

Milk and dairy products consumption and the risk of oral or oropharyngeal cancer: A meta-analysis

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Abstract

Background Previous studies have been conducted to assess the association of milk and dairy products consumption and oral or oropharyngeal cancer risk, with inconsistent results. We therefore conducted a meta-analysis to explore the role of milk and dairy products consumption on oral or oropharyngeal cancer risk.

Methods Databases of PubMed, Embase and Chinese Wanfang database were investigated until June 30th, 2019. The overall and subgroup associations were pooled with odds ratios (OR) and 95% confidence intervals (CI).

Results This study involving 4635 cases and 50777 participants from 12 publications suggested that an inverse association was found between milk and dairy products consumption and oral or oropharyngeal cancer risk (OR= 0.74, 95%CI= 0.59-0.92; I²= 65.9%, Pfor heterogeneity = 0.001). Four studies reported milk consumption on oral cancer risk, but no significant association was found (OR= 0.91, 95%CI= 0.61-1.37). Six studies about milk consumption and oropharyngeal cancer risk found that there was a positive association between them (OR= 0.63, 95%CI= 0.44-0.90).

Conclusion Findings from our meta-analysis indicated that milk and dairy products consumption may be associated with decreased risk of oral or oropharyngeal cancer.

Introduction

Oral cavity and pharyngeal cancer, which includes cancer from the tongue, buccal mucosa, upper and lower gums, mouth and hard palate, pharynx, is the eighth most common cancer in the world [1]. Previous paper showed that oral cancer may account for approximately 34,000 new cases and 7,000 deaths in United States in 2018 [1]. Therefore, primary prevention is important to reduce the incidence and mortality of oral cavity and pharyngeal cancer. Many researches have explored the association of dietary factors and the risk of oral or oropharyngeal cancer, such as tea consumption [2], fruit and vegetable consumption [3], coffee consumption [4], meat consumption [5]. But, there is no meta-analysis about milk and dairy products consumption and oral or oropharyngeal cancer risk. Notani et al. first explored the association about milk consumption of the risk of oral cancer in 1987 [6]. Since then, more studies had attempted to assess their relevance. However, no exact conclusion was obtained probably due to the small sample size and inadequate statistical power in each individual study. Thus, the current study used a meta-analysis to pool all the eligible studies to get a more exact result about milk and dairy products consumption and oral or oropharyngeal cancer risk.

Methods

Identification of eligible studies

All the suitable studies about milk consumption and oral cancer risk were investigated by two independent authors (JY and WL) until June 30th, 2019. The database included PubMed, Embase and Chinese Wanfang database. The associated keywords were ('milk' or 'dairy') combined with ('oral cancer' or 'oral cavity cancer' or 'oral oncology' or 'oropharyngeal cancer' or 'pharyngeal cancer'). Meanwhile, we also manually searched for the references which cited in the eligible articles or reviews to identify relevant studies. Disagreement was resolved by a third reviewer (WS).

The inclusion criteria were as follows: (1) observational study; (2) assessed the association of milk and dairy products consumption and oral or oropharyngeal cancer risk; (3) provided odds ratios (OR) and 95% confidence intervals (95%CI) or enough information for calculating them in independent study; (4) reported in humans.

Data extraction

Information which was provided in Table 1 from all suitable publications was independently extracted with two investigators (JY and WL). Disagreement was resolved by a third reviewer (WS).

Statistical analysis

Pooled association of milk and dairy products consumption and oral or oropharyngeal cancer risk was calculated with OR and 95%CI [7]. The I^2 was used to evaluate the heterogeneity and $I^2 > 50\%$ was considered as significant heterogeneity [8,9]. A random-effect model was used on the overall and subgroup analyses. Sensitivity analysis was assessed to explore if a single study had significant impact on the pooled OR while omitted a study one by one. Publications bias was detected using Begg's funnel plots [10] and Egger's test [11]. All analyses in the current study were calculated with Stata 10.0 software (College Station, TX). $P < 0.05$ was set as statistics significant.

