

## SECTION 5

# Alcohol Use and Mortality in the Japan Collaborative Cohort Study for Evaluation of Cancer (JACC)

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## Abstract

Alcohol use was examined for its influence on mortality in the Japan Collaborative Cohort. While overall risk of death, as well as ischemic heart disease, were reduced with moderate consumption, increase was noted with heavy intake, even after cessation. With heavy consumption, overall cancers were also increased. In males, risk of oesophageal cancer was particularly elevated and risk of liver and renal cancer was found to be increased in ex-drinkers. Heavy consumption appears to be also a risk factor for rectal and gallbladder cancer. Furthermore, cerebrovascular disease was increased with dose-dependence.

**Keywords:** Alcohol - consumption level - mortality - cancer - circulatory disease

*Asian Pacific J Cancer Prev*, 8, JACC Supplement, 81-88

## Introduction

Alcohol use was surveyed in all areas of the Japan Collaborative Cohort Study for Evaluation of Cancer (JACC) and assessed for its influence on mortality.

## Materials and Methods

Each participant was asked about his or her drinking habits and was classified accordingly as a drinker, ex-drinker, or rare/non-drinker. Drinkers were further classified by their drinking frequency, level of alcohol consumption per day, duration of drinking habit, and age at which drinking started. Ex-drinkers were classified according to number of years since drinking ceased. Level of alcohol consumption was self-estimated as a volume equivalent to Japanese sake by the participants. Sex-specific and age- and study area-adjusted hazard ratios and 95% confidence intervals of major causes of death were calculated.

## Results

### *Risk of death from all causes*

The overall risk of death was found to be decreased in both male and female drinkers, in particular, in occasional (3-4/week) drinkers compared with rare/non-drinkers (Age-adjusted Hazard Ratio (HR) = 0.84,  $P < 0.01$  for males, and HR = 0.87,  $P < 0.01$  for females) (Table 1). This was particularly the case for male and female light drinkers (HR = 0.86,  $P < 0.01$ , and HR = 0.90,  $P < 0.01$ , respectively), who consumed less than 54 ml of alcohol per day (Table 2). In contrast, the risk of death from all

causes was increased in male heavy drinkers who consumed more than 81 ml of alcohol per day (HR = 1.33,  $P < 0.01$ ). A drinking habit lasting less than 20 years decreased the risk of death (HR = 0.75,  $P < 0.01$ ) (Table 3). Commencing alcohol use before the age of 20 years increased the risk of death from all causes (HR = 1.20,  $P < 0.01$ ) (Table 4). Risk was increased in both male and female ex-drinkers (HR = 1.59,  $P < 0.01$ , and HR = 1.51,  $P < 0.01$ , respectively) (Table 1). Risk of death from all causes appeared to remain high even after cessation of drinking (Table 5).

### *Risk of death from all cancers*

The risk of death from all cancers in male and female drinkers was no different to that in rare/non-drinkers, but it was increased in male heavy drinkers who consumed amounts of alcohol equal to or greater than 81 ml per day (HR = 1.39,  $P < 0.01$ ) (Table 2). A drinking habit of less than 20 years duration decreased the risk (HR = 0.82,  $P < 0.01$ ) (Table 3), whereas a drinking habit of 30 years or longer increased the risk of death from all cancers (HR = 1.11,  $P < 0.05$ ). Younger age (<20 years) at which drinking started also increased the risk (HR = 1.23,  $P < 0.05$ ) (Table 4). The risk was increased in both male and female ex-drinkers (HR = 1.50,  $P < 0.01$ , and HR = 1.60,  $P < 0.01$ , respectively) (Table 1). In males, the risk of death from all cancers appeared to decrease gradually after permanent cessation of alcohol consumption (Table 5).

### *Risk of death from esophageal cancer*

Compared with rare/non-drinkers, the risk of death from esophageal cancer was increased in male drinkers, especially in those drinking daily (HR = 2.84,  $P < 0.01$ )

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**Table 1. Hazard Ratios (HRs)<sup>#</sup> and 95% Confidence Intervals (95% CI) for Selected Causes of Death with Reference to Alcohol Drinking and its Frequency**

