including laryngeal cancer in a large prospective Netherlands cohort study (NLCS) of

120,852 participants, aged 55-69 years from 204 Dutch population registries. After 17.3 years of follow-up, 199 cases of laryngeal cancer were found by record linkage to the Netherlands Cancer Registry. They carried out analyses on both the cancer cases and a sub-cohort of 4,288 members, randomly sampled from the entire cohort at baseline. Baseline information on alcohol consumption was obtained using a food frequency questionnaire (FFQ) including details on habitual intake of alcoholic beverage type during the year preceding the study, the frequency of consumption and the number of glasses consumed per occasion. Standard glass sizes were defined as 200ml for beer (8 g ethanol), 105 ml for wine (10 g ethanol) and 45 ml of liquor/spirits (13 g ethanol). Information was also obtained on drinking habits 5 years prior to baseline questionnaire. Abstainers were considered as those participants who indicated they never consumed alcohol or consumed alcohol less than once a month. Relative Risks (RR) and 95% CI were estimated using Cox proportional hazard models and adjusted for age (years), sex, education, non-occupational physical activity, energy intake, coffee and tea consumption, intake of fruit, vegetables, fat, red meat, meat products, family history of head-neck cancers and smoking. The different types of alcoholic beverages were also analysed and adjusted for ethanol intake to examine whether other components of the beverage may have an effect on the cancer risk. Abstainers were the reference category. They did not observed a statistically significant dose-response with increased consumption and laryngeal cancer risk compared to abstainers but did find an increased RR at highest level of consumption (RR = 1.03 (0.60-1.77) for >0 - <5 g ethanol/day; 0.94 (0.56-1.58) for 5 - <15 g ethanol/day; 1.10 (0.66-1.83) for 15 - <30 g ethanol/day and 1.54 (0.91-2.60) for ≥30 g ethanol/day). They did not observe an interaction between sex and continuous alcohol consumption in overall laryngeal cancer risk, though women had lower RRs than men. After adjusting for total alcohol intake, beer and liquor consumption were not significantly associated with laryngeal cancer risk. An inverse trend was observed for wine consumption but this was not statistically significant.

18. Kim et al. (2010) examined the association between alcohol consumption and all-cause and cancer mortality in a large-scale prospective study among 1.34 million Koreans aged 49 years or more. 49 cases of laryngeal cancer were identified. Medical staff at local hospitals obtained information on alcohol consumption such as frequency of consumption and amount of alcohol consumed per occasion in relation to a traditional Korean alcoholic drink “Soju”. Daily alcohol consumption was calculated into five categories for men (non-drinker, 1.0 -14.9, 15.0 – 29.9, 30.0 - 89.9 and ≥ 90 g ethanol/day) and three categories for women (non-drinker, 1.0 -14.9 and ≥15 g ethanol/day). Non-drinkers were the reference category for the analysis. Relative risks and 95% CI for alcohol consumption were obtained using Cox proportional hazard regression analysis and adjustments were made for age, residence, smoking, exercise, BMI, systolic and diastolic blood pressure, and fasting blood sugar. Only data for men were presented on laryngeal cancer. They observed an increased risk of laryngeal cancer among male heavy drinkers (RR = 2.50 (95% CI 1.07–5.85 for ≥90g ethanol/day)) compared to non-drinkers. No association was observed at the lower levels of alcohol intake. They found no association between lower categories of alcohol consumption and laryngeal cancer (1.0 -14.9 g ethanol/day (RR = 1.31, 95% CI 0.60–2.85); 15.0 – 29.9 g ethanol/day (RR = 0.87, 95 % CI 0.32–2.35) and 30.0 - 89.9 g ethanol/day (RR = 1.14, 95% CI 0.45–2.90)) compared to non-drinkers.

19. Jayaleshmi et al. (2013) examined the association of alcohol drinking and tobacco smoking with laryngeal cancer risk in a cohort of 65,553 men from the Karunagappally area in India. 85 cases of laryngeal cancers were identified by the Karunagappally Cancer registry between 1990 and 2009. Information on lifestyle including details of alcohol drinking status (never, former or current) was obtained using a standardised questionnaire. RR and 95% CI were obtained from Poisson regression analysis of grouped survival data and stratified by attained age, income and education. Never drinker was the reference category. They observed an increased risk of laryngeal cancer with both past and current alcohol consumption (RR = 2.0 (95% CI 1.1 - 3.7) for former drinkers and RR= 2.1 (95% CI 1.3 – 3.5) for current drinkers) compared to never drinkers. When they considered the combined effects of current alcohol drinking with current tobacco chewing, bidi smoking or cigarette smoking, respectively, the reported RR's of 1.7 (95% CI 1.5-5.5), 2.9 (95% CI 1.5 -5.5) and 5.7 (95% CI 2.6 – 12.8) compared to never drinker/never smokers.

