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ABO blood types and cancer risk—A cohort study of 339,432 subjects in Taiwan

Wenjie Sun[a,b,1], **Chi-Pang Wen**[c,d,1], **Jie Lin**[a], **Christopher Wen**[e], **Xia Pu**[a], **Maosheng Huang**[a], **Min Kuang Tsai**[c], **Chwen Keng Tsao**[f], **Xifeng Wu**[a,*], and **Wong-Ho Chow**[a]

[a]Department of Epidemiology, The University of Texas MD Anderson Cancer Center, Houston, TX 77030, USA

[b]Tulane University School of Public Health and Tropical Medicine, New Orleans, LA, USA

[c]Institute of Population Health Science, National Health Research Institutes, Zhunan, Taiwan

[d]China Medical University Hospital, Taichung, Taiwan

[e]Department of Radiological Sciences, University of California at Irvine, Irvine, CA, USA

[f]MJ Health Management Institution, Taipei, Taiwan

Abstract

Background—The associations of laboratory-based ABO phenotypes with cancer risks and mortality have not been systematically determined.

Methods—The study subjects were 339,432 healthy individuals with laboratory-based blood types from a Taiwan cohort.

Results—Compared to blood type O, blood type A was significantly associated with an elevated risk of stomach cancer incidence (Hazard Ratio [HR], 1.38 [95% CI, 1.11–1.72]) and mortality (HR, 1.38 [95% CI, 1.02–1.86]) compared with blood type O, after adjusting for age, sex, education, smoking, alcohol drinking, physical activity, and body mass index. Non-O blood types were associated with an elevated risk of pancreatic cancer, with blood type B reaching statistical significance for incidence (HR, 1.59 [95% CI, 1.02–2.48]) and mortality (HR, 1.63 [95% CI, 1.02–2.60]). In contrast, kidney cancer risk was inversely associated with blood type AB (HR, 0.41 [95% CI, 0.18–0.93]) compared to type O.

Conclusion—Cancer risks vary in people with different ABO blood types, with elevated risks of stomach cancer associated with blood type A and pancreatic cancer associated with non-O blood types (A, B, and AB).

*Corresponding author at: Department of Epidemiology, Unit 1340, The University of Texas MD Anderson Cancer Center, 1155 Pressler Blvd., Houston, TX 77030, USA. Tel.: +1 713 745 2485; fax: +1 713 745 1165. xwu@mdanderson.org (X. Wu).

[1]These authors contributed equally to this work.

Conflicts of interest

The authors declare no conflict of interest.

Authorship contribution

CW, XW, and WC contributed to study conception and design; WS, CW, JL, CW, XP, MH, MT, CT, XW, and WC contributed to acquisition of data, or analysis and interpretation of data; WS, CW, JL, XW, and WC contributed to drafting or revision of the article for important intellectual content; and all authors have approved the final version of the manuscript for submission.

Keywords

ABO blood type; Cancer risk; Cancer mortality; Cohort

1. Introduction

ABO blood type has been extensively studied in relation to human diseases and blood transfusion complications since its discovery by Karl Landsteiner in 1900 [1,2]. An association between blood type and cancer was initially suggested through the observation that stomach cancer patients were more likely to have blood type A than control subjects [3]. A variety of other cancers have since been linked to ABO blood group [4], including cancers of the oral cavity [5], larynx [6], esophagus [7], lung [8], pancreas [9], breast [10], colorectum [11], bladder [12], prostate [13], and skin [14], but the associations generally have been inconsistent. For instance, some studies showed that blood type was not associated with pancreatic cancer [15,16]. Most previous studies were based on self-reporting of blood type which is prone to recall and information biases. For example, in a study of health professionals, about 10% of the participants incorrectly reported their blood types [9]. Additionally, the relative small size of most previous studies has limited the opportunity to comprehensively evaluate the link between ABO blood type and cancer risks, particularly for rare cancers. The majority of studies on blood type and cancer risks were conducted in the Western world [4], and published evidence in other populations is limited. ABO blood type distribution has been shown to vary substantially among populations [17,18]. Phenotypic frequencies of ABO type in two large series of hospital patients and blood donors showed a higher percentage of type A among Caucasians (38%) than Chinese (29%), but a lower percentage of type B among Caucasians (14%) than Chinese (27%) [19,20].

To address the gaps in findings from existing studies, we conducted a large cohort study with laboratory-based ABO blood type to investigate the association of blood type with cancer risk and mortality among Chinese in Taiwan.

