significant. Another case–control study also presented the results by subsite, and drinking dose showed a stronger association with middle gastric cancer than with other subsites in men and women (39). Three studies reported no clear difference in risk pattern according to histologic subtype (intestinal and diffuse type) (25,32,39).

There were several methodological concerns in the Japanese studies reviewed here. First, assessment of drinking status was not detailed. Few studies assessed drinking status with validated questionnaires (25,27,28) in cohort studies. Therefore, it is necessary to consider the possible misclassification of drinking dose or frequency that would attenuate the association between alcohol drinking and gastric cancer risk. Moreover, early studies reviewed here did not differentiate between never and past drinkers. It is important to evaluate the risk of gastric cancer in past drinkers, because past drinkers could include those who gave up drinking due to ill health. Some recent studies have investigated the association with gastric cancer by distinguishing between past and never drinkers (24,26–28,34,35,38). Compared with never drinkers, two studies reported an increased risk of gastric cancer in past drinkers (24,38). In addition, the types of alcoholic beverages consumed among Japanese differ from those consumed by other populations, but this was considered in only two studies (22,31).

Second, few studies reported an adjusted risk of gastric cancer by important possible confounding factors. Although *H. pylori* is an established risk factor for gastric cancer (40), only one case–control study reported the OR adjusted for *H. pylori* infection (39). If alcohol drinking is related to *H. pylori* infection status, it could confound the association between alcohol drinking and gastric cancer. However, a cross-sectional study among Japanese men showed that alcohol drinking was not associated with *H. pylori* IgG antibody seropositivity (41). Thus, *H. pylori* infection status may not confound the association between alcohol drinking and gastric cancer risk. In fact, one case–control study presented the association between alcohol drinking and gastric cancer after adjustment for *H. pylori* infection and smoking status (39), and the magnitude of the association was similar to that in studies without adjustment for *H. pylori* infection status. Compared with never drinkers, the OR in the highest category of drinking dose (pure alcohol intake/day multiplied by years of drinking) was 1.40 (0.85–2.31) in men and 0.75 (0.43–1.30) in women. In the evaluation from the IARC, confounding by *H. pylori* infection was not considered as a major concern, because an association was seen in areas where the majority of the population had been infected by *H. pylori* (2).

Smoking is a potential confounder. Our previous review of Japanese studies regarding smoking and gastric cancer concluded that there is convincing evidence that tobacco smoking moderately increases the risk of gastric cancer (14). Since alcohol drinking is often related to smoking, confounding by smoking could elevate the risk of alcohol drinking. Of all the 22 studies reviewed, seven cohort studies (18,19,21–23,25,27) and three case–control studies (35,36,39) reported their results after adjustment for, or stratification by, smoking status.

Dietary factors are also potential confounders to be considered. Especially, it is important to consider salt intake, and fruit and vegetable consumption, which potentially increase and decrease gastric cancer risk (3), respectively. Two cohort studies reported their results after adjustment for consumption of fruit and vegetables (25,27), and one cohort study reported its results after adjustment for consumption of salty foods (25).

Third, misclassification of cardia cancer could occur because, until recently in Japan, the upper third of the stomach was called the cardia based on the guidelines for gastric cancer classification (42). This misclassification might have attenuated any positive association between alcohol drinking and cardia cancer if there is a causal relationship between alcohol drinking and cardia cancer, as suggested by several case–control studies among Western populations (3).

In experimental animals, the IARC evaluated the carcinogenic effect of ethanol on various sites including the forestomach, and concluded that there is sufficient evidence of carcinogenicity (1,2). However, epidemiologic findings on the association between alcohol drinking and gastric cancer among the Japanese population are inconclusive due to the quality of the methodology employed. Further, well designed epidemiologic studies are needed to provide a more detailed assessment of alcohol drinking, possible important confounding factors and anatomical subsites of gastric cancer.

Evaluation of Evidence on Alcohol Drinking and Gastric Cancer Risk in Japanese

From these results, and on the basis of assumed biological plausibility, we conclude that there is insufficient evidence that alcohol drinking increases the risk of gastric cancer in the Japanese population.

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Conflict of interest statement
None declared.

APPENDIX

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