Results

Researches characteristics

Figure 1 shows the process of included or excluded reason. Totally, 834 relevant publications about milk and dairy products consumption and oral or oropharyngeal cancer risk were searched. At last, 12 papers [6,12–22] including 4635 cases and 50777 participants were used in the final analysis. Six studies were from Europe, four from Asia and two from America. All included studies were with case-control design. Table 1 presents the characteristics of each individual study.

Meta-analysis results

Pooled result suggested that an inverse association was found between milk and dairy products consumption and oral or oropharyngeal cancer risk (OR = 0.74, 95%CI = 0.59–0.92; $I^2 = 65.9\%$, $P_{\text{for heterogeneity}} = 0.001$) (Figure 2)..

Four studies [6,19,20,22] reported milk consumption on oral cancer risk, but no significant association was found (OR = 0.91, 95%CI = 0.61–1.37) (Figure 3).. Six studies [14–18,21] about milk consumption and oropharyngeal cancer risk found that there was a positive association between them (OR = 0.63, 95%CI = 0.44–0.90) (Figure 3)..

When we explored the association of milk and dairy products consumption and oral or oropharyngeal cancer geographic location, significant association was only found in European populations (OR = 0.58, 95%CI = 0.40–0.85; $I^2 = 71.2\%$, $P_{\text{for heterogeneity}} = 0.004$), but not in Asia populations (OR = 0.90, 95%CI = 0.61–1.34; $I^2 = 75.5\%$, $P_{\text{for heterogeneity}} = 0.007$) or in America populations (OR = 0.91, 95%CI = 0.60–1.38; $I^2 = 1.7\%$, $P_{\text{for heterogeneity}} = 0.313$).

Sensitive analysis and publication bias

Sensitivity analysis showed that no single study had essential impact on the overall result while removed a study sequentially. There was no significant publication bias detected by funnel plots and Egger's test ($P = 0.868$).

Discussion

Whether milk and dairy products consumption is associated with reduced the risk of oral or oropharyngeal cancer is still attracting attention for researchers. So far, no meta-analysis had been performed regarding milk and dairy products consumption on oral or oropharyngeal cancer risk. Thus, the current meta-analysis was carried out to pool all the suitable studies that met our inclusion criteria. Our meta-analysis included 12 studies, comprising 4635 cases and 50777 participants. Findings from our study indicated that milk and dairy products consumption may reduce the risk of oral or oropharyngeal cancer.

To our attention, significant heterogeneity was found in the overall analysis. Though between-study heterogeneity is common in a meta-analysis, we did our best to explore the sources of heterogeneity. Meta-regression was first performed to evaluate if

this high heterogeneity was caused by publication years, geographic locations, study design or sample size. Results from meta-regression suggested that all the above mentioned factors were not associated with this high heterogeneity. We then performed subgroup analyses by geographic location and study design to further explore the sources of heterogeneity. However, the heterogeneity was significant in subgroup analyses. Thus, some other factors, such as genetic or environmental or their interaction may affect the development of oral cancer.

Milk and dairy products consumption had been studied on risk of many cancers [23–25]. The mechanism of milk and dairy products consumption on the risk of oral or oropharyngeal cancer is still unclear. Milk contains high-quality protein, which can enhance the body's immunity and promote the body to return to health. Therefore, drinking milk and dairy products may protect against the oral or oropharyngeal cancer. In our study, we also obtained an inverse association about milk and dairy products consumption and oral or oropharyngeal cancer risk.

