

## Effect of Coffee and Tea Consumption on Oral Cancer Risk: A Meta-Analysis

### Abstract

**Background:** Oral cancer is a global public health problem whose incidence and mortality have not considerably improved in recent decades. Its etiology is multifactorial with risk factors such as smoking, alcohol intake, human papillomavirus infection, or dietary factors. **Objective:** The objective is to assess the possible effect of coffee and/or tea consumption on oral cancer. **Methods:** A PubMed database search through December 2018 of articles on the effect of coffee or tea consumption on oral cancer using the following Medical Subject Headings terms (“coffee” or “tea”) and “mouth neoplasms” was conducted. One hundred and two articles were found between 1990 and 2017. From 79 studies with full-text availability, 61 were excluded for several reasons: studies on cancers that did not exclusively affect the oral cavity (29) and studies with non-usable data (32). **Statistical Analysis:** For dichotomous outcomes, the estimates of effects of an intervention were expressed as odds ratios (ORs) using Mantel-Haenszel method with a 95% confidence interval and, also the Pearson Chi-square test was applied when required. **Results:** Eighteen studies on the effect of coffee and/or tea consumption on oral cancer were included in this meta-analysis. High consumption of coffee ( $\geq 6$  cups daily) had no relevant effect on oral cancer risk (OR: 1.01,  $P = 79\%$ ,  $P = 0.88$ ). Tea intake (OR: 0.78,  $P = 79\%$ ,  $P < 0.001$ ) and consumption of  $\geq 6$  cups/day (OR: 0.79,  $P = 80\%$ ,  $P = 0.02$ ) did have a significant protective effect on oral cancer. **Conclusions:** Only the consumption of tea had a protective effect on oral cancer.

**Keywords:** Coffee, mouth neoplasms, risk factors, tea

### Introduction

Oral cancer is a global public health problem with an important incidence, and its mortality rate has not improved significantly in recent decades. In 2018, these mouth neoplasms were responsible for 354,864 new cases (2.0% of all cancers) and 177,384 deaths (1.9%).<sup>[1]</sup> Its etiology is multifactorial with classic factors such as tobacco and/or alcohol consumption in addition to human papillomavirus infection or dietary factors.<sup>[2]</sup> Coffee and tea, after water, are probably the most consumed beverages in the world. Several studies<sup>[3,4]</sup> analyze the possible effect of the consumption of these beverages on the risk of oropharyngeal cancer with contradictory results, some point out that it is a risk factor, others that it is a protective factor. However, there are differences between oral cancer and pharyngeal cancer, so the effect of these drinks on oral cancer could

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be different. The aim of this study was to assess the possible effect of coffee and/or tea consumption on oral cancer.

### Methods

A PubMed search of case-control studies about the consumption of coffee and/or tea on oral cancer patients was conducted through December 2018. Search strategies included terms from the Medical Subjects Headings (MeSH) and free-text terms such as “mouth neoplasms” [MeSH Terms], “oral cancer” [All Fields] AND “coffee” [MeSH Terms], “coffee” [All Fields] OR “tea” [MeSH Terms], “tea” [All Fields]. After this initial search, 102 articles were found between 1990 and 2017.

Solely articles with full-text availability were considered ( $n = 79$ ). The exclusion criteria were: (a) studies on cancers that did not exclusively affect the oral cavity ( $n = 29$ ) and (b) studies with non-usable data ( $n = 32$ ). Finally, 18 studies were included in this meta-analysis [Figure 1].

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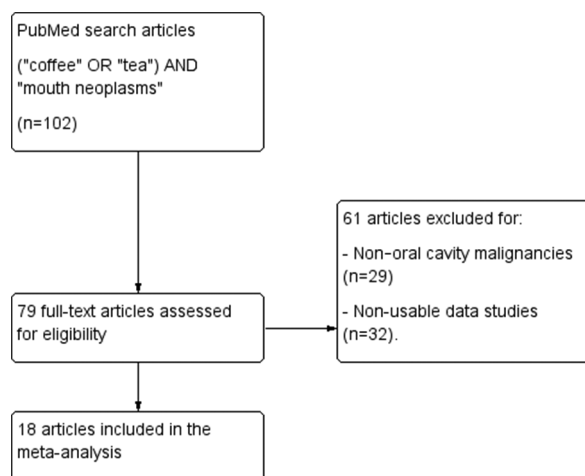


