

Alcohol and cancer risk, with focus on moderate drinkers

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Alcohol substantially increases the risk of head and neck and oesophageal cancers. The risks are essentially due to total ethanol intake. Alcohol drinking has also been associated with primary liver cancer, with cancers of the large bowel in both sexes, of the female breast, and -at high doses only- of the pancreas [1].

To evaluate the strength of the evidence provided by the epidemiological literature on the association between alcohol consumption and the risk of 18 known or potentially alcohol-related neoplasms, we performed a search of the epidemiological literature from 1966 to 2012 using major bibliographic data-bases. We fitted meta-regression models considering linear and non-linear effects of alcohol intake. We also investigated the effects of selected characteristics of the studies (e.g., allowance for tobacco) and of individuals included in the studies (e.g., gender, age, etc.), as possible sources of heterogeneity of the estimates. A total of approximately 600 studies including 200,000 cases were considered. Strong trends in risk were observed for cancers of the oral cavity, oesophagus and larynx, the strongest one being for oral cancer, with a relative risk (RR) around 5 for 50 g/day of alcohol. Direct relations were also observed for cancers of the colon and rectum, liver, breast, and (for high doses only) pancreas [2].

We also specifically considered the association between light alcohol consumption and cancer risk for those sites for which there is sufficient or limited evidence for carcinogenicity of alcohol [1, 3]. Thus, we considered cancers of the upper digestive and respiratory tract (oral and pharyngeal cancer, esophageal squamous cell carcinoma - but not adenocarcinoma of the esophagus, that is not associated to alcohol drinking [4] - and laryngeal cancer), liver, colorectum, pancreas and breast.

Quantification of the association between low doses of alcohol consumption and cancers known to be alcohol-related is particularly important, as it is still unclear

whether there is any threshold in intake below which no effect of alcohol drinking on cancer is evident.

Data on light alcohol drinking, defined as 1 or less drink/day, were derived from meta-analyses of all studies to December 2010 [5].

For oral and pharyngeal cancer, two meta-analyses provided evidence that an increased risk is present also at low doses of consumption [6, 7]. The overall RR of oral and pharyngeal cancer, based on 20 case-control and 3 cohort studies, was 1.17 (95% confidence interval, CI, 1.06-1.29) for 1 or less drink/day vs. non/occasional drinkers [5].

For esophageal squamous cell carcinoma [8], the summary RR for light drinking was 1.30 (95% CI, 1.09-1.56) for the overall analysis, based on 27 studies. When the analysis was stratified by geographical area, the association was stronger in Asia (RR=1.49; 95% CI, 1.12-1.98) than in other regions of the world (RR=1.17; 95% CI, 0.99-1.39), suggesting a potential effect modification by genetic susceptibility. No increase in risk with consumption of low doses of alcohol was observed in never-smokers, but the estimate was based on 5 studies only.

In contrast, laryngeal cancer was not associated with light alcohol consumption [9]. The summary RR for light drinking, based on 10 case-control and 3 prospective studies, was 0.90 (95% CI, 0.73-1.10). Results were materially unchanged in several subgroup analyses, including those of studies adjusted for smoking.

A total of 54 studies provided information on low doses of alcohol and colorectal cancer risk. No overall association was reported with colorectal (RR=1.00; 95% CI, 0.95-1.05), colon (RR=0.96; 95% CI, 0.90-1.02) nor rectal (RR=1.06; 95% CI, 0.98-1.14) cancers. Results were consistent across strata of sex, geographical area and various other covariates.

For breast cancer, on the basis of 110 studies and over 60,000 cases, the RR was 1.05 (95% CI, 1.02-1.08).

A meta-analysis on alcohol and pancreatic cancer considered moderate alcohol consumption, defined as less than 3 drinks/day, and found strong evidence for a lack of any positive association at low to moderate intakes [10]. Seventeen case-control and 7 cohort studies were included, and the summary RR was 0.92 (95% CI, 0.86-0.97).

For liver cancer, on the basis of 20 studies, the RR was 1.03 (95% CI, 0.90-1.17). This estimate should however be interpreted with caution, since most alcohol related liver cancers follow liver diseases - particularly cirrhosis - which lead to a reduction in alcohol consumption, and thus to a substantial under-estimation of the real associations [11].

Approximately 400,000 cases of cancer were attributable to alcohol drinking worldwide in 2002, representing 3.6% of all cancers (5.2% in men, 1.7% in women) [12]. The corresponding figure for mortality is about 250,000 deaths (3.5% of all cancer deaths). Most recent unpublished estimates for 2012 gave a total of over 800,000 alcohol related cancers worldwide (5.8% of the total), 580,000 (7.8%) in men and 230,000 (2.3%) in women. This proportion is particularly high among men in Central and Eastern Europe. Among women, breast cancer comprised 60% of alcohol-attributable cancers. Thus, the global burden of alcohol associated cancers is substantial. Low alcohol drinking may account for about 12 to 15% of alcohol-related cancers (50 to 60,000) and cancer deaths (30 to 40,000). Thus, restricting alcohol drinking to up to 2 drinks per day in men and to one drink in women would avoid over 85% of all alcohol-related cancers worldwide [5, 13].

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