Cohort studies examining alcohol consumption and laryngeal cancer mortality

20. Lopez et al. (2011) investigated the association between lifestyle factors such as education, tobacco smoking, alcohol consumption as well as interleukin-2 and interleukin-6 polymorphisms and the survival of head and neck cancers including laryngeal cancer in a Brazilian cohort of 445 subjects. 105 cases of laryngeal cancer were found. Information on alcohol consumption prior to cancer diagnosis was obtained using a structured questionnaire and reported in grams of ethanol per day (g ethanol/day) considering the equivalence of ethanol in different beverages such as beer, wine and spirits. Hazard ratios (HR) and corresponding 95% CI were estimated using Cox proportional hazard regression and were adjusted for age and gender. HR for alcohol consumption was calculated for each g ethanol/day increase. In this study, alcohol consumption did not exert any effect on the survival in laryngeal cancer (HR = 1.00; 95% CI 1.00-1.01).

Case-Control studies (Table 3)

21. Only one case-control study investigating alcohol consumption and laryngeal cancer risk was identified in the literature search. The study was a good quality European study as evaluated using the modified Newcastle-Ottawa scoring scheme.

Case-control studies examining alcohol consumption and laryngeal cancer risk

22. Marron et al. (2012) investigated the association of drinking different alcoholic beverage types and upper aero-digestive tract cancers (UADT) including laryngeal cancer in a large European case-control study. The data presented here was generated from the Alcohol-Related Cancers and Genetic Susceptibility in Europe (ARCAGE) study, which was initiated by IARC. It involved 14 centres in 10 European countries. The majority of centres used hospital based controls with the exception of the three UK centres where population-based controls were recruited. Information on lifestyle including information on alcohol consumption was obtained by a trained interviewer using a questionnaire. They obtained information on volume of alcohol consumed, frequency and duration of various alcoholic beverages (beer, wine, hard liquor and aperitifs) in different periods of life, details of binge drinking (drinking large volumes in short periods of time, ascertained by asking whether more than 10 drinks

had been consumed in a couple of hours) and details on the specific type of alcohol consumed ("pure drinker" consuming one beverage type exclusively; "predominant drinker" consuming one beverage type to more than 66% of the time and "mixed drinker" consuming more than one type of alcoholic beverage type to similar proportions). Odds ratios (OR) and 95 % confidence intervals (CI) were estimated using unconditional logistic regression and adjusted for the following potential confounding factors: age, sex, centre, education level, vegetable, smoking (duration, frequency and time since quitting of tobacco, type of tobacco and smoking status) and alcohol drinking (adjusting liquor consumption on wine and beer, beer consumption on wine and liquor, and wine consumption on beer and liquor). The analysis included 631 laryngeal cancer cases and 2,125 controls.

23. Stratifying the results for laryngeal cancer adjusting for cumulative alcohol consumption, the OR and 95 %CI of laryngeal cancer among 'pure drinkers' of wine, beer and liquor drinking, respectively, were 2.01 (95% CI 1.02 – 3.94), 1.56 (95% CI 0.77 – 3.15) and 1.41 (95% CI 0.48 – 4.18) in men and 0.44 (95% CI 0.12 – 1.59), 0.25 (95% CI 0.04 – 1.72) and 0.11 (95% CI 0.01 -1.48) in women compared to never drinkers. Among predominant drinkers, they observed OR and 95% CI for wine, beer and liquor drinking, respectively, of 1.28 (95% CI 0.68 – 2.41), 1.12 (95% CI 0.58 – 2.19) and 2.08 (95% CI 0.98 – 4.38) in men and 0.48 (95% CI 0.13 – 1.74), 0.43 (95% CI 0.08 – 2.37) and 1.23 (95% CI 0.26 – 5.72) in women compared to never drinkers. Among mixed drinkers, they observed OR and 95% CI for wine, beer and liquor drinking, respectively, of 1.18 (95% CI 0.64 – 2.19), 1.36 (95% CI 0.75 – 2.45) and 1.34 (95% CI 0.73 – 2.44) in men and 0.44 (95% CI 0.13 -1.42), 0.64 (95% CI 0.20 - 2.05) and 0.63 (95% CI 0.19 - 2.07) in women compared to never drinkers.

