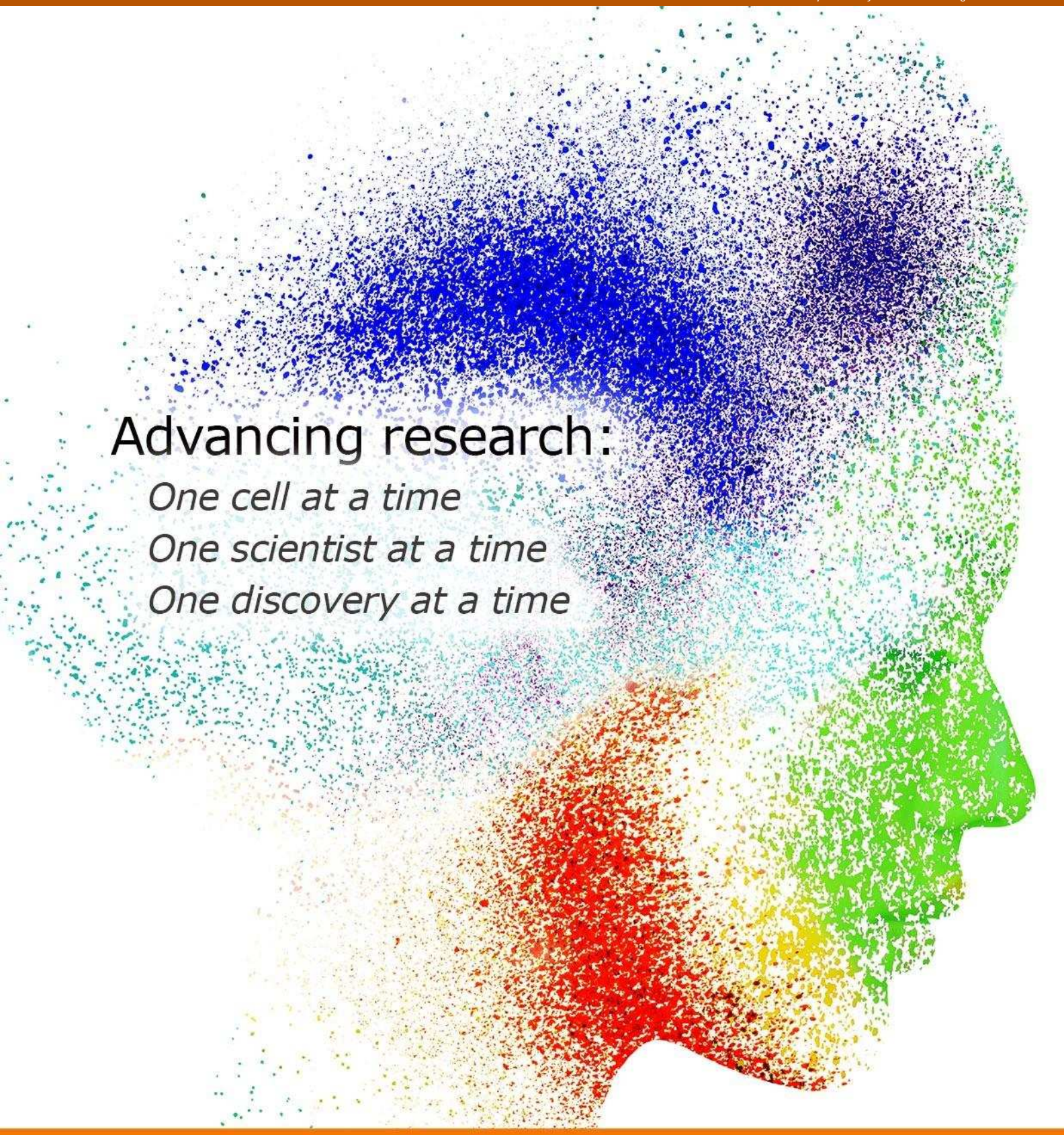

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The burden of cancer attributable to alcohol drinking

