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High-temperature beverages and Foods and Esophageal Cancer Risk -- A Systematic Review

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Abstract

Coffee, tea, and maté may cause esophageal cancer (EC) by causing thermal injury to the esophageal mucosa. If so, the risk of EC attributable to thermal injury could be large in populations in which these beverages are commonly consumed. In addition, these drinks may cause or prevent EC via their chemical constituents. Therefore, a large number of epidemiologic studies have investigated the association of an indicator of amount or temperature of use of these drinks or other hot foods and beverages with risk of EC.

We conducted a systematic review of these studies, and report the results for amount and temperature of use separately. By searching PubMed and the ISI, we found 59 eligible studies.

For coffee and tea, there was little evidence for an association between amount of use and EC risk; however, the majority of studies showed an increased risk of EC associated with higher drinking temperature which was statistically significant in most of them. For maté drinking, the number of studies was limited, but they consistently showed that EC risk increased with both amount consumed and temperature, and these two were independent risk factors. For other hot foods and drinks, over half of the studies showed statistically significant increased risks of EC associated with higher temperature of intake.

Overall, the available results strongly suggest that high-temperature beverage drinking increases the risk of EC. Future studies will require standardized strategies that allow for combining data, and results should be reported by histological subtypes of EC.

Introduction

Recurrent thermal injury to the esophageal mucosa due to consuming large amounts of hot drinks has long been suspected to be a risk factor for esophageal cancer (EC). In 1939, WL Watson, after reviewing clinical records from 771 EC cases, wrote: "thermal irritation is probably the most constant factor predisposing to the cancer of the esophagus".1 If hot drinks indeed cause EC, they can explain a large proportion of all cases in populations in which drinking tea, coffee, or maté (an herbal infusion of *Ilex paraguariensis*, commonly

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consumed in several South American countries), or eating hot foods are common. Nevertheless, the association of hot drinks with EC has been questioned both based on biologic reasons and empirical evidence.

It has been argued that the temperature of hot foods and drinks may fall rapidly in the mouth and oropharynx so that it cannot cause thermal injury to the esophageal mucosa.2 To test this hypothesis, De Jong and colleagues measured intraesophageal temperature after consuming hot drinks. The results of their study showed that drinking hot beverages could substantially increase the intra-esophageal temperature and this increase was a function of the initial drinking temperature and more importantly, the size of the sip.3 For example, drinking 65 °C coffee increased the intra-esophageal temperature by 6–12 °C, depending on the sip size.3

Tea, coffee, and maté may affect cancer risk not only through thermal effects but also via their chemical constituents. Although some studies have shown mutagenic effects for tea, coffee, and unprocessed maté herb (*Ilex paraguariensis*) extracts,4⁻10 a number of more recent experimental studies in animals have reported cancer preventive activities for these beverages (reviewed in refs. 11⁻15). A number of epidemiological studies have investigated a possible effect of these beverages on cancer risk. With respect to gastrointestinal cancers, recent meta-analyses did not find any significant association between tea drinking and gastric and colorectal cancers,16⁻18 but coffee drinking was shown to be inversely associated with risk of liver cancer.19،20

In 1990, a Working Group of the International Agency for Research on Cancer (IARC) concluded that there was not sufficient evidence to recognize tea, coffee, or maté, *in toto*, as risk factors of human cancer, but they found that drinking hot maté was a probable risk factor in humans.21 The strongest evidence was for an association with EC. Since then, a large number of additional studies have investigated the association of the beverages and EC. We conducted a systematic review of the results of epidemiologic studies on the association of tea, coffee, or maté drinking or of high-temperature food consumption with EC.

Materials and Methods

We conducted a comprehensive search of the PubMed and ISI-Web of Knowledge databases for all case-control or cohort studies published in English language on the association of tea, coffee, maté, or other hot drinks or high temperature foods and risk of EC. All results were updated on January 23, 2009. The following terms were used in the PubMed Database search: “(esophag* OR oesophag*) AND (cancer OR carcinoma OR adenocarcinoma OR neoplasm OR neoplasia OR neoplastic) AND (tea OR mate OR coffee OR beverage)”; the search was repeated by replacing the last phrase with “(liquid OR drinks OR alcohol OR food) AND (hot OR cold OR warm OR temperature)”. The same terms were used to search text words in the ISI Database. In addition, references cited in the identified articles were searched manually. Two of the authors (FI and FK) reviewed the search results to reduce the possibility of missing the published papers.

Using the above-mentioned approach, a total of 536 articles were retrieved. Figure 1 shows a summary of the article selection process. After reading the abstracts of the retrieved articles, we excluded 417 articles because they were not case-control or cohort studies of hot drinks and EC; the excluded articles were reviews, animal studies, *in vitro* studies, case-series, studies of cancers other than EC, or studies of treatment and complications of EC. In case of any doubt, we also reviewed the full texts of those articles. After reviewing the full texts of the remaining 119 articles, we excluded another 57 because they did not present data

on the variables of interest, but we found an additional 14 articles by searching the references of the articles. We also included a study which was in press at the time of our review.22 Therefore, a total of 77 relevant articles were found. Of these, 7 articles 23–29 were excluded because they reported data on EC in combination with other cancers and an additional 10 publications 30–39 were excluded because their results were reported in other publications or in combined analyses. One more study that referred to drinking of hot Calvados,40 a strong spirit which is a well established cause of EC, was excluded because separating the effect of temperature from that of the spirit per se would be difficult. Finally, a total of 59 full-text articles were included in this systematic review.22,41–98

Tea, coffee, and maté constitute the three major types of hot drinks consumed around the world. Therefore, we present data for each one of these, as well as for the mixed group of other hot foods and drinks, in separate tables. The two main variables of interest were: 1) an indicator of amount consumed (frequency per day, amount per day, duration of use, or a composite variable indicating cumulative use); and 2) temperature.

The etiological factors responsible for the two main histological of EC, esophageal squamous cell carcinoma (ESCC) and esophageal adenocarcinoma (EAC), may be different, and any role of hot drinks and foods might be more relevant for ESCC etiology.99 Therefore, where data are available, we present the results for ESCC and EAC separately.

Where both crude and adjusted odds ratios (ORs) and 95% confidence intervals (95% CIs) were reported in the paper, we only present the adjusted results. A small number of studies showed crude numbers but not ORs and 95% CIs, in which case we calculated these statistics using simple logistic regression models and present them. Throughout the article, *P* values < 0.05 were considered as statistically significant.

Results

Tea

After excluding duplicate publications, we found 38 papers, published between 1974 and 2008, that reported on the association of tea drinking with EC (Table 1). These included 33 individual case-control studies, a pooled analysis of 5 case-control studies, a pooled analysis of 2 case-control studies, and 3 prospective studies. The studies were conducted in United States, South America, Europe, South-Africa, Middle-East, and South and East Asia, and included both high-risk and low-risk regions. Two of the prospective studies were from Japan and one was from China. There were large differences in study size, but the majority of the studies had between 100 and 400 EC cases. Whereas some studies described the type of tea consumed (e.g., green tea or black tea), the large majority did not report on tea type; however, black tea represents the predominant type of tea traditionally drunk in most regions outside East Asia.21

Amount consumed—Most studies (n = 33) provided results for one of the indicators of amount consumed, e.g., amount per day, frequency per day, duration of use, or an indicator of cumulative use. However, not all studies reported ORs (95% CIs) or crude numbers. There was no clear pattern of association between amount of tea consumed and EC risk; 7 studies showed an increase in risk (4 were statistically significant), and this was counterbalanced by 15 individual studies and a pooled analysis of 5 case-control studies that showed an inverse association between tea drinking and EC risk, either in the main analyses or in subgroup analyses (the association in 8 studies was statistically significant). Four studies reported ORs close to one, on both sides of the null line, which were not statistically significant. In addition, 6 other studies only stated that the results were not statistically significant, without reporting detailed results. We did not find a clear pattern of association

by geographic region. However, the majority of the inverse associations were from East-Asian countries, especially China, where mostly green tea is used.

Temperature—Results for the association of tea drinking temperature and EC were reported in 14 publications. Of these, 7 individual case-control studies, a combined analysis of 5 other case-control studies, and a prospective study found an increased risk; of these, the association was statistically significant in 8 studies. Two case-control studies reported statistically non-significant inverse associations, and 3 other studies only stated that the results were not statistically significant, without reporting crude numbers or ORs.

Coffee

We found 22 independent papers, published between 1974 and 2008, that reported on the association between coffee intake and EC (Table 2). These included 17 individual case-control studies, a pooled analysis of 5 case-control studies, a pooled analysis of 2 case-control studies, and 3 cohort studies. Most reports (n = 14) were from the United States or Europe. Most studies included between 100 and 400 EC cases.

Amount consumed—Most studies (n = 20) reported one of the indicators of amount consumed and EC. Four case-control studies showed statistically non-significant positive associations. Seven studies reported an inverse association between coffee drinking and EC risk, of which only 1 prospective study from Japan and a combined analysis of 2 case-control studies from Italy and Switzerland showed statistically significant results for drinking 3 or more cups per day. Four other studies, including 2 prospective studies, showed non-significant results with ORs close to one, on both sides of null line. The remaining 5 studies only reported that the results were not statistically significant.

Temperature—Six individual case-control studies and a pooled analysis of 5 other case-control studies reported on temperature of coffee consumption in relation to EC risk. Of these, 2 individual studies and the pooled analysis showed an increased risk with drinking hot or very hot coffee, either in the main analyses or in subgroup analyses; 2 studies suggested statistically non-significant inverse associations, and 2 other studies only reported that the results were not statistically significant.

Maté

We found 4 independent papers, including 3 individual case-control studies and a combined analysis of 5 other case-control studies. These reports were published between 1985 and 2008 and all came from South American countries (Table 3).

Amount consumed—All reports showed significantly increased EC risk with amount consumed, with approximately 3-fold higher risk in those in the highest category of consumption compared to those who did not consume maté. The pooled analysis of the case-control studies found that amount per day and duration of drinking both increased risk.

Temperature—Three of these publications reported on the association of temperature of maté drinking and EC risk and all showed significant increased risk with increasing temperature. Mutual adjustment for temperature and amount in the pooled analysis suggested that amount and temperature of use were independent risk factors for EC.

High temperature food or other drinks

We found 19 publications (17 individual case-control studies, a combined analysis of 5 other case-control studies, and 1 prospective study) that presented results on the association of

consumption of high temperature food, other drinks, or all beverages combined with risk of EC (Table 4). The reports were published between 1974 and 2008, and the studies were conducted in South Americas, Europe, Africa, and South and East Asia. For this category, we only present results on temperature.

Temperature—In all, 11 individual case-control studies and the combined analysis showed positive associations (11 were statistically significant), whereas 2 case-control studies found statistically non-significant inverse associations. Two case-control studies and the prospective study reported ORs close to one, on both sides of null line, with no statistically significant association. Two other studies only stated that the results were not statistically significant, without reporting crude numbers or ORs.

Summary of all hot foods and drinks

A summary of the associations between amount or temperature of consumed tea, coffee, or maté, or consumption of high temperature food or other beverages, and risk of EC is presented in Table 5.

