

Alcohol Consumption and the Risk of Cancer

A Meta-Analysis

VINCENZO BAGNARDI, MS.C., MARTA BLANGIARDO, MS.C.,
CARLO LA VECCHIA, M.D., AND GIOVANNI CORRAO, PH.D.

Alcohol consumption has been linked to an increased risk for various types of cancer. A combined analysis of more than 200 studies assessing the link between alcohol and various types of cancer (i.e., a meta-analysis) sought to investigate this association in more detail. This meta-analysis found that alcohol most strongly increased the risks for cancers of the oral cavity, pharynx, esophagus, and larynx. Statistically significant increases in risk also existed for cancers of the stomach, colon, rectum, liver, female breast, and ovaries. Several mechanisms have been postulated through which alcohol may contribute to an increased risk of cancer. Concurrent tobacco use, which is common among drinkers, enhances alcohol's effects on the risk for cancers of the upper digestive and respiratory tract. The analysis did not identify a threshold level of alcohol consumption below which no increased risk for cancer was evident. KEY WORDS: AOD (alcohol or other drug) consumption; chronic AODE (effects of AOD use, abuse, and dependence); cancer; carcinogenesis; oral disorder; esophageal disorder; dose-response relationship; gender differences; tobacco in any form; distilled alcoholic beverage; drug concentration; risk analysis; meta-analysis

Regular alcohol consumption can have numerous consequences, beneficial or detrimental, on the health of the drinker. For example, light-to-moderate alcohol consumption¹ may protect against certain types of heart disease and stroke. Conversely, heavy drinking has been associated with liver disease; cardiovascular disease; disorders of the digestive tract; and illness or death from alcohol-related injuries, motor vehicle crashes, and violence. Another group of disorders that has been linked to drinking is cancer, particularly cancers of the upper airway and digestive tract (e.g., mouth, pharynx, larynx, and esophagus). Although alcohol has not been shown to cause cancer (i.e.,

be carcinogenic) in animal studies, strong epidemiological evidence indicates that consumption of alcoholic beverages increases the risk of those cancers. Alcohol consumption also is associated with primary liver cancer. This relationship is difficult to investigate in epidemiological studies, however, because it is more indirect. Thus, alcohol causes cirrhosis of the liver in a substantial proportion of heavy drinkers, which then can lead to liver cancer. In addition, heavy alcohol consumption can increase the drinker's risk for infection with the hepatitis C virus (HCV), which in turn can also result in liver cancer (for more information on the relationship between alcohol consump-

tion and HCV infection, see the article in this issue by Lieber, pp. 245–254).

Alcohol consumption also has been linked to cancers of the large bowel (i.e., colon and rectum) in both men and women and to breast cancer in women, although these associations have not yet been proven unequivocally. Nevertheless, because these are the two most common types of cancer in developed countries after lung cancer, even a moderate increase in risk may result in

¹The definitions of light, moderate, and heavy alcohol consumption vary across studies. In the United States, the U.S. Department of Health and Human Services and the U.S. Department of Agriculture have defined moderate drinking as no more than one drink per day for women and no more than two drinks per day for men.

a relatively large number of additional cases and therefore have important public health implications. The association between alcohol consumption and other types of cancer (e.g., stomach, pancreatic, prostate, and endometrial cancer) is still controversial (International Agency for Research on Cancer [IARC] 1988; Doll et al. 1999).

The increased risk of cancer among heavy drinkers is primarily attributed to the alcohol (chemically referred to as ethanol) in alcoholic beverages. Thus, the risk tends to increase with the overall amount of ethanol consumed. It is still unclear, however, whether any defined consumption threshold exists below which no increased risk for cancer is evident (IARC 1988; Doll et al. 1999).

To evaluate the overall effects of alcohol on the cancer risk of a population, one must accurately quantify its effects on various types of tumors. To this end, researchers have performed comprehensive meta-analyses of published studies investigating the relationship between alcohol intake and the risk for numerous types of cancer. Meta-analyses are studies that pool data from several studies, thereby substantially enhancing the overall number of cases evaluated. This approach allows researchers to detect relationships that may have been overlooked in the individual studies because

of the relatively small sample size and insufficient statistical power of those individual studies. This article summarizes the major findings of one such meta-analysis (Corrao et al. 1999, 2000).

METHODS USED FOR THE META-ANALYSIS

To identify scientific articles to include in the meta-analysis, the researchers followed three steps: First, they conducted a search of several bibliographic databases (e.g., *MEDLINE*, *Current Contents*, *EMBASE*, *CAB Abstracts*, and *Core Bio-medical Collection*) for studies published between 1966 and 2000. Second, the investigators reviewed all references in the resulting articles to identify any studies that had not been found in the database search. And third, to ensure that the list of studies included was as complete as possible, the investigators conducted a manual search of the most relevant journals of epidemiology and medicine and compared their search results with those of other general reviews and meta-analyses published on this topic.