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We estimated the number of cancer cases and deaths attributable to alcohol drinking in 2002 by sex and WHO subregion, based on relative risks of cancers of the oral cavity, pharynx, esophagus, liver, colon, rectum, larynx and female breast obtained from recent meta- and pooled analyses and data on prevalence of drinkers obtained from the WHO Global Burden of Disease project. A total of 389,100 cases of cancer are attributable to alcohol drinking worldwide, representing 3.6% of all cancers (5.2% in men, 1.7% in women). The corresponding figure for mortality is 232,900 deaths (3.5% of all cancer deaths). This proportion is particularly high among men in Central and Eastern Europe. Among women, breast cancer comprises 60% of alcohol-attributable cancers. Although our estimates are based on simplified assumptions, the burden of alcohol-associated cancer appears to be substantial and needs to be considered when making public health recommendations on alcohol drinking.

Key words: alcohol; neoplasms; epidemiology

A causal link has been established between alcohol drinking and cancers of the oral cavity, pharynx, esophagus, colon, rectum, liver, larynx and breast.[1] For other cancers, a causal association is suspected.[1]

Despite the importance of alcohol as a human carcinogen,[2,3] a detailed estimate of the global burden of alcohol-related cancers is lacking. We aimed to estimate the worldwide burden of alcohol-related cancer by combining the relative risk of cancer with the distribution of drinkers and the number of incident cases of cancer and of deaths from cancer. Although cancer incidence is a more relevant measure to estimate the burden of cancer, we have also included mortality in our estimates because of the higher quality of this type of data in many low- and medium-resources countries.[4]

Methods

We calculated the number of cases of cancer of the oral cavity and pharynx, esophagus, colorectal, liver and larynx for both sexes and for breast cancer for women. For each cancer site and each WHO subregion (Table I), we obtained the age-specific distribution of drinkers among adults from the Global Burden of Disease project.[2] These distributions are based on surveys conducted in 69 countries. We considered 5 categories of drinkers: abstainers, and drinkers of 1–19, 20–39, 40–59 and 60 and more grams of alcohol/day. We combined the first 2 categories of drinkers for men, and the last 2 categories for women. We obtained relative risks (RR) for all cancers, but female breast cancer from a recent meta-analysis.[5] In this meta-analysis, the authors provided summary RR estimates for intake of 25 g/day (used for the 20–39 g/day category), 50 g/day (used for the 40–59 g/day category) and 75 g/day (used for the 60+ g/day category). For the 1–19 g/day category, we estimated the excess risk to be half of that reported for the 25 g/day category (as the midpoint of the 1–19 g/day category lies close to 25/2), and we estimated the excess risk for the 1–39 g/day category in men to be 75% of that reported in the meta-analysis for the 25 g/day category (as the midpoint of the 1–39 g/day category lies close to 25 × 0.75). In the case of female breast cancer, we used the results of a recent pooled analysis, which concluded for a linear dose-response relationship with relative risk of 1.07 per 10 g/day of alcohol intake.[6]

We obtained the age-specific numbers of incident cases of cancer and of cancer deaths in 2002 from the Globocan 2002 project.[4] We then calculated the numbers of cases (or deaths) attributable to alcohol drinking (AC_{alc}) in each sex according to the formulae:

$$AC_{alc} = \Sigma_{jk}(AF_{jk} * N_{jk})$$

and

$$AF_{jk} = \Sigma_i(P_{ijk} * (RR_i - 1)/(P_{ijk} * (RR_i - 1) + 1))$$

where, for each category of drinking i, each age group j, and each WHO subregion k, P is the proportion of drinkers, N is the number of cases (or deaths) and AF is the attributable fraction. The RR (reported in Table II) are specific for sex, but not for age or WHO subregion. We used the same RR for cancer mortality and cancer incidence (*i.e.*, we assumed that alcohol drinking does not affect cancer survival).

Results

Table III shows the overall results for cancer incidence: a total of 389,100 cases of cancer were attributed to alcohol drinking worldwide, representing 3.6% of all cancers (5.2% in men, 1.7% in women). Among men, more than 60% of all alcohol-associated cancers were from the upper digestive tract (oral cavity, pharynx and esophagus); among women, about 60% of alcohol-associated cancers were from the breast. Table IV reports comparable figures for mortality: the proportions of attributable cancer deaths were similar to those found for incidence, resulting in a total of 232,900 cancer deaths attributable to alcohol drinking (3.5% of all cancer deaths).

