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Burden of cancer attributable to consumption of alcohol in Japan in 2015

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Abstract: Alcohol can cause or contribute to the development of many non-communicable diseases, including cancer. We calculated the proportion of cancer incidence and mortality in 2015 attributable to alcohol consumption in 2005. Data on alcohol consumption, provided in *go*, a traditional Japanese alcohol measurement unit, was derived from the 2005 Japanese National Health and Nutrition Survey for each sex and age group, then converted into grams of ethanol per day. The optimal consumption of alcohol for the purpose of this study was determined to be none, based on a global assessment derived from previous observational studies that have looked at the association between alcohol consumption and cancer. Using standard formulas, population attributable fractions (PAFs) for all cancers positively associated with alcohol drinking - oral cavity, pharynx, esophagus, stomach, colorectum, liver, larynx, and female breast - were calculated for each sex and age group and aggregated to obtain the PAF among total cancer incidence and mortality. For Japan in 2015, 59,838 cases of cancer incidence and 23,929 cancer deaths were attributable to alcohol consumption. The estimated PAF for cancer incidence and mortality attributable to alcohol consumption was 6.2% and 6.5%, respectively. For both cancer incidence and mortality, the highest percentage of alcohol-attributable cancer sites was esophageal (54.0% for incidence, 52.3% for mortality). Avoidance of alcohol consumption would reduce the burden of alcohol on cancer in Japan.

***Keywords*:** cancer, alcohol, population attributable fraction, Japan

Introduction

Since 1998, alcohol consumption has been classified as a human carcinogen by the International Agency for Research on Cancer (IARC) (*1*). In the most updated review in 2010, the IARC concluded that alcohol consumption is a risk factor for cancers of the oral cavity, pharynx, larynx, esophagus, liver, colorectum, and breast (women only) (*2*). In addition to these cancer sites, the World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) concluded that alcoholic drinks increase the risk of colorectal and stomach cancer in their latest report (*3*). The report also noted that there is no evidence of safe level of alcohol consumption (*3*).

Despite these established evidences, drinking patterns between countries and regions differ due to their cultural background. In this report, we examined the fraction of cancers occurring in 2015 attributable to alcohol consumption in Japan.

Materials and Methods

Cancers associated with alcohol

The IARC reconfirmed the consumption of alcohol as "group 1", carcinogenic to humans (*1,2,4,5*). For this study, we selected cancer sites associated with the consumption of alcoholic beverages that IARC reports found sufficient evidence for a positive association, and for which relative risk estimates were available. The cancer sites included in this study were oral cavity, pharynx, esophagus, stomach, colorectum, liver, larynx, and breast (women only).

Prevalence of exposure to alcohol

The latent period between 'exposure' to alcohol and the appropriate increase in risk of these cancers has not been well established. We assumed that this would be 10 years on average, and therefore examined the

effects of cancer incidence and mortality in 2015 from non-optional levels of alcohol consumption in the year 2005.

We used data from the Japanese National Health and Nutrition Survey (JNHNS) from 2005 (*6*). JNHNS targets household members aged at least one year old in all households within 300 districts (10 districts per prefecture; 15 districts for Tokyo) selected through stratified random sampling, which totaled about 5,000 households and 15,000 participants in November of 2005. The survey provides the proportions of individuals (by sex and age group) consuming different quantities of alcohol per day in *go*. In Japan, one unit of alcohol is measured by a traditional measurement, "*go*", which assumes 23g of ethanol for 180mL of sake, 10g ethanol for 30mL of whiskey or brandy, 6g ethanol for 60mL of wine, or 23g of ethanol for 633mL of beer, for ages 20 and over. Table 1 summarizes the sex- and age-group-specific proportion of alcohol drinkers (1-3 times/month or more) and average consumption amount of alcohol (g of ethanol/day) in Japanese in 2005.

Theoretical minimum risk exposure level

The optimum level of alcohol consumption was considered to be none, based on previous observational studies that looked at the association between alcohol consumption and cancer and found that cancer risk increases with increased consumption of alcohol.

Cancer incidence and mortality in Japan in 2015

Cancer incidence data in 2015 were estimated using the annual estimate of cancer incidence in 2013 by the Monitoring of Cancer Incidence in Japan (*7*). This was done using an age and period spline model, a type of model which is used for short-term projections of cancer incidence in Japan (*8*). The sex- and age-specific incidence data for target cancers were coded in accordance with the International Statistical Classification of Diseases and Related Health Problems, 10th edition (ICD-10), using morphology codes of the International Classification of Disease for Oncology, 3rd edition (ICD-O-3).

The data on cancer mortality statistics from 2015 were based on the vital statistics of Japan (*9*). We obtained sex- and age-specific mortality data by cause of death from available data sources from the Health, Labour, and Welfare Statistics Association (*10*), and used 4-digit ICD-10 codes to classify the cause of death.

