Original Article

Consumption of processed food and risk of nasopharyngeal carcinoma: a systematic review and meta-analysis

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Background: Consumption of processed foods has been associated with nasopharyngeal carcinoma (NPC), but with inconsistent results. Therefore, we conducted a systematic review and meta-analysis to compute results regarding the association between processed foods and risk of NPC in included studies.

Methods: Studies exploring the association between consumption of processed food and risk of NPC were included in the present study. All included studies were case-control or cohort designed. PubMed, Web of Science, EMBASE, Medline and Google Scholar databases were searched for articles published before July 2021. We recorded the following data: author, publication year, sample size, study type, study location, years of diagnosis, food item and comparison, and the covariates considered were multivariate adjusted odds ratios (ORs) or relative risks (RRs) with corresponding 95% confidence intervals (CIs) for the highest *vs.* lowest categories of processed food intake. STATA 12.0 software was used to compute the multivariate ORs or RRs and 95% CIs of the association. Quality appraisal was made using the Cochrane Risk of Bias Tool.

Results: A meta-analysis was made for 29 case-control studies (including 14,378 NPC patients and 17,928 controls). The meta-analysis showed that the highest categories of processed food intake were associated with a 65% increase in NPC risk compared with the lowest categories in a random effects model (OR =1.67; 95% CI: 1.56–1.79; P value for Q test <0.001; I^2=86.9%). Subgroup study showed significant positive associations regarding consumption of processed food and risk of NPC in both Asians and Caucasians (Asian: OR =1.68, 95% CI: 1.56–1.81; Caucasian: OR =1.36, 95% CI: 1.09–1.71).

Conclusions: The association of processed foods with NPC risk might be significant. Further prospective studies and experimental research are needed to explore this relationship.

Keywords: Meta-analysis; nasopharyngeal carcinoma (NPC); processed food

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Introduction

Nasopharyngeal carcinoma (NPC) is a malignancy with distinct geographical distribution, with an estimated 129,079 new cases and 72,987 deaths in 2018 worldwide, and most NPC patients are geographically localized to southern China and east and southeast Asia (1). According to relevant epidemiological data, the incidence and mortality of NPC in China were 3.09/100,000 and 1.57/100,000, respectively, which was higher the global data, and the top three incidence and mortality provinces are all located in southern China (2). NPC is a head and neck cancer with poor prognosis, and epidemiological trends in the past decades have shown the incidence and mortality of NPC have been decline (3). It is thought that NPC is the result of both genetic susceptibility and exposure to environmental factors such as Epstein-Barr virus infection (4).

Salt-preserved and fermented foods such as salted fish are traditional southern Chinese food, and favored by the local population due to the unique flavor of preserved foods and local food culture. Previous studies have proved that the intake of traditional salt-processed food is associated with gastrointestinal tumors including esophageal and gastric cancer (5,6). Pro-cancer factors in processed meat, including excess fat, excess protein, excess iron and heat-induced mutagens, may also be involved in carcinogenesis, plus the salt and nitrite added during the curing process (7). Several studies (8-20) have demonstrated that the consumption of processed foods is associated with risk of NPC. However, some inconsistent results exist. Some studies (21-24) showed no significant association between consumption of processed foods and risk of NPC. Therefore, we conducted a systematic review and meta-analysis to summarize the association of processed foods and NPC and assess the relationship. We present the following article in accordance with the MOOSE reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-690/rc).

Methods

Search strategy

PubMed, Web of Science, EMBASE, Medline and Google Scholar databases were searched by investigators for articles published before July 2021 regarding the association between consumption of processed food and risk of NPC. We used the search terms: ('processed' OR 'pickle' OR 'pickled' OR 'moldy' OR 'fermented' OR 'saltextractible' OR 'salted') AND ('nasopharyngeal') AND ('cancer' OR 'carcinoma' OR 'neoplasm' OR 'neoplasia' OR 'neoplastic'). All articles were published in English.