In Figure 1 the alcohol-attributable fraction of overall cancer incidence is presented for each WHO subregion: alcohol drinking is responsible for a large proportion of cancer in Europe (in particular, in Central and Eastern Europe [Europe C]), America, East Asia, Oceania and sub-Saharan Africa, while in Northern Africa, and Western and Southern Asia this proportion is smaller. As shown in Table V, the largest number of cases of alcohol-attributable cancer in men originates from Eastern Asia, in particular China, and from Europe, while Europe and North America are the regions with the largest contribution of alcohol-attributable cancers among women.

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TABLE I – WHO SUBREGIONS

Africa D	Algeria, Angola, Benin, Burkina Faso, Cameroon, Cape Verde, Chad, Comoros Equatorial Guinea, Gabon, Gambia, Ghana, Guinea, Guinea-Bissau, Liberia, Madagascar, Mali, Mauritania, Mauritius, Niger, Nigeria, Sao Tome and Principe, Senegal, Seychelles, Sierra Leone, Togo
Africa E	Botswana, Burundi, Central African Republic, Congo, Côte d'Ivoire, Democratic Republic of the Congo, Eritrea, Ethiopia, Kenya, Lesotho, Malawi, Mozambique, Namibia, Rwanda, South Africa, Swaziland, Uganda, United Republic of Tanzania Zambia, Zimbabwe
America A	Canada, Cuba, United States of America
America B	Antigua and Barbuda, Argentina, Bahamas, Barbados, Belize, Brazil, Chile, Colombia, Costa Rica, Dominica, Dominican Republic, El Salvador, Grenada, Guyana, Honduras, Jamaica, Mexico, Panama, Paraguay, Saint Kitts and Newis, Saint Lucia, Saint Vincent and the Grenadines, Suriname, Trinidad and Tobago, Uruguay, Venezuela
America D	Bolivia, Ecuador, Guatemala, Haiti, Nicaragua, Peru
Eastern Mediterranean B	Bahrain, Cyprus, Iran (Islamic Republic of), Jordan, Kuwait, Lebanon, Libyan Arab Jamahiriya, Oman, Qatar, Saudi Arabia, Syrian Arab Republic, Tunisia, United Arab Emirates
Eastern Mediterranean D	Afghanistan, Djibouti, Egypt, Iraq, Morocco, Pakistan, Somalia, Sudan, Yemen
Europe A	Andorra, Austria, Belgium, Croatia, Czech Republic, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Luxembourg, Malta, Monaco, Netherlands, Norway, Portugal, San Marino, Slovenia, Spain, Sweden, Switzerland, United Kingdom
Europe B	Albania, Armenia, Azerbaijan, Bosnia and Herzegovia, Bulgaria, Georgia, Kyrgyzstan, Poland, Romania, Slovakia, Tajikistan, The Former Yugoslav Republic of Macedonia, Turkey, Turkmenistan, Uzbekistan, Yugoslavia
Europe C	Belarus, Estonia, Hungary, Kazakhstan, Latvia, Lithuania, Republic of Moldova, Russian Federation, Ukraine
South-East Asia B	Indonesia, Sri Lanka, Thailand
South- East Asia D	Bangladesh, Bhutan, Democratic People's Republic of Korea, India, Maldives, Myanmar, Nepal, Timor Leste
Western Pacific A	Australia, Brunei Darussalam, Japan, New Zealand, Singapore
Western Pacific B	Cambodia, China, Cook Islands, Fiji, Kiribati, Lao People's Democratic Republic, Malaysia, Marshall Islands, Micronesia (Federated States of), Mongolia, Nauru, Niue, Palau, Papua New Guinea, Philippines, Republic of Korea, Samoa, Solomon Islands, Tonga, Tuvalu, Vanuatu, Viet Nam

