

Public Health Report

## Green Tea Consumption and Gastric Cancer Risk: An Evaluation Based on a Systematic Review of Epidemiologic Evidence Among the Japanese Population

Shizuka Sasazuki<sup>1,\*</sup>, Akiko Tamakoshi<sup>2</sup>, Keitaro Matsuo<sup>3</sup>, Hidemi Ito<sup>3</sup>, Kenji Wakai<sup>4</sup>, Chisato Nagata<sup>5</sup>, Tetsuya Mizoue<sup>6</sup>, Keitaro Tanaka<sup>7</sup>, Ichiro Tsuji<sup>8</sup>, Manami Inoue<sup>1</sup> and Shoichiro Tsugane<sup>1</sup> for the Research Group for the Development and Evaluation of Cancer Prevention Strategies in Japan

<sup>1</sup>Epidemiology and Prevention Division, Research Center for Cancer Prevention and Screening, National Cancer Center, Tokyo, <sup>2</sup>Department of Public Health, Aichi Medical University School of Medicine, Nagakute, <sup>3</sup>Division of Epidemiology and Prevention, Aichi Cancer Center Research Institute, <sup>4</sup>Department of Preventive Medicine, Nagoya University Graduate School of Medicine, Nagoya, <sup>5</sup>Department of Epidemiology and Preventive Medicine, Gifu University Graduate School of Medicine, Gifu, <sup>6</sup>Department of Epidemiology and International Health, Research Institute, International Medical Center of Japan, Tokyo, <sup>7</sup>Department of Preventive Medicine, Saga Medical School, Faculty of Medicine, Saga University, Saga and <sup>8</sup>Division of Epidemiology, Department of Public Health and Forensic Medicine, Tohoku University Graduate School of Medicine, Sendai, Japan

\*For reprints and all correspondence: Shizuka Sasazuki, 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: ssasazuk@ncc.go.jp

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**Objective:** Numerous *in vitro* and animal studies have shown that green tea has a protective effect against cancer. However, results from epidemiologic studies are conflicting. We evaluated the association between green tea consumption and risk for gastric cancer risk among the Japanese population based on a systematic review of epidemiologic evidence.

**Methods:** Original data were obtained from MEDLINE searches using PubMed or from 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 biologic plausibility.

**Results:** Eight cohort studies and three case–control studies were identified. Overall, we found no preventive effect on gastric cancer for green tea intake in cohort studies. However, a small, consistent risk reduction limited to women was observed, which was confirmed by pooling data of six cohort studies (hazard ratio = 0.79, 95% confidence interval 0.65–0.96 with  $\geq 5$  cups/day of green tea intake). Case–control studies consistently showed a weak inverse association between green tea intake and gastric cancer risk.

**Conclusions:** We conclude that green tea possibly decreases the risk of gastric cancer in women. However, epidemiologic evidence is still insufficient to demonstrate any association in men.

*Key words:* systematic review – epidemiology – green tea – gastric cancer – Japanese

## BACKGROUND

Although the age-standardized mortality rate has been continuously declining, gastric cancer is still the second leading cause of cancer deaths among men and women in Japan (1). In addition to *Helicobacter pylori* infection or cigarette smoking, dietary factors are suggested to be associated with gastric carcinogenesis (2).

Numerous *in vitro* and animal studies have shown that green tea has a protective effect against cancer (3). These experimental studies have suggested that green tea polyphenols might have a protective effect against gastric cancer through its apoptosis-inducing, antimutagenic and antioxidant activities. In 1997, a review of the World Cancer Research Fund, based on the results of case–control studies and several animal models that showed a protective effect of green tea, stated that ‘green tea possibly reduce the risk of stomach cancer’ (4). Since then, results from cohort studies generally have not supported the findings from case–control studies, and the more recent 2007 report concluded that ‘the evidence was so limited that no firm conclusion can be made’ (5).

In Japan, green tea is one of the most commonly consumed beverages, and therefore, the effect of green tea on the risk for gastric cancer may be of particular concern. We reviewed epidemiologic studies of green tea consumption and gastric cancer risk among Japanese. This work was conducted as a systematic review of epidemiologic studies on lifestyle factors and cancer based on previous publications targeting Japanese (6).

