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Original Article

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Alcohol consumption and cancer risk in South Korea and the UK: prospective cohort studies

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Abstract

Background: This study aimed to compare cancer incidence rates between South Korea and the UK, and assess the associated cancer risks due to alcohol consumption.

Methods: Data were pooled from the Korean Cancer Prevention Study-II and the Korean Genome Epidemiology Study Biobank for South Korea, and from UK Biobank (UKB) for the UK, with follow-up until 2020. Age-standardized incidence rates were calculated by using the World Health Organization standard population. Hazard ratios (HRs) for cancer incidence were analysed in relation to alcohol consumption levels.

Results: The overall cancer incidence rates were similar between South Korea and the UK. However, the incidence of liver, stomach, and thyroid cancers was more than five times higher in the Korean cohort. Compared with never drinkers, consuming ≥50 g of alcohol daily increased the overall cancer risk by 24% in the Korean data and by 11% in the UKB data. In Korea, heavy drinking (≥50 g/day) was associated with higher risks of esophageal cancer (HR = 12.59), liver cancer (HR = 1.65), head and neck cancer (HR = 2.06), alcohol-related cancers (HR = 1.60), and stomach cancer (HR = 1.43). In the UKB cohort, it was linked to increased risks of head and neck cancer (HR = 1.95), breast cancer (HR = 1.12), and alcohol-related cancers (HR = 1.18). Both cohorts showed a lower risk of thyroid cancer with increased alcohol consumption.

Conclusion: Alcohol consumption is associated with an increased risk of alcohol-related cancers in both South Korean and UK populations.

Keywords: cohort studies; South Korea; United Kingdom; risk; alcohol drinking; neoplasms.

Key Messages

- This study investigated the differences in cancer incidence rates between South Korea and the UK, focusing on the impact of alcohol consumption on cancer risk.
- The findings revealed that, while overall cancer rates were similar, South Korea had higher rates of liver, stomach, and thyroid cancers, and alcohol consumption increased the risk of various cancers, particularly esophageal cancer in South Korea and breast cancer in the UK.
- These results highlight the public health importance of addressing alcohol consumption as a modifiable risk factor for cancer, with implications for targeted prevention strategies in different populations.

Introduction

It is estimated that alcohol consumption is responsible for 3 million deaths every year, which represents 5.3% of all deaths [1]. Alcohol is a well-known cause of >200 diseases and injury conditions [2].

Cancer accounted for a large proportion of alcohol-related all causes of deaths, especially among those over the age of 50 years. These alcohol-related deaths accounted for 27.1% of cancer deaths in women and 18.9% of cancer deaths in men [3].

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There is a strong scientific consensus that alcohol drinking can cause several types of cancer [4, 5]. The International Agency for Research on Cancer also stipulates that alcohol is a carcinogen. In particular, cancer of the oral cavity, pharynx, larynx, esophagus, liver, colorectal, and breast cancer in women is classified as alcohol-related cancer [6]. However, the association between alcohol consumption and cancer showed inconsistent results according to cancer site and ethnicity [7–11].

Despite the well-established link between alcohol consumption and cancer, there is a lack of country-specific evidence on this association in South Korea. Notably, the annual total economic cost of alcohol consumption in South Korea is ~24 914 million US dollars, accounting for 3.3% of the gross domestic product, which is a higher proportion than that of the USA (2.7%) [12]. Given the significant economic and public health burden of alcohol in South Korea, it is crucial to investigate the cancer risk associated with alcohol consumption in the Korean population.

Therefore, we aimed to compare the association between alcohol consumption and cancer risk by using data from the pooled Korean Biobank for Asians and the UK Biobank (UKB) for Europeans.

Methods

Data source and study population

Korean Cancer Prevention Study-II biobank

The Korean Cancer Prevention Study (KCPS)-II biobank is a prospective population-based cohort with adults recruited from 18 health examination centers across South Korea. Detailed descriptions of KCPS-II have been previously reported [13]. KCPS-II comprises 156 701 participants who underwent routine health assessments between 2004 and 2013, provided blood samples, and gave informed consent for long-term follow-up. Among them, after excluding those <20 years of age, those with missing smoking status (2001) and alcohol status information (3339), and cancer prevalence cases (2282), there were 149 079 people. After excluding current drinkers whose alcohol amount was missing (8501), the final number of subjects was 140 578. The mean follow-up period of the subjects was a total of 952 223 person-years over 12.8 years. At baseline, participants provided information on socio-demographic factors, alcohol drinking, smoking habits, diet, exercise, and past medical history according to the questionnaire (IRB no. 4-2011-0277).

Korean Genome Epidemiology Study biobank

The Korean Genome Epidemiology Study (KoGES) biobank consists of two community-based prospective cohorts that were started in 2001 and 2004, respectively, and a population-based prospective cohort established with subjects who visited the screening center between 2004 and 2013. Detailed descriptions of KoGES have been previously reported [14]. The KoGES subjects were established for men and women >40 years of age. KoGES comprises 195 544 participants who provided blood samples and gave informed consent for long-term follow-up.

UKB

UKB is a prospective population-based cohort with >0.5 million adults recruited from 22 assessment centers across the UK between 2006 and 2010. Detailed descriptions of UKB have been previously reported [15]. The UKB subjects were established with 502 619 male and female adults aged 39–73 years. Participants filled in questionnaires and provided information on health and lifestyle in the baseline survey.