TABLE II – RELATIVE RISKS USED IN THE ANALYSIS OF ATTRIBUTABLE FRACTIONS

Sex	Drinking category	Oral cav., pharynx	Esophagus	Colon, rectum	Liver	Larynx	Breast
Men	Abstainers[1]	1.00	1.00	1.00	1.00	1.00	NA
	1–39 g/day	1.65	1.29	1.05	1.14	1.32	NA
	40–59 g/day	3.11	1.93	1.12	1.40	2.02	NA
	60+ g/day	6.45	3.59	1.25	1.81	3.86	NA
Women	Abstainers[1]	1.00	1.00	1.00	1.00	1.00	1.00
	1–19 g/day	1.43	1.19	1.03	1.09	1.21	1.07
	20–39 g/day	1.86	1.39	1.06	1.19	1.43	1.21
	40+ g/day	3.11	1.93	1.12	1.40	2.02	1.35
Reference		[5]	[5]	[5]	[5]	[5]	[6]

NA, not applicable.
[1]Reference category.

TABLE III – ALCOHOL-ATTRIBUTABLE CANCER CASES WORLDWIDE BY SEX, 2002

	Men		Women		Total	
	AF%	Cases	AF%	Cases	AF%	Cases
Oral cavity, pharynx	38.8	109,500	10.9	13,300	30.4	122,800
Esophagus	25.0	79,000	4.5	6,600	18.5	85,500
Colon and rectum	4.6	25,200	1.7	7,800	3.2	33,000
Liver	12.2	53,800	2.9	5,400	9.4	59,100
Larynx	25.3	35,200	7.3	1,500	23.0	36,700
Breast (women)	NA	NA	4.5	51,900	4.5	51,900
Total	5.2[1]	302,600	1.7[1]	86,400	3.6[1]	389,100

NA, not applicable. Numbers might not add up because of rounding. AF%, fraction of cancers attributable to alcohol drinking.
[1]Denominator comprises all cancer cases.

TABLE IV – ALCOHOL-ATTRIBUTABLE CANCER DEATHS WORLDWIDE BY SEX, 2002

	Men		Women		Total	
	AF%	Deaths	AF%	Deaths	AF%	Deaths
Oral cavity, pharynx	33.3	49,500	8.6	5,400	25.9	54,900
Esophagus	24.6	64,200	4.4	5,500	18.1	69,700
Colon and rectum	4.4	12,300	1.6	4,000	3.1	16,300
Liver	12.1	50,600	3.0	5,500	9.4	56,100
Larynx	23.5	18,500	6.4	700	21.4	19,200
Breast (women)	NA	NA	4.1	16,800	4.1	16,800
Total	5.1[1]	195,000	1.3[1]	37,900	3.5[1]	232,900

NA, not applicable. Numbers might not add up because of rounding. AF%, fraction of cancer deaths attributable to alcohol drinking.
[1]Denominator comprises all cancer deaths.

Discussion

We found that 3.6% of all cases of cancer and a similar proportion of cancer deaths are attributable to alcohol drinking. These figures are higher in selected regions of the world, in particular in Central and Eastern Europe. It is worth noting that among women 60% of cancers attributable to alcohol occur in the breast.

Our results are likely to represent a conservative estimate of the burden of alcohol-associated cancer, since they are restricted to cancers with an established association with alcohol drinking. An association with alcohol drinking is suspected also for other types of cancer, such as pancreatic, lung, bladder and kidney cancer.[1] On the other hand, the estimate for head and neck and esophageal cancers does not take into consideration the interaction between