Figure 1: Study flow diagram

### Statistical analysis

Meta-analysis was implemented using the RevMan 5.3 program (The Cochrane Collaboration, Oxford, UK). For dichotomous outcomes, the odds ratio (OR) was used with the Mantel-Haenszel Chi-square formula with 95% confidence intervals (95% CIs). Heterogeneity was established considering the values of  $P$  and the Higgins statistic ( $I^2$ ). The random-effects model was applied in cases of high heterogeneity. Pearson's Chi-square test was also used when required. The minimum level of significance was set at  $P < 0.05$ .

### Results

The main descriptive characteristics of the 18 articles included in the meta-analysis are shown in Table 1.<sup>[5-22]</sup>

Thirteen studies<sup>[5-17]</sup> analyzed coffee consumption in patients with oral cancer and in controls without the disease [Figure 2a]. A higher percentage of patients with oral cancer than controls who consumed coffee was found. Nevertheless, the coffee consumption was not a risk factor for oral cancer, and no statistically significant relationship was observed (OR = 0.98, 95% CI: 0.88–1.09,  $P = 0.68$ ).

Regarding the consumption of decaffeinated coffee [Figure 2b], three studies<sup>[7,9,17]</sup> also found no statistically significant influence of the consumption of this type of coffee on oral cancer risk (OR = 0.89, 95% CI: 0.58–1.38,  $P = 0.61$ ).

Figure 2c presents the 15 studies<sup>[6-9,11-14,16-22]</sup> that considered the possible influence of tea intake on oral cancer risk. About 52.8% of the controls and 39.8% of the patients with oral cancer reported tea ingestion. The consumption of this drink had a protective effect against oral cancer with statistically significant differences (OR = 0.78, 95% CI: 0.67–0.90,  $P < 0.001$ ).

Table 2 shows the comparison of coffee or tea intake in patients with oral cancer and in controls without the

disease. The coffee intake was slightly higher in patients with oral cancer (86.9%) than in controls (86.1%) with no statistically significant association ( $P = 0.14$ ). In the case of tea consumption, there was higher percentage of controls (40.5%) than in patients with oral cancer (38.1%) who ingested tea. After the statistical analysis, significant differences were observed ( $P < 0.01$ ).

Twelve studies<sup>[5,7-17]</sup> evaluated high coffee intake ( $\geq 6$  cups/day) in patients with oral cancer and in controls without the disease [Figure 3a]. A lower percentage of patients with oral cancer than controls with high coffee consumption was observed. After statistical analysis, no significant differences were found (OR = 1.01, 95% CI: 0.84–1.23,  $P = 0.88$ ).

With regard to high tea intake [Figure 3b], 13 studies<sup>[8,9,11-14,16-22]</sup> assessed the intake of  $\geq 6$  cups of tea/day in patients with oral cancer and in controls. There was a lower percentage of patients with oral cancer (22.7%) than controls (29.1%) with this high tea consumption, with a statistically significant association (OR = 0.79, 95% CI: 0.64–0.97,  $P = 0.02$ ).

The comparison between the quantity (low/high) of coffee or tea consumed by patients with oral cancer and by controls without the disease is shown in Table 3. Controls had higher intakes of both coffee (57.4%) and tea (48.6%) compared to oral cancer patients (34.5% and 36.4%, respectively). After the analysis, highly significant differences were found in both comparisons ( $P < 0.001$ ).

### Discussion

In this meta-analysis on the effects of coffee and/or tea consumption on oral cancer risk, data from 18 studies have been included.