Observed person /Male -years /Female Site ICD10	Deaths	Alcohol drinking				Frequency of drinking in drinkers (Compared with rare/none)					
		Rare/none	Drinkers	Ex-drinkers		Almost every day	3-4/week or less				
		No	HR (95% CI)	No	HR (95% CI)	No	HR (95% CI)	No	HR (95% CI)		
<b>Male</b>											
All causes	10,230	2,038	1.00	6,326	0.95 (0.90, 1.00) <sup>+</sup>	1,157	1.59 (1.48, 1.71)**	4,405	1.01 (0.96, 1.06)	1,496	0.84 (0.78, 0.90)**
All cancers	3,894	718	1.00	2,571	1.04 (0.95, 1.13)	373	1.50 (1.32, 1.70)**	1,811	1.11 (1.02, 1.22)*	621	0.93 (0.83, 1.04)
Esophagus C15	153	14	1.00	123	2.26 (1.29, 3.95)**	10	2.08 (0.92, 4.70) <sup>+</sup>	106	2.84 (1.62, 4.99)**	14	0.89 (0.42, 1.88)
Stomach C16	777	149	1.00	519	1.03 (0.85, 1.23)	61	1.16 (0.86, 1.57)	359	1.06 (0.87, 1.29)	138	1.01 (0.80, 1.28)
Colon C18	219	36	1.00	148	1.16 (0.80, 1.68)	19	1.57 (0.90, 2.75)	108	1.23 (0.84, 1.80)	37	1.01 (0.63, 1.61)
RectumC19-20	164	25	1.00	120	1.33 (0.86, 2.06)	15	1.89 (0.99, 3.60) <sup>+</sup>	92	1.48 (0.94, 2.31)	21	0.80 (0.44, 1.45)
Liver C22	463	79	1.00	271	0.89 (0.69, 1.15)	79	3.16 (2.32, 4.31)**	171	0.90 (0.68, 1.18)	79	0.89 (0.65, 1.23)
Gall bladder C23	72	10	1.00	48	1.47 (0.74, 2.92)	7	2.00 (0.76, 5.29)	38	1.74 (0.86, 3.53)	9	0.99 (0.40, 2.47)
Pancreas C25	224	40	1.00	163	1.23 (0.87, 1.75)	10	0.70 (0.35, 1.41)	100	1.18 (0.81, 1.73)	49	1.42 (0.92, 2.18)
Lung C33-34	904	184	1.00	582	0.94 (0.80, 1.12)	90	1.40 (1.09, 1.80)**	411	1.02 (0.85, 1.22)	130	0.82 (0.65, 1.03) <sup>+</sup>
Prostate C61	169	45	1.00	103	0.79 (0.55, 1.13)	12	0.76 (0.40, 1.44)	69	0.82 (0.55, 1.21)	31	0.92 (0.57, 1.47)
Kidney C64	46	4	1.00	32	2.26 (0.79, 6.43)	6	4.43 (1.24, 15.8)*	25	2.60 (0.90, 7.54) <sup>+</sup>	6	1.62 (0.45, 5.85)
Urothelial tract											
C65-67	94	18	1.00	63	1.12 (0.66, 1.91)	7	1.07 (0.44, 2.57)	42	1.27 (0.71, 2.28)	17	1.32 (0.66, 2.64)
Non-Hodgkin's lymphoma											
C82-85	93	26	1.00	55	0.59 (0.37, 0.95)*	7	0.80 (0.34, 1.86)	35	0.62 (0.37, 1.06)	16	0.69 (0.36, 1.31)
Multiple myeloma											
C90	49	11	1.00	28	0.70 (0.34, 1.42)	4	1.23 (0.39, 3.90)	16	0.57 (0.26, 1.24)	10	0.85 (0.35, 2.04)
Myeloid leukemia											
C92	44	7	1.00	34	1.28 (0.56, 2.91)	1	0.47 (0.05, 3.89)	25	1.38 (0.59, 3.21)	7	1.02 (0.35, 2.94)
Ischemic heart disease											
I20-25	666	150	1.00	394	0.82 (0.68, 1.00) <sup>+</sup>	78	1.45 (1.10, 1.91)**	252	0.79 (0.64, 0.97)*	113	0.89 (0.69, 1.14)
Cerebrovascular disease											
I60-69	1,322	228	1.00	812	1.15 (0.99, 1.34) <sup>+</sup>	179	2.13 (1.75, 2.60)**	576	1.25 (1.06, 1.46)**	172	0.93 (0.76, 1.14)
<b>Female</b>											
All causes	7,174	4,817	1.00	1,110	0.91 (0.85, 0.97)**	162	1.51 (1.29, 1.77)**	277	1.01 (0.89, 1.14)	724	0.87 (0.80, 0.95)**
All cancers	2,325	718	1.00	2,571	0.98 (0.88, 1.10)	373	1.60 (1.21, 2.10)**	104	1.13 (0.93, 1.38)	289	0.95 (0.84, 1.08)
Esophagus C15	27	18	1.00	7	1.70 (0.69, 4.16)	0	NA	3	2.79 (0.80, 9.70)	2	0.73 (0.16, 3.22)
Stomach C16	386	262	1.00	69	1.00 (0.76, 1.31)	8	1.44 (0.71, 2.93)	12	0.79 (0.44, 1.41)	51	1.09 (0.79, 1.48)
Colon C18	220	153	1.00	33	0.82 (0.55, 1.20)	4	1.12 (0.41, 3.03)	9	0.96 (0.48, 1.89)	23	0.83 (0.53, 1.31)
RectumC19-20	89	63	1.00	12	0.60 (0.31, 1.13)	2	1.51 (0.36, 6.21)	1	0.28 (0.03, 2.02)	9	0.57 (0.28, 1.18)
Liver C22	227	141	1.00	36	0.83 (0.57, 1.21)	10	2.89 (1.51, 5.53)**	12	1.38 (0.76, 2.52)	22	0.69 (0.43, 1.10)
Gall bladder C23	95	62	1.00	16	0.97 (0.55, 1.71)	1	0.75 (0.10, 5.47)	3	0.81 (0.25, 2.63)	12	1.10 (0.58, 2.09)
Pancreas C25	217	138	1.00	50	1.48 (1.06, 2.07)*	5	1.68 (0.68, 4.12)	9	1.17 (0.59, 2.32)	38	1.71 (1.18, 2.48)**
Lung C33-34	268	181	1.00	49	0.93 (0.67, 1.29)	6	1.52 (0.67, 3.45)	15	1.30 (0.76, 2.22)	29	0.78 (0.52, 1.16)
Breast C50	103	63	1.00	31	1.34 (0.85, 2.09)	2	1.38 (0.33, 5.69)	4	1.04 (0.37, 2.89)	26	1.55 (0.95, 2.51) <sup>+</sup>
Cervix uteri C53	36	24	1.00	6	0.73 (0.29, 1.83)	1	1.69 (0.22, 12.7)	1	0.61 (0.08, 4.61)	4	0.70 (0.23, 2.10)
Kidney C64	19	11	1.00	1	0.37 (0.04, 2.92)	2	7.88 (1.71, 36.2)**	1	1.63 (0.21, 12.7)	0	NA
Urothelial tract											
C65-67	41	30	1.00	8	1.02 (0.45, 2.28)	0	NA	2	1.31 (0.31, 5.54)	6	1.07 (0.43, 2.69)
Non-Hodgkin's lymphoma											
C82-85	65	40	1.00	11	0.97 (0.49, 1.93)	2	2.45 (0.58, 10.3)	4	1.59 (0.56, 4.54)	7	0.85 (0.37, 1.94)
Multiple myeloma											
C90	49	34	1.00	9	1.00 (0.47, 2.14)	1	1.34 (0.18, 9.85)	2	1.07 (0.25, 4.55)	4	0.68 (0.23, 1.97)
Myeloid leukemia											
C92	33	20	1.00	7	1.23 (0.50, 2.99)	1	2.24 (0.29, 16.9)	3	2.32 (0.67, 7.97)	3	0.76 (0.22, 2.64)
Ischemic heart disease											
I20-25	458	302	1.00	76	1.09 (0.84, 1.41)	6	0.85 (0.38, 1.92)	21	1.28 (0.82, 2.00)	47	1.04 (0.76, 1.43)
Cerebrovascular disease											
I60-69	1,151	787	1.00	155	0.86 (0.72, 1.02)	21	1.17 (0.76, 1.82)	40	0.92 (0.67, 1.28)	91	0.77 (0.62, 0.97)*

