

Nakaya et al. (2005) (18)	1990-97 (7 years)	21,201 men	Residential registry (40-64 years old)	Incidence	882 men	150-299 g	19	0.49 (0.27-0.91)	Follow-up by residential register and population-based cancer registry
						300-449 g	7	0.33 (0.14-0.78)	
						450+ g	10	0.55 (0.26-1.16)	
Lin et al. (2005) (19)	1988-99 (10 years)	97,432 (42,072 men and 55,360 women)	JACC study (45 areas throughout Japan, 40-79 years old)	Death	2418 men	Current smokers	81	1.43 (0.89-2.31)	Follow-up by residential register and death certificate
						Non-drinker	23	1.00	
						Occasional drinker	83	1.68 (1.04-2.69)	
						1-149 g of ethanol/week	84	1.52 (0.94-2.44) $P < 0.001$	
						150-299 g	99	2.15 (1.35-3.44)	
						300-449 g	114	2.57 (1.62-4.09)	
						450+ g	1170	0.94 (0.80-1.11)	
						Non-drinker	178	1.00	
						Occasional drinker	118	0.80 (0.63-1.01)	
						1-149 g of ethanol/week	20	0.68 (0.42-1.11) $P = 0.659$	
						150-299 g	6	0.73 (0.32-1.66)	
						300-449 g	7	0.68 (0.32-1.46)	
						450+ g	368	1.08 (0.79-1.49)	
						Non-drinker	43	1.00	
						Occasional drinker	28	0.79 (0.49-1.27)	
1-149 g of ethanol/week	6	0.54 (0.19-1.52) $P = 0.896$							
150-299 g	3	1.27 (0.39-4.15)							
300-449 g	2	0.68 (0.16-2.86)							
450+ g	92	1.3 (1.0-1.8)							
Ex-drinker	122	1.0							
Never-drinker	668	1.3 (1.0-1.5) $P = 0.001$							
Current drinkers, all	158	1.1 (0.8-1.3)							
<22.8 g of alcohol/day	175	1.3 (1.0-1.7)							
22.8-45.5 g	335	1.3 (1.1-1.7)							
45.6+ g	498	1.00							
Never-drinker	253	1.50 (1.29-1.75)							
Ex-drinker	251	0.82 (0.70-0.95)							
Current drinker									
0.1-22.9 g									

Continued

Table 1. Continued

Reference	Study period	Study population			Category	Number among cases	Relative risk (95% CI or P)	P for trend	Confounding variables considered	Comments
		Number of subjects for analysis	Source of subjects	Event followed						
					23.0-45.9 g	422	0.96 (0.84-1.10)	P = 0.001		
					46.0-68.9 g	351	1.05 (0.91-1.20)			
					69.0+ g	185	1.31 (1.10-1.56)			
				1363 women	Never-drinker	1054	1.00			
					Ex-drinker	30	1.21 (0.83-1.74)			
					Current drinker					
					0.1-22.9 g	119	1.03 (0.85-1.25)	P = 0.53		
					23.0-45.9 g	26	1.20 (0.81-1.77)			
					46.0+ g	6	1.04 (0.46-2.33)			

increased risk associated with alcohol was seen only among current smokers (17). In that report, alcohol intake was associated with a decreased risk of both cancer incidence and mortality in male non-smokers. These findings suggest the existence of interaction of smoking and drinking in the risk of cancer. Cytochrome P450 2E1 (CYP2E1), the expression of which is induced by alcohol, metabolizes procarcinogens present in tobacco smoke and food such as *N*-nitroso compounds (27) and catalyzes the conversion of alcohol to acetaldehyde. Animal experiments suggest that carcinogens in tobacco smoke are metabolized more slowly in drinkers (27,28). While epidemiological evidence is limited, these findings from experimental studies support the biological plausibility of this interaction, which may contribute to both the incidence and mortality of overall cancer risk.

Further, approximately half of all Japanese have been found to have a phenotype deficient for aldehyde dehydrogenase-2, a key enzyme for the conversion of acetaldehyde to acetate (29), which results in higher levels of acetaldehyde exposure. To our knowledge, no studies have investigated the impact of alcohol drinking on total cancer risk among those deficient in aldehyde dehydrogenase, although some evidence has been reported for a difference in impact on alcohol-related cancers such as esophageal cancer by polymorphism of aldehyde dehydrogenase (30,31). On this basis, we speculate that the fraction of cancer risk attributable to alcohol drinking might be greater among Japanese than non-mongoloid populations. This deficiency in the key enzyme for alcohol metabolism indicates the need for caution in interpreting the results for non-drinkers. In addition, care is probably also required when non-drinker categories include ex-drinkers, since some of these subjects are unable to drink due to a diagnosis of cancer, resulting in risk inflation in this category.