Overall Summary

24. Since 2009, the majority of published papers on alcohol consumption and laryngeal cancer have been either meta-analysis or pooled analysis. In line with previous IARC evaluations, the meta-analysis of Bagnardi et al. (2015) and pooled analysis of Lubin et al. (2010 and 2011) added further weight that the increased risk of laryngeal cancer with increased consumption of alcohol. In the cohort studies of Maasland et al. (2014) and Kim et al. (2010), heavy drinking was associated with increased laryngeal cancer risk. The case-control study of Marron et al. (2012) reported an increased risk of laryngeal cancer among male drinkers of wine, beer and liquor but the data for female drinkers was less consistent. The relevance of the results from Asian populations to the UK population requires consideration.

Questions for the Committee

1) What are the views of the Committee on the recently available epidemiological studies (case-control, cohort, pooled and meta-analysis) on alcohol exposure and laryngeal cancer risk?

2) Do the studies reviewed here add further weight to the existing view that alcohol consumption is causally associated with laryngeal cancer risk?

Secretariat
April 2015

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Table 1.Pooled and meta-analysis studies examining Alcohol Consumption and laryngeal cancer risk, published since 2009							
Reference, location, name of study	**Description (No. in analysis)**	**Exposure assessment**	**Exposure categories**	**No. of cases/ controls, n**	**Pooled odds ratio (95% CI)[a]**	**Adjustment factors**	**Comments**
Hashibe et al 2009 European and American studies International Head and Neck Cancer Epidemiology (INHANCE) consortium	Pooled analysis with 17 case-control studies 2,959 laryngeal cancer cases 13,130 controls	Varied	**<u>Drinking Status</u>** ***Alcohol alone*** ***Tobacco alone*** ***Alcohol and tobacco*** Never smoker/never drinker Never smoker/1–2 drinks/day 1–20 cigs/day/1–2 drinks/day >20 cigs/day/1–2 drinks/day Never smoker/>=3 drinks/day 1–20 cigs/day/>=3 drinks/day >20 cigs/day/>=3 drinks/day	 284/ 1308 89/3041 2541/ 6850	 1.21 (0.77- 1.92) 6.76 (4.58 - 9.96) 14.22 (8.26 -24.46) 1.00 (ref) 1.20 (0.72 - 2.02) 8.33 (5.07- 13.69) 16.91 (9.66 - 29.61) 3.16 (1.23 - 8.16) 18.94 (10.64 - 33.71) 36.87 (16.60 - 81.90)	Age, sex, education, race/ethnicity and study centre	

Table 1.Pooled and meta-analysis studies examining Alcohol Consumption and laryngeal cancer risk, published since 2009							
Reference, location, name of study	**Description (No. in analysis)**	**Exposure assessment**	**Exposure categories**	**No. of cases/ controls, n**	**Pooled odds ratio (95% CI)[a]**	**Adjustment factors**	**Comments**
Lubin et al 2010 European and American studies International Head and Neck Cancer Epidemiology (INHANCE) consortium	Pooled analysis with 15 case-control studies of the 17 studies analysed in Hashibe et al 2009	Varied	**<u>Drinking status</u>** 0 1-49 drink-yrs 50–99 drink-yrs 100–149 drink-yrs 150–199 drink yrs ≥200 drink yrs < 1 drink/day 1–2.9 drinks/day 3.0-4.9 drinks/day 5-10 drinks/day	 243/2,783 536/3,766 264/1,594 221/954 201/628 508/971 390/2,783 435/2,571 322/1,347 583/1,206	 1.00 0.98 (0.8 - 1.2) 0.94 (0.6 -1.4) 1.20 (0.8 - 1.8) 1.35 (0.8 - 2.2) 1.80 (1.1 - 3.1) 1.00 (Ref) 1.05 (0.8 - 1.4) 1.08 (0.7 - 1.6) 1.64 (1.0 - 2.6)	Sex, education, BMI, smoking and use of other tobacco products.	Never drinker was the reference category