Exclusion criteria

Studies exploring the association between consumption of processed food and risk of NPC were included in the present study. All included studies were case-control or cohort designed. Exclusion criteria were: (I) not provide information regarding the relative risk (RR) or odds ratio (OR) estimates and the 95% confidence interval (CI) for the association between consumption of processed food and risk of NPC; (II) not case-control or cohort design; and (III) reviews, meta-analyses and case studies were removed.

Data collection

We recorded the following data: author, publication year, sample size, study type, study location, years of diagnosis, food item and comparison, and the covariates considered were multivariate adjusted ORs or RRs with corresponding 95% CI for the highest *vs.* lowest categories of processed food intake.

Statistical analysis

STATA 12.0 software was used to compute the multivariate ORs or RRs and 95% CIs regarding the association between consumption of processed food and risk of NPC. Q test and I^2 were used to evaluate heterogeneity between studies. With invariably high heterogeneity (P value for Q test ≤0.05 and $I^2 \geq 50\%$), a random effects model was used to generate summary effect size of studies; conversely, in the absence of between-study heterogeneity (P value for Q test >0.05 and $I^2 < 50\%$), a fixed effects model was used to summarize the effect size. Meta-regression analysis was applied to explore source of heterogeneity. Subgroup analysis for different ethnicities was used to explore the effect of heterogeneous ethnicities on the heterogeneity of the meta-analysis. Subgroup analysis for studies adjusted for confounders and studies which did not report covariates was used to explore the source of heterogeneity. Sensitivity analysis was conducted by removing 1 individual study each time to assess the source of heterogeneity. Publication bias was evaluated with Egger's regression test, Begg's adjusted rank correlation test, and funnel plots. Quality appraisal was made using the Cochrane Risk of Bias Tool. Data were analyzed using Review Manager 5.3.

Results

Search results

Figure 1 shows procedure for exclusion and Table S1 shows the studies' characteristics and results. A meta-analysis was made for 29 case-control studies (including 14,378 NPC patients and 17,928 controls). N=13 case-control studies (8-20) reported consumption of processed foods is associated with risk of NPC, whereas n=16 studies (21-36) showed no significant association between consumption of

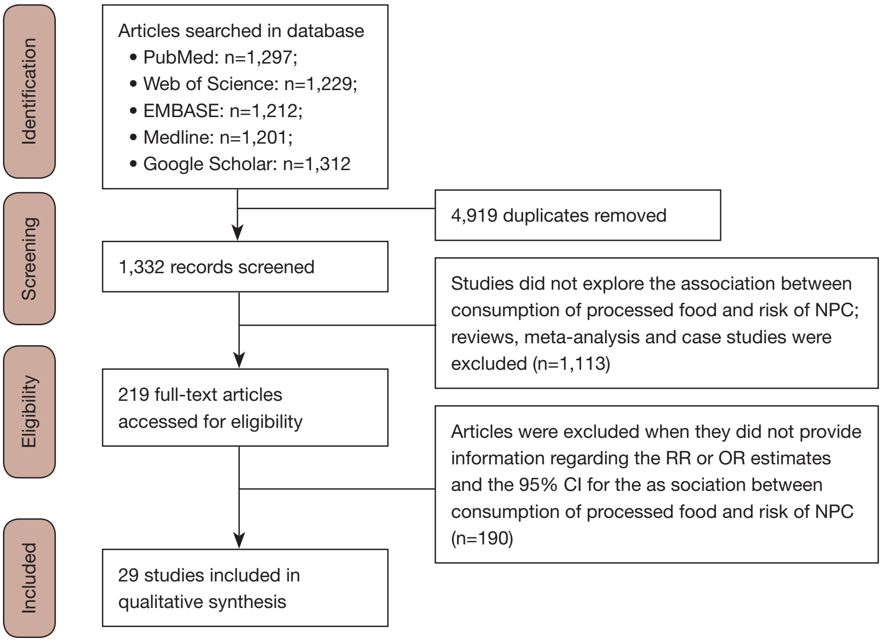

Figure 1 Flow of information through the different phases of meta-analysis. NPC, nasopharyngeal carcinoma; RR, relative risk; OR, odds ratio; CI, confidence interval.

processed foods and risk of NPC.