The confounding factors used for adjustment differ among studies. Most early studies adjusted age only. In the recent prospective studies, however, the association of alcohol drinking and total cancer risk has been adjusted by tobacco smoking at least. These studies also included any or all of vegetable and fruit intake, body mass index, physical activity and a history of diabetes as confounders, but the results have indicated that the effect of these factors may be small compared with that of smoking.

The present study identified a difference in the magnitude of risk between men and women. Only three of eight cohort studies evaluated risk in women, and no clear association was observed. We speculate that this was because of the low number of regular/heavy women drinkers in whom risk could be assessed, rather than any sex difference in disease susceptibility.

Finally, our systematic review confirms a positive association between alcohol drinking and total cancer risk.

Table 2. Summary of cohort studies of the association between alcohol drinking and total cancer risk

Reference	Study period	Study population					Magnitude of association*
		Sex	Number of subjects	Age range	Event	Number of incident cases or deaths	
Kono et al. (1986) (12)	1965–1983	Men	5135	27–89	Death	381	↑ ↑
Hirayama T. (1990) (14)	1965–1982	Men	122,261	40 +	Death	8794	↑
		Women	142,857	40 +	Death	5946	—
Takezaki et al. (1999) (15)	1988–1997	Men	7662	40–79	Death	240	↑
Inoue et al. (2005) (17)	1990–2001	Men	35,007	40–59	Incidence	1904	↑ ↑
		Women	38,274	40–59	Incidence	1499	—
Nakaya et al. (2005) (18)	1990–1997	Men	21,201	40–64	Incidence	882	↑
Lin et al. (2005) (19)	1988–1999	Men	42,072	40–79	Death	2418	↑
		Women	55,630	40–79	Death	1363	—

* ↑ ↑ ↑ or ↓ ↓ ↓, strong; ↑ ↑ or ↓ ↓, moderate; ↑ or ↓, weak; —, no association (see text for more detailed definition).

Because the studies included in this review used different alcohol consumption categories, however, meta-analysis for quantitative assessment could not be conducted. A meta-analysis of Japanese populations using common alcohol consumption categories, which is now on-going, will likely provide further clues to the quantitative contribution of alcohol drinking to total cancer risk.

EVALUATION OF EVIDENCE ON ALCOHOL DRINKING AND TOTAL CANCER RISK IN JAPANESE

From these results, and on the basis of assumed biological plausibility, we conclude that there is convincing evidence that alcohol drinking increases the risk of total cancer in the Japanese population, specifically among heavy drinking men. The clear implication of this conclusion is that the total burden of cancer in the Japanese population can be reduced by the avoidance of heavy alcohol drinking.

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Conflict of interest statement

None declared.

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Alcohol Drinking and Gastric Cancer Risk: An Evaluation Based on a Systematic Review of Epidemiologic Evidence among the Japanese Population

Taichi Shimazu^{1,2}, Ichiro Tsuji¹, Manami Inoue², Kenji Wakai³, Chisato Nagata⁴, Tetsuya Mizoue⁵, Keitaro Tanaka⁶ and Shoichiro Tsugane² for the Research Group for the Development and Evaluation of Cancer Prevention Strategies in Japan

¹Division of Epidemiology, Department of Public Health and Forensic Medicine, Tohoku University Graduate School of Medicine, Sendai, ²Epidemiology and Prevention Division, Research Center for Cancer Prevention and Screening, National Cancer Center, Tokyo, ³Department of Preventive Medicine/Biostatistics and Medical Decision Making, Nagoya University Graduate School of Medicine, Nagoya, ⁴Department of Epidemiology and Preventive Medicine, Gifu University Graduate School of Medicine, Gifu, ⁵Department of Epidemiology and International Health, Research Institute, International Medical Center of Japan, Tokyo and ⁶Department of Preventive Medicine, Saga Medical School, Faculty of Medicine, Saga University, Saga, Japan

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Background: We reviewed epidemiologic studies on the association between alcohol drinking and gastric cancer among the Japanese population. This report is one of a series of articles by our research group, which is evaluating the existing evidence concerning the association between health-related lifestyles and cancer.

Methods: Original data were collected by searches of MEDLINE using PubMed, or searches of the *Ichushi* database, complemented with manual searches. Evaluation of associations was based on the strength of evidence and the magnitude of association, together with biological plausibility as evaluated previously by the International Agency for Research on Cancer.

Results: Of the 11 cohort studies evaluated, nine showed no association between alcohol drinking and gastric cancer, and one study showed a strong positive association among men. All of 11 case–control studies found no association between alcohol drinking and gastric cancer. By anatomical subsites of gastric cancer, only three studies have evaluated the association between alcohol drinking and gastric cancer, and one cohort study found a positive association for cardia and upper-third gastric cancer in men. Few studies conducted among the Japanese population have made a detailed assessment of alcohol drinking, possible important confounding factors such as smoking and diet and anatomical subsites of gastric cancer.