Discussion

In this systematic review, we collected the published literature on the association between consuming tea, coffee, maté, or other high-temperature beverages or foods and risk of EC. We analyzed the results for amount consumed and temperature of drinking separately. For tea and coffee, there was little evidence that the amount consumed was associated with EC risk, but the majority of the publications reported statistically significant increased risks associated with higher temperature of use. For maté, individual studies and the combined analyses showed increased risk of EC associated with both amount consumed and with temperature of drinking, and these two seemed to be independent risk factors. For other hot foods and drinks, the majority of studies showed higher risk of EC associated with higher temperature of use.

There are several limitations to making definitive conclusions about the association of amount or temperature of these drinks with EC risk. Some of these limitations are due to the design of the published studies (retrospective nature of the data, subjective questions, incomplete questionnaires, and lack of information on histologic type of EC) and others are due to incomplete analysis or reporting of the data. The large majority of the reports were based on retrospective case-controls studies, so the data might have been subject to interviewer bias or recall bias. This is further complicated by asking subjective questions, such as “how hot do you drink your tea?”, which can be particularly prone to such biases. To our knowledge, very few published studies have actually measured the actual temperature of tea, coffee, or maté drinking (reviewed in ref 22). Obtaining data on amount or frequency of drinking per day, total duration of drinking, sip size (or an indicator of this), and temperature of drinking are important. Unfortunately, many of the published studies did not collect data on several of these factors or did not report the results; studying the effect of hot temperature drinks was not the main aim of most of these studies. Furthermore, few studies adjusted the results of drinking temperature for amount consumed and vice versa, and many studies failed to adjust the results for other confounders. Also, many studies combined the results for several types of beverages (e.g., tea and coffee), which made it difficult to look at effects of these drinks separately; this problem was more prominent for black and green tea use. A number of studies reported that the results were not significant, but provided no counts or ORs (95% CIs). Such incomplete reporting prohibits use of the results in future meta-analyses. There is a large body of evidence suggesting that the risk factors for ESCC and EAC may be different. For example, there is strong evidence for a positive dose-response

association between body mass index and risk of EAC,100 whereas several studies have reported an inverse association between body mass index and risk of ESCC.99 Nevertheless, few studies reported the results for ESCC and EAC separately.

Because of large heterogeneity in design and reporting, and also incomplete reporting in several studies, we conducted a systematic review but avoided formal combination of the results as a meta-analysis. However, many of the limitations mentioned above can be addressed in future studies. Using a standard questionnaire across studies would help in collecting uniform data. Actual measurement of tea temperature is already being conducted in a cohort study in Iran,22،101 where very high rates of ESCC are seen.102،103 In this study, two simultaneous cups of tea are poured; one is given to the study subject and a thermometer is put in the second cup.101 At intervals of 5°C (75°C, 70°C, 65°C, …) the subject is asked to sip the tea and tell the interviewer whether this is the usual temperature at which he/she drinks tea. This method for measuring tea temperature had shown a very good repeatability 101 and can be used in future studies, especially in areas with very high risk of EC. Measurement of relevant metabolites in biological samples might be helpful to validate the self-reported data on amount of consumed beverages.

Thermal injury may cause EC via both direct and indirect pathways. Inflammatory processes associated with chronic irritation of the esophageal mucosa by local hyperthermia might stimulate the endogenous formation of reactive nitrogen species, and subsequently, nitrosamines.104 This hypothesis is supported by high rates of somatic G > A transitions in CpG dinucleotides of the *TP53* gene in ESCC tumor samples from areas in which drinking hot beverages is considered an important risk factor for ESCC;105–108 these mutations may indicate increased nitric oxide synthase activity in tumors.109 Thermal injury can also impair the barrier function of the esophageal epithelium, which may increase the risk of damage from exposure to intra-luminal carcinogens.110 An association between hot drinks and precancerous lesion of the esophagus has also been reported.111،112 Nevertheless, further prospective studies are indicated to investigate the association between high-temperature beverage or food consumption and risk of EC.

Chemical composition of tea, coffee, and maté has been reviewed in detail elsewhere.21 Some constituents of tea, coffee, and maté may have anti-carcinogenic properties; for example, flavonoids and caffeine show antioxidant activities.12،13،113 Composition of the beverages may change during production procedures; for example, in production of black tea and coffee, fermentation of tea leaves reduces a large percentage of some flavonoids, 12،13 and severe roasting of coffee beans can considerably reduce their total cholorogenic acid content.21 Furthermore, black tea and maté may acquire some potentially carcinogenic contaminants, such as polycyclic aromatic hydrocarbons (PAH) and mycotoxins, when being processed;114،115 high levels of PAH exposure has been reported among black tea and maté drinkers.116،117 Both black and green tea drinking may increase plasma antioxidant activity in humans.118 On the other hand, in a clinical trial in Linxian and Huixian, China, decaffeinated green tea was not shown to have beneficial effects in alleviating esophageal precancerous lesions and abnormal cell proliferation patterns after 11 years of follow-up.119 Other hot foods and drinks, such as foods containing processed meat and preserved fish,120 may potentially have carcinogenic chemical constituents. However, most studies used in this review compared the intake of the same food in higher versus lower temperatures. Therefore, unless higher temperature results in further formation or release of carcinogens, the results should not be confounded by chemical constituents, and any association should be attributed to thermal injury.

Although the number of studies that reported inverse associations between amount of tea or coffee consumed is higher than the number of studies that showed positive associations, the

overall results are mixed. Despite cancer preventive activity of tea in experimental studies, it is not clear why epidemiological studies have not consistently shown an inverse association between tea drinking and risk of EC. Furthermore, all of the epidemiological studies that showed a statistically significant inverse association between tea drinking and risk of EC were case-control studies. In case-control studies, a possible reduction in tea intake by EC cases following their symptoms might lead to under-reporting of past tea consumption, and subsequently, resulting in spurious inverse associations. Tea and coffee contain several compounds other than flavonoids21 and may have some contaminants, which their interactions and their complex metabolisms might alter the protective effect of the individual compounds.17 It has also been suggested that flavonoids, or other anti-oxidants, in high doses may act as pro-oxidant that can generate free radicals, which may lead to DNA damage and finally irreversible pre-neoplastic lesions (reviewed in refs. 8,121).

In conclusion, there was little evidence for an association between EC risk and amount of tea or coffee consumed but the results suggest an increased risk of EC associated with higher drinking temperature. Amount, duration, and temperature of maté intake were all associated with higher EC risk, but number of the studies that investigated these associations was limited. For other hot foods and drinks, there was some evidence showing increased risk with higher temperature. Overall, the available results strongly suggest that high-temperature beverage drinking increases the risk of EC. Future studies will require standardized strategies that allow for combining data, and results should be reported by histological subtypes of EC.

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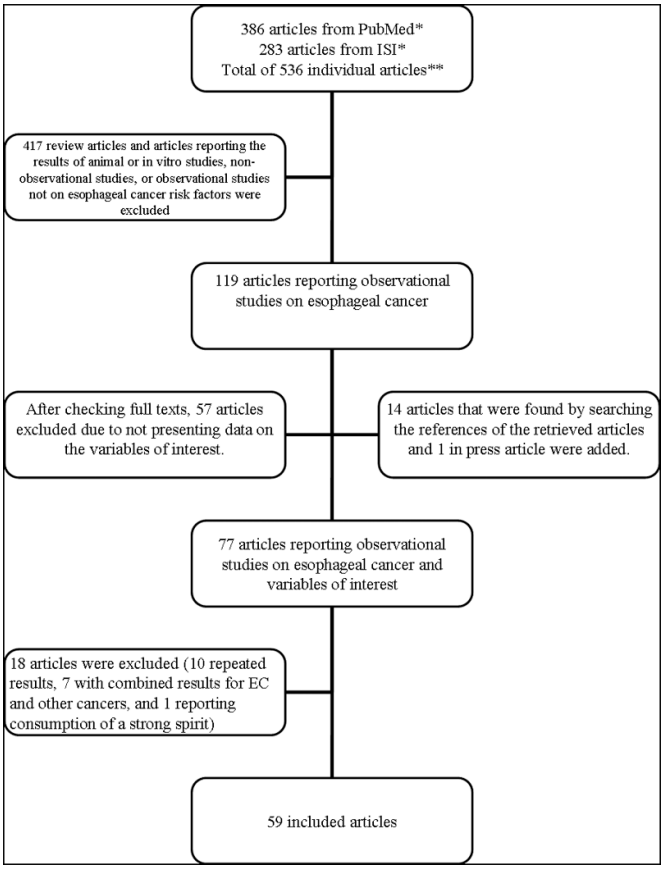

Figure 1.
A summary of the search process

Table 1

A summary of studies on the association between tea consumption and risk of esophageal cancer

First author; year of publication (Country; period of study)	Case / control[a]	Amount, frequency, duration, or status of tea drinking	OR/RR/HR (95% CI)[b]	Tea drinking temperature	OR/RR/HR (95% CI)[b]	Comments (1. Study design; 2. histological subtypes of EC, if available; 3. matching criteria, if applicable; and 4. the adjustments in statistical models that were done for the presented results)
De Jong; 197441 (Singapore; 1970–1972)	131 / 665 (95 / 465 men and 36 / 200 women)	**Tea drinking frequency (men)** Not daily Daily **(women)** Not daily Daily	1 0.99 (NS/NR) 1 0.82 (NS/NR)	**(men)** Other Burning hot **(women)** Other Burning hot	1 2.96 (P <0.01) 1 2.28 (NS/NR)	**1** Hospital-based case-control study **2** EC was confirmed histologically in 82% of cases, all were ESCC **3** Controls were individually matched for age and sex **4** Results were adjusted for dialect group
Cook-Mozaffari; 197942 (Iran; 1975–1976)	344 / 688 (217 / 434 men and 127 / 254 women)	**Tea drinking amount**	NS/NR	**(men)** Other Hot tea **(women)** Other Hot tea	1 1.72 (P <0.01) 1 2.17 (P <0.01)	**1** Population-based case-control study **2** EC was mainly diagnosed on the basis of clinical symptoms, radiological signs, and results of the follow-up study. EC was confirmed histologically in 4% of cases **3** Controls were individually matched for age, sex, place of residence, and in high incidence areas, the first language of the subjects **4** The matched results were adjusted for several socioeconomic indicators (e.g. education), fruit and vegetable intake, and tobacco use
Van Rensburg; 198543 (South Africa; 1978–1981)	211 / 211	**Tea with milk drinking amount**	NS/NR	-	-	**1** Hospital-based case-control study **2** EC diagnosis method was not reported **3** Controls were individually matched for age and urban-rural background **4** Results came from stepwise multivariate analyses (with adjustment for age effects), which included tobacco and alcohol use and some SES indicators Note: the frequency of tea with milk drinking was associated with increased risk of EC (P = 0.01) in crude analyses
Notani; 198744 (India; 1976–1984)	236 / 392	**Tea drinking frequency (vs. hospital controls)** ≤ 2 cups/day 2+ cups/day **(vs. pupulation controls)** ≤ 2 cups/day 2+ cups/day	1 1.18 (0.8–1.8) 1 2.39 (1.5–3.9)	-	-	**1** Case-control study with only male participants; hospital-based cases, 215 hospital-based and 177 population-based controls **2** EC diagnosis method was not reported **3** No other matching was reported