Some limitations existed in the current study should be noticed. Firstly, we only pooled the overall results about milk and dairy products consumption and oral or oropharyngeal cancer risk. To our knowledge, milk contains many different types, such as whole milk, low-fat milk, nonfat milk. Different types of milk may affect the role on the risk of oral or oropharyngeal cancer. However, there is no detailed information about milk types in each individual study. Thus, more studies with different milk types are warranted to further confirm these results. Secondly, all the included studies are case-control design. As far as we knowledge, case-control studies may cause some bias, such as selected bias, recalling bias and so on. Therefore, more cohort studies are needed to further explore the association of milk and dairy products consumption and risk of oral or oropharyngeal cancer. Thirdly, when we performed the subgroup analysis of milk consumption on oral cancer or oropharyngeal cancer independently, we only found an inverse association on oropharyngeal cancer, but not on oral cancer. This may be affecting by the small number of included studies of milk consumption on oral cancer risk.

Conclusion

In summary, our meta-analysis indicated that milk and dairy products consumption may be associated with decreased the risk of oral or oropharyngeal cancer. While some limitations existed in our meta-analysis, further studies with large participants are warranted to confirm this association.

Abbreviations

OR: odds ratios; CI: confidence intervals

Declarations

Author's contribution

Guarantor of integrity of the entire study: JY; study concepts: JY, WL, WS; study design: JY, WL, WS; definition of intellectual content: JY, WL; literature research: JY, WL, WS; data analysis: SLD; manuscript preparation: JY; manuscript editing: SLD.

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Availability of data and materials

The tables and figures listed the relevant data.

Ethics approval and consent to participate

Not applicable.

Consent for publication

None.

Competing interests:

None.

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Tables

Table 1 Characteristics of the included studies.

Study, year	Design	Age	Country	Participants, Cases	Dietary intake	Outcomes	Category	OR (95%CI)	Adjusted for or matched for
Bravi et al. 2013	Case-control	22-79	Switzerland	2846, 768	Milk and yoghurt	Oropharyngeal cancer	Q4 vs. Q1	0.98(0.70-1.38)	Age, sex, centre, education, year of interview, body mass index, tobacco smoking, alcohol drinking and nonalcohol energy intake.
Chen et al. 2017	Case-control	20-80	China	3597, 930	Milk and dairy products	Oral cancer	≥1 time/week vs. <1 times/week	0.63(0.53-0.74)	Adjusted for age, gender, education, residence, BMI, family history of cancer, tobacco smoking, alcohol consumption, denture wearing, recurrent oral ulceration.
De Stefani et al. 1994	Case-control	40-89	Uruguay	499, 246	Milk	Oropharyngeal cancer	≥14 times/week vs. <7 times/week	1.1(0.6-1.8)	Age, residence, education, pack-yrs and total alcohol consumption.
Fernandez Garrote et al. 2001	Case-control	28-91	Cuba	400, 200	Milk	Oropharyngeal cancer	≥7 times/week vs. <1 time/week	0.72(0.39-1.33)	Age, sex, area of residence, education, and smoking and drinking habits.
Gallus et al. 2006	Case-control	22-77	Italy	2089, 598	Milk	Oropharyngeal cancer	>7 times/week vs. <7 times/week	0.84(0.61-1.33)	Age, sex, centre, education, smoking habit, alcohol and energy intake.
La Vecchia et al. 1991	Case-control	37-74	Italy	1274, 105	Milk	Oropharyngeal cancer	>7 times/week vs. <1 time/week	0.3(0.2-0.7)	Age, sex.
Levi et al. 1998	Case-control	26-72	Switzerland	440, 156	Milk	Oropharyngeal cancer	T3 vs. T1	0.38(0.21-0.70)	Age, sex, education smoking, alcohol and total energy (other than alcohol) intake.
Lissowska et al. 2003	Case-control	23-80	Poland	246, 122	Milk	Oral cancer	≥7 times/week vs. <2 times/week	0.41(0.19-0.89)	Age, sex, race, residence, tobacco use (smoking habits), alcohol consumption