## METHODS

### RESEARCH REVIEW

Details of the evaluation method have been described previously (6). Briefly, original data for this review were identified through searches of the MEDLINE (PubMed) and *Ichushi (Japana Centra Revuo Medicina)* databases, complemented by manual searches of references from relevant articles where necessary. All epidemiologic studies on the association between green tea intake and gastric cancer incidence/mortality among the Japanese from 1950 (or 1983 for the *Ichushi* database) to June 2011 were identified using the search terms ‘green tea’, ‘tea’, ‘gastric cancer’, ‘stomach cancer’, ‘cancer’, ‘cohort study’, ‘case-control study’, ‘Japan’ and ‘Japanese’ as key words. In addition, we manually searched through references from relevant articles where necessary. Papers written in either English or Japanese were reviewed, and only studies on Japanese populations living in Japan were included. In the case of multiple publications of analyses of the same or overlapping data sets, only data from the largest or the most recent studies were included. The individual results were summarized in the tables separately as cohort or case–control studies. Pooled data of Japanese cohort studies, including some of the individual studies already listed, were also available through the review

process. To better understand the results from individual studies and finally evaluate the evidence for green tea intake and gastric cancer risk in Japanese, findings from recent pooled analyses were also listed and considered in this report.

### EVALUATION OF STRENGTH OF ASSOCIATION BETWEEN GREEN TEA INTAKE AND GASTRIC CANCER RISK

The evaluation was made based on the magnitude of association and the strength of evidence. First, the former was assessed by classifying the relative risk (RR) in each study into the following four categories, while considering statistical significance (SS) or no statistical significance (NS), as strong (symbol  $\downarrow\downarrow\downarrow$  or  $\uparrow\uparrow\uparrow$ ),  $<0.5$  or  $>2.0$  (SS); moderate (symbol  $\downarrow\downarrow$  or  $\uparrow\uparrow$ ), either (i)  $<0.5$  or  $>2.0$  (NS), (ii)  $>1.5-2$  (SS) or (iii)  $0.5$  to  $<0.67$  (SS); weak (symbol  $\downarrow$  or  $\uparrow$ ), either (i)  $>1.5-2$  (NS), (ii)  $0.5$  to  $<0.67$  (NS) or (iii)  $0.67-1.5$  (SS); or no association (symbol  $-$ ),  $0.67-1.5$  (NS). In cases where the frequency or amount of green tea intake had been separated into levels in a study, we used the RR derived from comparing the highest intake with the lowest. To consider the intermediate categories of intake, however, the *P* value for the trend was also considered when judging the statistical significance. After this process, the strength of evidence was evaluated in a manner similar to that used in the WHO/FAO Expert Consultation Report, where evidence was classified as convincing, probable, possible and insufficient (7). We assumed that biologic plausibility was based on evidence in experimental models, human studies and other relevant data.

### MAIN FEATURES AND COMMENTS

Through the review process, we identified eight cohort studies (8–15), one pooled analysis of six cohort studies (16) (Table 1) and three case–control studies (17–19) (Table 2). Among cohort studies, the events followed were death in five studies (8,10,12,14,15) and incidence in the other three studies (9,11,13). Five studies showed the results for men and women separately (9,10–14), whereas three studies showed combined results only (8,13,15). The pooled analysis included four cohorts (9,10 and two cohorts in 11) listed in Table 1 and two other cohorts (20,21). For all case–control studies, the results were shown for men and women combined.