Meta-analysis results

The meta-analysis showed that the highest categories of processed food intake were associated with a 67% increase in NPC risk compared with the lowest categories in a random effects model (OR =1.67; 95% CI: 1.56–1.79; P value for Q test <0.001; I^2=86.9%; *Figure 2*). Subgroup study showed significant positive associations regarding consumption of processed food and risk of NPC in both Asians and Caucasians (Asian: OR =1.68, 95% CI: 1.56–1.81; Caucasian: OR =1.36, 95% CI: 1.09–1.71; *Figure 3*). Meta-regression analysis indicated that publication year, gender and age were not responsible for heterogeneity across studies (publication year: P value =0.242; gender: P value =0.509; age: P value =0.837). Subgroup study showed significant positive associations between consumption of processed food and risk of NPC in studies adjusted for confounders and studies which did not report covariates (studies adjusted for confounders: OR =1.64, 95% CI: 1.52–1.76; studies which did not report covariates: OR =2.10, 95% CI: 1.65–2.67; *Figure 4*). A sensitivity analysis showed no changes in the direction of effect when any 1 study was excluded (*Figure 5*). In addition, Begg's test, Egger's test and funnel plot showed no significant publication bias in the included studies (Egger's test: P=0.066; Begg's test: P=0.082; *Figure 6*). Risk of bias graph was showed in Figure S1. Details of the risk of bias summary was showed in Figure S2.

Discussion

In this meta-analysis, we included 29 case-control studies with 14,378 NPC patients and 17,928 controls. Our results suggested a significant association of processed foods to NPC risk with a random effects model score showing OR of 1.67 at 95% CI of 1.56–1.79 (P<0.01). And for both Asians and Caucasians, processed foods were a high-risk factor for NPC.

Our result was consistent with that of previous several studies. Okekpa *et al.* reported that salted fish consumption was significantly associated with an increased risk in NPC (OR =1.41; 95% CI: 1.13–1.75) (37). Similarly, Li *et al.* reported a significant association between total processed meat consumption dose and risk of NPC, and the risk of NPC increased with increased consumption dose of processed meat (low-rank intake: RR =1.46, 95% CI: 1.34–1.64; moderate-rank intake: RR =1.59, 95% CI: 1.30–1.90; high-rank intake: RR =2.11, 95% CI: 1.31–3.42) (38).

Due to the process of salted preservation, salted fish can accumulate high levels of nitrosamines, which have a

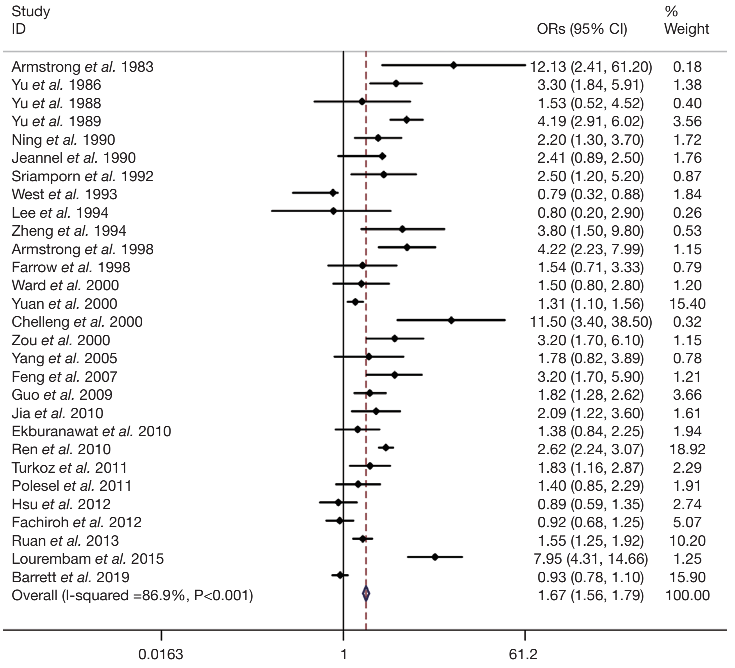

Figure 2 Forest plot of the association between processed food intake and NPC risk. OR, odds ratio; CI, confidence interval; NPC, nasopharyngeal carcinoma.