First author; year of publication (Country; period of study)	Case / control[a]	Amount, frequency, duration, or status of tea drinking	OR/RR/HR (95% CI)[b]	Tea drinking temperature	OR/RR/HR (95% CI)[b]	Comments (1. Study design; 2. histological subtypes of EC, if available; 3. matching criteria, if applicable; and 4. the adjustments in statistical models that were done for the presented results)
						4 Results were adjusted for age and tobacco use
Yu; 198845 (USA; 1975–1981)	275 / 275	**Tea drinking frequency** and the manner of drinking (sipped or gulped)	NS/NR	Temperature	NS/NR	**1** Population-based case-control study **2** All cases were histologically confirmed EC (88% ESCC, 8% EAC, 4% unspecified carcinoma) **3** Controls were individually matched for age, sex, race, and neighborhood **4** Multivariate analyses were used in the study, details of the adjustments for tea drinking variables were not reported
Brown; 198846 (USA; 1982–1984 for 'incidence series',1977–1981 for 'mortality series')	207 / 422	**Tea drinking amount (both regular tea and local herbal teas)**	NS/NR	Temperature	NS/NR	**1** The study participants were recruited with 2 methods: a hospital-based case-control study (incidence series) and a population-bases case-control study with the outcome of EC death (mortality series) **2** All cases in the incidence series were histologically confirmed EC (85% ESCC, 13% EAC, 2% carcinosarcoma), similar detailed information on histology was not ascertained for the cases in the mortality series **3** Controls were individually matched for age, race, hospital for incidence series and age, race, county of residence and year of death for mortality series **4** Results were adjusted for tobacco and alcohol use
Graham; 199047 (USA; 1975–1986)	178 / 174	**Tea drinking frequency** Nil 1–15 cups/month 16–28 cups/month 29–280 cups/month	1 1.12 (0.60–2.09) 1.21 (0.68–2.17) 0.76 (0.41–1.41)	-	-	**1** Case-control study; hospital-based cases, population-based controls **2** All cases were histologically confirmed EC; no information about EC subtypes was reported **3** Controls were individually matched for age, sex, and neighborhood **4** Results were adjusted for age, sex, education, and tobacco and alcohol use
La Vecchia; 199248 (Italy; 1983–1990)	294 / 6147	**Tea drinking status** Non-drinkers Drinkers	1 1.0 (0.7–1.4)	-	-	**1** Hospital-based case-control study (the data were derived from an integrated series of case-control studies based on a network **2** All cases were histologically confirmed EC; no information about EC subtypes was reported

First author; year of publication (Country; period of study)	Case / control[a]	Amount, frequency, duration, or status of tea drinking	OR/RR/HR (95% CI)[b]	Tea drinking temperature	OR/RR/HR (95% CI)[b]	Comments (1. Study design; 2. histological subtypes of EC, if available; 3. matching criteria, if applicable; and 4. the adjustments in statistical models that were done for the presented results)
						3 No matching was reported **4** Results were adjusted for age, sex, area of residence, education, smoking, and coffee use
Wang, YP; 199249 (China, Shanxi; 1988–1989)	326 / 396	**Tea drinking amount**	NS/NR	-	-	**1** Case-control study; hospital-based cases, population-based controls **2** All cases were initially diagnosed by X-ray. 72% of diagnoses in the high-risk and 83% in the moderate-risk area were confirmed histologically **3** Controls were frequency matched on age, sex, and residence **4** Results were adjusted for age, sex, and farm/nonfarm occupation
Memik; 199250* (Turkey; not reported)	78 / 558	**Tea drinking frequency** 0–3 glasses/day 4–10 glasses/day 11+ glasses/day	1 0.28 (0.16–0.46) 0.25 (0.11–0.59)	-	-	**1** Hospital-based case-control study **2** EC diagnosis method was not reported **3** Controls were matched for age **4** No adjustment was reported
Hu; 199451 (China; 1985–1989)	196 / 392	**Tea drinking amount** Nil 50–1500 g/year 1501–3000 g/year 3000+ g/year **Strength of tea** Non-drinkers Weak Medium Strong	1 1.2 (0.7–2.1) 1.8 (1.04–3.3) 3.9 (1.7–9.1) 1 0.8 (0.3–2.0) 1.1 (0.6–1.9) 2.5 (1.4–4.3)	-	-	**1** Hospital-based case-control study **2** All cases were histologically confirmed EC; no information about EC subtypes was reported **3** Controls were individually matched for age, sex, and area of residence **4** The matched results were adjusted for tobacco and alcohol use, income, and occupation
Gao, YT; 199452 (China; cases were ascertained during 1990–1993, controls were ascertained during 1986–1987)	902 / 1552	**Green tea** **Amount (men)** Non-tea drinker Tea drinker 1–199 g/month 200+ g/month **(women)** Non-tea drinker Tea drinker 1–149 g/month 150+ g/month **Amount × duration (men)**	1 0.80 (0.58–1.09) 0.79 (0.53–1.17) 0.79 (0.56–1.13) 1 0.50 (0.30–0.83) 0.77 (0.39–1.53) 0.34 (0.17–0.69) 1 0.73 (0.48–1.11) 0.83 (0.59–1.16) 1	See Table 4.		**1** Population-based case-control study **2** EC was confirmed histologically in 81% of cases (of them: 83% ESCC, 7% EAC, 3% other, 7% unspecified) **3** Controls were frequency matched to cases with 4 types of GI cancer cases in the original study (in accordance with the age and sex distribution among the cases) **4** Results were adjusted for age, education, birthplace, and tobacco and alcohol use.

First author; year of publication (Country; period of study)	Case / control[a]	Amount, frequency, duration, or status of tea drinking	OR/RR/HR (95% CI)[b]	Tea drinking temperature	OR/RR/HR (95% CI)[b]	Comments (1. Study design; 2. histological subtypes of EC, if available; 3. matching criteria, if applicable; and 4. the adjustments in statistical models that were done for the presented results)
		Non-tea drinker 1–3499 (g/month × years) 3500+ (g/month × years) **(women)** Non-tea drinker 1–3499 3500+ ***Never smoker/drinkers*** **Amount (men)** Non-tea drinker Tea drinker 1–199 g/month 200+ g/month **(women)** Non-tea drinker Tea drinker 1–149 g/month 150+ g/month **Amount × duration (men)** Non-tea drinker 1–3499 (g/month × years) 3500+ (g/month × years) **(women)** Non-drinker 1–3499 (g/month × years) 3500+ (g/month × years)	0.74 (0.40–1.38) 0.29 (0.13–0.65) 1 0.43 (0.22–0.86) 0.33 (0.14–0.80) 0.62 (0.25–1.54) 1 0.40 (0.20–0.77) 0.70 (0.31–1.58) 0.17 (0.05–0.58) 1 0.24 (0.08–0.72) 0.63 (0.29–1.41) 1 0.66 (0.32–1.37) 0.07 (0.01–0.54)			Note: In the analyses for men and women, the numbers of cases/controls were 417 / 654 and 242 / 658, respectively. In the analyses for never smoker/never alcohol drinker men and women, the number of cases/controls were 69 / 192 and 184 / 564, respectively.
Srivastava; 199553 (India; not reported)	75 / 75	-	-	Hot Very hot	1 NS/NR	**1** Hospital-based case-control study **2** All cases were histologically confirmed EC (85% ESCC, 15% EAC) **3** No matching was reported **4** In the stepwise multivariate analysis, tea temperature variable was dropped out because it did not have any significant association with the risk (in the final model only vegetable intake and alcohol use had significant associations with the risk) Note: in the crude analyses, drinking very hot tea vs. hot tea was associated with increased risk of EC (OR= 2.63, 95% CI 1.13–6.19)
Inoue; 199854 (Japan; 1990–1995)	185 / 21128	**Green tea frequency** Rarely Occasionally 1–3 cups/day 4-6 cups/day 7+ cups/day	1 1.02 (0.50–2.10) 1.07 (0.58–2.00) 0.96 (0.50–1.83) 1.14 (0.55–2.34) 1	-	-	**1** Hospital-based case-control study **2** All cases had histologically confirmed EC. No information about EC subtypes was reported **3** Controls were non-cancer outpatients; no matching was reported

First author; year of publication (Country; period of study)	Case / control[a]	Amount, frequency, duration, or status of tea drinking	OR/RR/HR (95% CI)[b]	Tea drinking temperature	OR/RR/HR (95% CI)[b]	Comments (1. Study design; 2. histological subtypes of EC, if available; 3. matching criteria, if applicable; and 4. the adjustments in statistical models that were done for the presented results)
		Black tea frequency Rarely Occasionally Daily	0.44 (0.26–0.74) 1.03 (0.53–2.00)			**4** Results were adjusted for age, sex, year and season at hospital-visit, tea and coffee intake, tobacco and alcohol use, regular physical exercise, fruit, rice, and beef intake
Kinjo; 199855 (Japan; 1966–1981)	440 / 220272	-	-	**Green tea** Non hot Hot	1 1.5 (1.1–1.9)	**1** Cohort study; the outcome was EC death within the cohort **2** EC diagnosis method was not reported **3** Controls were the non-cancer cohort members. No matching was reported **4** Results were adjusted for age, sex, prefecture, occupation, vegetable intake, and tobacco and alcohol use
Gao, CM; 199956 (China, 1995)	81 / 234	**Tea drinking amount** Nil 1–199 g/month 200+ g/month	1 0.63 (0.28–1.42) 0.42 (0.19–0.95)	-	-	**1** Population-based case-control study **2** All cases had histologically confirmed EC. No information about EC subtypes was reported **3** Controls were individually matched to EC and stomach cancer cases for age, sex, and neighborhood. For the analysis, the enrolled controls for the 2 types of cancer were combined **4** Results were adjusted for age and sex
Tao; 199957 (China; 1984–1988)	71 / 1122	**Tea drinking frequency** < 1 cup/day 1+ cup/day	1 0.70 (0.39–1.25)	-	-	**1** Population-based case-control within a cohort study with only male participants; the outcome was EC death within the cohort **2** EC diagnosis method was not reported **3** Controls were the 1% of total non-cancer cohort members, stratified by community. No other matching was reported **4** Results were adjusted for age, medical history, occupational history, pesticide exposure, lifestyle factors, dietary habits, education and monthly food expenses

First author; year of publication (Country; period of study)	Case / control[a]	Amount, frequency, duration, or status of tea drinking	OR/RR/HR (95% CI)[b]	Tea drinking temperature	OR/RR/HR (95% CI)[b]	Comments (1. Study design; 2. histological subtypes of EC, if available; 3. matching criteria, if applicable; and 4. the adjustments in statistical models that were done for the presented results)
Castellsagué; 200058 (Argentina, Brazil, Uruguay, Paraguay;1985–1992)	830 / 1779	**Tea drinking status** Never-drinker Ever-drinker **Amount** Non-drinker 1–500 ml/day >500 ml/day	1 0.81 (0.62–1.06) 1 0.90 (0.67–1.20) 0.62 (0.40–0.96)	Cold/warm Hot Very hot	1 0.66 (0.35–1.25) 3.73 (1.41–9.89)	**1** A pooled analysis of 5 other hospital-based case-control studies 35–38; the results from Uruguay came from 2 studies: one from 1985 to 1988 38 and the other was an extension of that study (1989–1992) **2** Cases from Argentina, Brazil, and Uruguay had histologically confirmed ESCC; in Paraguay, a cytological or radiological diagnosis of EC was acceptable **3** Controls were individually matched for age and sex, admission to the same hospital and during the same period as the corresponding case **4** Results were adjusted for age group, sex, hospital, residency, education, tobacco and alcohol use
Bosetti; 200059 (Italy; 1992–1997)	304 / 743	**Coffee & tea frequency** ≤ 7.9 times/week 8–14.4 times/week 14.5–20.9 times/week 21.0–24.9 times/week 25+ times/week (quintiles)	1 0.91 (0.56–1.48) 0.82 (0.47–1.43) 0.91 (0.57–1.44) 0.71 (0.42–1.19)	-	-	**1** Hospital-based case-control study **2** All cases were histologically confirmed EC; only ESCC cases **3** Controls were frequency matched for age, sex, year of interview, area of residence **4** Results were adjusted for age, sex, area of residence, education, tobacco and alcohol use, non-alcohol energy
Nayar; 200060 (India; 1994–1997)	147 / 140	-	-	Warm Hot Burning hot	1 1.11 (0.62–1.96) 1.27 (0.60–2.69)	**1** Hospital-based case-control study **2** All cases had histologically confirmed EC. No information about EC subtypes was reported **3** Controls were individually matched for age, sex, and socioeconomic status **4** For tea temperature variable, only crude analysis was done
Cheng; 200061 (England, Scotland; 1993–1996)	74 / 74	**Tea drinking amount** Never/<1 /day ≤ 6 dcl/day 7–11 dcl/day	1 0.83 (0.26–2.63) 0.95 (0.30–3.08)	**Tea or coffee** Warm Hot	1 0.75 (0.32–1.76) 0.51 (0.18–1.45)	**1** Population-based case-control study, only female participants **2** All cases were histologically confirmed EC; only EAC cases **3** Controls were matched for age and general practice