The summary of the magnitudes of association for the cohort study and the case–control study is presented in Tables 3 and 4, respectively. As shown in Table 3, among eight cohort studies, one study showed a weak positive association between green tea intake and gastric cancer risk in men (9). Women in the study and all other studies showed no association at all. When the anatomic subsite was considered, one study observed a moderate inverse association for distal cancer in women (11). On the other hand, case–

**Table 1.** Gastric cancer risk and consumption of green tea in cohort studies of Japanese populations

References	Study period	Study population				Category	No. among cases	Relative risk (95% CI or P)	P for trend	Confounding variables considered	Comments
		No. of subjects for analysis	Source of subjects	Event followed	No. of incident cases or deaths						
Nakachi et al. (8)	1986–99	8552	Population-based Saitama Prefecture	Death	140	Green tea, cups/day				Sex and lifestyle factors	
						≤3	1.0				
						≥10	0.69 (0.23–1.88)				
Tsubono et al. (9)	1984–92	26 311 11 902 men 14 409 women	Population-based Miyagi Prefecture	Incidence	419 296 men 123 women	Green tea, cups/day				Age, sex, types of health insurance, history of peptic ulcer, smoking status, alcohol consumption, daily consumption of rice, black tea, coffee, meat, green or yellow vegetables, pickled vegetables, other vegetables, fruits and bean-paste soup	
						Total					
						<1	66	1.0			
						1–2	68	1.1 (0.8–1.6)			
						3–4	79	1.0 (0.7–1.4)			
						≥5	206	1.2 (0.9–1.6)	0.13		
						Men					
						<1	41	1.0			
						1–2	49	1.3 (0.8–1.9)			
						3–4	55	1.2 (0.8–1.8)			
						≥5	151	1.5 (1.0–2.1)	0.03		
						Women					
<1	25	1.0									
1–2	19	0.8 (0.5–1.5)									
3–4	24	0.7 (0.4–1.3)									
≥5	55	0.8 (0.5–1.3)	0.46								
Hoshiyama et al. (10)	Mean 8 years	72 851 30 370 men 42 481 women	Population-based 45 areas of Japan	Death	359 240 men 119 women	Green tea, cups/day				Age, smoking status, history of peptic ulcer, family history of stomach cancer, consumption of rice, miso soup, green–yellow vegetables, white vegetables, fruits and preference for salty foods	
						Men					
						<1	24	1.0			
						1–2	51	1.6 (0.9–2.9)			
						3–4	51	1.1 (0.6–1.9)			
						5–9	76	1.1 (0.6–1.9)			
						≥10	38	1.0 (0.5–2.0)	0.634		
						Women					
						<1	20	1.0			
						1–2	18	1.1 (0.5–2.5)			
						3–4	40	1.0 (0.5–2.1)			
						5–9	32	0.8 (0.4–1.6)			
≥10	9	0.7 (0.3–2.0)	0.476								

Continued

Table 1. *Continued*

References	Study period	Study population				Category	No. among cases	Relative risk (95% CI or <i>P</i> )	<i>P</i> for trend	Confounding variables considered	Comments
		No. of subjects for analysis	Source of subjects	Event followed	No. of incident cases or deaths						
Sasazuki et al. (11)	1990–2001	72,943 34,832 men 38,111 women	Population-based	Incidence	892 665 men 227 women	Green tea, cups/day				Age, area, cigarette smoking, consumption of fruits, green or yellow vegetables, fishgut, miso soup, black tea and coffee	
						Men					
						All sites					
						<1	1.0				
						1–2	0.95 (0.72–1.22)				
						3–4	0.84 (0.65–1.08)				
						≥5	0.98 (0.77–1.25)	0.65			
						Upper-third including cardia					
						<1	1.0				
						1–2	1.06 (0.51–2.18)				
						3–4	0.73 (0.34–1.57)				
						≥5	1.17 (0.60–2.30)	0.75			
						Distal					
						<1	1.0				
						1–2	0.88 (0.64–1.20)				
						3–4	0.79 (0.59–1.07)				
						≥5	0.92 (0.69–1.22)	0.37			
						Women					
						All sites					
						<1	1.0				
1–2	0.85 (0.53–1.38)										
3–4	1.04 (0.68–1.58)										
≥5	0.67 (0.43–1.04)	0.08									
Upper-third including cardia											
<1	1.0										
1–2											
3–4	0.89 (0.34–2.33)										
≥5		0.81									
Distal											
<1	1.0										
1–2	0.88 (0.52–1.49)										
3–4	1.00 (0.63–1.59)										
≥5	0.51 (0.30–0.86)	0.01									