Table 1.Pooled and meta-analysis studies examining Alcohol Consumption and laryngeal cancer risk, published since 2009

Reference, location, name of study	Description (No. in analysis)	Exposure assessment	Exposure categories	No. of cases/ controls, n	Pooled odds ratio (95% CI)[a]	Adjustment factors	Comments
Lubin et al 2011 European and American studies International Head and Neck Cancer Epidemiology (INHANCE) consortium	Pooled analysis with 15 case-control studies of the 17 studies analysed in Hashibe et al 2009	Varied	**Drinking status** **Men** 0 drink-yrs 1-49 drink-yrs 50–99 drink-yrs 100–149 drink-yrs 150–199 drink yrs ≥200 drink yrs **Women** 0 drink-yrs 1-49 drink-yrs 50–99 drink-yrs 100–149 drink-yrs 150–199 drink yrs ≥200 drink yrs **Men** < 1 drink/day 1–2.9 drinks/day 3.0-4.9 drinks/day 5-10 drinks/day **Women** < 1 drink/day 1–2.9 drinks/day 3.0-4.9 drinks/day 5-10 drinks/day	 91/2,111 94/1,862 22/339 16/ 131 8/47 6/22 142/1,765 416/3,478 219/1,483 176/927 151/634 399/1,030 85/1,447 32/686 21/133 8/ 38 287/2,583 368/2,354 247/1,327 459/1,288	 1.00 0.91 (0.7 – 1.2) 0.78 (0.5 -1.2) 0.99 (0.6 - 1.6) 1.13 (0.7 – 1.9) 1.51 (0.9 – 2.7) 1.00 1.14 (0.8 – 1.7) 2.68 (1.0 – 7.1) 3.18 (1.0 – 11.0) 3.84 (0.8 – 19.0) 3.79 (0.6 – 26.0) 1.00 1.20 (0.9 - 1.6) 1.20 (0.8 - 1.9) 1.89 (1.1 – 3.1) 1.00 0.45 (0.2 -1.0) 0.67 (0.2 – 2.3) 0.52 (0.1-2.7)	Study, age, education, BMI, cigarette per day, years since smoking cessation, use of other tobacco products, drinks per day in the drink-year analysis and drink-years in the drinks per day analysis.	Never drinker was the reference category

Table 1.Pooled and meta-analysis studies examining Alcohol Consumption and laryngeal cancer risk, published since 2009

Reference, location, name of study	Description (No. in analysis)	Exposure assessment	Exposure categories	No. of cases/ controls, n	Pooled odds ratio (95% CI)[a]	Adjustment factors	Comments
Ismali et al, 2010	Meta-analysis of 40 studies (38 case-controls and 2 cohort studies.	Varied	**Drinking status** Non-drinker /occasional drinker Drinker Non/occasional drinker Light drinker Moderate drinker Heavy drinker ***Subgroup analyses*** ***Any intake*** Population-based controls Only non-drinkers as ref Adjusted results ***Light Drinkers*** Population-based controls Only non-drinkers as ref Adjusted results ***Moderate Drinkers*** Population-based controls Only non-drinkers as ref Adjusted results ***Heavy Drinkers*** Population-based controls Only non-drinkers as ref Adjusted results		 1.0 1.90 (1.59 – 2.28) 1.00 0.88 (0.71–1.08) 1.47 (1.25–1.72) 2.62 (2.13–3.23) 1.87 (1.32–2.65) 1.62 (1.27–2.08) 1.84 (1.50–2.26) 0.78 (0.59–1.03) 0.87 (0.69–1.08) 0.88 (0.70–1.12) 1.41 (1.11–1.80) 1.61 (1.28–2.15) 1.50 (1.23–1.83) 2.55 (1.71–3.81) 2.15 (1.50–3.10) 2.46 (1.88–3.22)	Age, sex, and smoking	The reference category for the meta-analysis included both non-drinkers and occasional drinkers Light drinking = ≤12.5 g ethanol = ≤ 1 drink Moderate drinking = > 12.5 - <50g ethanol = > 1 drink - <4 drinks Heavy drinking = ≥ 50g ethanol = ≥4 drinks.