2. Methods

Details of the study methods were reported previously [21,22]. Briefly, the cohort consists of healthy people at least 20 years of age who were provided health management by a private firm (MJ Health Management Institution, Taipei City, Taiwan) beginning in 1994. All cohort members took part in a standard medical screening program and donated an overnight fasting blood sample at baseline, and were followed until December 31, 2007. All participants underwent a standard panel of clinical tests, including hemogram, blood sugar tests, liver function tests, renal function tests, blood lipid tests, thyroid function tests, blood grouping, the presence of HBV surface antigen in blood (HBsAg), and the presence of HCV antibody in blood [23]. Individuals were defined as having diabetes if they had a history of diabetes or if they had positive diabetes screening results (fasting blood glucose concentration ≥7 mmol/L). This is to provide a complete picture of diabetes diagnosis as diabetic patients whose disease is under control may decide not to undergo screening test or

the test results may be negative. Individuals with either type I or type II diabetes were included. The ABO blood typing (A, B, O and AB) was conducted using the standard forward antigen typing with antisera reagents (anti-A, anti-B) made from monoclonal antibodies. Every participant completed a self-administered questionnaire of their medical history and lifestyle information. All participants were encouraged to visit on a yearly basis; the same questionnaires were filled out on every visit, but results from the initial visit only were used for the current analysis. All study participants signed an informed consent. The study was approved by the Institutional Review Boards (IRB) of MJ Health Management Institution and National Health Research Institutes in Taiwan and MD Anderson Cancer Center.

Of 440,630 individuals enrolled in the MJ Health Management Institution between January 1, 1994 and December 31, 2007, 339,432 were included in the current analysis with a total of 2,969,357 person-years of follow-up. The participants were followed for an average of 8.75 years (s.d. 3.15) with a range of 1.0–12.9 years. Excluded from the current analysis were subjects who reported a history of any cancer at baseline ($n = 3714$) or were followed up for less than 1 year ($n = 27,035$) or death in less than 1 year ($n = 447$). Also excluded were subjects with no information on ABO blood type ($n = 70,002$).

The principal outcome variables were cancer incidence and cause-specific mortality, including the most common cancers occurring in Taiwan. The procedures to ascertain these outcomes have been described in detail previously [24]. Incident cancer and vital status were ascertained from the Taiwan National Cancer Registry and National Death File, respectively, via record linkage using the unique national identification numbers assigned to each Taiwan resident. Cancer cases were classified according to the International Classification of Diseases (ICD-9) and were based on histological discharge forms and oncology reports [22].

The Cox proportional hazards regression analysis was used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for cancer incidence and mortality in relation to ABO blood type. The time of study entry was the date of enrollment, and the time of exit was the date of first cancer diagnosis, death, or the end of follow-up (December 31, 2007), whichever came first. Participants who died of any causes other than cancer were censored on the date of death. The proportional hazards assumption was evaluated by inspection of plots of log (−log[S]) against time [25], in which S was the estimated survival function. Baseline potential confounders were adjusted, including sex, age, education, physical activity, smoking, alcohol drinking, and body mass index (BMI). The age- and sex-adjusted model included 339,432 individuals and the fully adjusted model included 297,187 individuals after excluding those with missing values for covariates. In addition, HBV infection was included as a covariate for estimating risk of liver cancer incidence and mortality. The potential confounders were categorized as in Table 1. We also considered whether the association of ABO blood type with cancer varied with age, sex, or BMI group from the significance of interaction terms. All analyses were conducted using the STATA statistical software program (version 10.1; Stata Corp., College Station, TX, USA).

3. Results

Of the 339,432 participants, 42.9% had blood type O, and 26.8, 24.3, and 6.0% had blood types B, A, and AB, respectively. The mean and median ages at baseline were 41 and 39 years, with little variations in subgroups defined by blood type (Table 1). Only 7.9% of the cohort participants were age 65 years or older and 53.6% was female. About 42% of the cohort had attended at least some college. The majority were never smokers (69.8%) and never alcohol drinkers (76.6%). Overweight (BMI 25–<30) and obesity (BMI ≥ 30) were reported by 23.4 and 3.8% of the cohort, respectively. Over 85% were inactive or had low physical activity level. There were no meaningful differences in the distributions of the demographic variables and exposures by ABO blood groups.