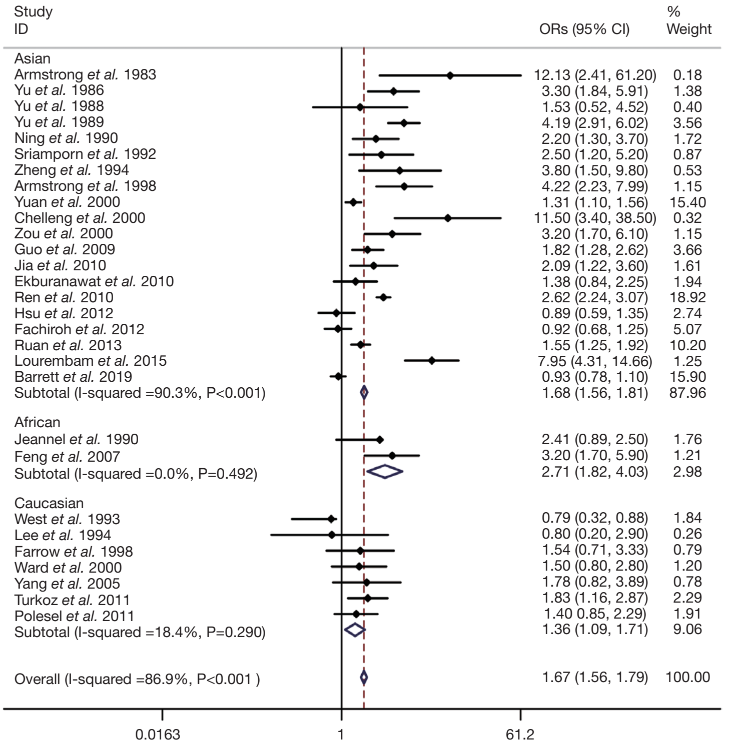

Figure 3 Subgroup study of the associations between processed food intake and NPC risk in Asians, Africans, and Caucasians. OR, odds ratio; CI, confidence interval; NPC, nasopharyngeal carcinoma.

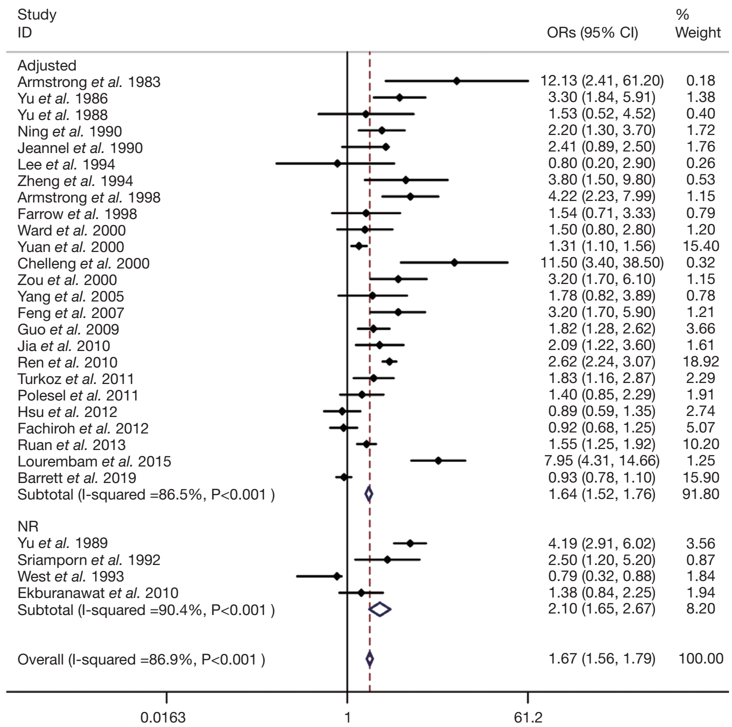

Figure 4 Subgroup study of the associations between processed food intake and NPC risk in studies adjusted for confounders and studies which did not report covariates. OR, odds ratio; CI, confidence interval; NR, not reported; NPC, nasopharyngeal carcinoma.