First author; year of publication (Country; period of study)	Case / control[a]	Amount, frequency, duration, or status of tea drinking	OR/RR/HR (95% CI)[b]	Tea drinking temperature	OR/RR/HR (95% CI)[b]	Comments (1. Study design; 2. histological subtypes of EC, if available; 3. matching criteria, if applicable; and 4. the adjustments in statistical models that were done for the presented results)
		12+ dcl/day	0.49 (0.14–1.72)	Very/burning hot		**4** No adjustment for tea- or coffee-related variables
Terry; 200162 (Sweden; 1995–1997)	167 ESCC and 189 EAC / 815	-	-	**Tea or coffee (ESCC)** None, cold, lukewarm Hot Very hot **(EAC)** None, cold, lukewarm Hot Very hot	1 1.0 (0.6–1.6) 0.8 (0.4–1.8) 1 0.7 (0.5–1.1) 0.6 (0.3–1.3)	**1** Population-based case-control study **2** All cases were histologically confirmed EC (47% ESCC, 53% EAC) **3** Controls from the Sweden population register were frequency matched to resemble the age and sex distribution among the cases **4** Results were adjusted for age, sex, BMI, socioeconomic status, tobacco and alcohol use, gastro-esophageal reflux symptoms, frequency of hot beverage drinking, energy, fruit, and vegetable intake
Takezaki; 200163 (China; 1995–2000)	195 / 333	**Tea drinking amount** 0 g/month 1–149 g/month 150+ g/month	1 0.73 (0.44–1.22) 0.64 (0.36–1.15)	-	-	**1** Case-control study; hospital-based cases, population-based controls **2** All cases had histologically confirmed EC. No information about EC subtypes was reported **3** No matching was reported **4** Adjusted for age, sex, tobacco and alcohol use
Sharp; 200164 (England, Scotland; 1993–1996)	159 / 159	**Tea drinking amount** Nil/<1 dcl/day ≤ 6 dcl/day 7-11 dcl/day 12+ dcl/day	1 2.33 (0.62–8.86) 2.99 (0.85–10.56) 3.36 (0.99–11.29)	**Tea or coffee** Very/burning hot Hot Warm	1 0.75 (0.38–1.47) 0.34 (0.13–0.88)	**1** Population-based case-control study, only female participants **2** All cases were histologically confirmed EC; only ESCC cases **3** Controls were matched for age and general practice **4** Results were adjusted for slimming diet, breakfast, salad, years smoking, regular use of aspirin, aspirin centre, and temperature of tea/coffee
Ke; 200265 (China; 1997–2000)	1248 / 1248	**Congou tea** Non-drinker Drinker **(amount)** 500− g/year 10000− g/year 20000− g/year 30000+ g/year **Hot Congou tea** Non-drinker Drinker	1 0.40 (0.28–0.57) 1 0.52 (0.38–0.70) 0.44 (0.29–0.67) 0.05 (0.01–0.22) 1 0.04 (0.01–0.13) 1 0.41 (0.28–0.62) 0.57 (0.34–0.97)	-	-	**1** Hospital-based case-control study **2** All cases were histologically confirmed EC; only ESCC cases **3** Controls were individually matched for age, sex, and hospital **4** Results were adjusted for age, sex, region, occupation, income, tobacco and alcohol use, some dietary items, including fish sauce, pickled vegetable, sowbelly, fruit and vegetable intake

First author; year of publication (Country; period of study)	Case / control[a]	Amount, frequency, duration, or status of tea drinking	OR/RR/HR (95% CI)[b]	Tea drinking temperature	OR/RR/HR (95% CI)[b]	Comments (1. Study design; 2. histological subtypes of EC, if available; 3. matching criteria, if applicable; and 4. the adjustments in statistical models that were done for the presented results)
		(amount) 500− g/year 10000− g/year 20000− g/year 30000+ g/year	0.03 (0.00–0.23)			Note: Congou tea is a grade of Chinese black tea
Sun; 200266 (China; 1986–1998)	42 / 209	**Urinary tea polyphenols (epigallocatechin)** Negative Positive ≤ 0.196 mg/g creatinine > 0.196 mg/g creatinine **(epicatechin)** Negative Positive ≤ 0.311 mg/g creatinine > 0.311 mg/g creatinine **(M4)** Negative Positive ≤ 0.220 mg/g creatinine > 0.220 mg/g creatinine **(M6)** Negative Positive ≤ 0.448 mg/g creatinine > 0.448 mg/g creatinine	1 0.87 (0.38–2.02) 0.84 (0.32–2.19) 0.91 (0.36–2.31) 1 1.22 (0.48–3.10) 1.32 (0.51–3.45) 0.99 (0.32–3.04) 1 0.91 (0.44–1.89) 0.96 (0.43–2.15) 0.83 (0.32–2.14) 1 0.79 (0.38–1.66) 0.90 (0.40–2.01) 0.61 (0.22–1.65)	-	-	**1** Nested case-control study, only male participants. Urinary level of 4 tea polyphenols was measured **2** All cases were histologically confirmed EC (67% ESCC, 5% EAC, 28% other or unspecified) **3** Controls were individually matched for age, month and year of sample collection, and neighborhood of residence **4** The matched Results were adjusted for age at starting to smoke and alcohol use; the cutting points for the urinary levels were the median positive values among all control subjects Note: for subjects with an interval of four years or more between sample collection and cancer diagnosis, the ORs (95% CIs) for level of epigallocatechin for gastric cancer and gastric cancer and EC combined were 0.52 (0.28–0.97) and 0.58 (0.34–0.98), respectively
Onuk; 200267 (Turkey; 1999–2000)	44 / 100	-	-	Not hot Hot	1 8.7 (2.5–30.2)	**1** Hospital-based case-control study **2** All cases had histologically confirmed EC. No information about EC subtypes was reported **3** No matching was reported **4** It is not clear in the article but it seems the results were adjusted for tobacco use, fruit, vegetable, coffee and pickle intake, and type of bread
Gao, CM; 200268 (China; 1998–2000)	141 / 223	**Tea drinking amount** 0 g/month 1+ g/month	1 0.45 (0.26–0.78)	-	-	**1** Population-based case-control study **2** All cases had histologically confirmed EC. No information about EC subtypes was reported **3** Controls were individually matched for age, sex, and ethnicity **4** Results were adjusted for age, sex, tobacco and alcohol use, raw vegetables, pickled vegetables, fruit, meat, soybean products, GSSTT1 and GSTM1

First author; year of publication (Country; period of study)	Case / control[a]	Amount, frequency, duration, or status of tea drinking	OR/RR/HR (95% CI)[b]	Tea drinking temperature	OR/RR/HR (95% CI)[b]	Comments (1. Study design; 2. histological subtypes of EC, if available; 3. matching criteria, if applicable; and 4. the adjustments in statistical models that were done for the presented results)
Tavani; 200369 (Italy, Switzerland; 1991–1997)	395 / 1066	**Tea drinking frequency** <1 cup/day 1+ cup/day	1 0.9 (0.7–1.2)	-	-	**1** A pooled analysis of 2 hospital-based case-control studies; in the articles from the original studies the association between EC and the variables of interest were not reported **2** All cases had histologically confirmed EC. No information about EC subtypes was reported **3** No matching was reported **4** Results were adjusted for age, sex, study center, education, tobacco and alcohol use, and fruit and vegetable intake
Hung; 200470 (Taiwan; 1996–2002)	365 / 532	**Tea drinking frequency (age 20–40 years)** <1 time/week 1–6 times/week 7+ times/week **(age 40+ years)** <1 time/week 1–6 times/week 7+ times/week	1 1.0 (0.5–1.7) 0.7 (0.4–1.1) 1 0.7 (0.4–1.2) 0.5 (0.3–0.8)	-	-	**1** Hospital-based case-control study, only male participants **2** All cases were histologically confirmed EC; only ESCC cases **3** Controls were individually matched for age and hospitalization date **4** Results were adjusted for age, education, ethnicity, hospital location, tobacco, alcohol use and areca nut chewing
Chitra; 200471 (India; 1999–2000)	90 / 90	**Tea drinking frequency** ≤3 cups/day 3+ cups/day	1 3.3 (1.7–6.3)	-	-	**1** Hospital-based case-control study **2** All cases were histologically confirmed EC; only ESCC cases **3** Controls were individually matched for age and sex **4** No adjustment was reported
Yang CX; 200572 (China; 2003–2004)	185 / 185	**Tea drinking frequency** ≤ 1 time/week 2–4 times/week >4 times/week	1 0.45 (0.15–1.36) 0.57 (0.25–1.31)	-	-	**1** Case-control study; hospital-based cases, population-based controls **2** All cases had histologically confirmed EC; 179 ESCC cases and 6 EAC cases **3** Controls were individually matched for age and sex **4** The matched results were adjusted for family history of EC, occupation, tobacco and alcohol use, some dietary items, including fruit and vegetable intake, hot food, water supply, eating speed, and intake of pickled vegetables, fresh meat, processed meat, eggs and tea