During an average of 8.75 years of follow-up, 9164 participants developed cancer and 3803 participants had died of the disease. Compared to type O, type AB was associated with a slight decrease in risk of developing cancer overall (HR = 0.90, 95% CI 0.81–1.00; P = 0.049) after adjusting for age, sex, educational level, smoking, alcohol drinking, physical activity, and BMI (Table 2). When specific cancers were examined, a significant inverse association with type AB was observed only for kidney cancer (HR = 0.41, 95% CI 0.18–0.93). An inverse association relative to blood type O was also observed for other blood types, with kidney cancer risk for those with non-O blood type reduced 27% (HR = 0.73, 93% CI 0.56–0.96). In contrast, stomach cancer risk was significantly elevated for those with blood type A (HR = 1.38, 95% CI 1.11–1.72) compared to those with blood type O. No association was observed for blood type B or AB. For pancreas cancer, a significant excess risk associated with non-O blood type overall was observed (HR = 1.50, 95% CI 1.04–2.19), with an elevated risk found across all non-O blood types (HR for type A: 1.45; type B: 1.59; and type AB: 1.37).

No consistent patterns of association were observed between ABO blood type and other cancers, including cancers of the oral cavity, esophagus, lung, colon, rectum, leukemia, breast, and prostate (Table 2). The findings for cancer mortality generally mirrored those for incident cancers (Table 3). Compared to blood type O, individuals with blood type A had a significantly elevated risk of stomach cancer mortality (HR = 1.38; 95% CI 1.02–1.86), whereas risk of pancreas cancer mortality was elevated for those with non-O blood type (HR = 1.47, 95% CI 0.98–2.19). Consistent with findings for incident cancer, the elevated risk for pancreas cancer mortality was found across all blood types, with statistical significance reached for blood type B (HR = 1.63, 95% CI 1.02–2.60). Furthermore, adjustment for other variables such as history of diabetes, HBV infection, or family history of cancer did not materially alter the findings for either cancer incidence or mortality (data not shown). Age, sex, or BMI did not modify the associations between ABO blood type and cancer incidence or mortality (data not show).

4. Discussion

In this large cohort of Chinese men and women with laboratory typing of ABO blood group at baseline, we found that after an average follow-up of 8.75 years, subsequent risk of cancer varied in people with different blood types. Compared to people with blood type O, those

with non-O blood type (A, B, and AB combined as well as separately) had a reduced risk of kidney cancer but an elevated risk of pancreas cancer. In addition, blood type A was associated with an excess risk of stomach cancer whereas type AB was associated with a marginal reduction in overall cancer risk.

Since Aird et al. first reported an association between blood type A and gastric cancer 60 years ago [3], this observation has been confirmed in many case-control studies and a cohort of blood donors in Sweden and Denmark [18,26]. Assessment of ABO genotype, which is highly concordant with ABO phenotype [27], has also linked an increased risk of gastric cancer with AA genotype [28]. Our observation of an elevated risk of both gastric cancer incidence and mortality associated with blood type A add to the limited evidence from cohort study. Recently, a study of intestinal metaplasia and dysplasia, both precancerous gastric lesions, found that the association with ABO type was modified by *Helicobacter pylori* (*H. pylori*) and *cagA* status, a known risk factor for gastric cancer [29]. An elevated risk of these lesions was associated with blood type A only among carriers of the virulent cagA+ strains of *H. pylori*, hypothesized to be due to differential binding of the bacterium to the blood group antigens. Our study did not collect data on *H. pylori* and cagA status and therefore was unable to confirm an interactive effect of *H. pylori* and ABO blood group.

Our observation of an increased risk of pancreatic cancer associated with all non-O blood types (A, B, or AB) relative to blood type O is consistent with findings reported in two prospective cohort studies of health professionals in the USA [9]. These findings, however, differ from results in a recent European consortium study [30] and a large population-based case-control study in Shanghai, China [27]. Assessing ABO blood type based on genotype, these studies found an increased risk of pancreatic cancer associated only with blood type A, and not type B or AB, when compared with type O. To explore reasons for the diverse findings, Risch et al. conducted a meta-analysis of 24 studies worldwide totaling 10,415 cases and 869,044 controls [31]. When the studies were stratified by cagA+ *H. pylori* endemic (mostly East Asian populations) versus cagA non-endemic populations, an increased risk of pancreatic cancer was associated with blood type A in all populations, but with blood type B or AB only in cagA non-endemic populations (mostly Western populations) [31]. However, this observation is not supported in our cohort study in Taiwan, which is a cagA+ *H. pylori* endemic population [32]. The reasons for the diverse findings are unclear, but further assessment of interactions between ABO blood group and *H. pylori* carriage and other exposures could be informative. We were unable to examine *H. pylori* status as these data were not available in our study. The distributions of other potential cancer risk factors, including smoking and alcohol drinking, body mass index, and physical activity level, were not meaningfully different among people of various ABO blood groups in our cohort.

