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## Association of tea consumption and the risk of oral cancer: A meta-analysis

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## SUMMARY

**Objectives:** Epidemiological studies evaluating the association of tea consumption and the risk of oral cancer risk have produced inconsistent results. Thus, we conducted a meta-analysis to assess the relationship between tea consumption and oral cancer risk.

**Methods:** Pertinent studies were identified by a search in PubMed, Web of Knowledge and Wan Fang Med Online. The fixed or random effect model was used based on heterogeneity test. Publication bias was estimated using Egger's regression asymmetry test.

**Results:** Finally, 14 articles with 19 studies comprising 4675 oral cancer cases were included in this meta-analysis. The relative risk (95% confidence interval) of oral cancer for the highest versus the lowest category of tea consumption was 0.853 (0.779–0.934), and the association was significant between oral cancer risk and green tea consumption [0.798 (0.673–0.947)] but not in the black tea consumption [0.953 (0.792–1.146)]. The associations were also significant in Asian and Caucasian.

**Conclusions:** Our analysis indicated that tea consumption may have a protective effect on oral cancer, especially in green tea consumption.

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## Introduction

Oral cavity cancer, comprising cancer of tongue, buccal mucosa, upper or lower gingival, floor of mouth and hard palate, represents the eighth most frequent cancer worldwide [1]. In China, it was reported that the incidence rate and mortality rate of oral cavity cancer were 3.29 per 100,000 and 1.49 per 100,000 in 2008 [2]. Oral cancer is a serious problem in many parts of the world [3], mainly due to its low survival rate [4] and poor life quality [5,6], especially for advanced oral cancer cases. Thus, primary prevention is important. Many studies have shown that oral cancer is associated with genetic factors [7–9]. Furthermore, many environmental factors such as tobacco smoking [10], alcohol drinking [11], fruit and vegetables [12] can also affect the incidence of oral cancer.

Tea, which is derived from the leaves of the plant *Camellia sinensis*, is one of the most popular beverages consumed worldwide, and generally the most consumed are black tea and green tea. Evidence from laboratory studies strongly showed the inhibition of tumorigenesis by tea and its constituents [13,14]. Up to date, a number of epidemiologic studies have been published

to explore the relationship between tea consumption and oral cancer risk. However, the results are not consistent. Therefore, we conducted a meta-analysis to (1) first assess the oral cancer risk for the highest vs. lowest categories of tea consumption; (2) assess the heterogeneity among studies and publication bias.

## Methods

## Search strategy

We performed a literature search up to June 2013 using the databases of PubMed, Web of Knowledge and Wan Fang Med Online. The following search terms were used: 'tea' and 'oral cancer' without restrictions. Moreover, we reviewed the reference lists from retrieved articles to search for further relevant studies. Two investigators searched articles and reviewed of all retrieved studies independently. Disagreements between the two investigators were resolved by consensus with a third reviewer.

## Inclusion criteria

All relevant studies reporting the association of tea and oral cancer risk were considered for inclusion. The inclusion criteria were as follows: (1) case-control or cohort study assessing the

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association between tea consumption and oral cancer risk; (2) the exposure of interest was green tea, black tea or total tea consumption; (3) the outcome of interest was oral cancer; (4) results including relative risk (RR) or OR and its 95% CIs, or providing us with sufficient information to calculate them and (5) the abstracts were included if they provide the RR (95% CI) of oral cancer associated with tea consumption. Accordingly, the following exclusion criteria were also used: (1) reviews and (2) repeated or overlapped publications.

#### Data extraction

The following data were collected from all studies independently by two investigators: the design type (case-control study or cohort study), the first author's last name, publication year, location where the study was performed, sample size and number of cases, variables adjusted for in the analysis, RR estimates (we presented all results with RR for simplicity) with corresponding 95% CI for the highest versus lowest categories of tea and oral cancer, respectively. For studies that reported results from various covariate analyses, we abstracted the estimates based on the model that included the most potential confounders. If there was disagreement between the two investigators about eligibility of the data, it was resolved by consensus with a third reviewer.

#### Statistical analysis

The pooled measure was calculated as the inverse variance-weighted mean of the natural logarithm of multivariate adjusted RR with 95% CI for the highest vs. lowest levels to assess the association of tea consumption and oral cancer risk. The *Q* test and  $I^2$  of Higgins and Thompson [15] were used to assess heterogeneity among included studies.  $I^2$  describes the proportion of total variation attributable to between-study heterogeneity as opposed to random error or chance. In the presence of substantial heterogeneity ( $I^2 > 50%$ ) [16], the DerSimonian and Laird random-effect model was adopted as the pooling method; otherwise, the fixed-effect model was used as the pooling method. Publication bias was estimated using Begg' funnel plot [17] and Egger's regression asymmetry test [18]. A study of influence analysis [19] was conducted to describe how robust the pooled estimator is to removal of individual studies. An individual study is suspected of excessive influence if the point estimate of its omitted analysis lies outside the 95% CI of the combined analysis. All the statistical analyses were performed with STATA version 10.0 (Stata Corporation, College Station, TX, USA). Two-tailed  $P \leq 0.05$  was accepted as statistically significant.