Estimation of relative risks

Table 2 shows the increase in risk associated with alcohol consumption. The estimates derived from the studies listed below have been adjusted for potential major confounders.

Relative risks (RR) for esophagus, breast, and liver cancers were derived from epidemiological studies included in the WCRF/AICR's report (*3*). RR for oral, pharynx, larynx were derived from a published Japanese population-based cohort study (*11*). The RR for stomach cancer were estimated using a pooled analysis of Japanese studies (*12,13*). The RR for colorectal cancer was derived from a pooled analysis of five Japanese cohorts (*14*).

The risk for oral, pharynx, and larynx cancers was calculated in comparison to those who never drank.

Table 1. Sex- and age-group specific proportion of alcohol drinkers and average consumption amount of alcohol (g of ethanol/day) in Japanese in 2005

Age at exposure (2005)	Men		Women	
	Proportion of drinkers* (%)	Average intake (g/day) (Excess from 0 g/day)	Proportion of drinkers* (%)	Average intake (g/day) (Excess from 0 g/day)
0 - 4	0.0	0.0	0.0	0.0
5 - 9	0.0	0.0	0.0	0.0
10 - 14	0.0	0.0	0.0	0.0
15 - 19	0.0	0.0	0.0	0.0
20 - 24	60.3	15.9	52.4	10.1
25 - 29	66.2	21.1	49.0	13.0
30 - 34	68.1	31.5	52.1	14.8
35 - 39	71.9	30.4	50.8	17.3
40 - 44	75.8	33.7	49.1	16.0
45 - 49	78.7	33.9	47.5	14.5
50 - 54	79.8	34.2	41.9	15.1
55 - 59	78.7	34.2	36.4	12.8
60 - 64	75.7	31.3	31.6	12.2
65 - 69	72.3	28.6	25.4	11.0
70 - 74	70.2	24.0	19.4	7.8
≥ 75	57.9	20.2	15.0	7.8
Total	71.7	29.5	36.9	13.4

Data source: The National Health and Nutrition Survey, Japan, 2005 *Drinker: Frequency of drinking 1-3 times/month or more.

Table 2. Increase in risk associated with alcohol consumption

Cancer type	Studies	RR reference group	RR (95% CI)	Increase in risk per gram alcohol per day
Oral cavity, pharynx, larynx	Lu *et al.* (2018) (*11*)	Never	1.50 (1.02 - 2.22)	N/A
Esophagus	Ishiguro *et al.* (2009) (*24*)*	10g per day	1.34 (1.25 - 1.55)	0.02927
Stomach	Meta-analysis of six Japanese studies*	10g per day	1.03 (1.00 - 1.06)	0.00296
Liver	Ohishi *et al.* (2008) (*13*)*, Shimazu *et al.* (2012) (*12*)	10g per day	1.14 (0.90 - 1.44)	0.00677
Colorectal	Mizoue *et al.* (2008) (*14*)*	15g per day	1.07 (1.06 - 1.09)[b]	0.0131
Breast[a]	Suzuki *et al.* (2010) (*25*)*	10g per day	1.05 (0.98 - 1.14)	0.0131

*Included in the WCRF/AICR report (*3*). [a]Calculated for women only. [b]Adjusted for 10g per day. Abbreviations: RR = relative risk; CI = confidence interval; WCRF/AICR = World Cancer Research Fund, American Institute for Cancer Research

Table 3. Proportion (%) of cancer in 2015 attributable to alcohol consumption in Japan

Cancer Site (ICD-10)	Incidence			Mortality		
	Men	Women	Both sexes	Men	Women	Both sexes
Oral cavity and pharynx (C00 ─ C14)	26.8	12.9	22.5	26.6	10.5	21.9
Esophagus (C15)	58.7	28.3	54.0	57.4	26.7	52.3
Stomach (C16)	5.6	2.1	4.5	5.4	2.0	4.2
Colorectum (C18-C20)	18.1	7.2	13.4	17.3	6.6	12.4
Liver (C22)	31.9	12.7	25.2	30.8	11.8	24.3
Larynx (C32)	27.0	13.5	26.0	26.1	6.5	25.1
Breast (C50)		6.4	6.4		5.8	5.8
Total	8.3	3.5	6.2	8.8	3.0	6.5

For esophagus, breast, liver, and stomach cancers, risk was calculated based on that for 10g of ethanol intake per day. The risk of colorectal cancer was presented for 15g of ethanol intake per day, but was adjusted to that for 10g of ethanol intake per day. The increase in risk for an increase of one gram of ethanol consumption per day was calculated, based on a log-linear relationship between exposure and risk of cancer onset. The increased risk for one gram of increased ethanol consumption was calculated using the following formula:

$$Risk = exp^{[\ln(\text{risk per gram of ethanol}) \times \text{average exposure level}]}$$

Estimation of population attributable fractions (PAFs)

PAFs were calculated for each gender and age group. For cancers of the oral cavity, pharynx, and larynx, which compared the risk of ethanol consumption with never drinkers, PAFs were calculated according to the formula (*15*):

$$\text{PAF} = \frac{P \times (RR - 1)}{P \times (RR - 1) + 1}$$

where P refers to the proportion of those who were drinkers in the total population.