The inverse associations of kidney cancer with blood types A, B, and AB in our study are unexpected and in contrast to the elevated risk of renal cell cancer, the predominant form of kidney cancer, associated with the respective blood types in two prospective cohorts of health professionals [33]. This difference in findings cannot be explained by the inclusion of renal pelvis cancer in our study since the risk of bladder cancer, which has similar histology as renal pelvis cancer, is positively associated with blood types A, B, and AB. A registry-

based study comparing kidney cancer cases to other cancer patients reported no association with ABO blood type [4]. It is premature to link kidney cancer with ABO blood type based on the limited and inconsistent evidence.

Our study also found a weak inverse association between overall cancer risk and blood type AB compared to type O. To our knowledge, this observation has not been reported previously. Confirmation in other studies is needed before we can draw any inference from this finding.

The ABO blood group antigens are glycoproteins expressed on the surface of red blood cells and other tissues, including epithelial cells of the gastrointestinal tract [34]. Glycoconjugates are mediators of intercellular adhesion and membrane signaling and therefore can affect cell proliferation and malignant progression [9,34]. These cell surface molecules are also recognized by host immune response and may play a role in immunosurveillance of malignant cells [9,34,35]. Furthermore, individuals with various ABO blood types have been shown to have different inflammatory responses to *H. pylori* infection, indicated by the release of different levels of proinflammatory cytokines [36]. The cagA strains of *H. pylori* have been shown to modify the association between single nucleotide polymorphisms at the ABO locus and risk of pancreatic and gastric cancers and precancerous lesions [28–31]. Together these observations suggest that ABO blood type may influence risk of gastric and pancreatic cancers through differential immune function and inflammatory responses. Although mechanisms have been proposed for other cancers, such as kidney cancer, the evidence linking these cancers to ABO blood type is tenuous. Further evidence is needed before mechanisms can be fully considered.

Our study has several notable strengths. The large study size provides an opportunity to comprehensively examine the association between ABO blood type and cancer risks, including risk of uncommon cancers. Misclassification of ABO blood type is minimized by using a laboratory-based measurement. The relatively homogenous and stable study population diminishes potential confounding by other factors. The unique personal identification number and the availability of population-based cancer registry and vital statistics registry, along with continuing health management for the cohort, enhance the completeness and accuracy of follow-up for cancer incidence and mortality. Furthermore, MJ is a homogenous cohort of individuals belonging to the same ethnicity (Han Chinese). There are 98% Han Chinese in Taiwan. The original minority is only 2%. The distribution of blood type of the study population is similar to the Han Chinese: A 20–39%; B 20–39%, and O 30–40% [37]. Such a homogenous population could minimize potential confounding but may limit the generalizability of our study findings to other populations with more diverse prevalence of exposures. Our study is limited by the availability of only phenotype, and not genotype, for the classification of individuals into ABO blood type. It has been shown that compared with people with OO genotype, pancreatic cancer risk was higher among those with AA or BB genotype than those with AO or BO genotype, respectively [28,38]. Similar observations were also reported for gastric cancer, comparing groups with AA or AO with those with OO genotype [31]. Since our study was unable to classify cohort participants by ABO genotype, the cancer risk we observed for subjects with blood group A or B phenotype may be underestimated relative to those with homozygous A or B genotype. Our study is

also limited by not having information on *H. pylori* and cag A status, which could be an effect modifier in the relation between ABO blood group and risk of gastric and pancreatic cancers. Lastly, the number of cases with blood type AB is small for the less common cancers, despite the large study population.

5. Conclusion

In this cohort study with laboratory measured ABO phenotype, we confirmed previous observations linking blood type A to an excess risk of stomach cancer. Compared to people with blood type O, our study suggested that those with blood type A, B, or AB have an elevated risk of pancreas cancer. Further studies are needed to identify the mechanisms through which ABO blood type may influence risk of various cancers in different populations.

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Table 1

Characteristics of the study participants by ABO blood type (column %).