Each article identified by this search process was reviewed and included in the analysis if it met the following three criteria:

- The article was a case-control or a cohort study published as an original article. Case-control studies compare people with a certain disease (e.g., cancer)—the cases—with a similar group of people without the disease—the controls. Investigators then collect information (e.g., regarding alcohol consumption) for both groups to determine whether differences exist between the groups. For example, significant differences between the groups with respect to alcohol intake suggest that alcohol was a causative factor in the disease. Cohort studies follow a group of initially healthy people over a prolonged period of time. At the outset, the investigators determine the participants' drinking patterns so that they can relate drinking patterns and disease development during the followup period.

- The findings of the study were expressed as relative risk (RR) or odds ratio (OR) and considered at least three levels of alcohol consumption. The RR determines the strength of the relationship between a variable (e.g., alcohol consumption) and the development of a disease. The RR for a disease among people without the variable (e.g., among abstainers) is defined as 1.0. A RR among people with the variable (e.g., among drinkers) of greater than 1.0 indicates that the variable increases the risk of the disease. Conversely, an RR of less than 1.0 indicates that the variable has a protective effect. (The OR is used to estimate the RR under certain conditions.)
- The article reported the number of cases and non-cases (i.e., controls in case-control studies and person-time exposed during the followup in a cohort study) and estimates of the RR or OR for each exposure level.

Two readers, who received no information on the names and affiliations of the authors of each study or the alcohol-related results, independently determined the eligibility of each article for inclusion in the meta-analysis. When the results of a study were published in more than one article, only the most recent and complete article was included in the analysis.

To estimate the effect of alcohol consumption on the risk for each type of cancer studied, based on the pooled data from all studies included in the meta-analysis, the investigators used meta-regression models—statistical models developed specifically for such analyses (Corrao et al. 1999, 2000). For a more detailed description of these statistical analyses, see the textbox, p. 265, and the articles by Corrao and colleagues (1999, 2000).

RESULTS OF THE META-ANALYSIS

In all, 229 studies (183 case-control studies and 46 cohort studies) met the eligibility criteria and were included in

VINCENZO BAGNARDI, *Ms.C.*, and MARTA BLANGIARDO, *Ms.C.*, are *Ph.D. students in statistics*, and GIOVANNI CORRAO, *Ph.D.*, is a *full professor in statistics at the Department of Statistics, University of Milan-Bicocca, Milan, Italy*.

CARLO LA VECCHIA, *M.D.*, is an *associate professor in epidemiology at the Institute of Medical Statistics and Biometry, University of Milan*, and *head of the laboratory of general epidemiology at the Mario Negri Institute of Pharmacological Research, Milan, Italy*.

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Summary of the Studies Included in the Meta-Analysis

Cancer site	No. of Studies	No. of Cases	Study design		Pooled RR [and 95% CI] associated with alcohol intake of			Gender effect (p)	Heterogeneity test (p)
			Cohort	Case-control	25 g/day [range]	50 g/day [range]	100 g/day [range]		
Oral cavity	26	7,954	1	25	1.73 [1.67–1.78]	2.77 [2.67–2.95]	5.75 [5.22–6.34]	n.s.	< 0.01
Esophagus ^a	28	7,239	1	27	1.51 [1.48–1.55]	2.21 [2.11–2.31]	4.23 [3.91–4.59]	< 0.05	< 0.01
Males	18	3,310	1	17	1.43 [1.38–1.48]	1.98 [1.87–2.11]	3.49 [3.14–3.89]	-	< 0.01
Females	5	304	0	5	1.52 [1.42–1.63]	2.24 [1.95–2.58]	4.45 [3.37–5.87]	-	
Stomach	16	4,518	2	14	1.07 [1.04–1.10]	1.15 [1.09–1.22]	1.32 [1.18–1.49]	n.s.	< 0.01
Small intestine	2	415	0	2	-	-	-	-	-
Colon	17	5,948	4	13	1.14 [1.07–1.21]	1.21 [1.11–1.32]	1.32 [1.16–1.49]	n.s.	< 0.01
Rectum	16	3,872	3	13	1.11 [1.03–1.20]	1.17 [1.06–1.30]	1.32 [1.16–1.51]	n.s.	< 0.01
Liver ^a	19	1,961	3	16	1.20 [1.13–1.27]	1.41 [1.26–1.56]	1.83 [1.53–2.19]	< 0.05	< 0.01
Males	10	949	2	8	1.28 [1.13–1.45]	1.51 [1.27–2.10]	1.62 [1.18–2.24]	-	< 0.01
Females	3	231	1	2	1.97 [1.30–3.00]	3.57 [1.56–8.21]	9.15 [1.73–48.41]	-	
Gallbladder	2	81	1	1	-	-	-	-	-
Pancreas	17	2,524	4	13	0.98 [0.90–1.05]	1.05 [0.93–1.18]	1.18 [0.94–1.49]	n.s.	< 0.01
Larynx	20	3,759	0	20	1.35 [1.31–1.40]	1.83 [1.72–1.95]	3.24 [2.89–3.65]	n.s.	< 0.01
Lung	6	2,314	3	3	1.02 [1.00–1.04]	1.04 [1.00–1.08]	1.08 [1.00–1.18]	n.s.	< 0.01
Melanoma	2	708	0	2	-	-	-	-	-
Female Breast	49	44,033	12	37	1.31 [1.27–1.36]	1.67 [1.56–1.78]	2.71 [2.33–3.08]	-	< 0.01
Cervix	1	242	-	1	-	-	-	-	-
Endometrium	6	2,473	2	4	1.05 [0.88–1.24]	1.09 [0.78–1.54]	1.20 [0.60–2.37]	-	< 0.01
Ovary	5	1,651	-	5	1.11 [1.00–1.24]	1.23 [1.01–1.54]	1.53 [1.03–2.32]	-	n.s.
Prostate	11	4,094	4	7	1.05 [1.00–1.08]	1.09 [1.02–1.17]	1.19 [1.03–1.37]	-	n.s.
Bladder	11	5,997	2	9	1.04 [0.99–1.09]	1.08 [0.98–1.89]	1.17 [0.97–1.41]	n.s.	n.s.
Kidney	2	921	0	2	-	-	-	-	-
All sites combined	8	14,495	6	2	1.01 [0.90–1.05]	1.22 [1.11–1.27]	1.91 [1.77–2.06]	n.s.	< 0.01
Total*	229	115,199	46	183	-	-	-	-	-