Notani et al.	Case-control	30-70	India	670,278	Milk	Oral cancer	≥7 times/week vs. <7 times/week	0.87(0.47-1.67)	Age, sex and tobacco habits.
1987 Rajkumar et al.	Case-control	18-87	India	1173,591	Milk	Oral cancer	≥5 times/week vs. never	1.14(0.70-1.87)	Age, sex, centre, education, chewing, smoking and drinking habits.
2003									
Sanchez et al.	Case-control	20-91	Spain	750,375	Milk	Oropharyngeal cancer	≥9 times/week vs. ≤6 times/week	0.67(0.44-1.01)	Age, gender, centre, years of schooling, smoking and drinking habits.
2003									
Takezaki et al.	Case-control	20-79	Japan	36793,266	Milk	Oral cancer	T3 vs. T1	1.2(0.8-1.8)	Age, sex, smoking, drinking and year of visit.
1996									

Abbreviation: OR: odds ratio; CI: Confidence Intervals; BMI: Body mass index; Q4: Quartile 4; Q1: Quartile 1; T3: Tertile 3; T1: Tertile 1.

Figures

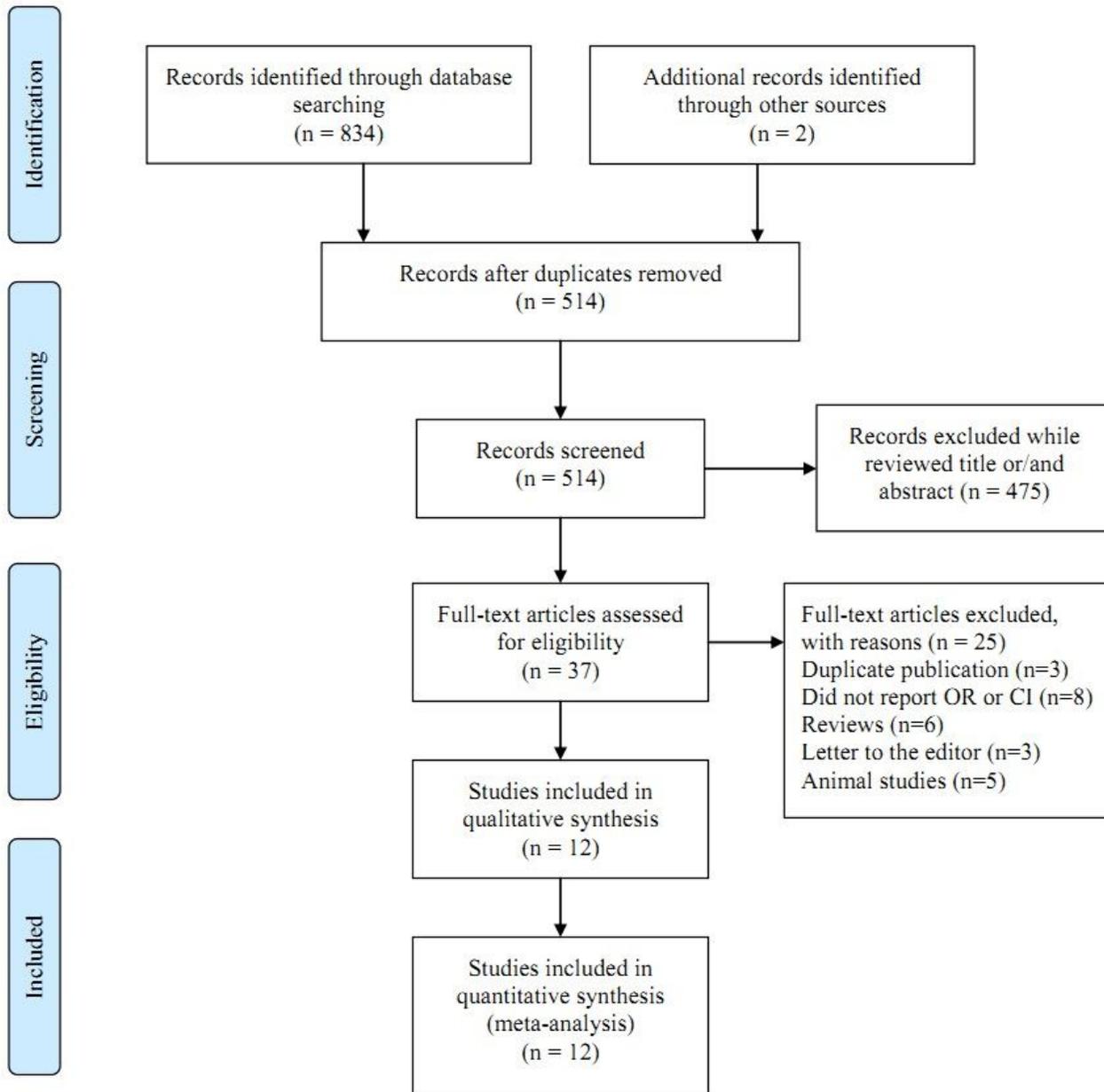


Figure 1

Flow chart of meta-analysis for exclusion/inclusion of studies.

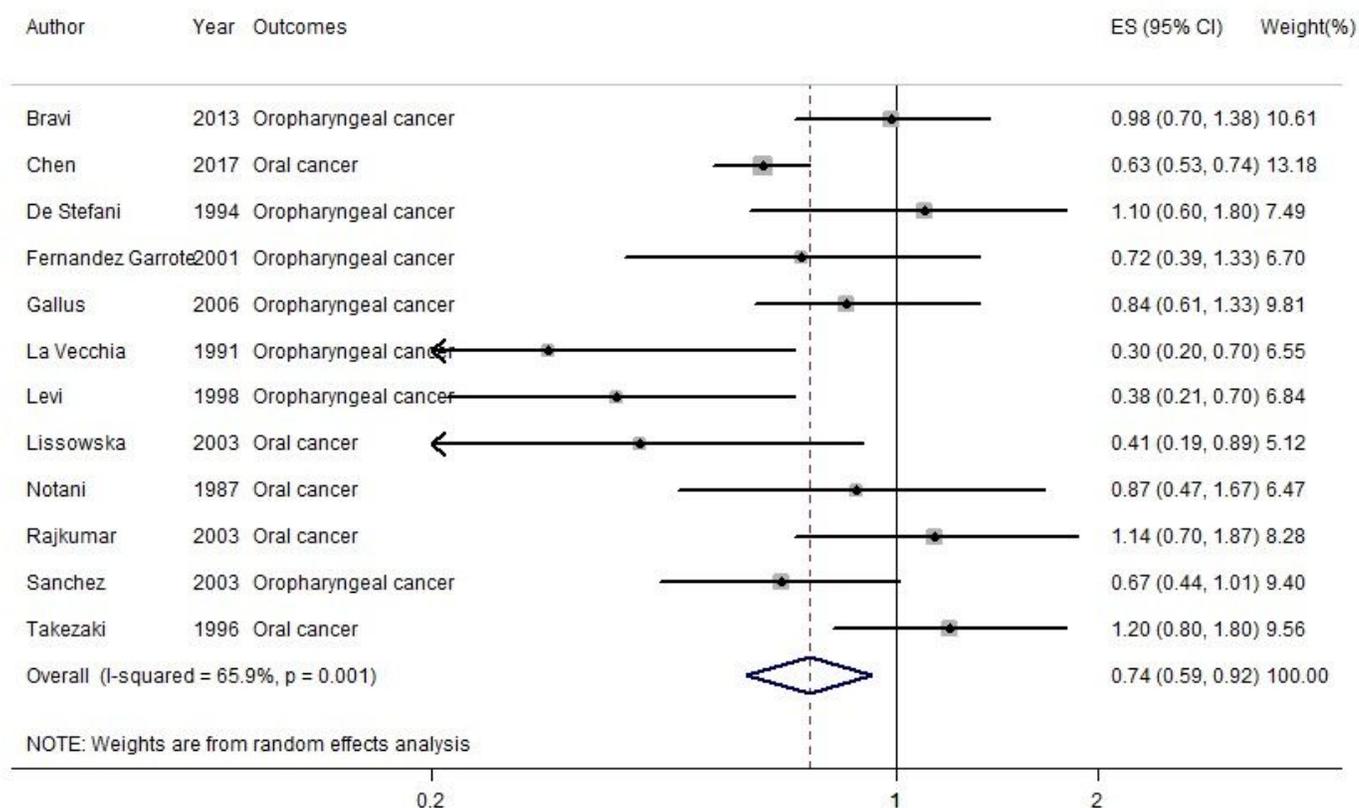


Figure 2

The forest plot of the association about milk and dairy products consumption on the risk of oral or oropharyngeal cancer.