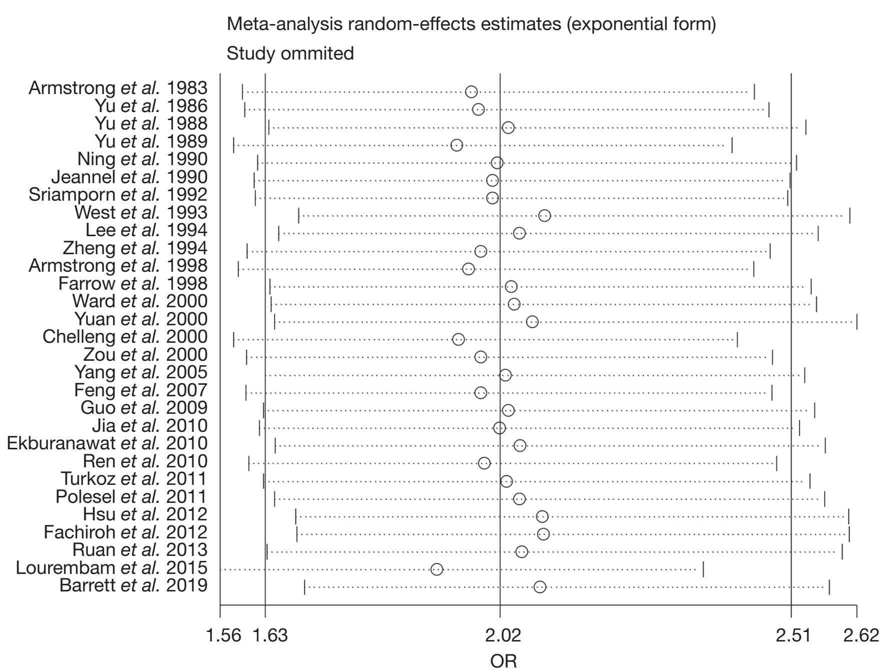

Figure 5 Sensitivity analysis of the association between processed food intake and NPC. OR, odds ratio; NPC, nasopharyngeal carcinoma.

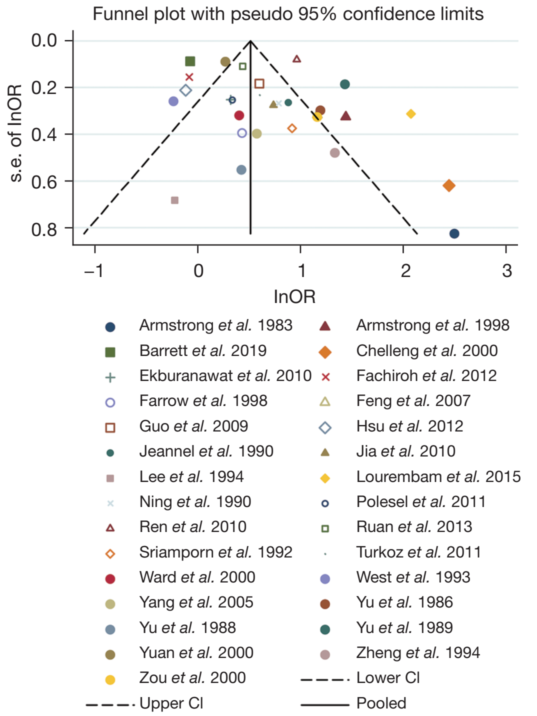

Figure 6 Funnel plot of the association between processed food intake and NPC. OR, odds ratio; CI, confidence interval; NPC, nasopharyngeal carcinoma.