Conclusion: We conclude that epidemiologic evidence for an association between alcohol drinking and gastric cancer risk remains insufficient due to the methodological quality of studies that have been conducted among the Japanese population.

Key words: systematic review – epidemiology – alcohol drinking – gastric cancer – Japanese

INTRODUCTION

The most recent evaluation from the International Agency for Research on Cancer (IARC) concluded in 2007 that

alcoholic beverages are carcinogenic to humans (Group 1) and are causally related to cancers of the oral cavity, pharynx, larynx, esophagus, liver, colorectum and female breast (1,2). However, epidemiologic studies on the association between alcoholic beverages and gastric cancer have been inconsistent and the interpretation of the findings is not clear (1–3).

For reprints and all correspondence: Taichi Shimazu, Epidemiology and Prevention Division, Research Center for Cancer Prevention and Screening, National Cancer Center, 5-1-1 Tsukiji, Chuo-ku, Tokyo 104-0045, Japan.
E-mail: tshimazu@gan2.res.ncc.go.jp

As the majority of these reports were based on evidence from Western populations, their applicability to the Japanese population is unknown. The Japanese commonly consume different types of beverages from Western populations and have a relatively high prevalence of the variant allele of *aldehyde dehydrogenase 2* (4), which is related to a high blood concentration of acetaldehyde (5). In addition to the factors related to alcohol, the prevalence of *Helicobacter pylori* infection (6) and the proportion of gastric cancers occurring in the distal stomach (7) are higher among the Japanese than among Western populations. Therefore, the magnitude of association among Japanese might differ from that among other populations.

The objective of the present study was to review epidemiologic studies on the association between alcohol drinking and gastric cancer among the Japanese population. The findings were summarized and the magnitude of the effect was evaluated. This report is one of a series of articles by our research group, which is investigating the associations between lifestyle factors and major types of cancer in Japan (8–15).

METHODS

Original data for this review were collected by searches of MEDLINE using PubMed complemented by manual searches of references from relevant articles when necessary. All epidemiologic studies on the association between alcohol drinking and gastric cancer incidence or mortality among Japanese from January 1966 to May 2007, including papers in press if available, were identified using the search terms 'alcohol', 'drinking', 'gastric cancer', 'stomach cancer', 'cohort studies', 'case-control studies', 'Japan' and 'Japanese' as key words found in the abstract. A search of the *Ichushi (Japana Centra Revuo Medicina)* database was also done to identify studies written in Japanese from 1983 to May 2007. Papers written in English or Japanese were reviewed, and only studies on Japanese populations living in Japan were included. The individual results were summarized in the tables separately by study design as cohort or case-control studies. In the case of multiple publications of analyses of the same or overlapping datasets, only data from the largest or the most recent studies were included, and incidence was also given priority in a single publication describing both incidence and mortality.

Evaluation was made based on the strength of evidence and the magnitude of association. Relative risks (RRs) or odds ratios (ORs) in each epidemiologic study were grouped by magnitude of association, giving consideration to statistical significance (SS) or not SS (NS), as strong, <0.5 or >2.0 (SS); moderate, either (i) <0.5 or >2.0 (NS), (ii) >1.5 – 2 (SS) or (iii) 0.5 to <0.67 (SS); weak, either (i) >1.5 – 2 (NS), (ii) 0.5 to <0.67 (NS) or (iii) 0.67 – 1.5 (SS); or no association, 0.67 – 1.5 (NS). After this process, the strength of evidence was evaluated in a similar manner to that used in the WHO/FAO Expert Consultation Report (16), where

evidence was classified as 'convincing', 'probable', 'possible' and 'insufficient'. In brief, the following criteria were used (8): convincing: evidence based on a substantial number of epidemiologic studies showing consistent associations between exposure and disease, with little or no evidence to the contrary, with a biologically plausible association. Probable: evidence based on epidemiologic studies showing fairly consistent associations, but with perceived shortcomings in the available evidence or some evidence to the contrary that precludes a more definite judgment. Possible: evidence based mainly on findings from case-control and cross-sectional studies, requiring more studies to support the tentative associations, which should also be biologically plausible. Insufficient: evidence based on findings of a few studies that are suggestive, but insufficient to establish an association, requiring more well-designed research to support the tentative associations. We assumed that biological plausibility corresponded to the judgment of the recent evaluation from the IARC (1,2,17). The final judgment is made based on the consensus of research group members and is not necessarily objective. In addition, when there was 'convincing' or 'probable' evidence of a positive or inverse association, we conducted a meta-analysis to obtain summary estimates of the association. Details of the evaluation methods are described elsewhere (8).

MAIN FEATURES AND COMMENTS

We identified 11 cohort studies (18–28) and 11 case-control studies (29–39) (Tables 1 and 2, respectively). Among the cohort studies, three presented results by gender (20,21,26), six for men only (18,19,22,23,25,27) and two for men and women combined (24,28). The respective numbers for the case-control studies were three (32,38,39), three (29,30,36) and five (31,33–35,37).