Data collection

Exposure

In the three biobanks, the individual drinking statuses of the subjects were classified as never drinkers, former drinkers, and current drinkers. In the case of current drinking, the type of alcohol, the duration of drinking, and the number of episodes of drinking in the past week were investigated. The alcohol consumption survey included the following questions: "How often do you drink alcohol per week?" and "On average, how many glasses do you drink per occasion?" Additionally, current drinkers were asked about their preferred type of alcoholic beverage, selecting from soju, makgeolli (rice wine), beer, whiskey, wine, or others. In this study, calculating alcohol consumption separately for each type of alcoholic beverage could have led to overestimation. Therefore, we assumed that each standard drink contains a similar amount of alcohol (13 g), regardless of the beverage type. Based on this assumption, individual alcohol intake was estimated by multiplying the frequency of drinking per week by the average number of drinks consumed per occasion. In addition, indices indicating the subject's height, weight, smoking history, family history of cancer, and socioeconomic status were investigated. For socioeconomic index rules, the education year and income variable were used for pooled Korean biobank subjects and the Townsend Deprivation Index was investigated for UKB [16].

Outcome

The main outcome of this study is the incidence of cancer. The cancer incidence information about the subjects was confirmed by linking the cancer registration data, which were a collection of diagnosed records from hospitals. In the case of both KCPS-II and KoGES, information on cancer site, cancer diagnosis date, and histological type was collected in connection with the national cancer registration data. Prevalent and incident cancer cases within the UKB cohort were identified through linkage to cancer and death registries. In this study, cancer incidence was defined as all cancer, esophageal cancer (C15), head and neck cancer, colorectal cancer (C18–C20), liver cancer (C22), stomach cancer (C16), lung cancer (C34), thyroid cancer (C73), and breast cancer (C50). Head and neck cancer was defined as including oral cavity cancer, pharynx cancer, and larynx cancer [17]. Alcohol-related cancer was defined as including oral cavity cancer, pharynx cancer, larynx cancer, esophagus cancer, liver cancer, colon cancer, rectum cancer, and female breast cancer [18]. Until 31 December 2020, the cancer registration data of the follow-up National Cancer Center and the cause-of-death data of the National Statistical Office were used.

Statistical analyses

Calculation of the cancer incidence

Data are presented as the mean for normally distributed continuous variables and as proportions for categorical variables. The incidence rates of cancers were calculated by dividing the number of events by 100 000 person-years (PY) at risk. To exclude differences in the age structure of the two biobanks, the age-standardized incidence rate was calculated

by using the World Health Organization (WHO) standard age structure [19].

Association between alcohol consumption and incident cancer risk

The drinking status of the subjects was classified as never, former, and current; current drinkers were classified according to the alcohol amount as <12.5, 12.5–24.9, 25–49.9, and ≥50 g/day. In East Asia, including Korea, alcohol consumption is lower than in other ethnic groups. This category was used to focus on light drinking [20]. To determine the independent association of drinking status and the amount of alcohol consumption with the risk of cancer incidence, the Cox regression model was used. We adjusted confounding variables including age and body mass index (BMI) as continuous variables, smoking status as a categorical variable with three categories (non-smoker, former smoker, current smoker), socioeconomic status as a categorical variable divided into quintiles, and family history of cancer as a binary variable (yes/no).

The hazard ratios (HRs) calculated from KCPS-II and KoGES were combined through meta-analysis. We used the Floating Absolute Risk (FAR) method to estimate the relative risk (RR) while minimizing the bias associated with the choice of a reference group and allowing the independent calculation of confidence intervals for each category. Unlike conventional approaches that require a specific reference group, FAR allows the estimation of RRs without selecting a baseline category. We implemented this approach by following Plummer's method to ensure accurate estimation and comparability across the exposure categories [21]. We estimated the association between drinking amount and incident cancer risk separately in the pooled Korean biobank data and the UKB data. To compare the effect estimates between these two populations, we calculated the Z-score for the difference between the two statistics [22].

Sensitivity analyses for association between alcohol consumption and incident cancer risk

We performed sex-stratified analyses to examine potential differences by gender. In addition, to reduce the potential influence of reverse causation, we conducted an analysis by excluding individuals with a follow-up period of <3 years. Given the potential interaction between alcohol consumption and smoking, we tested for statistical interaction by smoking status and further conducted stratified analyses accordingly.

Statistical analyses were performed by using SAS version 9.4 (SAS Institute, Cary, NC, USA) and R version 4.0.5 (The R Foundation for Statistical Computing, Vienna, Austria, http://www.Rproject.Org).

Results

Comparison of general characteristics of study subjects

The mean age of the 149 079 KCPS-II subjects was 41 years, which is younger than the mean age of the 195 544 KoGES subjects at 54 years old and the 464 7654 UKB subjects at 56 years old. The KCPS-II and KoGES subjects also had lower BMI than the UKB subjects. Smoking rates were higher in men in all of the KCPS-II, KoGES, and UKB subjects. More than 90% of the UKB subjects were current drinkers and there were more current drinkers than in the KCPS-II and KoGES subjects. Also, compared with KCPS-II and KoGES subjects, among the current drinkers in UKB, men were found to consume about two times and women four to five times more alcohol (Table 1).

Table 1. General characteristics of KCPS-II, KoGES, and UKB.