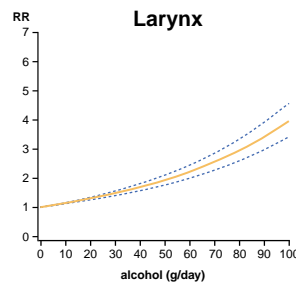
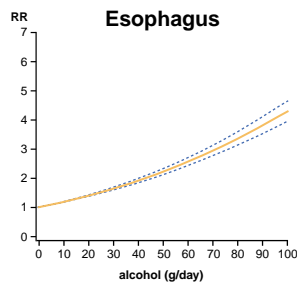
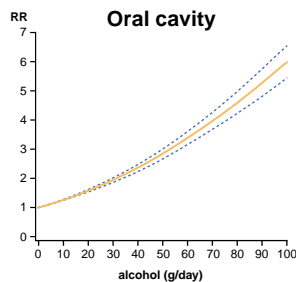
NOTE: Table gives the pooled relative risks (RR) and corresponding 95-percent confidence intervals (95% CI) for three alcohol consumption levels. Those levels specified corresponded to approximately two, four, and eight standard drinks per day, respectively. The effects of gender and differences (i.e., heterogeneity) in the study results for various cancer sites also are presented. The RR indicates the strength of the relationship between alcohol consumption and a given type of cancer. A RR greater than 1.0 means that alcohol consumption at the level indicated increased the risk for that type of cancer. The greater the value over 1.0, the greater the risk. The 95-percent confidence intervals indicate the range of RR that is 95 percent likely to show a true RR. A statistically significant heterogeneity level indicates that results varied greatly among the various studies analyzed and that, therefore, an overall summary of average effect across studies must be interpreted with caution.

* The number of individual studies does not add up to the total shown because several studies examined more than one type of cancer.

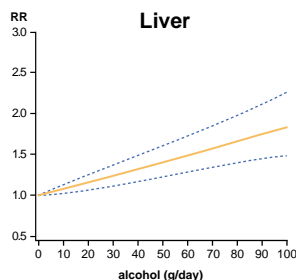
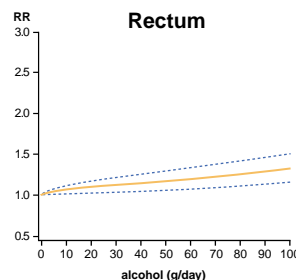
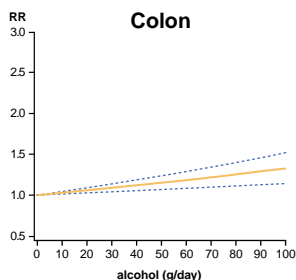
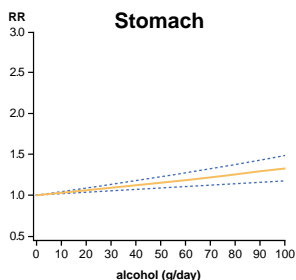
^a For this type of cancer, the RRs associated with alcohol consumption for males and females are listed separately because a statistically significant difference existed between the two sexes.