<sup>#</sup>Adjusted for age and area of study. Significance level: \*\* p<0.01, \* p<0.05, + p<0.1 NA: not applicable

and in heavy drinkers consuming 81 ml of alcohol or more per day (HR = 4.63, P < 0.01) (Table 2). Longer duration of drinking habit and younger age at which drinking commenced also increased the risk. The risk of death from esophageal cancer was increased in male ex-drinkers (Table 1), in particular in those in the 5 year interval post-quitting (HR = 3.75, P < 0.05) (Table 5).

#### Risk of death from liver cancer

The risk of death from liver cancer was increased in

both male and female ex-drinkers (HR = 3.16, P < 0.01, and HR = 2.89, P < 0.01, respectively) (Table 1), and the increased risk persisted even after cessation of alcohol consumption. In male and female drinkers, the risk of death from liver cancer was no different from the risk in rare/non-drinkers overall (Table 1). However, in male drinkers there appeared to be a dose-dependent relationship between the amount of alcohol consumed per day, duration of drinking habit and increased risk of death from liver cancer (Tables 2, 3).

**Table 2. Hazard ratios (HRs)<sup>#</sup> and 95% Confidence Intervals (95% CI) of Consumption of Alcohol per day in Current Drinkers, Compared with Rare/Nondrinkers**