Table 1.Pooled and meta-analysis studies examining Alcohol Consumption and laryngeal cancer risk, published since 2009							
Reference, location, name of study	**Description (No. in analysis)**	**Exposure assessment**	**Exposure categories**	**No. of cases/ controls, n**	**Pooled odds ratio (95% CI)[a]**	**Adjustment factors**	**Comments**
Bagnardi et al. (2013)	Meta-analysis of 20 studies (7 cohorts and 13 case-controls)	Varied	**Drinking Status** Non-drinker Light-drinker ***Stratified Results*** ***Study design*** Cohort Case–control ***Geographical area*** Europe North America Asia ***Sex*** Men Women		 1.0 0.90 (0.73 -1.10) 0.96 (0.71- 1.30) 0.83 (0.63- 1.09) 0.84 (0.43 -1.62) 0.89 (0.66- 1.20) 0.91 (0.60- 1.37) 0.89 (0.67-1.16) 0.93 (0.71 -1.22)	Age, Sex, Liver Disease, BMI or Diabetes	Light alcohol drinking = up to 1 drink/day (up to 12.5 g alcohol/day)
Bagnardi et al. (2015)	Meta-analysis 41 studies (3 cohort 38 case-control studies)	Varied	**<u>Drinking Status</u>** Non-Drinker Light drinker Moderate Drinker Heavy Drinker		 1.0 0.87 (0.68−1.11) 1.44 (1.25−1.66) 2.65 (2.19−3.19)	Age, Sex, Smoking	Light, moderate and heavy drinking was measured at intervals whose midpoint was ≤12.5, ≤50 and > 50g of alcohol per day respectively

Table 1.Pooled and meta-analysis studies examining Alcohol Consumption and laryngeal cancer risk, published since 2009							
Reference, location, name of study	**Description (No. in analysis)**	**Exposure assessment**	**Exposure categories**	**No. of cases/ controls, n**	**Pooled odds ratio (95% CI)[a]**	**Adjustment factors**	**Comments**
Marron et al. (2010)	8 case control studies used in pooled analysis 9167 cases 12593 controls	Exposure assessment varied slightly across the studies but the questionnaire were conceptually similar	**Drinking status** Current drinkers **Cessation of alcohol drinking** >1–4 years 5–9 years 10–19 years ≥ 20 years Never drinkers p trend **Frequency of consumption and effect after ≥ 20 cessation** <1 drink/day 1–2 drinks/day ≥3 drinks/day	1103/4961 141/353 112/358 199/553 157/514 243/	1.00 (Ref.) 1.16 (0.82–1.63) 0.88 (0.65–1.19) 0.93 (0.64–1.36) 0.69 (0.52–0.91) 0.69 (0.43–1.09) 0.28 0.99 (0.56 – 1.74) 0.78 (0.39 – 1.55) 0.28 (0.09 – 0.86)	Adjusted for age, sex, race/ethnicity, study centre, education level, tobacco pack years and drinking frequency	Results presented in this table are based on overall risk. Data available in study on the effect of cessation stratified by frequency of alcohol consumption.

Table 1.Pooled and meta-analysis studies examining Alcohol Consumption and laryngeal cancer risk, published since 2009							
Reference, location, name of study	**Description (No. in analysis)**	**Exposure assessment**	**Exposure categories**	**No. of cases/ controls, n**	**Pooled odds ratio (95% CI)[a]**	**Adjustment factors**	**Comments**
Ahmad-Kiadaliri et al. (2013) 9 studies included were: Altieri et al., 2002; Balaram et al.,2002; Castellsague et al., 2004; De Stefani et al., 2004; Garrote et al., 2001; Marron et al., 2009; Martinez, 1969; Szymanska et al., 2011; Takezaki	4 case- control studies were included in the meta-analysis for laryngeal estimates cancer	Exposure assessment varied across the studies	**Drinking status** Never Drinker Current Drinker		 1.00 (referent) 0.53 (0.37–0.75)		13 studies were included in the systematic review but only 9 were included in the meta-analysis Excluded from the meta-analysis were 1) Takezaki et al. (2000) as it did not present sufficient data for meta-analysis, 2) Rehm et al. (2007) as it was a meta-analysis including some of the other studies identified for inclusion, 3) Franceschi et al. (2000) and 4) Hayes et al. (1999) to avoid giving too much weight to these two specific samples as they were included in the pooled analysis of Marron et al. (2010). The risk of developing laryngeal cancer was 47% lower for never drinkers than for current drinkers. Alcohol-related elevated risk of laryngeal cancer would last 36 (95% CI: 11–106) years after drinking cessation. Majority of data was presented graphically in paper