Characteristic	O	A	B	AB	Total
Sex					
Male	67,190 (46.2)	42,277 (46.5)	38,711 (46.9)	9358 (46.1)	157,536 (46.4)
Female	78,360 (53.8)	48,695 (53.5)	43,920 (53.1)	10,921 (53.9)	181,896 (53.6)
Age (years)					
<65	134,506 (92.4)	83,652 (92.0)	75,859 (91.8)	18,636 (91.9)	312,653 (92.1)
≥65	11,044 (7.6)	7320 (8.0)	6772 (8.2)	1643 (8.1)	26,779 (7.9)
Education					
Middle school or lower	44,421 (30.5)	27,183 (29.9)	24,572 (29.7)	5908 (29.1)	102,084 (30.1)
High school	38,389 (26.4)	23,996 (26.4)	21,723 (26.3)	5388 (26.6)	89,496 (26.4)
Junior college	28,565 (19.6)	18,130 (19.9)	16,469 (19.9)	4096 (20.2)	67,260 (19.8)
College or higher	30,218 (20.8)	19,251 (21.2)	17,562 (21.2)	4360 (21.5)	71,391 (21.0)
Unknown	3957 (2.7)	2412 (2.6)	2305 (2.8)	527 (2.6)	9201 (2.7)
BMI (kg/m^2)					
≤18.5	11,937 (8.2)	7470 (8.2)	6868 (8.3)	1694 (8.4)	27,969 (8.2)
<25	94,103 (64.7)	58,636 (64.5)	53,158 (64.3)	13,111 (64.7)	219,008 (64.6)
<30	34,019 (23.4)	21,282 (23.4)	19,415 (23.5)	4665 (23.0)	79,381 (23.4)
≥30	5451 (3.7)	3563 (3.9)	3171 (3.9)	800 (3.9)	12,985 (3.8)
Unknown	40 (0.0)	21 (0.0)	19 (0.0)	9 (0.0)	89 (0.0)
Smoking status					
Never-smoker	95,653 (65.7)	59,367 (65.2)	53,779 (65.1)	13,254 (65.4)	222,053 (65.4)
Ex-smoker	8445 (5.8)	5534 (6.1)	5011 (6.1)	1197 (5.9)	20,187 (5.9)
Smoker	32,297 (22.2)	20,366 (22.4)	18,602 (22.5)	4547 (22.4)	75,812 (22.4)
Unknown	9155 (6.3)	5705 (6.3)	5239 (6.3)	1281 (6.3)	21,380 (6.3)
Drinking status					
Never-drinker	103,556 (71.1)	64,487 (70.9)	58,455 (70.7)	14,358 (70.8)	240,856 (71.0)
Ex-drinker	4341 (3.0)	2782 (3.0)	2421 (2.9)	594 (2.9)	10,138 (3.0)
Regular drinker	26,914 (18.5)	17,095 (18.8)	15,670 (19.0)	3863 (19.1)	63,542 (18.7)
Unknown	10,739 (7.4)	6608 (7.3)	6085 (7.4)	1464 (7.2)	24,896 (7.3)

Characteristic	O	A	B	AB	Total
Physical activity					
Inactive	74,051 (50.9)	46,700 (51.3)	42,606 (51.6)	10,513 (51.8)	173,870 (51.2)
Low	42,853 (29.4)	26,566 (29.2)	23,933 (29.0)	5886 (29.0)	99,238 (29.3)
Middle	16,324 (11.2)	10,008 (11.0)	9021 (10.9)	2124 (10.5)	37,477 (11.0)
High	4306 (3.0)	2740 (3.0)	2492 (3.0)	631 (3.1)	10,169 (3.0)
Unknown	8016 (5.5)	4958 (5.5)	4579 (5.5)	1125 (5.6)	18,678 (5.5)
Diabetes					
No	141,449 (97.2)	88,198 (97.0)	80,200 (97.1)	19,663 (97.0)	329,510 (97.1)
Yes	4100 (2.8)	2774 (3.1)	2431 (2.9)	616 (3.0)	9921 (2.9)
Unknown	1 (0.00)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.0)
Family history cancer					
No	109,117 (75.0)	67,523 (74.2)	61,722 (74.7)	15,230 (75.1)	253,592 (74.7)
Yes	36,433 (25.0)	23,449 (25.8)	20,909 (25.3)	5049 (24.9)	85,840 (25.3)
Unknown	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
HBV					
No	103,242 (70.9)	64,192 (70.6)	58,761 (71.1)	14,592 (72.0)	240,787 (70.9)
Yes	24,906 (17.1)	16,022 (17.6)	14,007 (17.0)	3337 (16.4)	58,272 (17.2)
Unknown	17,402 (12.0)	10,758 (11.8)	9863 (11.9)	2350 (11.6)	40,373 (11.9)

Table 2

HRs for over-all and cause-specific cancer incidence by ABO blood type.