	KCPS-II ($N = 149\,079$)		KoGES ($N = 195\,544$)		UKB ($N = 464\,765$)	
	Men 92 547	Women 56 532	Men 69 579	Women 125 965	Men 206 225	Women 258 540
	Mean (SD)		Mean (SD)		Mean (SD)	
Age, years	41.9 (9.8)	40.6 (11.2)	54.5 (9.1)	53.3 (8.5)	56.9 (8.2)	56.7 (8.0)
BMI, kg/m^2	24.4 (2.9)	22.2 (3.1)	24.4 (2.8)	23.9 (3.0)	27.7 (4.2)	27.0 (5.1)
Socioeconomic status[a]	14.9 (1.5)	13.3 (1.9)	9.6 (3.2)	8.3 (3.1)	−1.3 (3.1)	−1.4 (3.0)
Alcohol amount, g/day[b]	23.7 (29.2)	8.2 (15.1)	25.2 (38.1)	6.1 (13.3)	57.2 (39.0)	34.7 (22.8)
	N (%)		*N* (%)		*N* (%)	
Smoking status						
Never smoker	21 136 (22.8)	50 721 (89.7)	19 087 (27.4)	121 240 (96.2)	103 288 (50.1)	154 892 (59.9)
Former smoker	30 431 (32.9)	3486 (6.2)	27 425 (38.9)	1633 (1.3)	77 162 (37.4)	80 762 (31.2)
Current smoker	40 980 (44.3)	2326 (4.1)	23 425 (33.7)	3092 (2.5)	25 775 (12.5)	22 886 (8.9)
Family history of cancer	15 688 (17.0)	8569 (15.2)	14 503 (20.8)	29 934(23.8)	73 067 (35.4)	93 452 (36.2)
Alcohol consumption						
Abstainer	5681 (6.1)	18 340 (32.4)	14 422 (20.76)	85 275 (67.7)	5519 (2.7)	14 593 (5.6)
Former drinker	7583 (8.2)	9232 (16.3)	5628 (8.1)	2958 (2.3)	6825 (3.3)	9009 (3.5)
Current drinker	79 283 (85.7)	28 960 (51.2)	49 529 (71.2)	37 732 (30.0)	193 881 (94.0)	234 938 (90.9)
Current drinker (four categories)						
<12.5 g/day	33 224 (43.8)	19 198 (80.2)	22 642 (45.7)	33 290 (88.2)	4375 (2.6)	13 595 (7.6)
12.5–24.9 g/day	17 170 (22.7)	2670 (11.2)	10 476 (21.2)	2749 (7.3)	23 369 (14.0)	60 613 (34.0)
25.0–49.9 g/day	16 302 (21.5)	1463 (6.1)	9530 (19.2)	1242 (3.3)	62 066 (37.0)	75 404 (42.4)
≥50.0 g/day	9112 (12.0)	603 (2.5)	6881 (13.9)	451 (1.2)	77 695 (46.4)	28 415 (16.0)

SD: standard deviation.
[a] Education year for KCPS-II and KoGES; Townsend Deprivation Index for UKB.
[b] Alcohol amounts are among current drinkers with non-missing data.

Comparison of age-standardized cancer incidence rates in pooled Korean biobank and UKB

The age-standardized Korean biobank and UKB incidence rates were calculated by using the WHO standard population. The general characteristics of the subjects aged 40–69 years from the three biobanks used at this time are shown in Supplementary Table S1. First, each age-standardized rate of KCPS-II (Supplementary Table S2) and KoGES (Supplementary Table S3) was calculated, and the age-standardized incidence rate of the pooled Korean biobank was calculated by combining them. The age-standardized incidence rate of overall cancer in subjects aged 40–69 years was 1.04 times higher in the pooled Korean biobank subjects than in UKB. The age-standardized incidence rate was high in pooled Korean biobank subjects at colorectal, liver, stomach, lung, and thyroid cancer compared with UKB. The pooled Korean biobank showed the highest incidence ratio for thyroid cancer at 21.79 times, followed by stomach cancer at 10.44 times and liver cancer at 6.01 times (Table 2).

Comparison of cancer risk according to alcohol consumption in pooled Korean biobank and UKB

The overall cancer risk increased slightly as the amount of drinking increased compared with never drinkers. Compared with never drinkers, the risk of total cancer was increased in KCPS-II by 26% (Supplementary Table S4) and in KoGES by 23% (Supplementary Table S5) when drinking >50 g per day. In the pooled Korean biobank, the cancer that showed the strongest association was esophageal cancer, which was 12.59 times higher than that of non-drinkers when the amount of alcohol consumed per day was ≥50 g. In the case of stomach, head and neck, liver, and alcohol-related cancer, the cancer risk was higher in the pooled Korean biobank as the alcohol consumption increased (Fig. 1). In UKB, the cancer risk was higher as alcohol consumption increased in the cases of head and neck cancer, breast cancer, and alcohol-related cancer (Fig. 2). However, in the case of thyroid cancer, the pooled Korean biobank and UKB showed a lower risk as the alcohol consumption increased (Figs 1 and 2).