Khan et al. (12)	1984–2002	3158	Population-based Hokkaido	Death	51	Men			Age, smoking, health status, health education, health screening
		1524 men			36 men	Green tea ≤ several times/month	1.0		
		1634 women			15 women	Green tea ≥ several times/week	1.1 (0.4–2.5)		
						Women			
						Green tea ≤ several times/month	1.0		
						Green tea ≥ several times/week	0.7 (0.2–2.9)		
Sauvaget et al. (13)	1980–99	38 576	Atomic-bomb survivors: Hiroshima, Nagasaki	Incidence	1270	Green tea, cups/day			Sex, sex-specific age, city, radiation dose, sex-specific smoking habits and education level
		14 885 men			<2	242	1.0		
		23 691 women			2–4	680	1.03 (0.89–1.19)		
		34–98 years old			≥5	348	1.06 (0.89–1.25)	>0.50	
Kuriyama et al. (14)	All-cause	40 530	Population-based	Death	193	Green tea, cups/day			Age, sex, job status, years of education, BMI, sports or exercise, walking duration, history of HT, DM, GU, smoking, alcohol, total energy, rice, miso soup, soy bean product, total meat, total fish, dairy products, total fruits, total vegetables, oolong tea, black tea, and coffee
		1995–2005 (11 years)			19 060 men	<1	44	1.0	
	Cause-specific	21 470 women	1–2	44	1.33 (0.86–2.04)				
		1995–2001 (7 years)	3–4	38	1.00 (0.64–1.58)				
		5≤	67	1.17 (0.78–1.76)	0.72				
			138 men	<1	32	1.0			
				1–2	30	1.29 (0.78–2.16)			
				3–4	30	1.19 (0.71–2.00)			
				≥5	46	1.20 (0.74–1.95)	0.55		
			55 women	<1	12	1.0			
			1–2	14	1.32 (0.59–2.94)				
			3–4	8	0.64 (0.26–1.63)				
			≥5	21	1.08 (0.50–2.33)	0.84			
Suzuki et al. (15)	1999–2006	12 251	Population randomly chosen from all 74 municipalities in Shizuoka Prefecture	Death	68	Green tea, cups/day			Age, sex, smoking, alcohol, BMI, and physical activity
		6231 men			<1	2	1.0	Test for trend: HR = 1.04 (0.95–1.13)	
		6020 women			1–3	14	0.49 (0.11–2.28)		
		65–84y old			4–6	32	0.78 (0.19–3.30)		
					≥7	20	0.81 (0.18–3.54)		

Continued

Table 1. Continued

References	Study period	Study population				Category	No. among cases	Relative risk (95% CI or P)	P for trend	Confounding variables considered	Comments
Author		No. of subjects for analysis	Source of subjects	Event followed	No. of incident cases or deaths						
Pooled analysis of 6 cohort studies including those listed above (9,10, cohort I of 11, cohort II of 11) or mentioned in the text (20 and 21)											
Inoue et al. (16)	1985–2004	219 080	Population-based	Incidence	3577	Green tea, cups/day					
		100 479 men			2495 men	Men				Age, area (for three cohorts only), smoking, alcohol drinking, rice, soy bean paste soup, coffee, pickled vegetables, and green-yellow vegetables intake	
		118 601 women			1082 women	All sites					
						<1	420	1.0			
						1–2	452	0.97 (0.83–1.12)			
						3–4	610	0.93 (0.81–1.08)			
						≥5	1013	1.06 (0.86–1.30)	0.74		
						Proximal (upper third)					
						<1	38	1.0			
						1–2	41	1.10 (0.70–1.73)			
						3–4	42	0.79 (0.46–1.35)			
						≥5	96	1.43 (0.96–2.14)	0.08		
						Distal (lower two-thirds)					
						<1	185	1.0			
						1–2	185	0.91 (0.73–1.12)			
						3–4	249	0.95 (0.77–1.16)			
						≥5	328	0.96 (0.79–1.17)	0.86		
						Women					
						All sites					
						<1	215	1.0			
						1–2	174	0.90 (0.73–1.10)			
						3–4	303	0.92 (0.76–1.11)			
						≥5	390	0.79 (0.65–0.96)	0.04		
						Proximal (upper third)					
						<1	8	1.0			
						≥1	45	1.17 (0.52–2.60)	0.87		
						Distal (lower two thirds)					
						<1	83	1.0			
						1–2	64	0.80 (0.57–1.13)			
						3–4	117	0.96 (0.71–1.30)			
						≥5	106	0.70 (0.50–0.96)	0.04		