For the remaining cancers, for which the risk was calculated based on the risk for 10g of ethanol consumption per day, PAFs were calculated using the following formula (*16*):

$$\text{PAF} = \frac{(Risk - 1)}{Risk}$$

Cancer site-specific PAF was multiplied by the number of incident cases or mortality of the site-specific cancer to obtain a site-specific number of attributable cancer incidence and mortality.

By summing these site-specific numbers of attributed cases of cancer incidence and mortality, we obtained the attributed number of total cancer incidence and mortality. Total cancer PAF was then obtained by dividing the number of attributed total cancer incidence and mortality by the number of observed total cancer incidence and mortality.

Results

In Japan in 2005, 72% of male and 37% of female adults drank alcohol 1 to 3 times per month or more. The proportion peaked at nearly 80% among men aged 45-59 and around 50% in women aged 20-44. Average daily ethanol consumption was 29.5g in men and 13.4g women (Table 1).

Table 3 summarized the estimated PAF of cancer incidence and mortality in 2015 attributed to consumption of alcohol in Japan. The estimated cancer cases attributed to alcohol consumption were 8.3% for men and 3.5% for women, or 6.2% of cancers overall,

and the estimated cancer deaths were 8.8% for men, 3.0% for women, and 6.5% overall.

Cancers of the liver (25.2%), oral cavity and pharynx, larynx, and esophagus had the highest proportion of alcohol-attributed cases (22.5% for cancers of the oral cavity and pharynx, 26.0% of the larynx, and 54.0% of esophagus). Although fractions for cancers of the stomach (4.5%), colorectum (13.4%), and breast (6.4%) were much lower, the number of cases of alcohol-attributable cancers was high. Detailed results on cancer incidence for each cancer, sex and age-group are shown in Table S1 (online data, *https://www.ghmopen.com/site/supplementaldata.html?ID=33*).

The results of cancer mortality were similar to that of cancer incidence attributable to alcohol consumption. Cancers of aero-digestive sites also accounted for highest percentages of alcohol-attributed mortality (21.9% of cancers of the oral cavity and pharynx, 25.1% of cancers of larynx, and 52.3% of cancers of the esophagus Similar to cancer incidence attributable to alcohol consumption, there were a gender difference in the mortality of aero-digestive cancers. Deaths attributable to alcohol consumption for four of the cancers for men were about twice of those attributable for women (oral cavity and pharynx: 26.6% for men, 10.5% for women; larynx: 26.1% for men, 11.8% for women; esophagus: 57.4% for men, 26.7% for women; and stomach: 5.4% for men, 2.0% for women). Detail results on cancer mortality for each cancer, sex and age-group were shown in Table S2 (online data, *https://www.ghmopen.com/site/supplementaldata.html?ID=33*).

Discussion

In this study, we estimated that 59,838 (6.2%) newly diagnosed cancer cases and 23,929 (6.5%) cancer deaths in 2015 could be attributed to consumption of alcohol from 2005 in Japan. PAFs were highest for the oral cavity and pharynx, larynx, and esophagus, for both cancer incidence and mortality.

Our results are comparable to those of previous studies. A previous Japanese estimate for 2005 showed cancer incidence and mortality attributable to alcohol consumption of 6.3% and 6.2%, respectively (*17*). A Canadian study (*18*) published in 2019 found 5.2% of alcohol-associated cancer cases were attributable to alcohol consumption. A United Kingdom study (*19*) published in 2011 showed 4.0% of alcohol-associated cancer cases were attributable to alcohol consumption. These numbers are lower than those of our study. The difference in findings between Japan and Western countries could be explained in part by genetic differences. Mutation of the aldehyde dehydrogenase 2 gene (*ALDH2*) is one of the most common hereditary disorders, affecting over 8% of the world population (*20*). Prevalence is highest in East Asians, including Japanese (*21,22*). *ALDH2* deficiency leads to greater exposure to acetaldehyde, a possible carcinogenic metabolite of alcohol (*23*). This genetic difference may have resulted in the stronger association between alcohol consumption and cancer we found (*14*).

There are several limitations to the study. The calculation of PAF depends on the accuracy of self-reported alcohol consumption. Further, the number of recently published epidemiological studies on alcohol consumption and cancer in Japan from which risk estimates could be obtained is limited. Therefore, it is possible that our PAF estimate may have been underestimated.

Conclusion

Alcohol consumption was attributed to 6.2% of cancer incidence, and 6.5% of cancer mortality, respectively. The results of this study may provide useful evidence for reducing the cancer burden in Japan.

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