Sensitivity analysis

Drinking history and cancer risk showed a similar relationship when analysed by gender. As a result of analysing the cancer risk in men according to the amount of alcohol consumed, the results were similar to those in the analysis of all subjects (Supplementary Tables S6, S8, S10, and S11). In the Korean biobank, association and statistical significance were weakened because the drinking rate and amount of alcohol in female subjects were small (Supplementary Tables S7 and S9). In addition, especially in the case of overall and alcohol-related cancer, stronger associations could be observed when the analysis was performed by excluding cancer patients in the follow-up period of <3 years to reduce the possibility of reverse causation (Figs 3 and 4, and Supplementary Tables S12 and S13). We tested for interaction by smoking status and conducted stratified analyses. There was no significant interaction between alcohol consumption and smoking status in relation to overall cancer risk in either cohort. However, site-specific analyses in KCPS-II revealed significant interactions for liver, stomach, lung, and thyroid cancers, whereas, in UKB, interaction was observed only in alcohol-related cancers (Supplementary Table S14).

Discussion

This study compared the cancer risk according to drinking status by using the KCPS-II and KoGES biobanks in South Korea and UKB in the UK. The three biobanks are prospective cohorts of the general population and the development periods of the cohort were similar, with 2004–13 for KCPS-II, 2001–13 for KoGES and 2006–10 for UKB. However, the three biobanks have several different characteristics. First, in terms of the number of subjects, KCPS-II and KoGES have <200 000 while UKB has ∼480 000. The mean ages are 41 years for KCPS-II, 54 years for KoGES, and 56 years for UKB. The mean age for KCPS-II is ∼15 years younger than

Table 2. Age-adjusted cancer incidence and incidence ratio in pooled Korean biobank and UKB subjects aged 40–69 years

Cancer site	Pooled Korean biobank				UKB				Incidence ratio (KB/UKB)	
	Person-years of follow-up	Cancer event	Incidence per 100 000 PY		Person-years of follow-up	Cancer event	Incidence per 100 000 PY			
			Crude	Age-adjusted			Crude	Age-adjusted	Crude	Age-adjusted
All cancer	3 189 671	26 972	845.6	803.4	5 198 099	57 755	1 111.1	772.7	0.76	1.04
Esophagus cancer	3 356 775	194	5.8	5.1	5 595 545	1100	19.6	11.8	0.30	0.43
Head and neck cancer[a]	3 355 439	392	11.7	10.9	5 597 190	1068	19.1	15.4	0.61	0.71
Colorectal cancer	3 338 759	2834	84.9	77.6	5 576 900	5525	99.1	65.6	0.86	1.18
Liver cancer	3 348 528	1545	46.1	42.1	5 601 279	638	11.4	7.0	4.04	6.01
Stomach cancer	3 334 491	3589	107.6	99.2	5 600 275	837	14.9	9.5	7.22	10.44
Lung cancer	3 344 620	2546	76.1	67.8	5 594 804	3612	64.6	38.0	1.18	1.78
Thyroid cancer	3 323 878	4461	134.2	137.3	5 600 292	366	6.5	6.3	20.65	21.79
Breast cancer[b]	1 859 1952	2612	140.5	146.4	3 004 241	9049	301.2	266.9	0.47	0.55
Alcohol-related cancer[c]	3 309 645	7534	227.6	216.5	5 505 631	20 622	374.6	281.2	0.61	0.77

[a] Included oral cavity cancer, pharynx cancer, larynx cancer.
[b] Included only female cancer.
[c] Included oral cavity cancer, pharynx cancer, larynx cancer, esophagus cancer, liver cancer, colorectal cancer, female breast cancer.
[d] Using WHO world standard population.

Site of cancer	Alcohol amount, g/day	Hazard ratio (95% CI)
All cancer	Non Drinker	1.00 (0.98-1.03)
	Ex Drinker	1.20 (1.15-1.25)
	<12.5	1.08† (1.00-1.17)
	12.5-24.9	1.07 (0.95-1.20)
	25-49.9	1.08 (1.03-1.15)
	≥50	1.24† (1.17-1.31)
Esophagus cancer	Non Drinker	1.00 (0.63-1.58)
	Ex Drinker	4.47† (2.50-7.98)
	<12.5	1.77 (0.67-4.65)
	12.5-24.9	4.56† (0.85-24.44)
	25-49.9	5.49† (3.05-9.89)
	≥50	12.59† (3.11-50.91)
Head and neck cancer	Non Drinker	1.00 (0.79-1.26)
	Ex Drinker	1.74† (1.18-2.56)
	<12.5	1.53 (1.12-2.09)
	12.5-24.9	1.72 (1.20-2.46)
	25-49.9	1.77 (1.22-2.55)
	≥50	2.06 (1.41-3.02)
Colorectal cancer	Non Drinker	1.00 (0.93-1.07)
	Ex Drinker	1.00 (0.86-1.16)
	<12.5	1.04 (0.97-1.13)
	12.5-24.9	1.07 (0.94-1.21)
	25-49.9	1.13 (0.99-1.29)
	≥50	1.26 (0.99-1.59)
Liver cancer	Non Drinker	1.00 (0.89-1.12)
	Ex Drinker	1.78† (1.52-2.09)
	<12.5	0.91 (0.78-1.05)
	12.5-24.9	0.90† (0.75-1.08)
	25-49.9	1.12† (0.89-1.42)
	≥50	1.65† (1.40-1.94)
Stomach cancer	Non Drinker	1.00 (0.94-1.07)
	Ex Drinker	1.18 (0.95-1.47)
	<12.5	1.19† (1.01-1.39)
	12.5-24.9	1.21† (1.07-1.37)
	25-49.9	1.30† (1.16-1.45)
	≥50	1.43† (1.22-1.67)
Lung cancer	Non Drinker	1.00 (0.92-1.08)
	Ex Drinker	1.15 (0.98-1.33)
	<12.5	0.93 (0.83-1.03)
	12.5-24.9	0.92 (0.79-1.06)
	25-49.9	1.01 (0.86-1.17)
	≥50	1.10 (0.94-1.29)
Thyroid cancer	Non Drinker	1.00 (0.95-1.05)
	Ex Drinker	1.06 (0.90-1.25)
	<12.5	0.91 (0.79-1.06)
	12.5-24.9	0.85 (0.76-0.94)
	25-49.9	0.84 (0.75-0.93)
	≥50	0.76 (0.64-0.89)
Breast cancer	Non Drinker	1.00 (0.96-1.05)
	Ex Drinker	1.02 (0.89-1.17)
	<12.5	1.01† (0.94-1.09)
	12.5-24.9	0.87† (0.70-1.09)
	25-49.9	1.02 (0.76-1.37)
	≥50	0.75 (0.43-1.29)
Alcohol related cancer	Non Drinker	1.00 (0.96-1.05)
	Ex Drinker	1.35 (1.25-1.47)
	<12.5	1.11 (0.96-1.27)
	12.5-24.9	1.05 (0.96-1.15)
	25-49.9	1.22† (1.12-1.34)
	≥50	1.60† (1.42-1.79)