A summary of the magnitude of association for the cohort studies and case-control studies is shown in Tables 3 and 4, respectively. Of the 11 cohort studies evaluated, most showed no association between alcohol drinking and gastric cancer. Among these studies, nine showed no association (18,20,22–28), and the other two showed a strong positive (21) and a weak positive (19) association among men, respectively. All 11 case-control studies demonstrated no association between alcohol drinking and gastric cancer (29–39).

By anatomical subsites, few studies had evaluated the association between alcohol drinking and gastric cancer, and the association was inconsistent (25,38,39), similar to studies among other populations (3). In one cohort study (25), alcohol drinking showed a moderate positive association with cardia and upper-third gastric cancer, but not with distal gastric cancer in men. One case-control study analysed the association with cardia, middle and antrum gastric cancer separately (38). The point estimate of the OR in male drinkers tended to be highest for cardia cancer and decreased towards the distal part of the stomach compared with never drinkers, although the results were not statistically

Table 1. Alcohol drinking and gastric cancer risk, cohort studies among Japanese populations

References	Study period	Study population	Category	Number among cases	Relative risk, or odds ratio (95% CI or P)	P for trend	Confounding variables considered	Comments			
Author		Number of subjects for analysis	Source of subjects	Event followed	Number of incident cases or deaths						
Kono et al. (18)	1965–1983	5130 men	Male Japanese physicians	Death	116	Never or past	NA	Expressed as go of sake (1 go of sake; 27 ml alcohol)			
Ubukata et al. (19)	1961–1985	225 cases and 665 controls (nested case-control study)	14 229 persons who were screened for gastric cancer at the Center for Adult Diseases, Osaka	Incidence	225 men	Occasional	1.00	Matched (1:3) for sex, birth year (± 5 years), occupation and year of the initial screening of the case within the cohort Adjusted for smoking, dietary habit	Expressed as go of sake (1 go of sake; 27 ml alcohol)		
						<2 go/day	1.11 (0.69–1.79)				
						≥ 2 go/day	1.30 (0.79–2.12)				
						Non or occasional	1.17 (0.66–2.07)				
Hirayama (20)	1966–1982	122 261 men	95% of census population	Death	3414 men	<3 go/day	0.99 (0.70–1.39)				
						≥ 3 go/day	1.58 (0.99–2.53)				
						Men					
						None	1.00			NS	Age
						Rare	0.90 (0.82–0.99)				
						Occasional	0.85 (0.78–0.92)				
						Daily	0.92 (0.85–0.99)				
Women											
Kato et al. (21)	1985–1991	9753	Residential registry	Death	57	None	1.00		Ethanol content		
						Rare	0.81 (0.70–0.93)				
						Occasional	0.98 (0.82–1.16)				
						Daily	0.96 (0.66–1.40)				
						Total					
None	1.00	NA	Age, sex, smoking cooking methods and family history of stomach cancer								

Author	Year	Study Design	Location	Sample Size	Alcohol Intake	Incidence	Death	Registry	Matched for sex, birth year (± 2 years) and residential area (city or country)	In sake-equivalents (a cup of 180 ml of sake contains 27 ml of ethanol)
Masuda and Shigematsu (22)	1968-1987	8085 adults in Oku Islands, Shimane	Residential registry	97 men	Occasional	12	1.77 (0.85-3.68)	NA	NS	Number of male subjects was not available
					Daily, <50 ml	7	1.16 (0.46-2.89)			
					Daily, ≥50 ml	12	2.75 (1.20-6.29)			
					Men	35				
					None	8	1.00	Age		
					Occasional	9	2.31 (0.88-6.07)	NA		
					Daily, <50 ml	6	1.31 (0.45-3.81)			
					Daily, ≥50 ml	12	3.63 (1.44-9.11)			
					Women	22				
					None	18	1.00	Age		
					Occasional	3	1.12 (0.32-3.90)	NA		
					Daily	1	1.29 (0.17-9.69)			
					None	29	1.00	NS		
					Murata et al. (23)	1984-1993	246 male cases and 493 controls (nested case-control study)	17 200 male participants in a gastric mass screening by Chiba Cancer Association		
Daily	26	0.80 (NS)								
Total	NA	0.53 (0.26-1.06)								
Sake	NA	1.32 (0.36-4.84)								
Shochyu	NA	0.85 (0.10-6.92)								
Beer	NA	0.84 (0.30-2.34)								
Whisky	NA									
Alcohol intake (cups/day)	101	1.0	Matched for sex, birth year (± 2 years) and residential area (city or country)							
0	82	1.1								
0.1-1.0	51	1.1								
1.1-2.0	12	0.5								
2.1 +										
Nonsmoker										
Alcohol intake (cups/day)	62	1.0	NS							
0	39	1.0								
0.1-1.0										