n.s. = not significant

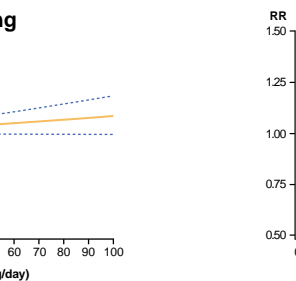
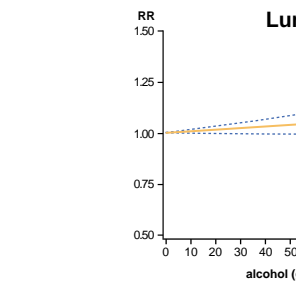
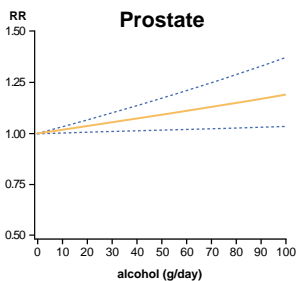
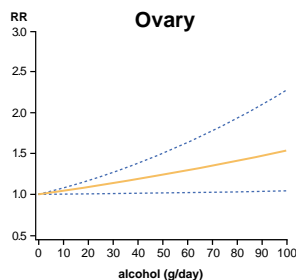
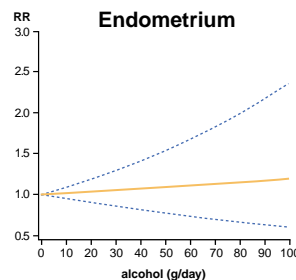
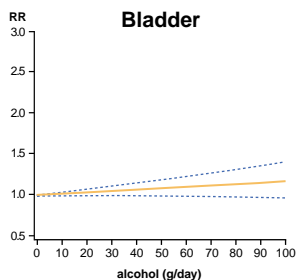
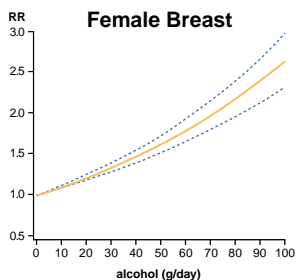
A. Neoplasms of the Upper-Aerodigestive Tract



B. Neoplasms of the Lower Digestive Tract



C. Other Neoplasms



Relationship between increasing amounts of alcohol and risk (i.e., relative risk or RR) for 14 types of cancer. The RR describes the strength of the relationship between a variable (e.g., alcohol consumption) and a disease (e.g., cancer). The RR for the disease in people without the variable (e.g., abstainers) is defined as 1.0. A RR among the people with the variable (e.g., drinkers) of greater than 1.0 indicates that the variable increases the risk for the disease. The greater the value, the greater the risk. The curves shown here were obtained by fitting certain statistical models to the data from several studies (i.e., a meta-analysis). Blue dotted lines indicate 95-percent confidence intervals; that is, the range of RR that is 95 percent likely to show a true RR.

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Materials Available on Underage Drinking

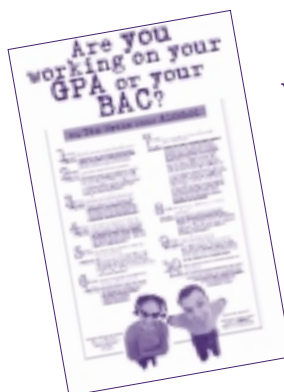
NIAAA has developed materials specifically aimed at addressing the problem of underage drinking. These materials may be ordered in quantities for school and other educational programs.



“Make a Difference: Talk to Your Child About Alcohol”

is a research-based guide geared to parents and caregivers of young people ages 10 to 14. Research shows that parents have an enormous impact on their children’s behavior.

This booklet covers a number of topics, from strategies to prevent underage drinking to recognizing the warning signs of a drinking problem. The booklet is available in both English and Spanish.



Are You Working on Your GPA or Your BAC?— Top Ten Myths About Alcohol.”

This colorful poster is geared to college-age students. It includes a tablet of tear-off sheets featuring 10 of the most common myths about drinking. Some of those myths include: “I can sober up quickly if I have to,”

“Beer doesn’t have as much alcohol as hard liquor,” “It’s okay for me to drink to keep up with my boyfriend,” and “I can manage to drive well enough after a few drinks.” Research-based facts are given to correct these common misconceptions.

To order, write to: National Institute on Alcohol Abuse and Alcoholism, Publications Distribution Center, P.O. Box 10686, Rockville, MD 20849-0686. Fax: (703) 312-5230. Full text of “Make a Difference: Talk to Your Child About Alcohol” is available on the World Wide Web at <http://www.niaaa.nih.gov>