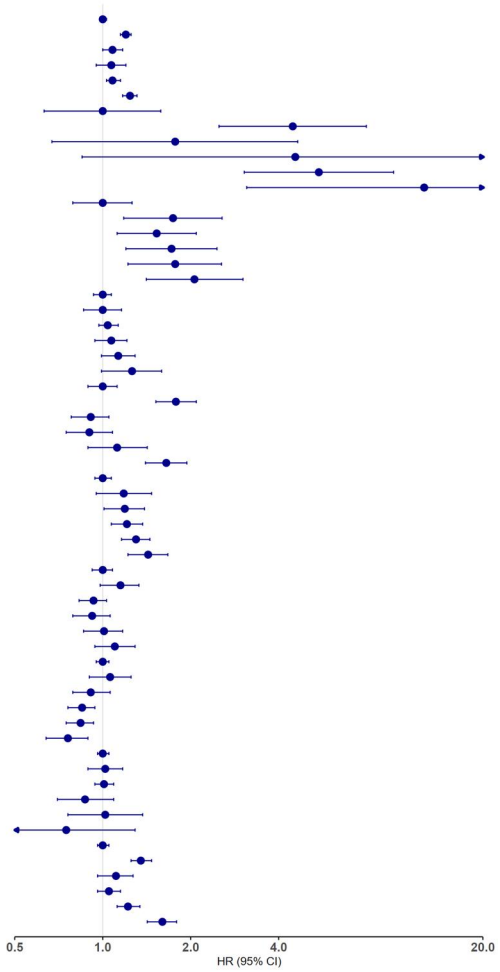

Figure 1. Association between drinking amount and incident cancer risk in all participants in the pooled Korean biobank. Adjusted for age, BMI, smoking status, socioeconomic status, family history of cancer; head and neck cancer included oral cavity cancer, pharynx cancer, larynx cancer; alcohol-related cancer included oral cavity cancer, pharynx cancer, larynx cancer, esophagus cancer, liver cancer, colorectal cancer, female breast cancer.
†The HR in the pooled Korean biobank is different from that in UKB (Z>1.96).

that for UKB. In the case of alcohol consumption, many more subjects drank alcohol in UKB than in the pooled Korean biobank and they drank more alcohol per day. Therefore, caution is needed to directly compare the cancer incidence rates of the two groups. This study compared the incidence rates by standardizing the age using the standard population of the WHO. At this time, the age was standardized for subjects aged 40–69 years in the pooled Korean biobank according to the age of 40–69 years of the UK subjects. As a result, the overall age-standardized cancer incidence rate was 1.04 times higher in the pooled Korean biobank subjects than in UKB—almost similar.

In around 2000, South Korea marketed a "health screening" program that included screening for thyroid cancer via ultrasound, and both the government and the media encouraged the early detection of cancer [23]. Thyroid cancer incidence increased slowly during the 1990s, but then increased rapidly in 2000. In 2011, the rate of thyroid cancer diagnoses was 15 times that observed in 1993 [24]. Therefore, the high incidence of thyroid cancer in South Korea might have contributed to the overall higher cancer incidence in South Korea compared with the UK. Careful interpretation is required when comparing cancer incidences in this study. This is because the comparison group is not a cohort that was made up of a representative sample of the country. In this study, to compare cancer incidence rates in South Korea and the UK, the age was set at 40–69 years and the age-standardized incidence rates were compared by using the WHO standard population.