Observed person- /Male years / Female	ICD10	Alcohol consumed per day (ml) <sup>##</sup>								
		Rare/none		<54		54-80		81+		
		No	HR	No	HR (95%CI)	No	HR (95%CI)	No	HR (95%CI)	
		100,388		162,193		112,169		52,405		
		545,032		88,499		6,264		2,586		
<b>Male</b>										
All causes		2,038	1.00	2,463	0.86 (0.81, 0.92)**	1,550	1.02 (0.95, 1.09)	775	1.33 (1.22, 1.46)**	
All cancers	C00-97	718	1.00	969	0.94 (0.85, 1.04)	672	1.17 (1.04, 1.31)**	312	1.39 (1.20, 1.60)**	
Esophagus	C15	14	1.00	28	1.33 (0.67, 2.62)	50	3.71 (1.95, 7.04)**	25	4.63 (2.28, 9.37)**	
Stomach	C16	149	1.00	198	0.93 (0.74, 1.16)	151	1.24 (0.97, 1.57) <sup>+</sup>	52	1.11 (0.79, 1.54)	
Colon	C18	36	1.00	66	1.32 (0.85, 2.04)	36	1.26 (0.76, 2.07)	20	1.75 (0.97, 3.14) <sup>+</sup>	
Rectum	C19-20	25	1.00	43	1.07 (0.64, 1.78)	26	1.08 (0.61, 1.92)	21	2.25 (1.22, 4.14)**	
Liver	C22	79	1.00	76	0.70 (0.49, 0.98)*	52	0.88 (0.60, 1.28)	36	1.47 (0.96, 2.25) <sup>+</sup>	
Gall bladder	C23	10	1.00	18	1.56 (0.65, 3.77)	12	2.02 (0.78, 5.25)	7	3.21 (1.09, 9.44)*	
Pancreas	C25	40	1.00	65	1.14 (0.75, 1.73)	47	1.52 (0.97, 2.38) <sup>+</sup>	15	1.22 (0.65, 2.26)	
Lung	C33-34	184	1.00	233	0.86 (0.70, 1.06)	144	0.96 (0.77, 1.21)	76	1.29 (0.98, 1.71) <sup>+</sup>	
Prostate	C61	45	1.00	53	0.90 (0.59, 1.38)	18	0.66 (0.37, 1.17)	8	0.82 (0.37, 1.79)	
Kidney	C64	4	1.00	15	2.88 (0.83, 9.97) <sup>+</sup>	8	2.93 (0.75, 11.3)	1	0.92 (0.09, 9.07)	
Urothelial tract	C65-67	18	1.00	29	1.37 (0.71, 2.65)	20	1.98 (0.96, 4.07) <sup>+</sup>	2	0.52 (0.11, 2.35)	
Non-Hodgkin's lymphoma	C82-85	26	1.00	21	0.60 (0.32, 1.10) <sup>+</sup>	14	0.76 (0.38, 1.52)	5	0.70 (0.26, 1.91)	
Multiple myeloma	C90	11	1.00	11	0.91 (0.35, 2.37)	4	0.53 (0.15, 1.87)	4	1.34 (0.38, 4.77)	
Myeloid leukemia	C92	7	1.00	15	1.21 (0.49, 2.97)	10	1.37 (0.51, 3.67)	2	0.69 (0.14, 3.42)	
Ischemic heart disease	I20-25	150	1.00	168	0.78 (0.62, 0.98)*	92	0.83 (0.63, 1.10)	40	0.94 (0.66, 1.36)	
Cerebrovascular disease	I60-69	228	1.00	305	0.95 (0.79, 1.14)	225	1.37 (1.13, 1.66)**	101	1.66 (1.30, 2.13)**	
<b>Female</b>										
All causes		4,817	1.00	506	0.90 (0.82, 0.99)*	28	1.03 (0.71, 1.50)	14	1.37 (0.81, 2.32)	
All cancers	C00-97	1,542	1.00	226	1.12 (0.97, 1.29)	9	0.80 (0.41, 1.54)	4	0.92 (0.34, 2.47)	
Esophagus	C15	18	1.00	5	2.06 (0.74, 5.73)	0	NA	0	N.A	
Stomach	C16	262	1.00	31	0.93 (0.63, 1.36)	0	NA	2	3.23 (0.80, 13.1)	
Colon	C18	153	1.00	22	1.04 (0.66, 1.64)	0	NA	1	2.14 (0.29, 15.4)	
Rectum	C19-20	63	1.00	5	0.62 (0.24, 1.57)	0	NA	0	NA	
Liver	C22	141	1.00	14	0.70 (0.40, 1.23)	1	1.02 (0.14, 7.37)	0	NA	
Gall bladder	C23	62	1.00	9	1.12 (0.55, 2.30)	1	2.17 (0.29, 15.8)	0	NA	
Pancreas	C25	138	1.00	34	2.02 (1.37, 2.98)**	1	1.05 (0.14, 7.56)	0	NA	
Lung	C33-34	181	1.00	25	1.01 (0.66, 1.56)	3	2.34 (0.74, 7.40)	0	NA	
Breast	C50	63	1.00	15	1.62 (0.90, 2.91)	0	NA	1	3.44 (0.47, 25.1)	
Cervix uteri	C53	24	1.00	2	0.52 (0.12, 2.27)	0	NA	0	NA	
Kidney	C64	11	1.00	0	NA	1	10.2 (1.24, 83.5)	0	NA	
Urothelial tract	C65-67	30	1.00	3	1.12 (0.33, 3.78)	0	NA	0	NA	
Non-Hodgkin's lymphoma	C82-85	40	1.00	8	1.25 (0.57, 2.72)	0	NA	0	NA	
Multiple myeloma	C90	34	1.00	5	1.21 (0.46, 3.18)	0	NA	0	NA	
Myeloid leukemia	C92	20	1.00	4	1.50 (0.50, 4.53)	0	NA	0	NA	
Ischemic heart disease	I20-25	302	1.00	32	1.03 (0.71, 1.49)	3	2.66 (0.84, 8.36)	3	7.60 (2.41, 23.9)**	
Cerebrovascular disease	I60-69	787	1.00	67	0.77 (0.60, 1.00)*	7	1.84 (0.87, 3.90)	3	2.06 (0.66, 6.42)	

<sup>#</sup>Adjusted for age, area of study. <sup>##</sup>One unit (gou) Japanese Sake = 27 ml alcohol = 22 g ethanol. Significance level: \*\* p<0.01, \* p<0.05, + p<0.1 NA: not applicable

#### Risk of death from cancers at other sites

The risk of death from renal cancer was increased in male and female ex-drinkers (HR = 4.43, P < 0.05, and HR = 7.88, P < 0.01, respectively) (Table 1). An increased risk of death from lung cancer was found in male ex-drinkers (HR = 1.40, P < 0.01). Although the risk of death from rectal or gall bladder cancers in drinkers overall did not differ from that in rare/non-drinkers, the risk was increased in heavy drinkers for rectal cancer (HR = 2.25, P < 0.01), and for gall bladder cancer (HR = 3.21, P <

0.05) (Table 2). In contrast, the risk of death from Non-Hodgkin's lymphoma was less in male drinkers (HR = 0.59, P < 0.05) (Table 1).