Cancer site	Blood type	*N*	Incidence rate (per 100,000 person-years)	HR[a] (95% CI)	HR[b] (95% CI)
Overall	O	3921	339.86	1.00 (Reference)	1.00 (Reference)
	A	2560	353.28	1.02 (0.97–1.07)	1.04 (0.98–1.10)
	B	2171	329.56	0.94 (0.89–0.99)	0.97 (0.91–1.02)
	AB	512	316.37	0.92 (0.84–1.01)	0.90 (0.81–1.00)
	Non-O	5243	339.30	0.97 (0.93–1.02)	0.99 (0.95–1.04)
Oral	O	262	22.71	1.00 (Reference)	1.00 (Reference)
	A	180	24.84	1.08 (0.89–1.30)	1.06 (0.86–1.30)
	B	147	22.31	0.96 (0.78–1.17)	0.97 (0.77–1.21)
	AB	38	23.48	1.03 (0.73–1.44)	0.93 (0.62–1.37)
	Non-O	365	23.62	1.02 (0.87–1.20)	1.01 (0.84–1.20)
Esophagus	O	52	4.51	1.00 (Reference)	1.00 (Reference)
	A	33	4.55	0.95 (0.61–1.48)	1.08 (0.67–1.74)
	B	27	4.10	0.85 (0.53–1.36)	0.96 (0.58–1.60)
	AB	8	4.94	1.08 (0.51–2.28)	1.01 (0.43–2.39)
	Non-O	68	4.40	0.92 (0.64–1.33)	1.02 (0.69–1.53)
Lung	O	429	37.18	1.00 (Reference)	1.00 (Reference)
	A	294	40.57	1.05 (0.91–1.22)	1.01 (0.85–1.19)
	B	281	42.66	1.08 (0.93–1.26)	1.08 (0.92–1.28)
	AB	61	37.69	0.97 (0.74–1.28)	1.03 (0.77–1.38)
	Non-O	636	41.16	1.06 (0.94–1.20)	1.04 (0.91–1.19)
Stomach	O	215	18.64	1.00 (Reference)	1.00 (Reference)
	A	180	24.84	1.28 (1.05–1.56)	1.38 (1.11–1.72)
	B	104	15.79	0.81 (0.64–1.03)	0.82 (0.63–1.07)
	AB	25	15.45	0.81 (0.54–1.23)	0.92 (0.59–1.44)
	Non-O	309	20.00	1.03 (0.87–1.23)	1.09 (0.90–1.33)
Liver[c]	O	625	54.17	1.00 (Reference)	1.00 (Reference)
	A	361	49.82	0.89 (0.79–1.02)	0.92 (0.80–1.07)
	B	339	51.46	0.92 (0.81–1.05)	0.96 (0.83–1.12)

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Cancer site	Blood type	*N*	Incidence rate (per 100,000 person-years)	HR[a] (95% CI)	HR[b] (95% CI)
	AB	69	42.64	0.77 (0.60–0.99)	0.81 (0.61–1.07)
	Non-O	769	49.77	0.89 (0.80–0.99)	0.93 (0.82–1.04)
Pancreas	O	51	4.42	1.00 (Reference)	1.00 (Reference)
	A	50	6.90	1.50 (1.02–2.22)	1.45 (0.94–2.26)
	B	45	6.83	1.47 (0.99–2.20)	1.59 (1.02–2.48)
	AB	10	6.18	1.36 (0.69–2.68)	1.37 (0.64–2.93)
	Non-O	105	6.80	1.48 (1.06–2.06)	1.50 (1.04–2.19)
Rectum	O	205	17.77	1.00 (Reference)	1.00 (Reference)
	A	159	21.94	1.20 (0.97–1.47)	1.19 (0.94–1.51)
	B	126	19.13	1.04 (0.83–1.30)	1.09 (0.85–1.40)
	AB	28	17.30	0.96 (0.65–1.42)	1.00 (0.65–1.55)
	Non-O	313	20.26	1.10 (0.93–1.32)	1.13 (0.93–1.38)
Colon	O	328	28.43	1.00 (Reference)	1.00 (Reference)
	A	226	31.19	1.06 (0.90–1.26)	1.12 (0.93–1.36)
	B	172	26.11	0.89 (0.74–1.07)	0.96 (0.78–1.17)
	AB	46	28.42	0.98 (0.72–1.34)	1.01 (0.71–1.42)
	Non-O	444	28.73	0.98 (0.85–1.13)	1.04 (0.89–1.22)
Kidney	O	125	10.83	1.00 (Reference)	1.00 (Reference)
	A	64	8.83	0.79 (0.58–1.07)	0.82 (0.58–1.14)
	B	58	8.80	0.78 (0.57–1.06)	0.72 (0.50–1.03)
	AB	12	7.42	0.67 (0.37–1.21)	0.41 (0.18–0.93)
	Non-O	134	8.67	0.77 (0.61–0.99)	0.73 (0.56–0.96)
Bladder	O	85	7.37	1.00 (Reference)	1.00 (Reference)
	A	68	9.38	1.21 (0.88–1.67)	1.11 (0.75–1.63)
	B	66	10.02	1.28 (0.93–1.77)	1.32 (0.91–1.93)
	AB	17	10.50	1.38 (0.82–2.32)	1.58 (0.88–2.82)
	Non-O	151	9.77	1.26 (0.97–1.64)	1.25 (0.91–1.71)
Leukemia	O	67	5.81	1.00 (Reference)	1.00 (Reference)
	A	38	5.24	0.89 (0.60–1.32)	0.86 (0.55–1.34)
	B	35	5.31	0.89 (0.59–1.35)	0.97 (0.63–1.51)
	AB	6	3.71	0.63 (0.27–1.46)	0.64 (0.25–1.59)