However, the purpose of this study was not to look at the incidence or burden of cancer according to drinking history, but to compare the RR of cancer according to drinking history. Therefore, the representativeness of the study subjects, selection bias, and detection bias are considered to be less problematic. Considering these points, in view of the results of this study, the pooled Korean biobank showed a higher incidence than UKB in some cancer sites, including gastric, thyroid, and liver cancer. This is obviously a big difference and we think that the explanation will be partially due to differences in eating habits, genetic differences, and healthcare systems [24, 25]. One of the key factors contributing to the differences in associations observed between these two cohorts is the disparity in smoking prevalence. Given that alcohol consumption and smoking are known to have a strong interaction, we conducted an interaction analysis to assess their combined effect on cancer risk. In the South Korean cohort, interactions were observed for liver, stomach, lung, and

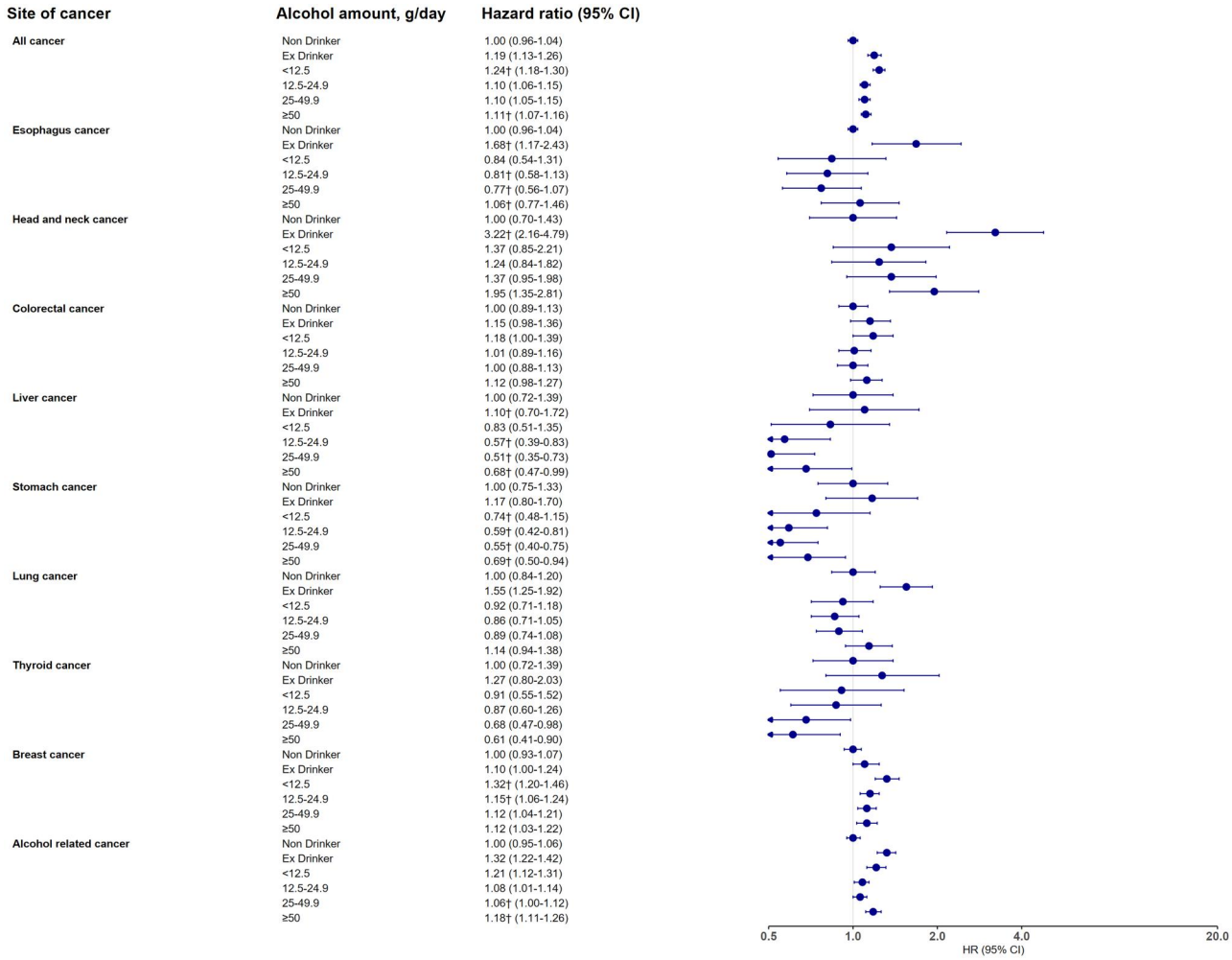

Figure 2. Association between drinking amount and incident cancer risk in total participants in UKB. Adjusted for age, BMI, smoking status, socioeconomic status, family history of cancer; head and neck cancer included oral cavity cancer, pharynx cancer, larynx cancer; alcohol-related cancer included oral cavity cancer, pharynx cancer, larynx cancer, esophagus cancer, liver cancer, colorectal cancer, female breast cancer.

†The HR in the pooled Korean biobank is different from that in UKB (Z>1.96).

thyroid cancer. In contrast, in the UKB cohort, an interaction was found only for alcohol-related cancers. These differences may be attributable to variations in smoking prevalence as well as other environmental and genetic factors between the two populations [26].

In cohort studies, cancers that develop within the first 2–3 years immediately after follow-up are suspected to be in the preclinical stage. These subjects are sometimes classified as past drinkers by reducing or stopping drinking at the baseline. In other words, as the actual risk corresponds to a high case, reverse causation can be seen.

In this study, after excluding the occurrence of cancer within <3 years, when looking at the alcohol consumption and cancer incidence results, the cancer risk was slightly increased in all alcohol consumption groups. In particular, for individuals consuming >50 g of alcohol per day, a slight increase in cancer incidence within 3 years was observed after the removal. In addition to total cancer, a similar phenomenon was also observed in gastric cancer and alcohol-related cancer. Although it was a small effect, it is considered that there was an effect of reverse causation. However, similar results were not obtained in UKB.