NS, not significant; BMI, body mass index; HT, hypertension; DM, diabetes mellitus; GU, gastric ulcer.

**Table 2.** Gastric cancer risk and consumption of green tea in case–control studies of Japanese populations

References	Study time	Study subjects				Category	Relative risk (95% CI)	P for trend	Confounding variables considered	Comments
Author		Type and source	Definition	No. of cases	No. of controls					
Tajima and Tominaga (17)	1981–83	Hospital-based (Aichi Cancer Center)	Cases: Histologically confirmed cases	93	186	Green tea, times/day ≥4	0.64	NS		Matched for age (± 5 years), sex, time of interviews (± 6 months)
			Controls: Patients without stomach cancer			≤3	1.0			
Kono et al. (18)	1979–82	Hospital-based (Karatsu Stomach Institute)	Cases: Newly diagnosed as having gastric cancer at the Institute	139	Hospital controls: 2574	vs. hospital controls Green tea, cups/day				
				74 men		None or 1–4	1.0		Age, sex	
				65 women	1171 men 1403 women	5–9	1.1			
						≥10	0.6	NS		
			Hospital controls: Patients without gastric cancer		General controls; 278	≤9	1.0		Age, sex, smoking, oranges, fruits	
					148 men	≥10	0.5 (0.3–1.1)			
			General population controls: Random sampling from the computerized file of residents		130 women	vs. general controls Green tea, cups/day			General population: Matched (1:2) for	
						None or 1–4	1.0		Sex	
						5–9	1.2		Age	
						≥10	0.4*	NS		
						≤9	1.0		Smoking, oranges, fruits	
						≥10	0.3 (0.1–0.7) <sup>†</sup>			

Continued

Table 2. Continued

References	Study time	Study subjects	Definition	No. of cases	No. of controls	Category	Relative risk (95% CI)	P for trend	Confounding variables considered	Comments
Inoue et al. (19)	1990–95	Hospital-based (Aichi Cancer Center)	Cases: Histologically diagnosed cases of gastric cancer at the Institute  Controls: Outpatients without cancer	893	21 128	Green tea Rarely  Occasional Daily 1–3 cups/day 4–6 cups/day ≥ 7 cups/day	1.00  1.00 (0.77–1.44)  0.96 (0.70–1.32) 1.01 (0.74–1.39) 0.69 (0.48–1.00) <sup>‡</sup>		Coffee intake, black tea intake, gender, age, year and season at first hospital visit, habitual smoking, habitual alcohol drinking, regular physical exercise, fruit intake, rice intake, and beef intake	

NS, not significant.  
<sup>\*</sup>*P* > 0.05.  
<sup>†</sup>*P* = 0.007.  
<sup>‡</sup>*P* > 0.05.

control studies consistently showed a weak negative association between intake of green tea and risk of gastric cancer (Table 4). Among them, when using the general population as a control setting, Kono et al. (18) observed a strong negative association between green tea intake and gastric cancer risk.