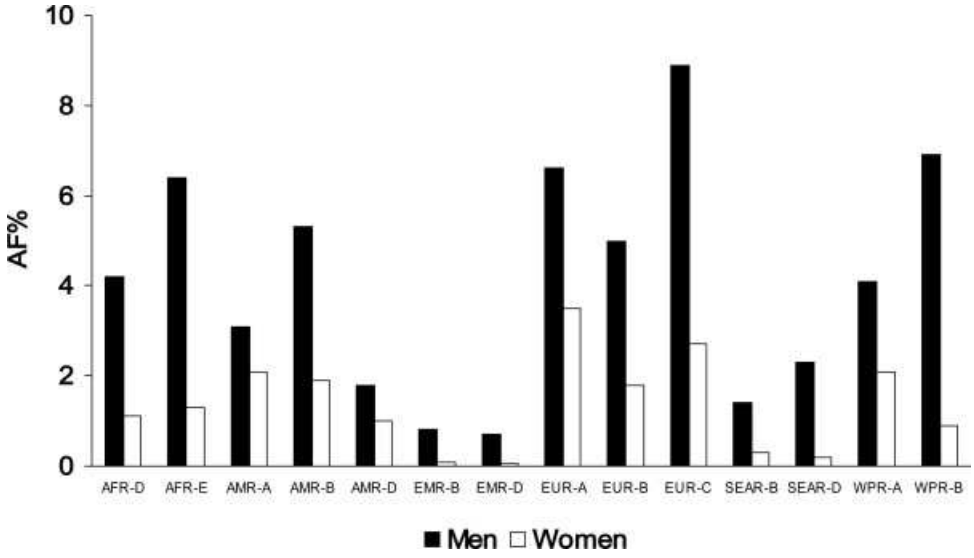

FIGURE 1 – Alcohol-attributable fraction (AF) of all cancers by sex and WHO subregion (see Table I for details on WHO subregions), 2002.

alcohol drinking and tobacco smoking in the etiology of these cancers.[7] A sizable proportion of cases of cancers of the upper aerodigestive tract can therefore be attributed to (*i.e.*, can be prevented by removing) either factor. Furthermore, in the case of lymphoma, a protective effect has been suggested by some studies.[8]

Our estimates of the proportion of cancer cases and deaths attributable to alcohol drinking are consistent among them. Minor differences are explained by the fact that WHO subregions with different survival rates contribute differently to the each cancer site. For example, the burden of breast cancer in women is greater for incidence (4.5%) than for mortality (4.1%), because a larger proportion of incident cases as compared to deaths occur in regions with better survival rates (*e.g.*, North America and Europe), which are also characterized by a higher prevalence of drinking women.

In 1981, Doll and Peto estimated two thirds of head and neck cancer deaths in the United States, as well as a lower proportion of deaths from esophageal and liver cancers were attributable to alcohol drinking, which represented 3% of total cancers.[3] The same figure of 3% was reported by the Harvard Center for Cancer Prevention in 1996, without a clear explanation on how it was derived.[9] Our results for the WHO subregion comprising the United States (America A) concur with these estimates, but they also indicate that the burden of alcohol-related cancer is likely to be higher in other regions of the world.

Three studies have provided a detailed assessment of the burden of alcohol-related cancers following an approach similar to ours. In an exercise aimed to assess the burden of deaths in Australia in 1995 from tobacco, alcohol and other addictive substances, it was estimated that 1.6% of total cancer deaths among men and 1.2% among women are attributable to alcohol drinking.[10] These estimates are lower than ours (4.1% among men and 2.1% among women in Western Pacific A sub-region, Fig. 1), because they did not consider colon and rectum among the target sites of alcohol carcinogenesis and used older data reporting a lower prevalence of drinkers. An estimate recently produced by the WHO Global Burden of Disease project and based on relative risks and prevalence data similar to ours resulted in an estimate of 355,000 cancer deaths attributable to alcohol drinking in 2000[2]: in that project, however, no detailed results were reported for cancer type and geographic region. Similar estimates (351,000 deaths worldwide in 2001) were reported in a further analysis of the role of 9 cancer risk factors, including alcohol drinking.[11] Our estimates are more conservative, in particular with respect to the role of alcohol drinking in mortality from esophageal and liver cancers, 2 neoplasms responsible for a large number of deaths in populations with limited alcohol consumption.