What is noteworthy in this study is the negative association between alcohol consumption and thyroid cancer. In South Korea, the issue of overestimating the incidence of thyroid cancer has been reported several times [27, 28]. It is hypothesized that such a medical system and environment in South Korea may have influenced the negative relationship between alcohol consumption and thyroid cancer. However, in this study, there is a limitation in specifically revealing how this detection bias affected the relationship between alcohol consumption and cancer incidence. There have been reports of meta-analysis studies synthesizing research results on alcohol consumption and thyroid cancer. A study by Wang *et al.* reported a meta-analysis of a total of 24 studies and included 9990 cases with thyroid cancer. This meta-analysis confirmed an inverse association between alcohol consumption and thyroid cancer risk. Further studies are needed to better understand the potential mechanisms underlying this association [27]. To gain a better understanding of the potential mechanisms, a Mendelian randomization study using genetic information as an instrumental variable found no evidence of an association between alcohol consumption and thyroid cancer [29, 30].

In conclusion, KCPS-II subjects had a higher rate of cancer incidence than UKB subjects at most cancer sites. For both KCPS-II and UKB subjects, alcohol consumption increased the risk of cancer. However, as this is a prospective cohort

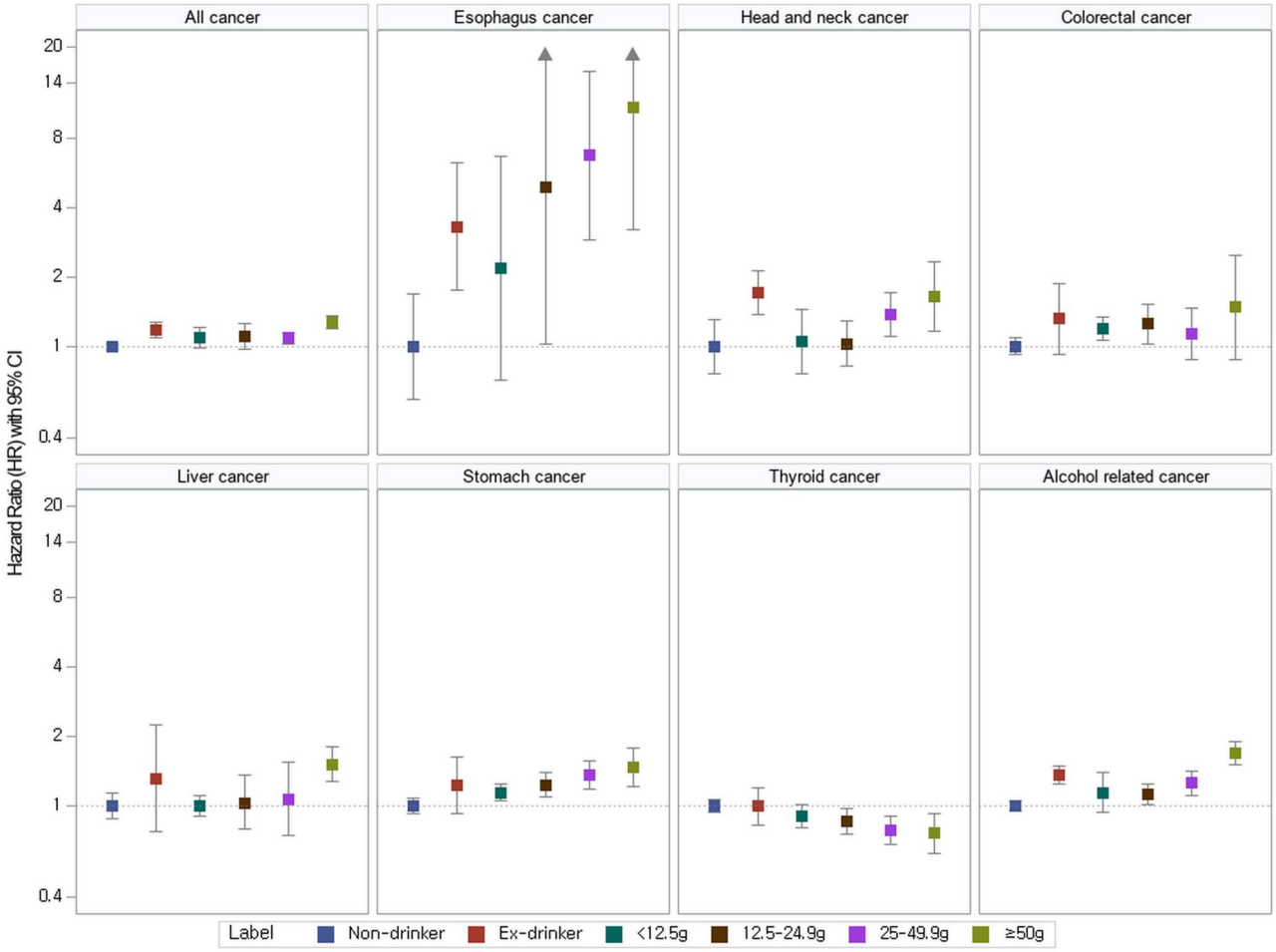

Figure 3. Association between drinking amount and incident cancer risk excluding F/U of <3 years in the pooled Korean biobank. Adjusted for age, BMI, smoking status, socioeconomic status, family history of cancer; head and neck cancer included oral cavity cancer, pharynx cancer, larynx cancer; alcohol-related cancer included oral cavity cancer, pharynx cancer, larynx cancer, esophagus cancer, liver cancer, colorectal cancer, female breast cancer.

study and has limitations as an observational study, causal conclusions cannot be drawn. In the future, further studies are needed to determine the causal relationship between alcohol consumption and cancer incidence.