During the review process, we were aware of the difference in effect by sex. In all studies that presented the analysis for men and women separately, although not statistically significant, the point estimate of highest category of green tea intake for women was consistently lower than that for men; i.e. based on incidence data, compared with <1 cup/day, the RRs of drinking ≥5 cups/day for men and women were estimated as 1.5 and 0.8 (9) and 0.98 and 0.67 (11), respectively (Table 1). Based on mortality data, the corresponding values for men and women were estimated as 1.0 and 0.7 (<1 vs. ≥10 cups/day) (10), and 1.1 and 0.7 (less than several times per month vs. more than several times per week) (12), respectively (Table 1). These results suggest a small protective effect, if any, of green tea intake and development of gastric cancer for women. However, applying our definition of magnitudes of association, they slightly failed to reach the level of weak association (weak association for 0.5 to <0.67, not significant). The null association observed among men may, in part, reflect insufficient adjustment for confounding factors such as cigarette smoking. Likewise, differences in the effect of green tea by subsite may point to an inconsistent effect on gastric cancer overall (11). However, evidence for such specific issues is sparse, probably due to the relatively small number of gastric cancer cases occurring in the upper subsite among cohorts, particularly in women. Results from pooled analysis may lead to a better understanding of these unresolved issues.

In a pooled analysis of six cohort studies (9–11,13,20,21) involving total of 219 080 subjects and 3577 gastric cancer cases, the role of green tea intake and gastric cancer risk was analyzed for men and women separately, with consideration of smoking status, anatomic subsite and so on (16). As a result, a statistically significant, weakly decreased risk of gastric cancer with ≥5 cups/day of green tea intake among women was observed [hazard ratio (HR) = 0.79, 95% confidence interval (CI) 0.65–0.96], although no association was observed among men (Tables 1 and 3). When the anatomic subsite was considered among four cohort studies in which the data were routinely collected, the risk reduction among women was more prominent in the distal gastric region (HR = 0.70, range 0.50–0.96; *P* for trend = 0.04). Together with the results of the systematic review, this finding from the pooled analysis was also considered to finally evaluate the evidence for green tea intake and gastric cancer risk in Japanese.

A difference in the effect of green tea intake by sex has also been observed for cardiovascular disease (14,22,23). The exact reason for the difference is unknown but may be explained, in part, by residual confounding effects of



smoking, phytoestrogens in tea and so on. It was suggested in some studies (9,14), but not all (16), that cigarette smoking might modify the effect of green tea. Tsubono et al. (9) observed a trend toward a positive association between green tea consumption and the risk of gastric cancer in subjects currently smoking  $\geq 20$  cigarettes/day ( $P$  for trend = 0.06), but not in other groups ( $P$  for the interaction term = 0.17). A similar interaction was suggested among studies investigating green tea intake and risk for cardiovascular disease (14). Higher rates of smoking may mask the effect of green tea consumption in men. Tea flavonoids such as kaempferol have been shown to exhibit estrogenic activity *in vitro* (24). In addition, tea contains lignan polyphenols, such as secoisolaracinol, which are considered phytoestrogenic (25). The phytoestrogens in tea might also partly account for the stronger protective effect of green tea in women than in men (26,27), although an estrogen-related protective mechanism against gastric cancer, if any, warrants further investigation.

Several aspects need to be discussed in relation to interpreting the present findings. Although cigarette smoking, which is suggested to have an interactive effect with green tea, was adjusted in most studies, *H. pylori* infection, a Group 1 carcinogen recognized by the International Agency for Research on Cancer (IARC), was not considered in any study. Based on the same origin of cohort study (10), Hoshiyama et al. (28) investigated whether green tea has any association with gastric cancer risk with considering *H. pylori* infection in a nested case–control study design within 157 incidence cases and 285 controls. They found that green tea intake had no protective effect against gastric cancer even after controlling for *H. pylori* infection. A previous nested case–control study that investigated plasma tea polyphenols and risk for gastric cancer reported that the decreased risk of gastric cancer by intake of tea polyphenols observed among women in the study remained even after adjusting for *H. pylori* infection (29). Some researchers used an animal model to report the inhibition of *H. pylori* urease by green tea extract (30) and the bactericidal effect on *H. pylori* infection by green tea catechins (31). A long-term habit of drinking green tea might lead to the elimination of *H. pylori*; if this is true, *H. pylori* may act as an intermediate rather than a confounding factor in the relationship between green tea and gastric cancer.