Continued

Table 1. Continued

References	Study period	Study population			Category	Number among cases	Relative risk, or odds ratio (95% CI or P)	P for trend	Confounding variables considered	Comments
		Number of subjects for analysis	Source of subjects	Event followed						
Inoue et al. (24)	1985-1995	5373	Patients who underwent gastroscopy at Aichi Cancer Center Hospital	Incidence 69	1.1-2.0	21	1.1			
					2.1 +	4	0.4			
					Smoker					
					Alcohol intake (cups/day)					
					0	39	1.0	NS		
					0.1-1.0	43	1.2			
					1.1-2.0	30	1.1			
					2.1 +	8	0.6			
					With atrophic gastritis					
Sasazuki et al. (25)	1990-1999	19 657 men	Residential registry (JPHC Study)	Incidence 293	None	22	1.00		Age and sex	
					Past	8	1.88 (0.78-4.50)			
					Occasional	15	0.85 (0.42-1.71)			
					Daily	20	1.13 (0.54-2.37)			
					Total					
					0-3 days/month	68	1.0	0.66	Age, area, smoking, consumption of fruit, green or yellow vegetable, salted cod roe or fish gut and body mass index	
					0-161.0 g/week	54	0.8 (0.6-1.2)			
					162.0-322.0 g/week	77	1.1 (0.8-1.5)			
					322.5 + g/week	74	1.1 (0.8-1.6)			

Cardia and upper-third gastric cancer
(all histologic type)

0-3 days/month 3 1.0 0.66

0-161.0 g/week 8 2.5 (0.7-9.5)

162.0-322.0 g/
week 13 3.3 (0.9-11.6)

322.5+ g/week 11 3.0 (0.8-11.1)

Distal gastric cancer (Differentiated type)

0-3 days/month 32 1.0 1.00

0-161.0 g/week 27 0.9 (0.5-1.5)

162.0-322.0 g/
week 38 1.1 (0.7-1.8)

322.5+ g/week 27 0.9 (0.5-1.5)

Distal gastric cancer (Undifferentiated type)

0-3 days/month 17 1.0 0.07

0-161.0 g/week 11 0.7 (0.3-1.4)

162.0-322.0 g/
week 15 0.9 (0.5-1.9)

322.5+ g/week 20 1.3 (0.7-2.6)

Fujino et al. 1988-1997 18 746 men (26)

261 men

Death

Participants in
municipal health
checkups, general
populations or
voluntary groups

26 184 women

Age

1.00

1.16 (0.71-1.87)

1.16 (0.84-1.59)

1.00

Age

1.00

0.99 (0.24-4.01)

1.01 (0.56-1.82)

(JACC Study)

118
women

Continued

Table 1. Continued

References	Study period	Study population		Category	Number among cases	Relative risk, or odds ratio (95% CI or P)	P for trend	Confounding variables considered	Comments
		Number of subjects for analysis	Source of subjects						
Nakaya et al. (27)	1990–1997	21 201 men	Residential registry	Never-drinkers	42	1.0	0.83	Age, smoking, education, daily consumption of orange and other fruit juice, spinach, carrot or pumpkin and tomato	
Sauvaget et al. (28)	1980–1999	38 576	(Miyagi cohort study)	Ex-drinkers	21	0.9 (0.5–1.5)			
				Current drinkers	184	1.0 (0.7–1.4)			
				< 22.8 g/day	49	1.0 (0.6–1.5)			
				> 22.8 g/day	135	1.0 (0.7–1.5)			
				Never	475	1.00			City, sex, sex-specific age, calendar period, education and radiation dose
				Incidence	1270				
			Atomic-bomb survivors in Hiroshima and Nagasaki	Past	690	1.09 (0.78–1.51)			
				Current	44	1.07 (0.94–1.23)			

CI, confidence interval; NA, not available; NS, not significant.

Table 2. Alcohol drinking and gastric cancer risk, case-control studies among Japanese populations

References	Study period	Study subjects	Definition	Number of cases	Number of controls	Category	Odds ratio (95% CI or P)	P for trend	Confounding variables considered	Comments
Hoshino (29)	1980-1982	Hospital-based (National Cancer Center)	Cases: gastric cancer patients operated at National Cancer Center hospital Controls: patients without gastric cancer in Adult Disease Clinic	460 men	460 men	Occasionally	NS	NA	Matched for age	
Tajima and Tomimaga (30)	1981-1984	Hospital-based (Aichi Cancer Center)	Cases: patients received surgical therapy and were newly diagnosed on the basis of both clinical and histopathological examinations	59 men	111 men	Versus non-drinkers			Matched for sex, age (\pm 5 years) and time of interview (\pm 6 months) Adjusted for age and sex	
						Yes	0.68 (NS)			
						Amount (sake)				
						Less than 360 ml/day	0.66 (NS)	NA		
						360 ml or more /day	0.81 (NS)			
						Frequency				
						Sometimes	0.80 (NS)	NA		
						Every day	0.64 (NS)			
			Controls: patients without cancer							
Kono et al. (31)	1979-1982	Hospital-based (Karatsu Stomach Institute)	Cases: newly diagnosed at a single institution	139	Hospital controls	Sake	NS		Matched for sex, and year of birth	The results were described in the text
						Shouchu	NS			
						General population controls	NS			
						Beer	NS			
						Whisky/brandy	NS			
			Controls: hospital control general population control							
Kato et al. (32)	1985-1989	Hospital-based (Aichi Cancer Center)	Cases: histologically confirmed cases	289 men	1247	Men			Adjusted for age and residence	
						Total				