Cancer site	Blood type	*N*	Incidence rate (per 100,000 person-years)	HR[a] (95% CI)	HR[b] (95% CI)
	Non-O	79	5.11	0.86 (0.62–1.20)	0.89 (0.62–1.27)
Breast (female)	O	506	81.33	1.00 (Reference)	1.00 (Reference)
	A	300	77.39	0.95 (0.82–1.09)	0.95 (0.82–1.12)
	B	271	77.31	0.94 (0.81–1.09)	0.92 (0.78–1.09)
	AB	70	80.21	0.99 (0.77–1.27)	0.87 (0.65–1.17)
	Non-O	641	77.65	0.95 (0.84–1.07)	0.93 (0.82–1.06)
Prostate (male)	O	223	41.95	1.00 (Reference)	1.00 (Reference)
	A	165	48.96	1.08 (0.88–1.32)	1.22 (0.98–1.53)
	B	122	39.58	0.87 (0.70–1.09)	0.95 (0.74–1.22)
	AB	32	42.92	0.95 (0.66–1.38)	0.89 (0.58–1.38)
	Non-O	319	44.32	0.98 (0.82–1.16)	1.07 (0.88–1.30)

[a]Adjusted for age and sex.

[b]Adjusted for age, sex, education level, smoking status, alcohol drinking status, physical activity, and BMI. Individuals with missing covariates were excluded from each model.

[c]Also adjusted for HBV infection.

Table 3

HRs for over-all and cause-specific cancer mortality by ABO blood type.

Cancer site	Blood type	*N*	Mortality rate (per 100,000 person-years)	HR[a] (95% CI)	HR[b] (95% CI)
Overall	O	1608	11.61	1.00 (Reference)	1.00 (Reference)
	A	1090	12.53	1.04 (0.96–1.12)	1.04 (0.95–1.13)
	B	900	11.39	0.94 (0.87–1.02)	0.96 (0.87–1.05)
	AB	205	10.56	0.89 (0.77–1.03)	0.90 (0.77–1.06)
	Non-O	2195	11.84	0.98 (0.92–1.05)	0.99 (0.92–1.06)
Oral	O	94	0.68	1.00 (Reference)	1.00 (Reference)
	A	59	0.68	0.97 (0.70–1.34)	0.82 (0.57–1.18)
	B	46	0.58	0.83 (0.58–1.18)	0.87 (0.60–1.26)
	AB	8	0.41	0.60 (0.29–1.23)	0.51 (0.22–1.17)
	Non-O	113	0.61	0.87 (0.66–1.15)	0.81 (0.60–1.09)
Esophagus	O	38	0.27	1.00 (Reference)	1.00 (Reference)
	A	24	0.28	0.96 (0.57–1.60)	1.05 (0.60–1.83)
	B	19	0.24	0.83 (0.48–1.44)	0.96 (0.53–1.75)
	AB	6	0.31	1.09 (0.46–2.57)	1.15 (0.45–2.96)
	Non-O	49	0.26	0.92 (0.60–1.40)	1.02 (0.64–1.63)
Lung	O	319	2.30	1.00 (Reference)	1.00 (Reference)
	A	213	2.45	1.02 (0.86–1.21)	0.95 (0.78–1.15)
	B	199	2.52	1.04 (0.87–1.24)	1.05 (0.86–1.27)
	AB	46	2.37	1.00 (0.73–1.36)	1.03 (0.73–1.44)
	Non-O	458	2.47	1.03 (0.89–1.18)	1.00 (0.85–1.17)
Stomach	O	110	0.79	1.00 (Reference)	1.00 (Reference)
	A	101	1.16	1.40 (1.07–1.84)	1.38 (1.02–1.86)
	B	60	0.76	0.91 (0.67–1.25)	0.79 (0.55–1.14)
	AB	9	0.46	0.57 (0.29–1.12)	0.70 (0.35–1.38)
	Non-O	170	0.92	1.11 (0.87–1.41)	1.06 (0.81–1.38)
Liver[c]	O	404	2.92	1.00 (Reference)	1.00 (Reference)
	A	247	2.84	0.94 (0.80–1.10)	1.00 (0.84–1.20)
	B	213	2.69	0.89 (0.75–1.05)	0.91 (0.75–1.09)