Table 2. Cohort studies examining the effect of alcohol consumption on laryngeal cancer risk, published since 2009

Reference, location, year of study	Cohort description (No. in analysis)	Exposure assessment	Exposure categories	No. of cases	Pooled odds ratio and confidence intervals (95% CI)	Adjustment factors	Comments	Star Rating for Quality
Maasland et al. (2014) Netherlands cohort study (NLCS) of 120,852 participants, aged 55-69 years from 204 Dutch population registries.	Prospective cohort 199 cases of laryngeal cancer and a sub-cohort of 4,288 members.	Food Frequency Question-naire (FFQ)	**Drinking status** Abstainers >0 - <5 g/day 5 - <15 g/day 15 - <30 g/day ≥30 g/day Continuous 10g/day Overall Men Women Alcohol consumption (g/day) stable users[1] Abstainers >0 - <5 g/day 5 - <15 g/day 15 - <30 g/day ≥30 g/day Continuous 1 g/day **Alcoholic beverages (glasses/day)** ***Beer*** None >0-<1 1-<2 ≥2 Continuous 1 glass/day ***Wine*** None >0-<1 1-<2 ≥2 Continuous 1 glass/day ***Liquor*** None >0-<1 1-<2 ≥2 Continuous 1 glass/day	 26 36 40 49 48 199 187 12 20 17 21 27 31 116 87 69 23 20 199 114 57 20 6 197 63 78 37 20 198	 1.0 1.03 (0.60-1.77) 0.94 (0.56-1.58) 1.10 (0.66-1.83) 1.54 (0.91-2.60) 1.10 (1.02-1.18) 1.10 (1.03-1.19) 0.85 (0.46–1.59) 1 (reference) 0.72 (0.35-1.46) 0.72 (0.37-1.40) 0.96 (0.50-1.83) 1.57 (0.82-3.02) 1.16 (1.04-1.28) 1.00 (reference) 0.85 (0.60-1.22) 1.19 (0.71-2.01) 1.30 (0.69-2.46) 1.08 (0.96-1.23) 1.00 (reference) 0.74 (0.52-1.05) 1.07 (0.63-1.83) 0.39 (0.15-0.99) 0.88 (0.68-1.14) 1.00 (reference) 1.17 (0.81-1.67) 1.08 (0.67-1.74) 0.95 (0.47-1.93) 0.98 (0.80-1.21)	Age (years), sex, education, non-occupational physical activity, energy intake, coffee and tea consumption, intake of fruit, vegetables, fat, red meat, meat products, family history of head-neck cancers and smoking	Abstainers were the reference category Subjects who had not changed their continuous alcohol consumption habits in the 5 years before baseline: for “beer” and “other alcoholic beverages”, participants could indicate whether 5 years before baseline they drunk (1) more than, (2) equal amounts of or (3) less than at baseline; the fourth answer option was (4) “I never use this”	[1]8

Table 2. Cohort studies examining the effect of alcohol consumption on laryngeal cancer risk, published since 2009								
Reference, location, year of study	**Cohort description (No. in analysis)**	**Exposure assessment**	**Exposure categories**	**No. of cases**	**Pooled odds ratio and confidence intervals (95% CI)**	**Adjustment factors**	**Comments**	**Star Rating for Quality**
Kim et al. 2010 KNHIC HEC 2000 Korea 2001–2005 (5 years)	Cohort consisted of 1,341,393 Korean men aged 40-69 years old. 49 laryngeal cancer cases	Interview based	**Drinking status** *Men* *g ethanol/d* Non-drinker 1.0 -14.9 15.0 – 29.9 30.0 - 89.9 ≥ 90		1.0 1.31(0.60–2.85) 0.87 (0.32–2.35) 1.14 (0.45–2.90) 2.50 (1.07–5.85)	Age, residence, smoking, exercise, BMI, systolic and diastolic blood pressure, fasting blood sugar, total cholesterol (only women); stratified by sex	Non-drinkers were the reference category for the analysis.	8 stars
Jayaleshmi et al. (2013) Cohort of 65,553 men from the Karunagappally area in India	85 cases of laryngeal cancers	Standardised questionnaire	**Drinking status** Never Former Current	 27 19 39	 1.0 (reference) 2.0 (1.1 - 3.7) 2.1 (1.3 – 3.5)	Attained age, income and education	Never drinker was the reference category	5
Lopez et al 2010 Brazilian cohort on laryngeal cancer mortality 445 subjects	105 cases of laryngeal cancer	Structured questionnaire	**Drinking status** ***Alcohol consumption g ethanol/day*** Never Drinker Drinker		 1.00 (reference) 1.00 (1.00 -1.01)	Age and gender	Hazard ratio calculated for each g ethanol/day increase	5