Thirteen studies<sup>[5-17]</sup> analyzed the coffee consumption in patients with oral cancer and in controls without the disease, five of them<sup>[5,6,8,9,14]</sup> with a higher number of oral cancer patients who consumed coffee and, another eight<sup>[7,10-13,15-17]</sup> with a greater number of controls. Coffee consumption had no significant protective effect on the risk of oral cancer (OR = 0.98, 95% CI: 0.88–1.09,  $P = 0.68$ ). Nevertheless, the results of Galeone *et al.*,<sup>[9]</sup> support the hypothesis of an inverse association between coffee consumption and the risk of oral and pharyngeal cancer, although other relevant risk factors for these cancers, such as tobacco and/or alcohol consumption, should be considered. This possible protective effect of coffee consumption on cancer could also be justified in that coffee beans contain several phenolic compounds with antioxidant properties, such as caffeic acid and chlorogenic acid, that would exert an anti-cancer activity.<sup>[15]</sup>

About the decaffeinated coffee consumption, three studies<sup>[7,9,17]</sup> found no statistically significant influence of

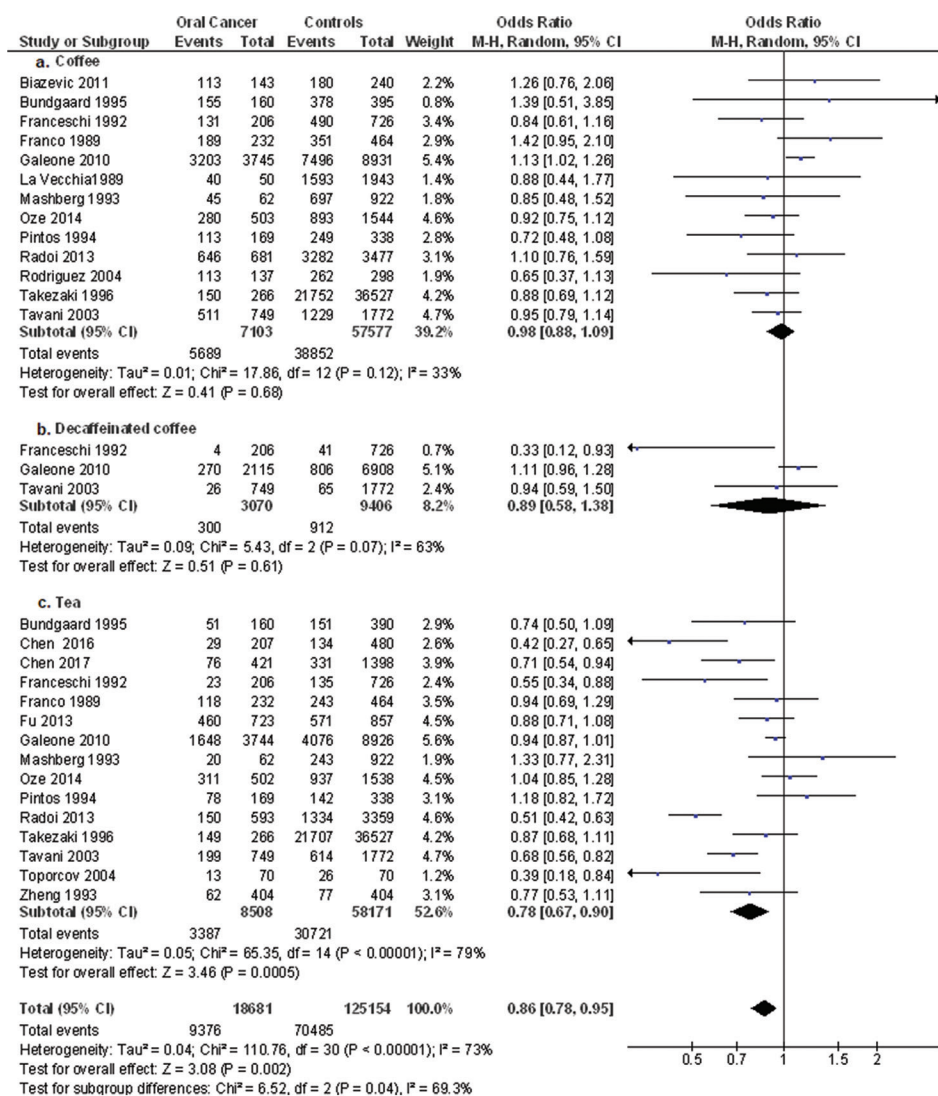


Figure 2: Study data and forest plot graph for coffee (a), decaffeinated coffee (b), and tea (c) consumption in oral cancer patients and controls

the consumption of this type of coffee on the risk of oral cancer ( $P = 0.61$ ). The consumption of decaffeinated coffee did not increase oral cancer risk. However, in these studies, data were scarce with low prevalences, and low amounts of decaffeinated coffee consumed. Nonalcoholic beverages such as coffee or tea could contribute to the mechanical cleaning of potential carcinogens from the oral cavity, providing greater protection against oral cancer.<sup>[9]</sup>