#### Risk of death from circulatory diseases

The risk of death from ischemic heart disease was decreased in males drinking daily (HR = 0.79, P < 0.05) (Table 1), in particular in light drinkers who consumed less than 54 ml of alcohol per day (HR = 0.78, P < 0.05) (Table 2) and in those drinkers who drank for less than 20

**Table 3. Hazard ratios (HRs)<sup>#</sup> and 95% Confidence Intervals (95% CI) of Duration of Drinking in Current Drinkers, Compared with Rare/Nondrinkers**

Observed person-years / Male / Female	ICD10	Rare/none		Duration of drinking (years)					
		100,388		<20		20-29		30+	
		No	HR	No	HR (95% CI)	No	HR (95% CI)	No	HR (95% CI)
		545,032		86,104		104,082		127,040	
				54,755		19,905		13,425	
<b>Male</b>									
All causes		2038	1.00	662	0.75 (0.68, 0.82)**	970	0.92 (0.84, 0.99)*	3085	1.03 (0.97, 1.09)
All cancers	C00-97	718	1.00	284	0.82 (0.70, 0.94)**	442	1.04 (0.92, 1.19)	1170	1.11 (1.01, 1.22)*
Esophagus	C15	14	1.00	11	1.19 (0.51, 2.77)	22	1.93 (0.93, 3.99) <sup>+</sup>	60	2.87 (1.53, 5.36)**
Stomach	C16	149	1.00	64	0.92 (0.67, 1.25)	92	1.10 (0.83, 1.45)	226	1.06 (0.85, 1.31)
Colon	C18	36	1.00	17	1.02 (0.55, 1.90)	32	1.59 (0.94, 2.68) <sup>+</sup>	64	1.31 (0.84, 2.03)
Rectum	C19-20	25	1.00	9	0.61 (0.27, 1.35)	24	1.35 (0.74, 2.46)	48	1.27 (0.77, 2.10)
Liver	C22	79	1.00	22	0.52 (0.31, 0.86)*	36	0.70 (0.46, 1.08)	114	1.13 (0.82, 1.54)
Gall bladder	C23	10	1.00	3	1.02 (0.26, 4.00)	9	2.63 (0.95, 7.29) <sup>+</sup>	25	2.01 (0.86, 4.67)
Pancreas	C25	40	1.00	19	0.96 (0.54, 1.69)	34	1.43 (0.88, 2.33)	71	1.16 (0.77, 1.73)
Lung	C33-34	184	1.00	56	0.63 (0.46, 0.86)**	106	0.97 (0.75, 1.25)	269	0.93 (0.77, 1.14)
Prostate	C61	45	1.00	15	1.03 (0.56, 1.89)	9	0.54 (0.25, 1.13)	52	0.80 (0.53, 1.21)
Kidney	C64	4	1.00	5	2.65 (0.61, 11.5)	5	2.18 (0.50, 9.44)	14	2.84 (0.81, 9.92)
Urothelial tract	C65-67	18	1.00	8	1.26 (0.51, 3.06)	6	0.80 (0.30, 2.15)	35	1.48 (0.79, 2.76)
Non-Hodgkin's lymphoma									
C82-85		26	1.00	6	0.45 (0.18, 1.14) <sup>+</sup>	8	0.51 (0.22, 1.18)	28	0.80 (0.45, 1.41)
Myeloma	C90	11	1.00	4	0.79 (0.22, 2.82)	7	1.15 (0.39, 3.41)	8	0.73 (0.26, 2.03)
Leukemia	C92	7	1.00	13	3.09 (1.12, 8.48)*	5	0.98 (0.29, 3.33)	9	0.96 (0.34, 2.73)
Ischemic heart disease	I20-I25	150	1.00	37	0.57 (0.39, 0.84)**	53	0.68 (0.49, 0.95)*	205	0.94 (0.75, 1.17)
Cerebrovascular disease	I60-I69	228	1.00	82	0.90 (0.69, 1.16)	97	0.90 (0.70, 1.15)	433	1.26 (1.06, 1.48)**
<b>Female</b>									
All causes		4817	1.00	283	0.98 (0.87, 1.11)	114	0.93 (0.77, 1.12)	142	0.93 (0.78, 1.10)
All cancers	C00-97	1542	1.00	128	1.15 (0.96, 1.39)	47	1.08 (0.80, 1.44)	49	1.05 (0.78, 1.39)
Esophagus	C15	18	1.00	1	0.78 (0.10, 5.98)	1	1.91 (0.25, 14.5)	3	5.32 (1.53, 18.4)**
Stomach	C16	262	1.00	19	1.06 (0.66, 1.70)	4	0.56 (0.20, 1.50)	7	0.86 (0.40, 1.84)
Colon	C18	153	1.00	11	0.99 (0.53, 1.84)	2	0.43 (0.10, 1.77)	6	1.13 (0.49, 2.57)
Rectum	C19-20	63	1.00	2	0.43 (0.10, 1.79)	2	1.13 (0.27, 4.69)	0	NA
Liver	C22	141	1.00	7	0.64 (0.30, 1.39)	5	1.20 (0.49, 2.96)	3	0.70 (0.22, 2.21)
Gall bladder	C23	62	1.00	9	2.02 (0.98, 4.15)	0	NA	0	NA
Pancreas	C25	138	1.00	20	2.17 (1.34, 3.51)**	4	1.09 (0.40, 2.96)	4	0.92 (0.34, 2.50)
Lung	C33-34	181	1.00	14	1.04 (0.60, 1.82)	5	0.97 (0.39, 2.38)	5	0.92 (0.38, 2.26)
Breast	C50	63	1.00	7	1.12 (0.50, 2.49)	4	1.73 (0.62, 4.83)	3	1.95 (0.60, 6.28)
Cervix uteri	C53	24	1.00	2	0.87 (0.20, 3.78)	1	1.19 (0.15, 8.90)	0	NA
Kidney	C64	11	1.00	0	N.A	1	3.11 (0.39, 24.4)	0	NA
Urothelial tract	C65-67	30	1.00	2	1.40 (0.32, 6.01)	0	NA	2	2.66 (0.62, 11.4)
Non-Hodgkin's lymphoma									
C82-85		40	1.00	6	1.67 (0.69, 4.04)	0	NA	2	1.67 (0.40, 7.04)
Multiple myeloma	C90	34	1.00	1	0.42 (0.05, 3.14)	3	3.25 (0.98, 10.8) <sup>+</sup>	1	0.91 (0.12, 6.76)
Myeloid leukemia	C92	20	1.00	2	1.41 (0.32, 6.17)	0	NA	3	5.12 (1.48, 17.6)**
Ischemic heart disease	I20-25	302	1.00	15	1.00 (0.59, 1.69)	8	1.13 (0.56, 2.30)	14	1.51 (0.88, 2.59)
Cerebrovascular disease	I60-69	787	1.00	38	0.88 (0.63, 1.22)	22	1.15 (0.75, 1.76)	29	1.14 (0.78, 1.65)