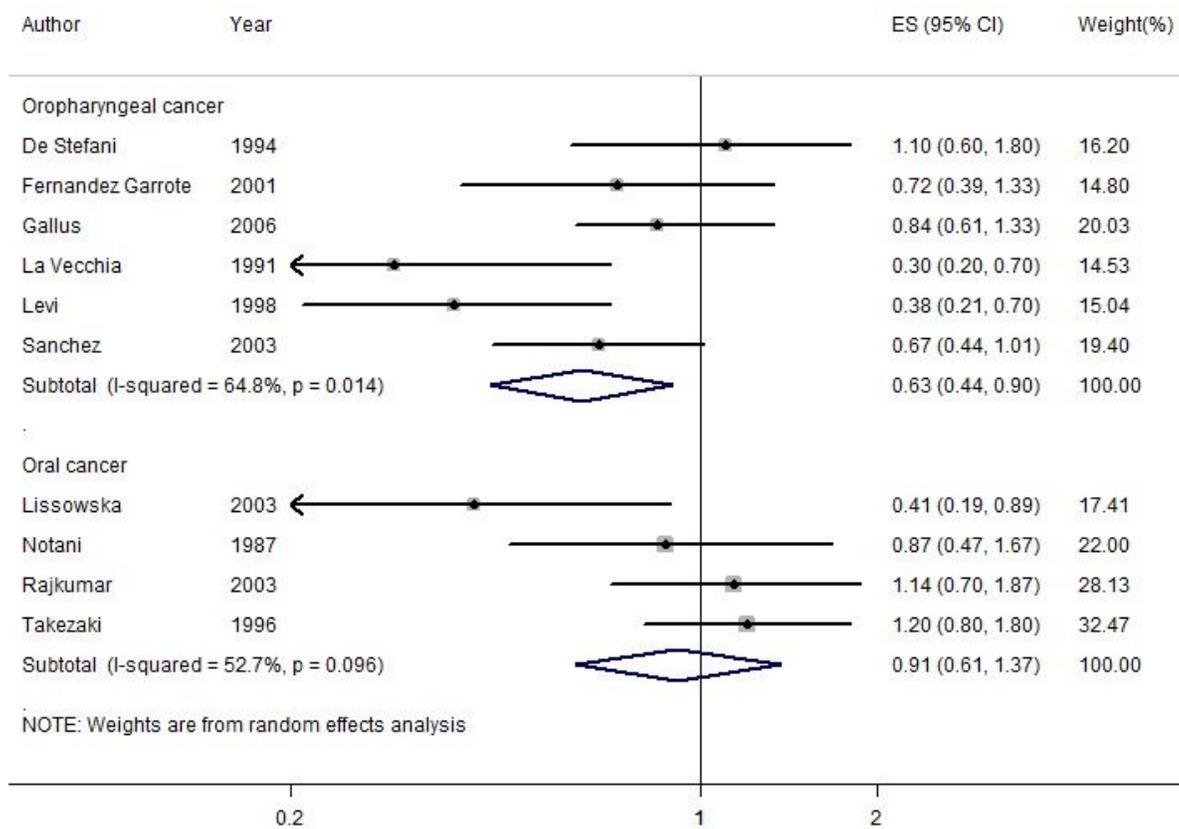


Figure 3

The forest plot of the association of milk consumption on the risk of oral cancer and oropharyngeal cancer independently.