Regarding high coffee consumption ( $\geq 6$  cups daily), in the present study, no statistically significant association was found between high coffee intake and oral cancer risk (OR = 1.01, 95% CI: 0.84–1.23,  $P = 0.88$ ). Twelve studies<sup>[5,7-17]</sup> evaluated high coffee consumption with respect to oral cancer, finding apparently contradictory results. One study<sup>[12]</sup> indicated that it was a protective factor and another two<sup>[9,14]</sup> that it was a risk factor. The consumption of three or more cups of coffee/day had a significant inverse association with oral cancer, although this association could

be modified by the influence of other important factors such as smoking and alcohol consumption. It is possible that the increase in coffee intake decreases the intake of alcohol and thus reduces the risk of oral cancer.<sup>[12]</sup> Conversely, other studies established a direct relationship between the amount of coffee consumed and the risk of oral cancer in the univariate analysis. However, when in the multivariate analysis, other factors were considered, such as the consumption of tobacco and/or alcohol or vegetables, the high intake of coffee ceased to be a risk factor.<sup>[9]</sup>

In the present meta-analysis, the ingestion of tea showed a significant protective effect against oral cancer (OR = 0.78, 95% CI: 0.67–0.90,  $P < 0.001$ ). Of the 15<sup>[6-9,11-14,16-22]</sup> that examined the possible role of tea consumption in oral cancer, six of them<sup>[7,14,17-19,21]</sup> observed a significant protective effect. Most studies coincided in pointing out a protective effect of tea consumption. However, the intake of other beverages and the dietary habits of the population

**Table 1: Descriptive characteristics of included studies**

First author	Years	Country	Study populations <i>n</i> (gender: Male/female)	Beverage assessed	Remarks
Biazevic <sup>[5]</sup>	2011	Brazil	115 OC (93 male/22 female) 240 controls (NA/NA)	Coffee	Cumulative coffee consumption during lifetime had a significant protective effect against OC
Bundgaard <sup>[6]</sup>	1995	Denmark	161 OC (97 male/64 female) 400 controls (250 male/150 female)	coffee, tea	Coffee and tea intake had no significant influence on oral cancer risk
Franceschi <sup>[7]</sup>	1992	Italy	206 OC (206 male/0 female) 726 controls (726 male/0 female)	Coffee, tea	Coffee and tea consumption had a significant protective effect against OC
Franco <sup>[8]</sup>	1989	Brazil	232 OC (201 males/31 females) 464 controls (NA/NA)	Coffee, tea	Coffee and tea intake had no significant influence on oral cancer risk
Galeone <sup>[9]</sup>	2010	Italy	1191 OC (905 males/286 females) 9028 controls (6356 males/2772 females)	Coffee, tea	Coffee, but not decaffeinated coffee, had a significant protective effect against OC. Tea intake did not have any influence
La Vecchia <sup>[10]</sup>	1989	Italy	50 OC (43 males/7 females) 1944 controls (1334 males/610 females)	Coffee	Coffee intake had no influence on oral cancer risk
Mashberg <sup>[11]</sup>	1993	USA	359 OC (NA/NA) 2280 controls (NA/NA)	Coffee, tea	Coffee and tea intake had no significant influence of oral cancer risk
Oze <sup>[12]</sup>	2014	Japan	503 OC (406 male/97 female) 1544 controls (1245 males/299 females)	Coffee, tea	Coffee, but not tea consumption, had a protective effect on oral cancer
Pintos <sup>[13]</sup>	1994	Brazil	169 OC (153 males/16 females) 338 controls (307 males/31 females)	Coffee, tea	Coffee and tea intake had no significant influence of oral cancer risk
Radoj <sup>[14]</sup>	2013	France	689 OC (556 males/133 females) 3481 controls (2720 males/761 females)	Coffee, tea	Tea intake and/or high coffee consumption had a significant protective effect on oral cancer
Rodriguez <sup>[15]</sup>	2004	Italy	137 OC (113 males/24 females) 298 controls (226 male/72 female)	Coffee	High coffee consumption had a significant protective effect on oral cancer
Takezaki <sup>[16]</sup>	1996	Japan	137 OC (113 males/24 females) 36527 controls (9858 males/26,669 females)	Coffee, tea	Coffee and tea consumption had no significant influence of oral cancer risk
Tavani <sup>[17]</sup>	2003	Italy	749 OC (634 male/115 female) 1772 controls (1252 males/520 females)	Coffee, tea	Coffee and tea consumption had no significant influence of oral cancer risk
Chen <sup>[18]</sup>	2016	China	207 OC (0 male/207 females) 480 controls (0 male/480 females)	Tea	Tea intake had a significant protective effect on oral cancer
Chen <sup>[19]</sup>	2017	China	421 OC (105 males/316 females) 1398 controls (402 males/996 females)	Tea	Tea consumption had a significant protective effect on oral cancer
Fu <sup>[20]</sup>	2013	China	723 OC (485 males/238 females) 857 controls (576 males/281 females)	Tea	Green tea intake, only in men had a significant protective effect on oral cancer
Toporcov <sup>[21]</sup>	2004	Brazil	70 OC (50 male/20 female) 70 controls (50 males/20 females)	Tea	Tea consumption had a significant protective effect on oral cancer
Zheng <sup>[22]</sup>	1993	China	404 OC (NA/NA) 404 controls (NA/NA)	Tea	Tea intake had no significant influence of oral cancer risk