Continued

Table 2. Continued

References	Study period	Study subjects		Definition	Number of cases	Number of controls	Category	Odds ratio (95% CI or P)	P for trend	Confounding variables considered	Comments
		Type and source	Definition								
Tominaga et al. (33)	1971-1985	Hospital-based (Tochigi Cancer Center)	Cases: newly histologically diagnosed gastric cancer at the center	Controls: patients with normal gastric mucosa or mild atrophic gastritis	138 women	1767 women	Occasional	0.77 (0.53-1.11)			
							Daily	0.99 (0.71-1.37)			
							Diffuse				
							Occasional	0.70 (0.41-1.21)			
							Daily	1.06 (0.67-1.69)			
							Intestinal				
							Occasional	0.79 (0.49-1.26)			
							Daily	0.95 (0.63-1.45)			
							Women				Adjusted for age and residence
							Total				
							Occasional	0.64 (0.40-1.01)			
							Daily	0.73 (0.26-2.08)			
							Diffuse				
							Occasional	0.70 (0.41-1.21)			
							Daily	1.06 (0.67-1.69)			
Intestinal											
Occasional	0.79 (0.49-1.26)										
Daily	0.95 (0.63-1.45)										
Non-drinker	1.0			Matched (1:2) for sex, age (± 5 years) and area of residency							
Kikuchi et al. (34)	1988-1990	Hospital-based	Cases: gastric carcinoma	Controls: randomly selected controls, who received the same early detection program and were verified as being free of gastric cancer	42	Hospital control 42	Versus hospital control				Matched for sex and age (± 3 years)
							Sometimes	0.85 (0.57-1.27)			
							Daily	1.16 (0.78-1.72)			
							Current or past drinker			1.04 (NS)	
							Current drinker			0.83 (NS)	

Controls: hospital control (inpatients with benign disease) participants in health check programs	Participants in health check programs	Versus participants in health check programs	Matched for sex, age and administrative division
Hoshiyama and Sasaba (35)	294	Current or past drinker	Adjusted for sex, age, administrative division and smoking status
1984-1990	General population controls	Current drinker	
Hospital-based (Saitama Cancer Center)	294	Versus general population controls	
Cases: newly diagnosed adenocarcinoma		Alcohol drinking	
		Never	1.0
		Past	0.7 (0.3-1.8)
		Occasional	0.8 (0.5-1.3)
		Daily	NA
		<50 ml/day	0.7 (0.4-1.2)
		≥50 ml/day	1.0 (0.5-1.7)
		Total alcohol consumption (1/lifetime)	
		Non-drinker	1.0
			P = 0.92
Controls: hospital control general population control	Hospitals controls	Versus hospital controls	
	202		
		<500	0.9 (0.5-1.6)
		≥500	1.0 (0.5-1.9)
		Versus hospital controls	
		Alcohol drinking	
		Never	1.0
		Past	0.3 (0.1-0.8)
		Occasional	1.1-(0.6-1.7)
		Daily	NA
		<50 ml/day	1.4 (0.7-2.8)
		≥50 ml/day	1.3 (0.6-2.4)
		Total alcohol consumption (1/lifetime)	
		Non-drinker	1.0
			P = 0.74

Table 2. *Continued*

References	Study period	Study subjects	Definition	Number of cases	Number of controls	Category	Odds ratio (95% CI or <i>P</i>)	<i>P</i> for trend	Confounding variables considered	Comments
		Type and source								
Iwasaki et al. (36)	1980–1986	Population-based (mountain villages in Shizuoka prefecture and farming-fishing villages in Chiba prefecture)	Cases: gastric cancer death	83 men	83 men	<500	1.4 (0.7–2.6)		Matched for sex, age (± 2 years), district and year of death (± 6 years) Adjusted for smoking, dietary habit	
						≥ 500	1.2 (0.6–2.3)			
						Everyday	0.945 (NS)			
Hirohata et al. (37)	1984–1986	Hospital-based (Kurume University Hospital)	Cases: histologically confirmed incident cases of gastric cancer at the First Department of Surgery	150	150	Versus controls from the department of surgery			Matched for sex, age (± 5 years) and residence	
						Quartiles of ethanol intake				
						Low	1.00	NS		
						Low moderate	0.63 (NS)			
						Moderate	1.30 (NS)			
						High	0.77 (NS)			
Controls: hospital control (inpatients of the First Department of Surgery and the Department of Orthopedics)		150								
Inoue et al. (38)	1988–1991	Hospital-based (Aichi Cancer Center)	Cases: histologically confirmed incident cases	420 men	420 men	Men			Matched for age (± 2 years) and time of first hospital visit (± 2 months)	
						Quartiles of ethanol intake				
						Low	1.00	NS		
						Low moderate	0.52 (NS)			
						Moderate	1.44 (NS)			
High	0.88 (NS)									