Table 3. Case-Control studies examining the effect of alcohol consumption on laryngeal cancer risk published since 2009

Reference, location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure category	Relative Risk (95% CI)[b]	Adjustment factors	Comments	Star Quality
Marron et al 2012 European Alcohol-Related Cancers and Genetic Susceptibility in Europe (Arcage) study, 14 centres in 10 European countries	631 laryngeal cancer cases Male and female cases identified with histologically or cyto-logically confirmed UADT cancer diagnosed within the past 6 months	2,125 controls UK population-based controls randomly selected from the same primary practice list as the corresponding case (N = 390) Hospital controls were randomly selected from subjects admitted as in- or out-patients in the same hospital as the case (N = 1837)	Interviewer based questionnaire	**Drinking Status** ***Men*** **Wine** Never Drinker Drinks only wine Drinks wine predominantly Drinks wine and other types **Beer** Never Drinker Drinks only beer Drink beer predominantly Drinks beer and other types **Liquor** Never Drinker Drinks only liquor Drink liquor predominantly Drinks liquor and other types ***Female*** **Wine** Never Drinker Drinks only wine Drinks wine predominantly Drinks wine and other types **Beer** Never Drinker Drinks only beer Drink beer predominantly Drinks beer and other types **Liquor** Never Drinker Drinks only liquor Drink liquor predominantly Drinks liquor and other types	 1.0 (ref) 2.01 (1.02-3.94), 1.28 (0.68-2.41), 1.18 (0.64 –2.19) 1.0 (ref) 1.56 (0.77 –3.15) 1.12 (0.58 –2.19) 1.36 (0.75 –2.45) 1.0 (ref) 1.41 (0.48 –4.18) 2.08 (0.98 –4.38) 1.34 (0.73 –2.44) 1.0 (ref) 0.44 (0.12 –1.59) 0.48 (0.13 –1.74) 0.44 (0.13 -1.42) 1.0 (ref) 0.25 (0.04 –1.72) 0.43 (0.08 –2.37) 0.64 (0.20 -2.05) 1.0 (ref) 0.11 (0.01 -1.48) 1.23 (0.26 –5.72) 0.63 (0.19 -2.07)	age, sex, centre, education level, vegetable, smoking (duration, frequency and time since quitting of tobacco, type of tobacco and smoking status) and alcohol drinking (adjusting liquor consumption on wine and beer, beer consumption on wine and liquor, and wine consumption on beer and liquor).		6

COMMITTEE ON CARCINOGENICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

Consumption of Alcohol and Laryngeal Cancer Risk

Extract from IARC Monographs on the Evaluation of Carcinogenic Risks to Humans Volume 96: Alchol Consumption and Ethyl Carbamate
Pages 329-351

Full document is available here:
http://monographs.iarc.fr/ENG/Monographs/vol96/mono96.pdf

Secretariat
April 2015

COMMITTEE ON CARCINOGENICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

Consumption of Alcohol and Laryngeal Cancer Risk

Extract from IARC Monographs on the Evaluation of Carcinogenic Risks to Humans Volume 100E: Personal Habits and Indoor Combustions

Pages 379-380, 446, 472 and Tables 2.6, 2.7, and 2.8

Full document is available here:
http://monographs.iarc.fr/ENG/Monographs/vol100E/mono100E.pdf
Tables are available here:
http://monographs.iarc.fr/ENG/Monographs/vol100E/100E-06-Table2.6.pdf
http://monographs.iarc.fr/ENG/Monographs/vol100E/100E-06-Table2.7.pdf
http://monographs.iarc.fr/ENG/Monographs/vol100E/100E-06-Table2.8.pdf

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Secretariat
April 2015