First author; year of publication (Country; period of study)	Case / control[a]	Amount, frequency, duration, or status of tea drinking	OR/RR/HR (95% CI)[b]	Tea drinking temperature	OR/RR/HR (95% CI)[b]	Comments (1. Study design; 2. histological subtypes of EC, if available; 3. matching criteria, if applicable; and 4. the adjustments in statistical models that were done for the presented results)
Ishikawa; 200673 (Japan; 1984–1992 cohort 1, 1990–1997 cohort 2)	78 / 196686 person-year	**Green tea Frequency** Never/occasionally 1–2 cups/day 3–4 cups/day 5+ cups/day	**HR (95% CI)** 1 1.03 (0.46–2.28) 1.13 (0.53–2.42) 1.67 (0.89–3.16)	-	-	**1** Cohort study with only male participants; cases were EC cases within 2 cohorts, controls were non-cancer members of the 2 cohorts **2** EC diagnosis method was not reported **3** No matching was reported **4** Results were adjusted for age, tobacco and alcohol use, and coffee and black tea consumption
Wang, Z; 200674 (China; 2002–2003)	107 / 107	**Green tea** Non-drinker Drinker	1 0.13 (0.03–0.62)	-	-	**1** Population-based case-control study **2** Cases were confirmed by endoscopy, X-ray or clinical histopathology. **3** Controls were individually matched for age, sex, and residency **4** Matched results were adjusted for family history of cancer, eating fast, utensil clean up, *H. pylori* infection, and esophageal lesions
Wang, JM; 200775 (China; 2004–2006)	355 / 408	**Green tea** **Status (men)** Non-drinker Drinker **(Women)** Non-drinker Drinker **Duration (men)** Nil <30 years 30+ years **(Women)** Nil <30 years 30+ years	1 1.37 (0.95–1.98) 1 0.26 (0.07–0.94) 1 1.31 (0.85–2.03) 1.44 (0.91–2.27) 1 0.33 (0.06–1.68) 0.18 (0.02–1.54)	-	-	**1** Population-based case-control study **2** All cases were histologically confirmed EC; only ESCC cases **3** Controls were group matched for age and sex **4** Results were adjusted for age, marital status, and education Note: Cases were enrolled from patients referred to one hospital, but they accounted for 85% of all histologically confirmed ECs in the study area during the study period
Gledovic; 200776 (Serbia; 1998–2002)	102 / 102	**Tea drinking status** Non-drinkers Drinkers	1 NS/NR	-	-	**1** Hospital-based case-control study **2** All cases were histologically confirmed EC; only ESCC cases **3** Controls were individually matched for age, sex and urban-rural residence **4** The matched results were adjusted for education, occupational exposure to chemicals, family history of

First author; year of publication (Country; period of study)	Case / control[a]	Amount, frequency, duration, or status of tea drinking	OR/RR/HR (95% CI)[b]	Tea drinking temperature	OR/RR/HR (95% CI)[b]	Comments (1. Study design; 2. histological subtypes of EC, if available; 3. matching criteria, if applicable; and 4. the adjustments in statistical models that were done for the presented results)
						cancer, non-carbonated beverages consumption, and tobacco and alcohol use Note: tea consumption was inversely associated with increased risk of ESCC in crude analyses
Wu; 200877 (China; 2003–2007)	1520 / 3879	**Green tea** **High-risk area (status)** Never drinker Ever drinker Former drinker Current drinker **(duration)** Never drinker <25 years 20–34 years 35+ years **(monthly consumption)** Never drinker 1–149 g 150–249 g 250+ g **(age at tea drinking start)** Never drinker <25 years 25–34 years 35–44 years 45+ years **Low-risk area (status)** Never drinker Ever drinker Former drinker Current drinker **(duration)** Never drinker <25 years 20–34 years 35+ years **(monthly consumption)** Never drinker 1–149 g 150–249 g 250+ g **(age at tea drinking start)** Never drinker <25 years 25–34 years 35–44 years	1 1.0 (0.7–1.3) 2.2 (1.6–5.3) 0.8 (0.6–1.1) 1 1.0 (0.6–1.4) 0.9 (0.6–1.4) 1.1 (0.7–1.8) 1 1.0 (0.7–1.3) 1.0 (0.6–1.8) 1.0 (0.6–2.0) 1 0.8 (0.4–1.5) 1.2 (0.8–1.8) 1.2 (0.7–1.9) 0.8 (0.6–1.2) 1 1.3 (0.9–1.7) 4.2 (2.3–7.6) 1.1 (0.8–1.5) 1 0.8 (0.5–1.5) 1.4 (1.0–2.0) 1.1 (0.8–1.6) 1 1.1 (0.7–1.7) 1.0 (0.7–1.6) 1.6 (1.1–2.2) 1 1.2 (0.8–1.9) 1.3 (1.0–1.9) 1.1 (0.7–1.8) 0.9 (0.4–1.9)	**Green tea** **High-risk area** Never drinking Normal temperature High temperature **Low-risk area** Never drinking Normal temperature High temperature	1 1.0 (0.7-1.3) 2.2 (1.6-5.3) 1 1.3 (0.9-1.7) 4.2 (2.3-7.6)	**1** Population-based case-control study **2** Cases were confirmed by endoscopy, X-ray, or histopathology **3** Controls were frequency matched for age, sex, and county of residence **4** Results were adjusted for age, gender, education level, income 10 years before, family history of cancer, body mass index, and tobacco and alcohol use. Results for amount of green tea consumed was also adjusted for tea temperature Note: the number of cases / controls in high- and low-risk areas was 637 / 1938 and 883 / 1941, respectively. In multivariate models that did not include tea temperature, most of the green tea consumption indicators were associated with increased risk of ESCC

First author; year of publication (Country; period of study)	Case / control[a]	Amount, frequency, duration, or status of tea drinking	OR/RR/HR (95% CI)[b]	Tea drinking temperature	OR/RR/HR (95% CI)[b]	Comments (1. Study design; 2. histological subtypes of EC, if available; 3. matching criteria, if applicable; and 4. the adjustments in statistical models that were done for the presented results)
		45+ years				
Islami; in press22 (Iran;	298 / 568	**Black tea (amount- quintiles)** 0–675 ml/day 676–920 ml/day 921–1215 ml/day 1216–1725 ml/day 1726+ ml/day **Green tea (frequency)** Never, <weekly Daily, weekly	1 0.91 (0.43–1.91) 0.68 (0.34–1.37) 1.46 (0.75–2.86) 1.83 (0.93–3.59) 1 0.86 (0.38–2.09)	**Temperature** Warm or lukewarm Hot Very hot **Time interval**[**] 4+ minutes 2–3 minutes <2 minutes	1 2.07 (1.28–3.35) 8.16 (3.93–16.91) 1 2.49 (1.62–3.83) 5.41 (2.63–11.14)	**1** Hospital-based case-control study **2** All cases were histologically confirmed EC; only ESCC cases **3** Controls were individually matched for age, sex and neighborhood of residence **4** The matched results were adjusted for ethnicity, duration of residence in rural areas, education, tobacco or opium use, alcohol use, vegetable intake, and owning an automobile Black tea consumption, green tea consumption, and tea temperature were also adjusted for each other Note: Amount of tea consumed was available for 266 cases and 386 controls. The fifth quintile of black tea consumption was significantly associated with increased risk of ESCC in crude analyses (OR = 1.86, 95% CI 1.07-3.23)

Abbreviations: EAC, esophageal adenocarcinoma; EC, esophageal cancer; ESCC, esophageal squamous cell carcinoma; HR, hazard ratio; M4, 5-(3′,4′,5′-trihydroxyphenyl)-γ-valerolactone (a metabolite of epigallocatechin); M6, 5-(3′,4′-trihydroxyphenyl)-γ-valerolactone (a metabolite of epicatechin); NR, not reported; NS/NR, non-significant/not reported (when the exact OR or 95% CI was not reported but the association was reported as non-significant); OR, odds ratio; RR, relative risk; 95% CI, 95% confidence interval.

[a] Number of cases and controls in case-control or prospective studies or number of person-years of follow-up in cohort studies, if it is indicated

[b] If studies reported both crude and adjusted ORs (95% CIs), we only present the adjusted results.

[*] These studies showed crude numbers but not ORs and 95% CIs; we calculated these statistics using simple logistic regression models and present them.

[**] Time interval between pouring tea into a cup and drinking it.

Table 2

A summary of studies on the association between coffee consumption and risk of esophageal cancer

First author; year of publication (Country; period of study)	Case / control [a]	Amount, frequency, or status of coffee drinking	OR/RR/HR (95% CI) [b]	Coffee drinking Temperature	OR/RR/HR (95% CI) [b]	Comments (1. Study design; 2. histological subtypes of EC, if available; 3. matching criteria, if applicable; and 4. the adjustments in statistical models that were done for the presented results)
De Jong; 197441 (Singapore; 1970–1972)	131 / 665	**Coffee drinking frequency (men)** Not daily Daily **(women)** Not daily Daily	1 0.93 (NS/NR) 1 1.42 (NS/NR)	**(men)** Other Burning hot **(women)** Other Burning hot	1 4.22 (NR, *P* <0.01) 1 4.09 (NR, *P* <0.01)	**1** Hospital-based case-control study **2** EC was confirmed histologically in 82% of cases, all were ESCC **3** Controls were individually matched for age and sex **4** Results are adjusted for dialect group
Jacobsen; 198678 (Norway; 1967–1978)	15 / See Notes	**Coffee drinking frequency (all)** ≤2 cups/day 7+ cups/day **(men)** ≤2 cups/day 7+ cups/day	1 1.19 (*P* = 0.85) 1 0.79 (*P* = 0.88)	-	-	**1** Cohort study with 16555 participants at baseline **2** EC diagnosis method was not reported **3** Mortality rates in the cohort were compared expected rates **4** Results for all cases were stratified by sex, age, and residence. Results for men were stratified for age, residence, and smoking Note: Coffee drinking frequency was categorized as ≤2, 3–4, 5–6, and 7+ cups/day; RR was presented only for 7+ vs. ≤2 cups/day groups, for which the number of cases were 3 and 4, respectively (the number of male cases were 1 and 1, respectively)
Yu; 198845 (USA; 1975–1981)	275 / 275	**Coffee drinking frequency**, the manner of drinking (sipped or gulped), and coffee type (caffeinated or decaffeinated)	NS/NR	Temperature	NS/NR	**1** Population-based case-control study **2** All cases were histologically confirmed EC (88% ESCC, 8% EAC, 4% unspecified carcinoma) **3** Controls were individually matched for age, sex, race, and neighborhood **4** Multivariate analyses were used in the study, details of the adjustments for tea drinking variables were not reported
Brown; 198846 (USA; 1982–1984 for ‘incidence series’,1977–1981 for ‘mortality series’)	207 / 422	**Coffee drinking amount**	NS/NR	Temperature	NS/NR	**1** The study participants were recruited with 2 methods: a hospital-based case-control study (incidence series) and a population-bases case-control study with the outcome of EC death (mortality series) **2** In the incidence series, all cases were histologically confirmed EC (85% ESCC, 13% EAC, 2%

First author; year of publication (Country; period of study)	Case / control [a]	Amount, frequency, or status of coffee drinking	OR/RR/HR (95% CI) [b]	Coffee drinking Temperature	OR/RR/HR (95% CI) [b]	Comments (1. Study design; 2. histological subtypes of EC, if available; 3. matching criteria, if applicable; and 4. the adjustments in statistical models that were done for the presented results)
						carcinosarcoma); detailed information on histology was not ascertained for the cases in the mortality series **3** Controls were individually matched for age, race, hospital, and county of residence **4** Results were adjusted for study series, tobacco and alcohol use
La Vecchia; 198979 (Italy; 1983–1988)	209 / 1944	**Coffee drinking frequency** 0–1 cup/day 2 cups/day 3+ cups/day	1 0.90 (NS) 0.98 (NS)	-	-	**1** Hospital-based case-control study **2** All cases were histologically confirmed EC. No information about EC subtypes was reported **3** No matching was reported **4** Results were adjusted for age, sex, social class, education, marital status, and tobacco and alcohol use
Graham; 199047 (USA; 1975–1986)	178 / 174	**Coffee drinking amount**	NS/NR	-	-	**1** Case-control study; hospital-based cases, population-based controls **2** All cases were histologically confirmed EC. No information about EC subtypes was reported **3** Controls were individually matched for age, sex, and neighborhood **4** Results are adjusted for age, sex, education, and tobacco and alcohol use
Memik; 199250 (Turkey; not reported)	78 / 610	**Coffee drinking amount**	NS/NR	-	-	**1** Hospital-based case-control study **2** EC diagnosis method was not reported **3** Controls were matched for age **4** No adjustment was reported
Garidou; 199680 (Greece; 1989–1991)	43 ESCC and 56 EAC / 200	**Coffee drinking frequency** **(ESCC)** 1 cup/day more **(EAC)** 1 cup/day more	1.15 (0.84–1.58) 1.11 (0.86–1.43)	-	-	**1** Hospital-based case-control study **2** All cases had histologically confirmed EC (43% ESCC, 57% EAC) **3** Controls were individually Matched for age and sex **4** Results are adjusted for age, sex, birthplace, education, height, analgesics, coffee drinking, tobacco and alcohol use, and energy intake