## Results

#### Characteristics of studies

The search strategy identified 343 articles from PubMed, 595 articles from the Web of Knowledge and 24 articles from Wan Fang Med Online. 30 articles were reviewed in full after reviewing the title/abstract. One article reported the upper aerodigestive tract cancer with tea consumption and one article reported the coffee and tea consumption with the risk of oral cancer. 12 articles were review. Two articles that did not report the risk estimate were also excluded. Finally, 14 articles [20–33] were included in this meta-analysis. Fig. 1 presents the flow chart for exclusion/inclusion process.

For tea consumption and oral cancer, data from 14 articles with 19 studies (4 prospective studies and 15 case-control studies) were used including 4675 oral cancer cases. 6 studies were carried out in China, 4 in United States, 3 in Brazil, 2 in Italy, 2 in Japan, 1 in

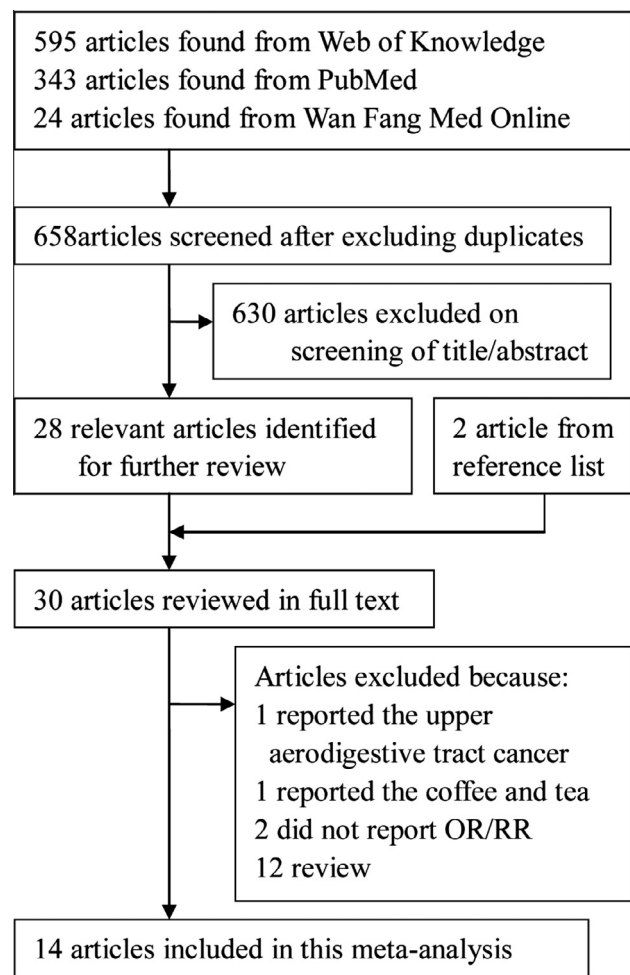


Figure 1. The flow chart for exclusion/inclusion process.

France and 1 in Denmark. Inverse association of tea consumption with risk of oral cancer was reported in 4 studies. Five studies were carried out to assess the association between green tea and oral cancer. The detailed characteristics of the relevant studies are shown in Table 1.

#### Quantitative synthesis

Highest tea consumption level versus lowest level was significantly associated with the risk of oral cancer [summary RR = 0.853, 95% CI = 0.779–0.934,  $I^2 = 23.8%$ ] (Fig. 2). Five studies with 1313 cases were carried out for green tea and three studies with 1127 cases were carried out for black tea to assess the risk of oral cancer. Significant association was found between oral cancer and green tea (RR = 0.798, 95% CI = 0.673–0.947,  $I^2 = 0.0%$ ) (Fig. 3), but not in black tea (RR = 0.953, 95% CI = 0.792–1.146,  $I^2 = 0.0%$ ). The associations were significant between tea consumption and oral cancer in Asian (RR = 0.866, 95% CI = 0.764–0.982,  $I^2 = 0.0%$ ) and Caucasian (RR = 0.822, 95% CI = 0.717–0.943,  $I^2 = 36.2%$ ). For the study design, significant associations were also found in prospective studies (RR = 0.796, 95% CI = 0.651–0.974,  $I^2 = 0.0%$ ) and case-control studies (RR = 0.868, 95% CI = 0.785–0.960,  $I^2 = 31.7%$ ), respectively. The main results are summarized in Table 2.

#### Influence analysis and publication bias

Influence analysis showed that no individual study had excessive influence on the association of tea consumption and oral

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