Discrepancies were noted in the effects of green tea on gastric cancer risk between case–control studies and cohort studies. The discrepancies were quantitatively shown from a recent meta-analysis of green tea intake and gastric cancer risk based on 13 studies from Japan and China (32). Compared with the lowest level of green tea intake, the RR of gastric cancer for the highest level of green tea intake was 0.73 (95% CI 0.64–0.83) for case–control studies, whereas no association was observed for cohort studies (RR = 1.04, 95% CI 0.93–1.17). The discrepancy may be partially explained by recall or selection biases that are inevitable in case–control studies. For example, it is possible that

individuals with gastric cancer reduce their green tea intake due to their gastric symptoms. In fact, it has been reported that among those with gastric cancer, black tea consumption was reduced even up to 2 years before their diagnosis was made (33). Therefore, the green tea intake for gastric cancer cases among case–control studies might be partly underreported. Another point is the variation of gastric cancer mortality rates across the country. The age-adjusted gastric cancer mortality rate under age 75 in 2009 in Japan was 11.8/100 000 and ranged from 6.3 (Okinawa prefecture) to 15.7 (Akita prefecture) (34). It is interesting that gastric cancer mortality rates in the two prefectures in the case–control studies are higher than the average level, whereas the situation for cohort studies is mixed. On the basis of wide variation in gastric cancer mortality rates by area, the approach such as pooled analysis might be important.

However, the null results in cohort studies also contradict the results of previous experimental studies that suggested the protective effect of tea polyphenols on gastric cancer using *in vivo* animal models and *in vitro* cancer cell lines (3). In most of the cohort studies where the validity of green tea intake was examined, a moderate validity was shown; the Spearman coefficient for the correlation between the green tea intake according to the questionnaire and the amounts consumed according to the food records ranged from 0.29 to 0.71 (9–11,13,14). However, in all epidemiologic studies investigating green tea intake and gastric cancer risk, green tea consumption was determined only in terms of self-reported frequency of drinking, and the size of the cup was not ascertained. Furthermore, the amount of tea polyphenols in one cup varies according to preparation, i.e. the type and amount of green tea leaves, the frequency of renewing a tea batch in the pot, the temperature of boiled water or time to brew the tea and so on. A number of studies have found that hot drinks have an effect on the risk for esophageal cancer (35). Yu et al. (36) also showed that boiling hot tea had a non-significant increased risk of causing gastric cancer (odds ratio = 1.18). The risk estimates for the cardia, pylori and antrum sites regarding boiling hot tea were 2.09, 0.56 and 0.82, respectively. Furthermore, the term ‘green tea’ might be ambiguous because some participants may include only ‘sencha’, which looks green, or others may also include ‘bancha/houjicha/genmaicha’, which is also a commonly consumed Japanese tea but looks brown. Sencha, one of the most popular green teas in Japan, contains higher levels of tannin, vitamin C and folate than bancha/houjicha/genmaicha (37). Inaccurate measurement of green tea consumption in epidemiologic studies necessarily attenuates the small effect of green tea. It is interesting that both studies using biomarkers of green tea intake showed a statistically significant association with gastric cancer. Sun et al. (38) reported that urinary (–)-epigallocatechin (EGC) showed a statistically significant inverse association with gastric cancer. In a case–control study nested within a cohort study (11), a high plasma level of EGC was associated with an increased risk of gastric cancer in men, whereas a high plasma level of

**Table 3.** Summary of associations between gastric cancer risk and consumption of green tea in cohort studies of Japanese populations

References			Study period	Study subjects					Strength of association
Author	Year	Ref. no.		Sex	No. of subjects	Age range	Event	No. of cases	
Nakachi et al.	2000	8	1986–99	Men and women	8552	40+	Death	140	–
Tsubono et al.	2001	9	1984–92	Men	11 902	40+	Incidence	296	↑
				Women	14 409			123	–
Hoshiyama et al.	2002	10	1988–97	Men	30 370	40–79	Death	240	–
				Women	42 481			119	–
Sasazuki et al.	2004	11	1990–2001	Men	34 832	40–59	Incidence	665	–
				Women	38 111			227	– (distal ↓↓)
Khan et al.	2004	12	1984–2002	Men	1524	40+	Death	36	–
				Women	1634			15	–
Sauvaget et al.	2005	13	1980–99	Men and women	38 576	34–98	Incidence	1270	–
Kuriyama et al.	2006	14	1995–2001	Men	19 060	40–79	Death	138	–
				Women	21 470			55	–
Suzuki et al.	2009	15	1999–2006	Men and women	12 251	65–84	Death	68	–
Pooled analysis of 6 cohort studies including those listed above (9,10, cohort I of 11, cohort II of 11) or mentioned in the text (20 and 21)									
Inoue et al.	2009	16	1985–2004	Men	100 479	40–103	Incidence	2495	–
				Women	118 601			1082	↓