First author; year of publication (Country; period of study)	Case / control [a]	Amount, frequency, or status of coffee drinking	OR/RR/HR (95% CI) [b]	Coffee drinking Temperature	OR/RR/HR (95% CI) [b]	Comments (1. Study design; 2. histological subtypes of EC, if available; 3. matching criteria, if applicable; and 4. the adjustments in statistical models that were done for the presented results)
						Note: The OR values here mean that how much the risk was increased when drinking one more cup per day
Inoue; 199854 (Japan; 1990–1995)	185 / 21128	**Coffee drinking frequency** Rarely Occasionally 1–2 cups/day 3+ cups/day	1 0.82 (0.51–1.31) 0.77 (0.52–1.12) 0.79 (0.46–1.36)	-	-	**1** Hospital-based case-control study **2** All cases had histologically confirmed EC. no information about EC subtypes was reported **3** Controls were non-cancer outpatients; No matching was reported **4** Results are adjusted for age, sex, tea and coffee intake, tobacco and alcohol use, regular physical exercise, fruit, rice, beef intake, and year and season at first hospital-visit
Castellsagué; 200058 (Argentina, Brazil, Uruguay, Paraguay; 1986–1992)	830 / 1779	**Coffee drinking (status)** Never-drinker Ever-drinker **(amount)** Non-drinker 1–500 ml/day >500 ml/day **Coffee with milk (status)** Never-drinker Ever-drinker **(amount)** Non-drinker 1–500 ml/day >500 ml/day	1 1.04 (0.83–1.30) 1 0.96 (0.74–1.24) 1.26 (0.88-1.81) 1 1.15 (0.94–1.42) 1 1.12 (0.90–1.40) 1.31 (0.89–1.95)	**Coffee** Cold/warm Hot Very hot **Coffee with milk** Cold/warm Hot Very hot	1 0.54 (0.33–0.87) 1.01 (0.52–1.98) 1 0.89 (0.62–1.29) 2.29 (1.37–3.81)	**1** A pooled analysis of 5 other hospital-based case-control studies 35–38; the results from Uruguay came from 2 studies: one from 1985 to 1988 38 and the other was an extension of that study (1989–1992) **2** Cases from Argentina, Brazil, and Uruguay had histologically confirmed ESCC; in Paraguay, a cytological or radiological diagnosis of EC was acceptable **3** Controls were individually matched for age and sex, admission to the same hospital and during the same period as the corresponding case **4** Results are adjusted for age group, sex, hospital, residency, education, tobacco and alcohol use
Bosetti; 200059 (Italy; 1992–1997)	304 / 743	**Coffee & tea frequency** ≤ 7.9 times/week 8–14.4 times/week 14.5–20.9 times/week 21.0–24.9 times/week 25+ times/week (quintiles)	1 0.91 (0.56–1.48) 0.82 (0.47–1.43) 0.91 (0.57–1.44) 0.71 (0.42–1.19)	-	-	**1** Hospital-based case-control study **2** All cases were histologically confirmed EC; only ESCC cases **3** Controls were frequency matched for age, sex, year of interview, area of residence **4** Results were adjusted for age, sex, area of residence, education, tobacco and alcohol use, non-alcohol energy
Terry; 200081 (Sweden; 1994–1997)	185 / 815	**Coffee drinking frequency** 0–2 cups/day 2–4 cups/day 4–7 cups/day	1 0.8 (0.5–1.4) 0.9 (0.5–1.5) 0.8 (0.5–1.4)	-	-	**1** Population-based case-control study **2** All cases were histologically confirmed EC; only EAC cases

First author; year of publication (Country; period of study)	Case / control [a]	Amount, frequency, or status of coffee drinking	OR/RR/HR (95% CI) [b]	Coffee drinking Temperature	OR/RR/HR (95% CI) [b]	Comments (1. Study design; 2. histological subtypes of EC, if available; 3. matching criteria, if applicable; and 4. the adjustments in statistical models that were done for the presented results)
		>7 cups/day (quartiles)				**3** Controls from the Sweden population register were frequency matched to resemble the age and sex distribution among the cases **4** Results are adjusted for age, sex, BMI, socioeconomic status, tobacco and alcohol use, use of antacids, energy, fruit, and vegetable intake
Cheng; 200061 (England, Scotland; 1993–1996)	74 / 74	**Coffee drinking amount** Never/<1 /day ≤ 3 dcl 4–7 dcl 8+ dcl	1 0.65 (0.27–1.53) 1.62 (0.53–4.94) 1.95 (0.68–5.57)	**Tea or coffee** Warm Hot Very/burning hot	1 0.75 (0.32–1.76) 0.51 (0.18–1.45)	**1** Population-based case-control study, only female participants **2** All cases were histologically confirmed EC; only EAC cases **3** Controls were matched for age and general practice **4** No adjustment for tea- or coffee-related variables
Terry; 200162 (Sweden; 1995–1997)	167 ESCC and 189 EAC / 815	-	-	**Tea or coffee** **(ESCC)** None, cold, lukewarm Hot Very hot **(EAC)** None, cold, lukewarm Hot Very hot	1 1.0 (0.6–1.6) 0.8 (0.4–1.8) 1 0.7 (0.5–1.1) 0.6 (0.3–1.3)	**1** Population-based case-control study **2** All cases were histologically confirmed EC (47% ESCC, 53% EAC) **3** Controls from the Sweden population register were frequency matched to resemble the age and sex distribution among the cases **4** Results were adjusted for age, sex, BMI, socioeconomic status, tobacco and alcohol use, gastro-esophageal reflux symptoms, frequency of hot beverage drinking, and energy, fruit, and vegetable intake
Sharp; 200164 (England, Scotland; 1993–1996)	159 / 159	-	-	**Tea or coffee** Very/burning hot Hot Warm	1 0.75 (0.38–1.47) 0.34 (0.13–0.88)	**1** Population-based case-control study, only female participants **2** All cases were histologically confirmed EC; only ESCC cases **3** Controls were matched for age and general practice **4** Results were adjusted for slimming diet, breakfast, salad, years smoking, regular use of aspirin, aspirin centre, and temperature of tea/coffee
Onuk; 200267 (Turkey; 1999–2000)	44 / 100	**Coffee drinking amount** Low High	1 0.8 (0.3–1.6)	-	-	**1** Hospital-based case-control study **2** All cases had histologically confirmed EC. No information about EC subtypes was reported

First author; year of publication (Country; period of study)	Case / control [a]	Amount, frequency, or status of coffee drinking	OR/RR/HR (95% CI) [b]	Coffee drinking Temperature	OR/RR/HR (95% CI) [b]	Comments (1. Study design; 2. histological subtypes of EC, if available; 3. matching criteria, if applicable; and 4. the adjustments in statistical models that were done for the presented results)
						3 No matching was reported **4** It is not clear in the article but it seems the results were adjusted for tobacco use, fruit, vegetable, coffee and pickle intake, and type of bread
Tavani; 200369 (Italy, Switzerland; 1991–1997)	395 / 1066	**Coffee drinking frequency** ≤1 cup/day >1–2 cup/day >2–3 cup/day 3+ cup/day **Decaffeinated coffee** <1 cup/day 1+ cup/day	1 1.1 (0.8–1.6) 0.9 (0.6–1.3) 0.6 (0.4–0.9) 1 0.6 (0.2–1.5)	-	-	**1** A pooled analysis of 2 hospital-based case-control studies; in the articles from the original studies the association between EC and the variables of interest were not reported **2** All cases had histologically confirmed EC. No information about EC subtypes was reported **3** No matching was reported **4** Results were adjusted for age, sex, study center, education, tobacco and alcohol use, and fruit and vegetable intake
Hung; 200470 (Taiwan; 1996–2002)	365 / 532	**Coffee drinking frequency (age 20–40 years)** <1 time/week 1+ times/week **(age 40+ years)** <1 time/week 1+ times/week	1 0.7 (0.4–1.2) 1 0.7 (0.4–1.2)			**1** Hospital-based case-control study, only male participants **2** All cases were histologically confirmed EC; only ESCC cases **3** Controls were individually matched for age, and hospitalization date **4** Results were adjusted for age, education, ethnicity, hospital location, tobacco, alcohol use and areca nut chewing
Ishikawa; 200673 (Japan; 1984–1992 cohort 1, 1990–1997 cohort 2)	78 / 196686 person-year	**Coffee drinking frequency** Never drinkers 1–2 cups/day 3+ cups/day	1 0.63 (0.32–1.27) 0.94 (0.36–2.45)	-	-	**1** Cohort study with only male participants; cases were EC cases within 2 cohorts, controls were non-cancer members of the 2 cohorts **2** EC diagnosis method was not reported **3** No matching was reported **4** Results were adjusted for age, tobacco and alcohol use, and green tea and black tea consumption
Gledovic; 200776 (Serbia; 1998–2002)	102 / 102	**Coffee ever drinking and amount**	NS/NR	-	-	**1** Hospital-based case-control study **2** All cases were histologically confirmed EC; only ESCC cases **3** Controls were individually matched for age and sex

First author; year of publication (Country; period of study)	Case / control [a]	Amount, frequency, or status of coffee drinking	OR/RR/HR (95% CI) [b]	Coffee drinking Temperature	OR/RR/HR (95% CI) [b]	Comments (1. Study design; 2. histological subtypes of EC, if available; 3. matching criteria, if applicable; and 4. the adjustments in statistical models that were done for the presented results)
						4 The matched results were adjusted for education, occupational exposure to chemicals, family history of cancer, and tobacco and alcohol use Note: Coffee consumption with frequency of more than 3 cups/day was associated with increased risk of ESCC in crude analyses
Rossini; 200882* (Brazil; 1995–2000)	36 / 290	**Coffee drinking frequency** <5 times a week 5+ times a week	1 1.89 (0.43–8.27)	-	-	**1** Hospital-based case-control study. Cases were head and neck cancer cases with second primary ESCC. Controls were head and neck cancer cases without second primary ESCC **2** All cases were histologically confirmed EC; only ESCC cases **3** No matching was reported **4** No adjustment was reported
Naganuma; 200883 (Japan; 1990–2003)	112 / 495138 person-year	**Coffee drinking frequency** Never Occasionally 1+ cup/day	1 0.56 (0.35–0.90) 0.60 (0.37–0.97)	-	-	**1** Cohort study **2** EC diagnosis method was not reported **3** No matching was reported **4** Results were adjusted for age, sex, BMI, tobacco and alcohol use, fruit and vegetable consumption, and green tea consupmtion

Abbreviations: BMI, body mass index; EAC, esophageal adenocarcinoma; ESCC, esophageal squamous cell carcinoma; HR, hazard ration; NR, not reported; NS/NR, non-significant/not reported (when the exact OR or 95% CI was not reported but the association was reported as non-significant); OR, odds ratio; RR, relative risk; 95% CI, 95% confidence interval.