carcinogenic effect on multiple organs (39). In addition, extracts of processed food have reactivated Epstein-Barr virus in cell lines (40). Lau *et al.* showed that decreasing incidence and mortality of NPC in Hong Kong correlated with declining salted fish consumption (41). Barrett *et al.* also reported an increased risk of NPC with a high level of intake of hard Chinese-style salted fish during adolescence (OR =1.19, 95% CI: 1.03–1.39) (26). As well as salted fish, salted and picked vegetables have also been proved to be associated with elevated risk of cancer incidence, including gastric cancer, and NPC (42,43). These findings indicated a need to reduce the consumption of processed foods.

However, several study limitations should be acknowledged. First, although observation studies can suggest an association between processed foods and NPC, the molecular mechanisms of the pathogenesis of NPC caused by processed foods are still unclear. Second, in our study we did not discuss the effect of some variates, including the intake dose and duration of consumption of processed foods, whether from adolescence or as an adult. Third, the status of Epstein-Barr virus may affect the result regarding the association between processed foods and NPC, so the lack of Epstein-Barr virus affection may lead to an inaccurate conclusion.

Conclusions

In summary, our findings of this present study voted that the result for the association of processed foods with NPC risk might be significant. And further prospective studies and experimental researches are needed to explore the relationship between processed foods and NPC risk.

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Footnote

Reporting Checklist: The authors have completed the MOOSE reporting checklist. Available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-690/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-690/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Supplementary

Table S1 Characteristics of the studies included in the meta-analysis

Reference	Numbers of cases/controls	Study type	Study location	Years of diagnosis	Food item; comparison	Covariates considered	OR/RR (95% CI)
Armstrong *et al*., 1983 (25)	100/100	Case-control	Malaysian	NR	Processed meat; < daily *vs.* never, daily *vs.* never	Age since, sex, exposure category, and occupational exposure to smoke and dust	2.49 (0.84, 7.36); 12.13 (2.41, 61.20)
Yu *et al*., 1986 (8)	250/250	Case-control	Hong Kong	NR	Processed meat; Q1–3 *vs.* <Q1; ≥Q4 *vs.* <Q1	Age, sex, dietary habits, occupational exposure to smoke, dust, or fumes, exposure to incense, antimosquito coils	2.32 (1.56, 2.45); 3.30 (1.84, 5.91)
Yu *et al*., 1988 (21)	128/174	Case-control	China	NR	Processed meat; Q1–3 *vs.* <Q1; ≥Q4 *vs.* <Q1	Age, sex, occupation, level of education, date, place of birth, and ethnic origin of both parents	1.58 (0.91, 2.76); 1.53 (0.52, 4.52)
Yu *et al*., 1989 (9)	110/139	Case-control	China	Between March 1, 1983 and August 31, 1985	Salted fish	NR	Hong Kong: 7.5 (3.9, 14.8); Guangzhou: 2.1 (1.2, 3.6)
Ning *et al*., 1990 (10)	100/300	Case-control	China	1985–1986	Processed meat; ever exposed *vs.* never exposed	The dietary risk factors had little effect on these occupational variables	2.2 (1.3, 3.7)
Jeannel *et al*., 1990 (22)	80/160	Case-control	Tunisia	Between November 1986 and November 1987	Processed meat; ever *vs.* never; ever *vs.* never (servings/week)	Age, sex, place of residence, and lifestyle	1.75 (0.79, 3.84); 2.41 (0.89, 2.50)
Sriamporn *et al*., 1992 (11)	120/120	Case-control	Thailand	NR	Processed meat; at least once a week *vs.* never	NR	2.5 (1.2, 5.2)
West *et al*., 1993 (34)	104/205	Case-control	USA	NR	Salted fish; processed meats; mid tertile *vs.* low tertile; high tertile *vs.* low tertile	NR	Salted fish: 1.1 [0.57, 2.3]; 1.3 [0.69, 2.6]; processed meats: 0.41 [0.21, 0.80]; 0.33 [0.17, 0.66]
Lee *et al*., 1994 (23)	200/406	Case-control	UK	Between March 1988 and December 1990	Salted fish; >3/week *vs.* nil	Confounding variables	0.8 (0.2, 2.9)
Zheng *et al*., 1994 (12)	88/176	Case-control	China	From 1 January 1986	Salted fish; monthly *vs.* rarely	Socioeconomic variables	3.8 (1.5, 9.8)
Armstrong *et al*., 1998 (13)	282/282	Case-control	China	NR	Processed meat; ≥Q3–4 *vs.* <Q1 (servings/month)	Age, sex, residence history, education, and social class	4.22 (2.23, 7.99)
Farrow *et al*., 1998 (24)	133/212	Case-control	USA	NR	Preserved meat; highest quartile *vs.* lowest quartile	Age, alcohol consumption, cigarette smoking, total caloric intake	1.54 (0.71, 3.33)
Ward *et al*., 2000 (33)	375/327	Case-control	USA	From July 15, 1991 through December 31, 1994	Salted fish; >0 *vs.* 0	Age, gender, and ethnicity	1.5 (0.8, 2.8)
Yuan *et al*., 2000 (36)	935/1,032	Case-control	China	Between January 1987 and September 1991	Salted fish; salted seafood pastes; preserved meats; preserved eggs; weekly or more *vs.* less than monthly	Age, gender (for "total" only), level of education, cigarette smoking, exposure to smoke from heated rapeseed oil and burning coal during cooking, occupational exposure to chemical fumes and history of chronic ear and nose condition	1.82 (0.86, 3.88); 1.44 (0.97, 2.15); 1.77 (1.12, 2.79); 1.17 (0.88, 1.55)
Chelleng *et al*., 2000 (14)	47/47	Case-control	India	NR	Processed meat; frequently *vs.* never/rarely	Age, sex, occupation, economic status, and history of smoking	11.50 (3.40, 38.50)
Zou *et al*., 2000 (15)	97/192	Case-control	China	1987–1995	Processed meat; 3 times every 10 days *vs.* less than 3 times every 10 days	Homemade pickles, and fermented soy beans, education levels, the history of chronic rhinitis, and the family history of NPC	3.2 (1.7, 6.1)