Explanation for each symbol is as follows when statistical significance (SS) or no statistical significance (NS), strong (symbol ↓↓↓ or ↑↑↑), <0.5 or >2.0 (SS); moderate (symbol ↓↓ or ↑↑), either (i) <0.5 or >2.0 (NS), (ii) >1.5–2 (SS) or (iii) 0.5 to <0.67 (SS); weak (symbol ↓ or ↑), either (i) >1.5–2 (NS), (ii) 0.5 to <0.67 (NS) or (iii) 0.67–1.5 (SS); or no association (symbol –), 0.67–1.5 (NS).

**Table 4.** Summary of associations between gastric cancer risk and consumption of green tea in case–control studies of Japanese populations

References			Study period	Study subjects				Strength of association	
Author	Year	Ref. no.		Sex	Age range	No. of cases	No. of controls		
Tajima and Tominaga	1985	17	1981–83	Men and women	40–70	93	186	↓	
Kono et al.	1988	18	1979–82	Men and women	20–75	139	Hospital	2547	↓
							General population	278	↓↓↓
Inoue et al.	1998	19	1990–95	Men and women	40+	893	21 128	↓	

Explanation for each symbol is as follows when statistical significance (SS) or no statistical significance (NS), strong (symbol ↓↓↓ or ↑↑↑), <0.5 or >2.0 (SS); moderate (symbol ↓↓ or ↑↑), either (i) <0.5 or >2.0 (NS), (ii) >1.5–2 (SS) or (iii) 0.5 to <0.67 (SS); weak (symbol ↓ or ↑), either (i) >1.5–2 (NS), (ii) 0.5 to <0.67 (NS) or (iii) 0.67–1.5 (SS); or no association (symbol –), 0.67–1.5 (NS).

(–)-epicatechin-3-gallate was associated with a statistically significant decreased risk of gastric cancer in women (29).

In conclusion, we found no preventive effect on gastric cancer for green tea intake in cohort studies, which have fewer biases and are more persuasive than case–control studies, where risk reduction was shown. However, a small, consistent risk reduction limited to women was observed, which was confirmed by pooling data from six cohort studies.

## EVALUATION OF EVIDENCE ON GREEN TEA CONSUMPTION AND GASTRIC CANCER RISK IN JAPANESE

From the results of the systematic review and pooled analysis of green tea intake and gastric cancer risk and on the basis of assumed biologic plausibility, we conclude that green tea possibly decreases the risk of gastric cancer in women. However, epidemiologic evidence is still insufficient to demonstrate any association in men.

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## Conflict of interest statement

None declared.

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### Appendix

Research group members: Shoichiro Tsugane (principal investigator), Manami Inoue, Shizuka Sasazuki, Motoki Iwasaki, Tetsuya Otani (until 2006), Norie Sawada (since 2007), Taichi Shimazu (since 2007) (National Cancer

Center, Tokyo); Ichiro Tsuji (since 2004), Yoshitaka Tsubono (in 2003) (Tohoku University, Sendai); Yoshikazu Nishino (until 2006) (Miyagi Cancer Research Institute, Natori, Miyagi); Akiko Tamakoshi (since 2010) (Aichi medical University, Aichi); Keitaro Matsuo (until 2010), Hidemi Ito (since 2010) (Aichi Cancer Center, Nagoya); Kenji Wakai (Nagoya University, Nagoya); Chisato Nagata (Gifu University, Gifu); Tetsuya Mizoue (National Center for Global Health and Medicine, Tokyo); Keitaro Tanaka (Saga University, Saga).