[a] Number of cases and controls in case-control or prospective studies or number of person-years of follow-up in cohort studies, if it is indicated

[b] If studies reported both crude and adjusted ORs (95% CIs), we only present the adjusted results.

* These studies showed crude numbers but not ORs and 95% CIs; we calculated these statistics using simple logistic regression models and present them.

Table 3

A summary of studies on the association between maté consumption and risk of esophageal cancer

First author; year of publication (Country; period of study)	Case / control [a]	Amount, frequency, duration, or status of maté drinking	OR (95% CI) [b]	Maté drinking temperature	OR (95% CI) [b]	Comments (1. Study design; 2. histological subtypes of EC, if available; 3. matching criteria, if applicable; and 4. the adjustments in statistical models that were done for the presented results)
Vassallo; 198584 (Uruguay; 1979–1984)	226 / 469	**Ever vs. never maté use** Men Women **Maté drinking amount (men)** Non-drinker 0.01–0.49 l/day 0.50–0.99 l/day 1.0+ l/day **(women)** Non-drinker 0.01–0.49 l/day 0.50–0.99 l/day 1.0+ l/day	3.9 (2.0–7.5) 11.9 (2.0–69.6) 1 1.1 (0.2–5.0) 3.1 (1.2–7.8) 4.8 (1.9–12.1) 1 2.1 (0.1–31.7) 12.5 (2.0–80.1) 34.6 (4.9–246.5)	-	-	**1** Hospital-based case-control study. Controls were patients with neoplastic conditions **2** All cases were histologically confirmed EC; only ESCC cases **3** No matching was reported **4** Results were adjusted for age (results for amount of maté drinking by men were also adjusted for tobacco and alcohol use. A few women were smoker or alcohol drinker)
Castellsagué; 200058 (Argentina, Brazil, Uruguay, Paraguay; 1986–1992)	830 / 1779	**Maté drinking (status)** Never-drinker Ever-drinker Ex-drinker Current-drinker **(amount)** Nil 0.01–0.50 l/day 0.51–1.00 l/day 1.01–1.50 l/day 1.51–2.00 l/day >2.00 l/day **(duration)** Nil 1–29 years 30-39 years 40–49 years 50–59 years 60+ years **(amount: cold/hot drinkers)** ≤0.50 l/day 0.51–1.00 l/day 1.01–1.50 l/day 1.50+ l/day **(amount: very hot drinkers)** ≤0.50 l/day 0.51–1.00 l/day 1.01–1.50 l/day 1.50+ l/day	1 1.52 (1.10–2.12) 1.87 (1.25–2.80) 1.47 (1.06–2.05) 1 1.39 (0.98–1.98) 1.34 (0.95–1.90) 1.96 (1.27–3.03) 2.03 (1.32–3.13) 3.04 (1.84–5.02) 1 1.40 (0.91–2.13) 1.39 (0.93–2.07) 1.53 (1.06–2.21) 1.47 (1.00–2.17) 1.92 (1.25–2.96) 1 0.91 (0.71–1.16) 1.50 (1.05–2.14) 1.38 (1.00–1.90) 0.99 (0.48–2.02) 1.59 (0.96–2.63) 0.73 (0.24–2.26) 4.14 (2.24–7.67)	Cold/warm Hot Very hot	1 1.11 (0.84–1.47) 1.89 (1.24–2.86)	**1** A pooled analysis of 5 other hospital-based case-control studies 35–38 the results from Uruguay came from 2 studies: one from 1985 to 1988 38 and the other was an extension of that study (1989–1992) **2** Cases from Argentina, Brazil, and Uruguay had histologically confirmed ESCC; in Paraguay, a cytological or radiological diagnosis of EC was acceptable **3** Controls were individually matched for age and sex, admission to the same hospital and during the same period as the corresponding case **4** Results are adjusted for age group, sex, hospital, residency, education, and tobacco and alcohol use

First author; year of publication (Country; period of study)	Case / control [a]	Amount, frequency, duration, or status of maté drinking	OR (95% CI) [b]	Maté drinking temperature	OR (95% CI) [b]	Comments (1. Study design; 2. histological subtypes of EC, if available; 3. matching criteria, if applicable; and 4. the adjustments in statistical models that were done for the presented results)
Sewram; 200385 (Uruguay; 1988–2000)	344 / 469	**Maté drinking (status)** Never-drinker Ever-drinker **(lifetime amount)** Nil 1–8000 l-years 8001–16000 l-years 16001–24000 l-years 24001+ l-years **(duration)** Nil 1–35 years 36–49 years 50–58 years 59+ years **(daily amount)** Nil 0.01–0.50 l 0.51–1.00 l 1.01+ l	1 2.26 (1.19–4.27) 1 1.43 (0.68–3.01) 2.21 (1.12–4.35) 2.43 (1.22–4.83) 3.07 (1.53–6.16) 1 1.31 (0.61–2.81) 2.29 (1.16–4.52) 2.58 (1.27–5.24) 4.31 (1.99–9.34) 1 1.69 (0.85–3.35) 2.47 (1.28–4.77) 2.84 (1.41–5.73)	Non-drinkers Warm/hot Very hot	1 2.00 (1.05–3.81) 3.98 (1.98–8.44)	**1** Hospital-based case-control study **2** All cases were histologically confirmed EC; only ESCC cases **3** Controls were frequency matched by gender **4** Results were adjusted for age, sex, urban/rural status, education, and tobacco and alcohol use
De Stefani; 200886* and 200887* (Uruguay; 1996–2004)	234/936 for drinking amount 234/468 for drinking temperature	**Maté drinking amount** Nil 0.01–0.99 l/day 1.00–1.99 l/day 2.00+ l/day	1 1.86 (0.93–3.72) 3.05 (1.59–5.85) 3.30 (1.64–6.62)	Warm Hot Very hot	1 2.03 (1.23–3.34) 5.76 (2.92–11.35)	**1** Hospital-based case-control study **2** All cases were histologically confirmed EC; only ESCC cases **3** Controls were individually matched for age, sex and residence **4** For maté drinking variables only raw data was presented

Abbreviations: EAC, esophageal adenocarcinoma; ESCC, esophageal squamous cell carcinoma; OR, odds ratio; RR, relative risk;95% CI, 95% confidence interval.

[a] Number of cases and controls

[b] If studies reported both crude and adjusted ORs (95% CIs), we only present the adjusted results.

* These studies showed crude numbers but not ORs and 95% CIs; we calculated these statistics using simple logistic regression models and present them.

Table 4

A summary of studies on the association between high temperature foods or drinks (other than tea, coffee and maté, unless the results have been reported as a combination of them) and risk of esophageal cancer

First author; year of publication (Country; period of study)	Case / control [a]	Food or drink temperature	OR/RR (95% CI)[b]	Comments (1. Study design; 2. histological subtypes of EC, if available; 3. matching criteria, if applicable; and 4. the adjustments in statistical models that were done for the presented results)
De Jong; 197441 (Singapore; 1970–1972)	131 / 665	**Barely temperature (men)** Other Burning hot **(women)** Other Burning hot	1 6.97 ($P < 0.01$) 1 15.28 ($P < 0.01$)	**1** Hospital-based case-control study **2** EC was confirmed histologically in 82% of cases, all were ESCC **3** Controls were individually matched for age and sex **4** Results are adjusted for dialect group
Astini; 199088* (Ethiopia; 1988–1989)	25 / 50	**High temperature food** Non-user User	1 36.0 (4.5–287.8)	**1** Hospital-based case-control study **2** EC was diagnosed on the basis of clinical symptoms and radiological signs **3** Controls were individually matched for age, sex and visiting the same hospital at the same time **4** In the matched analysis that was presented in the article, the OR (95% CI) could not be calculated (because most cells contained zeros)
Cheng; 199289 and 199590 (Hong Kong; 1989–1990)	400 / 1598 (68 never smoker & 52 never drinker / 540 never smoker & 407 never drinker)	**Preference for hot drinks or soups (all participants)** No Yes **(never smokers)** No Yes **(never drinkers)** No Yes	1 1.64 (1.30–2.08) 1 1.51 (0.80–2.83) 1 1.76 (0.90–3.45)	**1** Hospital-based case-control study. For each case, 2 controls were selected from the same hospital as the cases; 2 other controls were enrolled from the same clinic from which the cases were originally referred **2** All cases were histologically confirmed EC (85% ESCC, 12% EAC, and 3% other) **3** Controls were individually matched for age and sex **4** For all participants, the matched results were adjusted for age, education, and birth place; for never smokers and never drinkers, the matched results were adjusted for age, sex, education, place of birth, fruit and vegetable intake, and tobacco and alcohol use
Hu; 199451 (China; 1985–1989)	196 / 392	**Eaten gruel temperature** Cold Mild Hot Scalding	1 1.1 (0.4–3.4) 2.4 (0.9–6.4) 5.3 (1.4–20.9)	**1** Hospital-based case-control study **2** All cases were histologically confirmed EC; no information about EC subtypes was reported **3** Controls were individually matched for age, sex, and area of residence **4** The matched results were adjusted for tobacco and alcohol use, income, and occupation

First author; year of publication (Country; period of study)	Case / control [a]	Food or drink temperature	OR/RR (95% CI)[b]	Comments (1. Study design; 2. histological subtypes of EC, if available; 3. matching criteria, if applicable; and 4. the adjustments in statistical models that were done for the presented results)
Gao, YT; 199452 and 199491 (China; 1990–1993)	902 / 1552	**Burning hot fluids (men)** No + no green tea drinking Yes + no green tea drinking No + green tea drinking Yes + green tea drinking **(women)** No + no green tea drinking Yes + no green tea drinking No + green tea drinking Yes + green tea drinking **Soup/porridge (men)** Cold/lukewarm Hot Burning hot **(women)** Cold/lukewarm Hot Burning hot	1 4.80 (2.85–8.08) 0.88 (0.61–1.29) 3.09 (1.94–4.93) 1 4.78 (2.89–7.90) 0.50 (0.27–0.91) 2.00 (0.75–5.07) 1 1.21 (0.88–1.66) 4.75 (3.33–6.79) 1 1.90 (1.29–2.79) 6.77 (4.09–11.20)	**1** Population-based case-control study **2** EC was confirmed histologically in 81% of cases (of them: 83% ESCC, 7% EAC, 3% other, 7% unspecified) **3** Controls were frequency matched to cases with 4 types of GI cancer cases in the original study (in accordance with the age and sex distribution among the cases) **4** Results for burning hot fluids consumption were adjusted for age, education, birthplace, and tobacco and alcohol use. Results for soup/porridge temperature were adjusted for age, education, birthplace, tea drinking, tobacco and alcohol use, and consumption of preserved foods, vegetables and fruit
Hanaoka; 199492 (Japan; 1989–1991)	141 / 141	**High temperature food and drink** Dislike Indifferent Like	1 2.06 (0.94–4.52) 2.99 (1.18–7.55)	**1** Hospital-based case-control study; only male participants. 64% of controls had another malignant neoplasm **2** All cases had histologically confirmed EC. No information about EC subtypes was reported **3** Controls were individually matched for age, sex, and place of residence **4** The matched results were adjusted for alcohol use
Guo; 199493 (China; 1986–1991) and Tran; 200594 (China; 1986–2001)	640 / 3200	**Hot liquids** 0 time/month 1+ times/month	1 0.9 (0.7–1.0)	**1** Nested case-control study **2** EC was diagnosed on the basis of radiological signs, cytology, or histology. Nearly all cases with a microscopic diagnosis had ESCC **3** Controls were individually matched for age and sex **4** The matched results were adjusted for cancer history in first degree relatives and smoking
	1958 / 29584	**Hot liquid in summer** 0 time/year 1+ times/year **Hot liquid in winter** 0 time/year 1+ times/year	1 0.96 (0.87–1.07) 1 0.95 (0.87–1.04)	**1** Cohort study; controls were non-cancer members of the cohort **2** All cases had histologically confirmed EC; only ESCC cases **3** No matching was reported **4** Results were adjusted for age and sex