<sup>#</sup>Adjusted for age, area of study. Significance level: \*\* p<0.01, \* p<0.05, + p<0.1 NA: not applicable

years (HR = 0.57, P < 0.01) (Table 3). However the risk was increased in male ex-drinkers (HR = 1.45, P < 0.01) (Table 1). The risk of death from cerebrovascular disease was increased in males who drank daily (HR = 1.25, P < 0.01) and this relationship appeared to show dose-dependency with the amount of alcohol consumed. It was also increased in male ex-drinkers (HR = 2.13, P < 0.01). In contrast, risk of death from cerebrovascular disease was decreased in female occasional (3-4/week) drinkers (HR = 0.77, P < 0.05).

## Discussion

Heavy alcohol consumption is considered to cause cancer of the oral cavity, pharynx, larynx, esophagus, and liver, and may increase the risk of breast and colorectal cancer (IARC, 2003). In the JACC Study, drinking appeared to predispose individuals to increased risk of esophageal and liver cancer. Synergy between drinking and smoking has been reported for esophageal cancer (Sakata et al., 2005). Risk of breast cancer significantly

**Table 4. Hazard ratios (HRs)\* and 95% Confidence Intervals (95% CI) of Age at Which the Drinking Commenced in Current Drinkers, Compared with Rare/Nondrinkers**