Cancer site	Blood type	*N*	Mortality rate (per 100,000 person-years)	HR[a] (95% CI)	HR[b] (95% CI)
	AB	48	2.47	0.83 (0.61–1.12)	0.80 (0.56–1.13)
	Non-O	508	2.74	0.91 (0.79–1.03)	0.94 (0.81–1.09)
Pancreas	O	45	0.33	1.00 (Reference)	1.00 (Reference)
	A	43	0.49	1.47 (0.97–2.23)	1.34 (0.83–2.17)
	B	40	0.51	1.49 (0.98–2.29)	1.63 (1.02–2.60)
	AB	8	0.41	1.24 (0.59–2.64)	1.38 (0.61–3.09)
	Non-O	91	0.49	1.46 (1.02–2.08)	1.47 (0.98–2.19)
Rectum	O	52	0.38	1.00 (Reference)	1.00 (Reference)
	A	46	0.53	1.36 (0.91–2.02)	1.42 (0.91–2.21)
	B	41	0.52	1.32 (0.88–1.99)	1.49 (0.94–2.34)
	AB	7	0.36	0.94 (0.43–2.07)	1.21 (0.54–2.70)
	Non-O	94	0.51	1.30 (0.93–1.82)	1.42 (0.97–2.08)
Colon	O	112	0.81	1.00 (Reference)	1.00 (Reference)
	A	78	0.90	1.07 (0.80–1.43)	1.22 (0.89–1.69)
	B	48	0.61	0.72 (0.51–1.01)	0.79 (0.54–1.16)
	AB	15	0.77	0.94 (0.55–1.61)	1.00 (0.55–1.84)
	Non-O	141	0.76	0.90 (0.71–1.16)	1.02 (0.77–1.35)
Kidney	O	39	0.28	1.00 (Reference)	1.00 (Reference)
	A	22	0.25	0.86 (0.51–1.45)	0.95 (0.53–1.71)
	B	25	0.32	1.07 (0.65–1.77)	1.05 (0.58–1.89)
	AB	7	0.36	1.25 (0.56–2.80)	0.97 (0.34–2.76)
	Non-O	54	0.29	0.99 (0.66–1.50)	1.00 (0.62–1.61)
Bladder	O	24	0.17	1.00 (Reference)	1.00 (Reference)
	A	17	0.20	1.06 (0.57–1.98)	1.17 (0.51–2.67)
	B	19	0.24	1.30 (0.71–2.37)	1.30 (0.57–2.97)
	AB	3	0.15	0.86 (0.26–2.84)	0.54 (0.07–4.10)
	Non-O	39	0.21	1.14 (0.69–1.90)	1.16 (0.58–2.32)
Leukemia	O	32	0.23	1.00 (Reference)	1.00 (Reference)
	A	17	0.20	0.82 (0.46–1.48)	0.76 (0.39–1.46)
	B	14	0.18	0.74 (0.40–1.39)	0.83 (0.43–1.61)
	AB	2	0.10	0.44 (0.11–1.84)	0.52 (0.12–2.19)

Cancer site	Blood type	*N*	Mortality rate (per 100,000 person-years)	HR[a] (95% CI)	HR[b] (95% CI)
	Non-O	33	0.18	0.75 (0.46–1.22)	0.76 (0.45–1.29)
Breast (female)	O	50	0.67	1.00 (Reference)	1.00 (Reference)
	A	36	0.77	1.15 (0.75–1.77)	1.05 (0.64–1.71)
	B	35	0.83	1.23 (0.80–1.90)	1.06 (0.64–1.75)
	AB	7	0.67	1.01 (0.46–2.23)	0.89 (0.35–2.26)
	Non-O	78	0.79	1.17 (0.82–1.67)	1.03 (0.69–1.55)
Prostate (male)	O	45	0.71	1.00 (Reference)	1.00 (Reference)
	A	35	0.87	1.14 (0.73–1.77)	1.11 (0.66–1.84)
	B	23	0.62	0.82 (0.50–1.36)	0.76 (0.42–1.37)
	AB	5	0.56	0.74 (0.29–1.85)	0.77 (0.27–2.18)
	Non-O	63	0.73	0.96 (0.66–1.41)	0.92 (0.59–1.44)

[a]Adjusted for age and sex.

[b]Adjusted for age, sex, education level, smoking status, alcohol drinking status, physical activity, and BMI. Individuals with missing covariates were excluded from each model.

[c]Also adjusted for HBV infection.