*n*: Number of participants, OC: Oral cancer patients, NA: Data not available

**Table 2: Coffee and tea intake in oral cancer patients and controls without the disease**

Coffee intake	Oral cancer, <i>n</i> (%)	Controls, <i>n</i> (%)	Tea intake	Oral cancer, <i>n</i> (%)	Controls, <i>n</i> (%)
Yes	4202 (86.9)	13,758 (86.1)	Yes	1974 (38.1)	6269 (40.5)
No/occasional	633 (13.1)	2225 (13.9)	No/occasional	3213 (61.9)	9206 (59.5)
Total	4835 (100)	15,983 (100)	Total	5187 (100)	15,475 (100)
$\chi^2, P$	2.08, 0.14		$\chi^2, P$	9.65, <0.01*	

\*Statistically significant. *n*: Number of participants

must be taken into account to establish the true effect of the consumption of this beverage on the risk of oral cancer.<sup>[21]</sup>

Thirteen studies<sup>[8,9,11-14,16-22]</sup> investigated high tea consumption ( $\geq 6$  cups daily) in patients with oral cancer

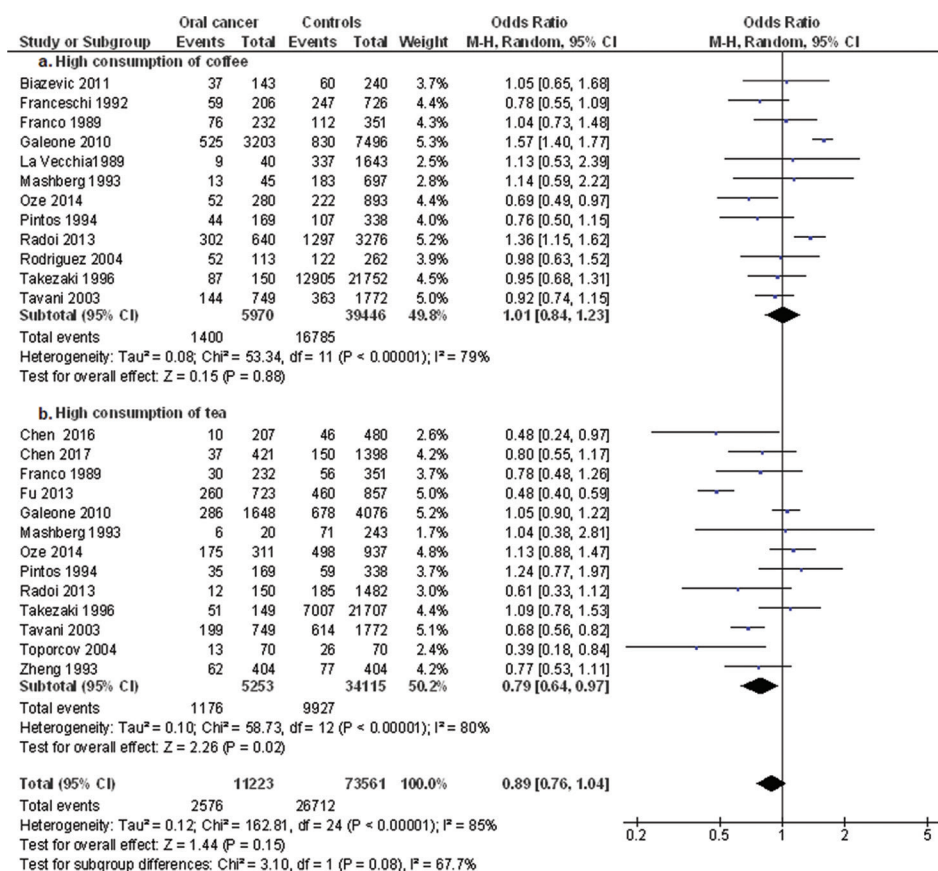
Figure 3: Study data and forest plot graph for high consumption ( $\geq 6$  cups daily) of coffee (a) or tea (b) in oral cancer patients and controls