Versus non-drinker		
Total		
Drinker	1.23 (0.92–1.65)	
Current drinker	1.16 (0.86–1.56)	
Ex-drinker	1.87 (1.11–3.15)	
<1-year after quitting	2.60 (1.09–6.19)	
≥1-year after quitting	1.60 (0.87–2.94)	
Cardia		
Drinkers	1.60 (0.92–2.78)	
Current drinker	1.45 (0.82–2.57)	
Ex-drinker	2.81 (1.21–6.54)	
<1-year after quitting	3.71 (1.02–13.5)	
≥1-year after quitting	2.47 (0.93–6.69)	
Middle		
Drinkers	1.47 (0.94–2.28)	
Current drinker	1.38 (0.88–2.16)	
Ex-drinker	2.29 (1.12–4.68)	
<1-year after quitting	3.63 (1.23–10.7)	
≥1-year after quitting	1.78 (0.75–4.23)	
Antrum		
Drinkers	1.00 (0.69–1.46)	
Current drinker	0.96 (0.65–1.41)	
Ex-drinker	1.36 (0.69–2.70)	
<1-year after quitting	2.16 (0.75–6.25)	
≥1-year after quitting	1.06 (0.46–2.45)	
Women		
Controls: outpatients of the same hospital	248 women	248 women
Drinker versus non-drinker		
Total	0.89 (0.58–1.36)	
Cardia	0.86 (0.39–1.90)	
Middle	1.17 (0.66–2.07)	
Antrum	0.65 (0.65–1.24)	

Continued

Table 2. Continued

References	Study period	Study subjects	Type and source	Definition	Number of cases	Number of controls	Category	Odds ratio (95% CI or <i>P</i>)	<i>P</i> for trend	Confounding variables considered	Comments
Kikuchi et al. (39)	1993–1995	Hospital-based (nine hospitals in Tokyo Metropolitan Area)	Hospital-based (nine hospitals in Tokyo Metropolitan Area)	Cases: newly hospitalized with historically confirmed cases aged 40 years and under	494 men	448 men	Drinking dose (alcohol-year) Men				Pure alcohol intake (ml)/day multiplied by years of drinking
							Total				
							Never drinker	1.0	<0.001		
							Occasional and 0.1–134.9 ml/day	0.57 (0.33–1.00)		Adjusted for age, smoking and <i>Helicobacter Pylori</i> status	
							135.0–1349.0 ml/day	1.23 (0.73–2.06)			
							1350.0 + ml/day	1.40 (0.85–2.31)			
							Intestinal type				
							Never drinker	1.76 (0.94–3.32)	0.02		
							Occasional and 0.1–134.9 ml/day	1.0			
							135.0–1349.0 ml/day	2.07 (1.22–3.53)			
							1350.0 + ml/day	2.14 (1.29–3.55)			
							Diffuse type				
							Never drinker	1.74 (0.80–3.79)	<0.01		
							Occasional and 0.1–134.9 ml/day	1.0			
							135.0–1349.0 ml/day	2.20 (1.19–4.07)			
							1350.0 + ml/day	3.05 (1.68–5.56)			
							Early				
							Never drinker	1.76 (0.90–3.44)	<0.01		
							Occasional and 0.1–134.9 ml/day	1.0			
							135.0–1349.0 ml/day	2.23 (1.29–3.87)			
							1350.0 + ml/day	2.50 (1.48–4.23)			
							Advanced				
							Never drinker	1.88 (0.94–3.77)	0.02		
							Occasional and 0.1–134.9 ml/day	1.0			
							135.0–1349.0 ml/day	2.17 (1.21–3.89)			