Ethics approval

This study protocol was approved by the Institutional Review Board of the Severance Hospital (approval number: 4-2011-0277). UKB was approved by North West—Haydock Research Ethics Committee (REC reference: 21/NW/0157; IRAS project ID: 299116). Data from UKB was accessed through a Material Transfer Agreement under Application Reference Number: 66486.

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Author contributions

J.K.J., L.K., and J.S.H. conceived and designed the study; J.K.J. and S.D.S. conducted data analysis, made tables and figures, and drafted the manuscript. All authors advised on statistical analyses and made critical revisions of the manuscript for important intellectual content. All authors have read and approved the final version of the manuscript.

Supplementary data

Supplementary data is available at *IJE* online.

Conflict of interest

Conflict of interest relevant to this article was not reported.

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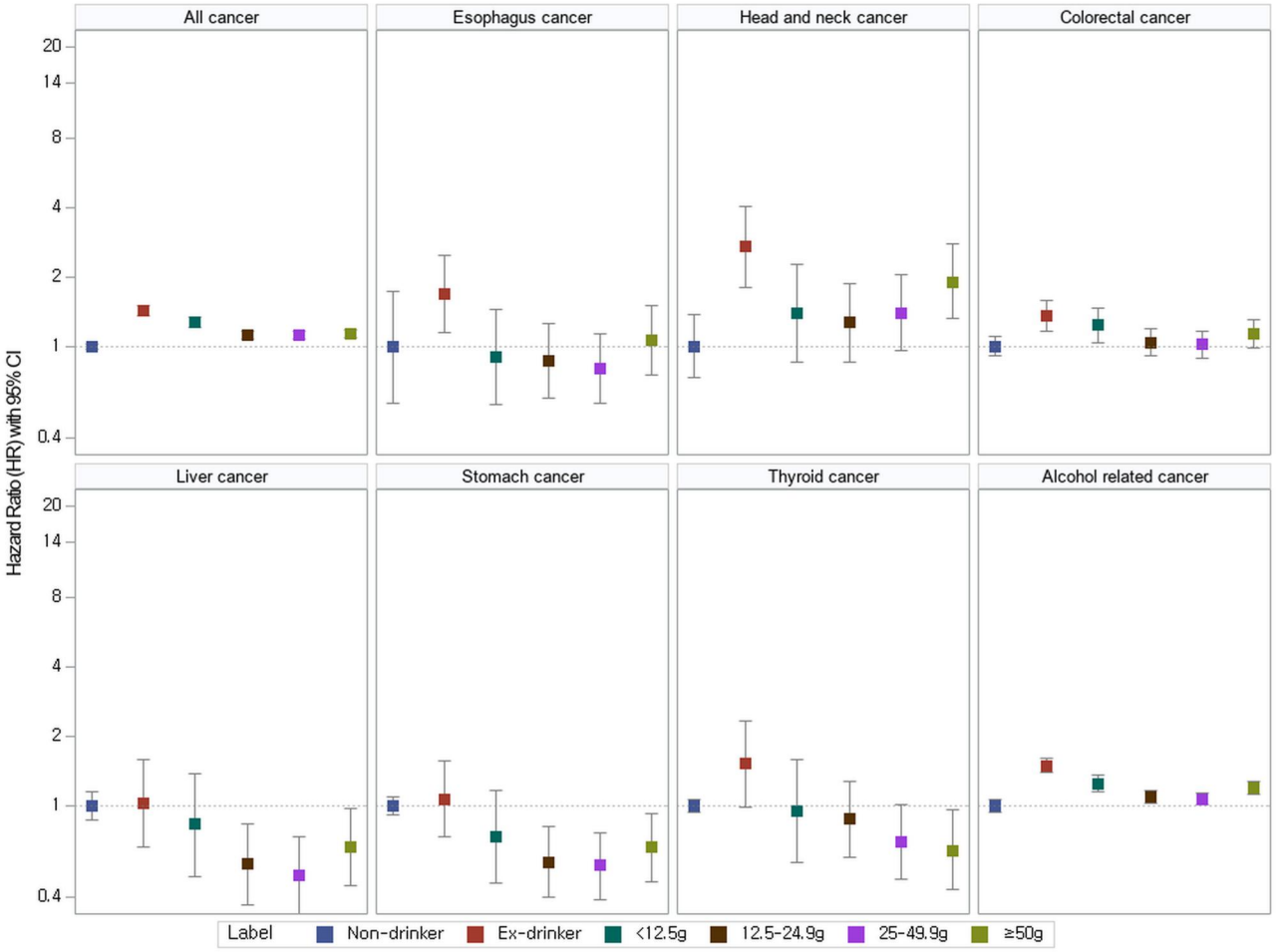

Figure 4. Association between drinking amount and incident cancer risk excluding F/U of <3 years in UKB. Adjusted for age, BMI, smoking status, socioeconomic status, family history of cancer; head and neck cancer included oral cavity cancer, pharynx cancer, larynx cancer; alcohol-related cancer included oral cavity cancer, pharynx cancer, larynx cancer, esophagus cancer, liver cancer, colorectal cancer, female breast cancer.

Use of artificial intelligence (AI) tools

AI tools were not used in this study or writing the paper.

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