Observed person- /Male years / Female	ICD10	Age at which the drinking commenced (years)								
		Rare/none		<20		20-29		30+		
		No	HR	No	HR (95% CI)	No	HR (95% CI)	No	HR (95% CI)	
		100,388		21,241		150,609		145,700		
		545,032		1,725		18,404		69,193		
<b>Male</b>										
All causes		2038	1.00	662	1.20 (1.05, 1.36)**	970	1.07 (1.01, 1.14)*	3085	0.86 (0.81, 0.92)**	
All cancers	C00-97	718	1.00	114	1.23 (1.01, 1.51)*	842	1.09 (0.98, 1.21)+	942	0.99 (0.90, 1.10)	
Esophagus	C15	14	1.00	10	4.56 (1.94, 10.7)**	37	2.07 (1.07, 4.00)*	46	2.30 (1.21, 4.37)*	
Stomach	C16	149	1.00	23	1.26 (0.80, 1.98)	167	1.07 (0.85, 1.36)	192	1.00 (0.79, 1.25)	
Colon	C18	36	1.00	5	1.15 (0.44, 3.00)	42	1.15 (0.71, 1.86)	66	1.45 (0.94, 2.26)	
Rectum	C19-20	25	1.00	4	1.10 (0.37, 3.22)	43	1.48 (0.88, 2.48)	34	0.94 (0.88, 2.48)	
Liver	C22	79	1.00	11	1.02 (0.53, 1.97)	90	1.08 (0.78, 1.51)	72	0.75 (0.53, 1.06)	
Gall bladder	C23	10	1.00	3	3.95 (0.99, 15.7)+	14	1.82 (0.72, 4.56)	20	1.94 (0.81, 4.61)	
Pancreas	C25	40	1.00	9	1.78 (0.85, 3.75)	58	1.33 (0.87, 2.03)	57	1.02 (0.67, 1.54)	
Lung	C33-34	184	1.00	21	0.83 (0.52, 1.31)	202	0.97 (0.79, 1.20)	209	0.84 (0.68, 1.03)+	
Prostate	C61	45	1.00	5	1.19 (0.46, 3.06)	29	0.74 (0.46, 1.21)	42	0.79 (0.51, 1.23)	
Kidney	C64	4	1.00	2	4.65 (0.76, 28.3)+	10	2.68 (0.72, 9.90)	12	2.48 (0.69, 8.81)	
Urothelial tract	C65-67	18	1.00	3	1.80 (0.50, 6.40)	21	1.37 (0.69, 2.73)	25	1.25 (0.64, 2.42)	
Non-Hodgkin's lymphoma										
	C82-85	26	1.00	0	NA	19	0.75 (0.40, 1.41)	23	0.66 (0.36, 1.19)	
Myeloma	C90	11	1.00	0	NA	9	0.93 (0.34, 2.54)	10	0.87 (0.33, 2.30)	
Leukemia	C92	7	1.00	3	2.73 (0.66, 1.95)	5	0.58 (0.17, 1.95)	19	1.92 (0.76, 4.83)	
Ischemic heart disease										
	I20-25	150	1.00	10	0.57 (0.30, 1.10)+	151	1.02 (0.80, 1.29)	134	0.71 (0.56, 0.91)**	
Cerebrovascular disease										
	I60-69	228	1.00	27	1.12 (0.75, 1.69)	273	1.23 (1.03, 1.49)*	312	1.06 (0.89, 1.27)	
<b>Female</b>										
All causes		4817	1.00	283	1.14 (0.59, 2.19)	114	0.96 (0.77, 1.20)	142	0.96 (0.87, 1.06)	
All cancers	C00-97	1542	1.00	2	0.63 (0.15, 2.55)	25	0.76 (0.51, 1.13)	199	1.19 (1.02, 1.38)	
Esophagus	C15	18	1.00	0	NA	0	NA	5	2.53 (0.91, 7.02)	
Stomach	C16	262	1.00	0	NA	2	0.38 (0.09, 1.53)	28	1.01 (0.68, 1.50)	
Colon	C18	153	1.00	0	NA	2	0.61 (0.15, 2.47)	17	0.97 (0.58, 1.61)	
Rectum	C19-20	63	1.00	0	NA	0	NA	4	0.60 (0.21, 1.68)	
Liver	C22	141	1.00	1	3.53 (0.49, 25.4)	2	0.65 (0.16, 2.64)	13	0.81 (0.45, 1.44)	
Gall bladder	C23	62	1.00	0	NA	0	N.A	9	1.34 (0.65, 2.73)	
Pancreas	C25	138	1.00	0	NA	2	0.70 (0.17, 2.85)	26	1.81 (1.18, 2.78)	
Lung	C33-34	181	1.00	0	NA	2	0.53 (0.13, 2.14)	22	1.10 (0.70, 1.73)	
Breast	C50	63	1.00	0	NA	3	1.40 (0.43, 4.54)	11	1.40 (0.72, 2.70)	
Cervix uteri	C53	24	1.00	0	NA	0	NA	3	0.96 (0.28, 3.25)	
Kidney	C64	11	1.00	0	NA	0	NA	1	0.82 (0.10, 6.47)	
Urothelial tract	C65-67	30	1.00	0	NA	0	NA	4	1.72 (0.59, 5.02)	
Non-Hodgkin's lymphoma										
	C82-85	40	1.00	0	NA	1	0.98 (0.13, 7.26)	7	1.38 (0.61, 3.14)	
Myeloma	C90	34	1.00	0	NA	2	2.85 (0.67, 12.1)	3	0.82 (0.25, 2.71)	
Leukemia	C92	20	1.00	0	NA	3	7.27 (2.08, 25.4)	2	0.95 (0.22, 4.16)	
Ischemic heart disease										
	I20-25	302	1.00	2	5.83 (1.43, 23.7)*	10	2.25 (1.19, 4.26)*	25	0.93 (0.61, 1.41)	
Cerebrovascular disease										
	I60-69	787	1.00	3	2.70 (0.86, 8.43)+	17	1.32 (0.82, 2.15)	70	0.94 (0.73, 1.20)	

\*Adjusted for age, area of study. Significance level: \*\* p<0.01, \* p<0.05, + p<0.1 NA: not applicable

increased in current drinkers, especially heavy drinkers (Lin et al, 2005b). Increased risk of incidence of colon cancer was observed in male current drinkers and ex-drinkers (Wakai et al, 2005c). Risk of hepatocellular carcinoma increased in ex-drinkers, and the association was further investigated (Ogimoto et al, 2004a). Risk of oral and pharyngeal cancer was also investigated (Ide et al, 2007). Increased risk of death from pancreatic cancer was not apparent in data obtained from follow-up to the end of 1997 (Lin et al., 2002b). No association with lung

cancer could be demonstrated (Nishino et al, 2006).

In contrast, the risk of death from all causes and some cardiovascular diseases appeared to decrease in occasional or light drinkers. In the JACC Study, a 12% to 20% decreased risk of all-cause mortality was observed in both men and women who consumed less than 23g/day of alcohol, although heavy drinking increased that risk (Lin et al, 2005a).

Increased risk of death from any disease in ex-drinkers might suggest that cohort subjects who were aware of

**Table 5. Hazard ratios (HRs)<sup>a</sup> and 95% Confidence Intervals (95% CI) of Period since Drinking Ceased in Ex-drinkers, Compared with Rare/Nondrinkers**