TABLE V – ALCOHOL-ATTRIBUTABLE CANCER CASES (ALL SITES) BY SEX AND WHO SUBREGION, 2002

WHO subregion	Men	Women
Africa D	3,700	1,100
Africa E	10,800	2,300
America A	26,100	15,500
America B	17,900	7,000
America D	800	600
Eastern Mediterranean B	500	100
Eastern Mediterranean D	900	100
Europe A	67,400	30,500
Europe B	11,300	3,700
Europe C	30,500	9,000
South East Asia B	1,700	400
South East Asia D	11,800	1,000
Western Pacific A	15,000	5,600
Western Pacific B	104,300	9,700

The regional differences in the burden of alcohol-attributable cancer resulted from variations in the prevalence of drinking: other potential sources of regional variability, including the carcinogenic effect of local alcoholic beverages and the pattern of drinking—*i.e.*, binge drinking—were not taken into consideration because of uncertainties in the quantification of the effect of such factors on cancer risk. In any case, studies conducted in different populations indicate that the most commonly used beverage is the one most strongly related to risk in each population, *i.e.*, spirits in northern Europe and wine in southern Europe.[12,13]

Our results are limited by the quality of available data on risk of cancer from alcohol drinking, prevalence of drinking and cancer incidence and mortality. Although a causal association between alcohol drinking and increased risk of cancer at several organs is well established, the quantification of the effect at different doses is subject to more uncertainties and relies on results of epidemiological studies, which may suffer from residual confounding (notably by smoking for cancers of upper aerodigestive organs, leading to an overestimate of the effect of alcohol), misclassification of past alcohol drinking (likely leading to an underestimate of the same effect), as well as other sources of bias (leading to unpredictable errors). It should be stressed that meta- and pooled-analyses, while improving the precision of the risk estimates, do not solve the problems of bias and confounding.

Several meta-analyses are available on the RR of specific cancers among drinkers.[3,10,14–17]. We have used the meta-analysis by Corrao *et al.*[5] because (*i*) it is recent, (*ii*) it includes all cancers that we considered causally associated with alcohol drinking and (*iii*) it provides RR for different levels of drinking.

Data on prevalence of drinking were obtained from the WHO Global Burden of Disease project[2]: these estimates are based on surveys conducted in 69 countries, including at least one (usually the largest) in each subregion, with the exception of the 2 Eastern Mediterranean subregions. Although these data suffer from variability in precision, quality and other validity issues, they represent the only comprehensive attempt to estimate the prevalence of alcohol drinking worldwide. Data on cancer incidence and mortality were derived from the IARC Globocan 2002 project.[4] While these data are reliable for most high-resource and many medium-resource countries, data from most low-resource countries are known to be of poor quality.

The burden of alcohol-associated cancer should be considered in the light of the evidence that alcohol drinking modifies the risk of numerous other diseases, but a detailed quantification of these effects goes beyond the scope of our study. The major non-neoplastic diseases caused by alcohol drinking are mental disorders, polyneuropathy, cardiomyopathy, hypertension, haemorragic stroke, gastritis, liver cirrhosis and fibrosis, and acute and chronic pancreatitis. In addition, alcohol drinking is a major cause of several types of injuries. On the other hand, there is strong evidence that moderate consumption of alcohol reduces the risk of ischemic heart disease, ischemic stroke and colelithiasis. A recent global estimate of the burden of disease due to alcohol drinking suggested that, in most populations, cancer is likely to represent an important, albeit not predominant component of alcohol-related morbidity and mortality.[2]

Our estimates required a number of simplifying assumptions: the relative risks of alcohol-associated cancer may be modified by smoking, ethnicity, age, and drinking patterns; in such case, differences in age structure, ethnicity, or smoking prevalence among WHO subregions would modify our estimates of the number of alcohol-attributable cancers. However, given the lack of definite evidence on the effect modification played by these covariates, we have not attempted to use them in our estimates. The rates of cancer among abstainers may also be influenced by dietary habits that are likely to differ in important ways from those who drink alcohol. This group may also include some individuals who were previous heavy consumers of alcohol, and it is plausible that the composition of these 2 types of abstainers will differ between WHO subregions.

In conclusion, although our estimates are based on simplified assumptions, a substantial number of cancer cases and cancer deaths appear to be attributable to alcohol drinking. Although cancer is only one of the health effects of alcohol drinking, its role needs to be kept in consideration when public health recommendations on drinking are made.

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