Table 3: Quantity of coffee/tea consumed by oral cancer patients and controls without the disease

Quantity of coffee consumed	Oral cancer, n (%)	Controls, n (%)	Quantity of tea consumed	Oral cancer, n (%)	Controls, n (%)
Low	2680 (65.5)	12,492 (42.6)	Low	2994 (63.6)	11,077 (51.4)
High	1411 (34.5)	16,839 (57.4)	High	1714 (36.4)	10,454 (48.6)
Total	4091 (100)	29,331 (100)	Total	4708 (100)	21,531 (100)
$\chi^2, P$	759.94, <0.001*		$\chi^2, P$	228.73, <0.001*	

\*Statistically significant. n: Number of participants

and in controls without the disease. In this study, the high intake of tea had a significant protective effect against oral cancer (OR = 0.79, 95% CI: 0.64–0.97,  $P = 0.02$ ). Similarly, four studies observed a significant protective effect of high tea consumption on oral cancer.<sup>[17,19-21]</sup> The consumption of green tea reduced the risk of cancer among women who drank more than 10 cups a day, pointing to a possible influence of gender. It is likely that tea intake stimulates the production of estrogens and exerts a protective effect on women. In addition, tea contains polyphenols, catechins, and other antioxidant compounds that could develop an anticarcinogenic activity through different mechanisms.<sup>[19]</sup> In contrast, another study observed a greater reduction in the risk of oral cancer in men, with a high intake of green tea, although more smokers.<sup>[20]</sup>

This study presents several limitations. When searching in PubMed database, almost exclusively,

English-language studies were included, representing a language restriction and the possibility of language and publication bias. Another possible limitation is the large differences in the sample sizes existing in the studies considered in this meta-analysis. Studies with small sample sizes tend to have low statistical power and may provoke erroneous interpretations. Furthermore, other interesting variables, such as the different types of coffee/tea consumed, or the drink temperature could not be properly analyzed.

New studies are needed to determine the true effect of the consumption of these beverages on the risk of cancer and, specifically, on oral cancer.

The results of this meta-analysis should be interpreted with caution due to the high heterogeneity of some of the studies included. These differences between studies may be conditioned by the study design, the methods to

gather information, the statistical analysis applied, the characteristics of the study populations, or the duration of the studies.

## Conclusions

In the present meta-analysis, tea consumption (OR: 0.78,  $P < 0.001$ ) but not that of coffee ( $P = 0.68$ ) or that of decaffeinated coffee ( $P = 0.61$ ), had a significant protective effect on oral cancer. On the other hand, high consumption ( $\geq 6$  cups daily) of coffee had no significant effect ( $P = 0.88$ ), while high tea consumption had a protective effect (OR: 0.79,  $P = 0.02$ ) for oral cancer.

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## Conflicts of interest

There are no conflicts of interest.

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