Observed person-years / Male / Female	ICD10	Rare/none 100,388 545,032		Years since drinking ceased					
				<5		5-15		15+	
				No	HR (95% CI)	No	HR (95% CI)	No	HR (95% CI)
<b>Male</b>									
All causes		2038	1.00	277	1.75 (1.54, 2.00)**	339	1.73 (1.53, 1.94)**	189	1.23 (1.06, 1.43)**
All cancers	C00-97	718	1.00	102	1.89 (1.53, 2.34)**	92	1.43 (1.15, 1.79)**	60	1.22 (0.93, 1.60)
Esophagus	C15	14	1.00	4	3.75 (1.16, 12.1)*	3	2.76 (0.76, 10.0)	1	1.03 (0.13, 8.12)
Stomach	C16	149	1.00	15	1.31 (0.76, 2.25)	11	0.77 (0.41, 1.44)	8	0.73 (0.35, 1.50)
Colon	C18	36	1.00	6	2.36 (0.97, 5.74) <sup>+</sup>	4	1.29 (0.45, 3.70)	3	1.30 (0.39, 4.32)
Rectum	C19-20	25	1.00	6	3.46 (1.37, 8.70)**	2	0.85 (0.19, 3.67)	2	1.17 (0.27, 5.06)
Liver	C22	79	1.00	19	3.79 (2.24, 6.42)**	26	4.56 (2.83, 7.33)**	10	2.43 (1.23, 4.79)*
Gall bladder	C23	10	1.00	3	4.65 (1.14, 19.0)*	1	1.18 (0.14, 10.1)	0	N.A
Pancreas	C25	40	1.00	4	1.39 (0.49, 3.97)	1	0.27 (0.03, 2.05)	0	N.A
Lung	C33-34	184	1.00	25	1.66 (1.08, 2.55)*	26	1.50 (0.98, 2.28) <sup>+</sup>	21	1.56 (0.98, 2.47) <sup>+</sup>
Prostate	C61	45	1.00	3	1.00 (0.30, 3.30)	3	0.77 (0.23, 2.53)	2	0.58 (0.13, 2.44)
Kidney	C64	4	1.00	0	NA	1	3.04 (0.30, 30.4)	2	6.82 (1.08, 42.8)*
Urothelial tract	C65-67	18	1.00	2	1.99 (0.43, 9.09)	1	0.77 (0.09, 6.01)	1	0.93 (0.11, 7.25)
Non-Hodgkin's lymphoma	C82-85	26	1.00	2	0.94 (0.21, 4.07)	1	0.41 (0.05, 3.12)	1	0.56 (0.07, 4.22)
Multiple myeloma	C90	11	1.00	0	NA	0	NA	3	5.52 (1.38, 22.1)*
Myeloid leukemia	C92	7	1.00	1	1.67 (0.19, 14.19)	0	NA	0	NA
Ischemic heart disease	I20-25	150	1.00	11	0.93 (0.50, 1.73)	28	1.99 (1.31, 3.02)**	17	1.60 (0.96, 2.68) <sup>+</sup>
Cerebrovascular disease	I60-69	228	1.00	52	2.97 (2.17, 4.05)**	50	2.18 (1.59, 2.99)**	26	1.42 (0.93, 2.15) <sup>+</sup>
<b>Female</b>									
All causes		4817	1.00	28	1.41 (0.97, 2.05) <sup>+</sup>	41	1.91 (1.40, 2.60)**	32	1.78 (1.25, 2.52)**
All cancers	C00-97	1542	1.00	8	1.16 (0.58, 2.33)	16	2.18 (1.33, 3.58)**	7	1.25 (0.59, 2.64)
Esophagus	C15	18	1.00	0	NA	0	NA	0	NA
Stomach	C16	262	1.00	0	NA	3	2.45 (0.78, 7.68)	2	2.09 (0.51, 8.45)
Colon	C18	153	1.00	0	NA	0	NA	1	1.50 (0.21, 10.8)
Rectum	C19-20	63	1.00	0	NA	0	NA	0	NA
Liver	C22	141	1.00	1	1.58 (0.22, 11.4)	5	7.53 (3.04, 18.7)**	1	1.92 (0.26, 13.8)
Gall bladder	C23	62	1.00	0	NA	1	2.92 (0.40, 21.4)	0	NA
Pancreas	C25	138	1.00	0	NA	1	1.58 (0.22, 11.4)	0	NA
Lung	C33-34	181	1.00	2	2.63 (0.65, 10.7)	3	3.58 (1.13, 11.3)*	1	1.58 (0.22, 11.4)
Breast	C50	63	1.00	1	3.18 (0.43, 23.2)	1	3.51 (0.48, 25.7)	0	NA
Cervix uteri	C53	24	1.00	0	NA	0	NA	1	13.0 (1.71, 99.1)*
Kidney	C64	11	1.00	0	NA	1	15.7 (1.99, 122.9)**	0	NA
Urothelial tract	C65-67	30	1.00	0	NA	0	NA	0	NA
Non-Hodgkin's lymphoma	C82-85	40	1.00	1	4.71 (0.64, 34.6)	0	NA	0	N.A
Multiple myeloma	C90	34	1.00	0	NA	0	NA	0	N.A
Myeloid leukemia	C92	20	1.00	0	NA	0	NA	0	N.A
Ischemic heart disease	I20-25	302	1.00	0	NA	1	0.82 (0.11, 5.92)	2	1.69 (0.41, 6.87)
Cerebrovascular disease	I60-69	787	1.00	5	1.51 (0.62, 3.66)	5	1.42 (0.59, 3.43)	2	0.66 (0.16, 2.67)

<sup>a</sup>Adjusted for age, area of study. Significance level: \*\* p<0.01, \* p<0.05, + p<0.1 NA: not applicable

alcohol-related health problems quit drinking prior to the baseline survey. For example, high risk individuals such as heavy drinkers or Hepatitis C virus carriers, who were aware of having abnormal liver function tests, may have quit drinking just before the baseline survey. In future studies of hazard ratios for individual cancers, such factors in drinkers and ex-drinkers should be considered.

Reported small numbers of deaths from cancers of the oral cavity (24 deaths) (ICD10; C03-C06), pharynx (27 deaths)(C10-C13) and larynx (21 deaths) (C32), up until

the end of 2003, indicated a nonsignificant increased risk (data not shown).

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