First author; year of publication (Country; period of study)	Case / control [a]	Food or drink temperature	OR/RR (95% CI)[b]	Comments (1. Study design; 2. histological subtypes of EC, if available; 3. matching criteria, if applicable; and 4. the adjustments in statistical models that were done for the presented results)
Srivastava; 199553 (India; not reported)	75 / 75	**Food temperature** Warm Hot	1 NS/NR	**1** Hospital-based case-control study **2** All cases were histologically confirmed EC (85% ESCC, 15% EAC) **3** No matching was reported **4** In the stepwise multivariate analysis, tea temperature variable was dropped out because it did not have any significant association with the risk (in the final model only vegetable intake and alcohol use had significant associations with the risk) Note: preference for high temperature food showed a significant association with ESCC risk in the crude analyses
Garidou; 199680 (Greece; 1989–1991)	43 ESCC and 56 EAC / 200	**Preference for beverage & food** **(ESCC)** Cold to hot Very hot **(EAC)** Cold to hot Very hot **(ESCC + EAC)** Cold to hot Very hot	1 1.89 (0.80–4.49) 1 1.82 (0.85–3.91) 1 >1 (NR, P = 0.02)	**1** Hospital-based case-control study **2** All cases had histologically confirmed EC (43% ESCC, 57% EAC) **3** Controls were individually Matched for age and sex **4** Results are adjusted for age, sex, birthplace, education, height, analgesics, coffee drinking, tobacco and alcohol use, and energy intake
Castellsagué; 200058 (Argentina, Brazil, Uruguay, Paraguay; 1986–1992)	830 / 1779	**Beverage temperature** **(any beverage, excluding maté)** Never very hot Ever very hot **(any beverage, including maté)** Never very hot Ever very hot	1 2.45 (1.72–3.49) 1 2.07 (1.55–2.76)	**1** A pooled analysis of 5 other hospital-based case-control studies 35¯38; the results from Uruguay came from 2 studies: one from 1985 to 1988 38 and the other was an extension of that study (1989–1992) **2** Cases from Argentina, Brazil, and Uruguay had histologically confirmed ESCC; in Paraguay, a cytological or radiological diagnosis of EC was acceptable **3** Controls were individually matched for age and sex, admission to the same hospital and during the same period as the corresponding case **4** Results are adjusted for age group, sex, hospital, residency, education, tobacco and alcohol use
Nayar; 200060 (India; 1994–1997)	150 / 150	**Food temperature** Warm Hot	1 0.68 (NS/NR)	**1** Hospital-based case-control study **2** All cases had histologically confirmed EC. No information about EC subtypes was reported **3** Controls were individually matched for age, sex, and socioeconomic status **4** For food temperature variable, only crude analysis was done

First author; year of publication (Country; period of study)	Case / control [a]	Food or drink temperature	OR/RR (95% CI)[b]	Comments (1. Study design; 2. histological subtypes of EC, if available; 3. matching criteria, if applicable; and 4. the adjustments in statistical models that were done for the presented results)
Phukan; 200195 (India; 1997–1998)	502 / 1004	**Food temperature** Moderate Cold Hot	1 1.2 (0.04–4.1) 2.8 (P <0.05) [See Note]	**1** Hospital-based case-control study **2** All cases had histologically confirmed EC. No information about EC subtypes was reported **3** Controls were individually matched for age and sex initially. Some cases and controls were dropped later on, the pairing identity was not retained **4** Results were adjusted for education, income, chewing betel nut and tobacco and alcohol use Note: For hot food category, the P value and 95% CI for the OR was reported as <0.05 and 0.6– 7.5, respectively. The statement in the text is "ingestion of food at very high temperature emerged as a very significant factor (OR=6.5) that seemed to persist, although in lower magnitude, even after adjustment for the other variables (OR=2.8)". Therefore, we considered that association as statistically significant
Yokoyama; 200296* (Japan; 2000–2001)	234 / 634	**Preference for high temperature food** (categories: Dislike very much, Dislike somewhat, Neither like nor dislike, Like somewhat, Like very much)	NS/NR	**1** Hospital-based case-control study, only male participants **2** All cases were histologically confirmed EC; only ESCC cases **3** No other matching was reported **4** Results were adjusted for age and tobacco and alcohol use Note: preference for high temperature food showed a significant association with ESCC risk in the crude analyses
Hung; 200470 (Taiwan; 1996–2002)	365 / 532	**Hot drink or soup** **(age 20–40 years)** <3 times/week 3+ times/week **(age 40+ years)** <3 times/week 3+ times/week **Eating overheated food** **(age 20–40 years)** No Yes **(age 40+ years)** No Yes	1 1.8 (1.1–3.0) 1 1.3 (0.8–2.1) 1 2.7 (1.6–4.4) 1 2.1 (1.3–3.4)	**1** Hospital-based case-control study, only male participants **2** All cases were histologically confirmed EC; only ESCC cases **3** Controls were individually matched for age, and hospitalization date **4** Results were adjusted for age, education, ethnicity, hospital location, tobacco, alcohol use and areca nut chewing
Yang; 200572 (China; 2003–2004)	185 / 185	**Eating high temperature food** Rarely Occasionally Often	1 0.43 (0.17–1.09) 0.40 (0.14–1.16)	**1** Case-control study; hospital-based cases, population-based controls **2** All cases had histologically confirmed EC; 179 ESCC cases and 6 EAC cases **3** Controls were individually matched for age, sex **4** The matched results were adjusted for family history of EC, occupation, tobacco and alcohol use, some dietary items, including fruit and vegetable intake, hot

First author; year of publication (Country; period of study)	Case / control [a]	Food or drink temperature	OR/RR (95% CI)[b]	Comments (1. Study design; 2. histological subtypes of EC, if available; 3. matching criteria, if applicable; and 4. the adjustments in statistical models that were done for the presented results)
				food, water supply, eating speed, and intake of pickled vegetables, fresh meat, processed meat, eggs and tea
Yokoyama; 200697 (Japan; 2000–2004)	52 / 412	**Preference for hot food or drinks** Dislike very much Dislike somewhat Neither like nor dislike Like somewhat Like very much	1 0.21 (0.01–3.60) 1.00 (0.12–8.17) 1.53 (0.18–12.92) 3.43 (0.39–30.46)	**1** Hospital-based case-control study, only female participants **2** All cases were histologically confirmed EC; only ESCC cases **3** No other matching was reported **4** Results were adjusted for age
Wu, M; 200698 (China; 2003–2005)	531 / 531 (291 / 291 from a high risk and 240 / 240 from a low risk area)	**Food temperature (high risk area)** Normal Hot **(low risk area)** Normal Hot	1 0.51 (0.24–1.09) 1 1.14 (0.55–2.41)	**1** Population-based case-control study **2** Of all the EC cases in the high-risk are (Dafeng), 46% were histologically confirmed, and 40% and 13% were diagnosed by endoscopy and radiology, respectively. In the low-risk area (Ganyu), 30% of EC cases were histologically confirmed, and 50% and 16% were diagnosed by endoscopy and radiology, respectively. **3** Controls were individually matched for age and sex **4** The matched results were adjusted for education, BMI, tobacco and alcohol use, family history of cancer, eating speed, and self-reported grain contamination with fungi
Wang, JM; 200775 (China; 2004–2006)	355 / 408 (223/252 men, 132/156 women)	**Food temperature (men)** Warm Hot **(women)** Warm Hot	1 2.13 (1.39–3.25) 1 3.05 (1.73–5.36)	**1** Population-based case-control study **2** All cases were histologically confirmed EC; only ESCC cases **3** Controls were matched for age and sex **4** Results were adjusted for age, marital status, and education Note: Cases were enrolled from patients referred to one hospital, but they accounted for 85% of all histologically confirmed ECs in the study area during the study period
Rossini; 200882* (Brazil; 1995–2000)	36 / 290	**Hot drinks** <1 time a week 1–2 times a week 3–4 times a week 5+ times a week **Food temperature** Cool Warm Hot	1 0.69 (0.20–2.41) 0.71 (0.09–5.75) 1.14 (0.44–2.97) 1 1.13 (0.27–4.66) 0.98 (0.20–4.82)	**1** Hospital-based case-control study. Cases were head and neck cancer cases with second primary ESCC. Controls were head and neck cancer cases without second primary ESCC **2** All cases were histologically confirmed EC; only ESCC cases **3** No matching was reported **4** No adjustment was reported

Abbreviations: EAC, esophageal adenocarcinoma; ESCC, esophageal squamous cell carcinoma; OR, odds ratio; RR, relative risk;95% CI, 95% confidence interval.

[a] Number of cases and controls

[b] If studies reported both crude and adjusted ORs (95% CIs), we only present the adjusted results.

* These studies showed crude numbers but not ORs and 95% CIs; we calculated these statistics using simple logistic regression models and present them.

Table 5

A summary of the associations between amount or temperature of consumed tea, coffee, maté, or consumption of high temperature food or other beverages and risk of esophageal cancer by study design

	Prospective				Case-control				
Variable	↓	↑	↔	**NS/NR**	↓	↑	↔	**NS/NR**	**Total**
Tea (38 papers)									
Amount	2 (0)	1 (0)	0	0	14 (8‡,**)	6 (4)	4**	6	33
Temperature	0 (0)	1 (1)	0	0	2 (0)	8 (7*)	0	3	14
Coffee (22 papers)									
Amount	1 (1)	0 (0)	2	0	6 (1**)	4*(0)	2	5	20
Temperature	0 (0)	0 (0)	0	0	2 (0)	3 (3*∫)	0	2	7
Maté (4 papers)									
Amount	0 (0)	0 (0)	0	0	0	4 (4*)	0	0	4
Temperature	0 (0)	0 (0)	0	0	0	3 (3*)	0	0	3
Temperature of food or other beverages (29 papers)	0 (0)	0 (0)	1⊥	0	2 (0)	12 (11*)	2	2	19

Numbers in parentheses represent statistically significant studies.

Associations: ↓, decreased risk; ↑, increased risk; ↔, ORs close to 1 or ORs with no clear trend in two sides of null line; NS/NR, there was no statistically significant association but crude numbers or ORs were not reported or ORs for adjusted models cannot be calculated.

‡ In two studies, the inverse association was observed only among women.

* One of the studies was a pooled analysis of 5 other studies.

** One of the studies was a pooled analysis of 2 other studies.

∫ In the pooled analysis of 5 other studies, the positive association was reported for drinking very hot coffee and milk.

⊥ In the nested control study, an odds ratio (95% confidence interval) of 0.9 (0.7–1.0) was reported. When the cases from an extended study were compared with a sub-cohort, no significant association was found.