1350.0 + ml/day	2.38 (1.36–4.17)	
Proximal		
Never drinker	2.72 (1.13–6.53)	
Occasional and 0.1–134.9 ml/day	1.0	
135.0–1349.0 ml/day	2.24 (1.01–4.96)	
1350.0 + ml/day	2.46 (1.17–5.17)	
Middle		
Never drinker	1.74 (0.84–3.57)	<0.01
Occasional and 0.1–134.9 ml/day	1.0	
135.0–1349.0 ml/day	2.34 (1.30–4.19)	
1350.0 + ml/day	3.29 (1.88–5.769)	
Distal		
Never drinker	1.28 (0.60–2.76)	0.25
Occasional and 0.1–134.9 ml/day	1.0	
135.0–1349.0 ml/day	1.85 (1.00–3.41)	
1350.0 + ml/day	1.56 (0.86–2.84)	
Women		
Controls: recruited from several health check programs in a hospital in the same area	224 women	435 women
Total		
Never drinker	1.0	0.016
Occasional and 0.1–134.9 ml/day	0.54 (0.35–0.82)	
135.0 + ml/day	0.75 (0.43–1.30)	
Intestinal type		
Never drinker	2.18 (1.18–4.03)	0.04
Occasional and 0.1–134.9 ml/day	1.0	
135.0 + ml/day	1.39 (0.55–3.53)	
Diffuse type		
Never drinker	1.74 (1.07–2.84)	0.06
Occasional and 0.1–134.9 ml/day	1.0	
135.0 + ml/day	1.02 (0.48–2.19)	

Continued

Table 2. *Continued*

References	Study period	Study subjects	Type and source	Definition	Number of cases	Number of controls	Category	Odds ratio (95% CI or P)	P for trend	Confounding variables considered	Comments
							Early				
							Never drinker	1.48 (0.88–2.49)	0.22		
							Occasional and 0.1–134.9 ml/day	1.0			
							135.0 + ml/day	0.88 (0.38–2.05)			
							Advanced				
							Never drinker	2.48 (1.42–4.33)	<0.01		
							Occasional and 0.1–134.9 ml/day	1.0			
							135.0 + ml/day	1.54 (0.68–3.44)			
							Proximal				
							Never drinker	1.50 (0.70–3.21)	0.21		
							Occasional and 0.1–134.9 ml/day	1.0			
							135.0 + ml/day	0.43 (0.10–2.05)			
							Middle				
							Never drinker	2.07 (1.22–3.53)	0.02		
							Occasional and 0.1–134.9 ml/day	1.0			
							135.0 + ml/day	1.34 (0.64–2.84)			
							Distal				
							Never drinker	1.69 (0.85–3.35)	0.28		
							Occasional and 0.1–134.9 ml/day	1.0			
							135.0 + ml/day	1.78 (0.67–4.71)			

Table 3. Summary of the association between alcohol drinking and gastric cancer risk, cohort study

References	Study period	Study subjects					Magnitude of association
		Author	Sex	No. of subjects	Age (years)	Event	
Kono et al. (18)	1965–1983	Men	5130	27–89	Death	116	–
Ubukata et al. (19)	1961–1985	Men	14 229	NA	Incidence	225	↑
Hirayama et al. (20)	1966–1982	Men	12 261	≥40	Death	3414	–
		Women	142 857	≥40	Death	1833	–
Kato et al. (21)	1985–1991	Men	9753	≥40	Death	35	↑↑↑
		Women		≥30	Death	22	–
Masuda and Shigematsu (22)	1968–1987	Men	NA	≥40	Death	97	–
Murata et al. (23)	1984–1993	Men	17 200	NA	Incidence	246	–
Inoue et al. (24)	1985–1995	Men and women	5373	NA	Incidence	69	–
Sasazuki et al. (25)	1990–1999	Men	19 657	40–59	Incidence	293	–
Fujino et al. (26)	1988–1997	Men	18 746	≥18 in 1949	Death	261	–
		Women	26 184	≥18 in 1949	Death	118	–
Nakaya et al. (27)	1990–1997	Men	21 201	40–64	Incidence	247	–
Sauvagat et al. (28)	1980–1999	Men and women	38 576	34–98	Incidence	1270	–

–, no association; ↑, weak positive association; ↑↑↑, strong positive association.
 Nested within the subjects.

Table 4. Summary of the association between alcohol drinking and gastric cancer risk, case-control study

References	Study period	Study subjects				Magnitude of association
		Author	Sex	Age (years)	Number of cases	
Hoshino et al. (29)	1980–1982	Men	20–84	460	460	–
Tajima and Tominaga (30)	1981–1984	Men	40–70	59	111	–
Kono et al. (31)	1979–1982	Men and Women	20–75	139	274 (in hospital)	–
					278 (in general population)	–
Kato et al. (32)	1985–1989	Men	NA	289	1247	–
		Women	NA	138	1767	–
Tominaga et al. (33)	1971–1985	Men and women	NA	294	588	–
Kikuchi et al. (34)	1988–1990	Men and women	–40	42	42	–
Hoshiyama and Sasaba (35)	1984–1990	Men and women	NA	294	202 (in hospital)	–
					294 (in general population)	–
Iwasaki et al. (36)	1980–1986	Men	NA	83	83	–
Hirohata et al. (37)	1984–1986	Men and women	–70	150	150	–
Inoue et al. (38)	1988–1991	Men	NA	420	420	–
		Women	NA	248	248	–
Kikuchi et al. (39)	1993–1995	Men	20–69	494	448	–
		Women	20–69	224	435	–