Table S1 (*continued*)

Table S1 (*continued*)

Reference	Numbers of cases/controls	Study type	Study location	Years of diagnosis	Food item; comparison	Covariates considered	OR/RR (95% CI)
Yang *et al.*, 2005 (35)	502/1,942	Case-control	USA	Initiated in 1996	Guangdong salted fish; ≥1/week *vs.* never	Age, sex, cigarette smoking, betel nut consumption, wood and formaldehyde exposure, and Guangdong and other salted fish consumption during childhood	1.78 (0.82, 3.89)
Feng *et al.*, 2007 (16)	636/614	Case-control	African (multicenter)	2002–2005	Preserved meat; ≥3 *vs.* <1 (servings/week); ≥1 *vs.* <1 (servings/month)	Age, sex, occupation, education, household type, exposure to chemicals, smokes, alcohol, and tobacco consumption	3.20 (1.70, 5.90); 1.95 (1.30, 2.94)
Guo *et al.*, 2009 (29)	1,049/785	Case-control	China	2004–2005	Salty fish; preserved meat; 3 times/month *vs.* never	All environmental exposures	1.9 (1.05, 3.47); 1.03 (0.51, 2.05)
Jia *et al.*, 2010 (17)	1,387/1,459	Case-control	China	Between October 2005 and October 2007	Processed meat; ≥4 *vs.* <1; ≥1 *vs.* <1 (servings/month)	Age, sex, education, dialect, and habitation household type	2.09 (1.22, 3.60); 1.67 (1.09, 2.54)
Ekburanawat *et al.*, 2010 (27)	327/327	Case-control	Thailand	NR	Salted fish	NR	1.38 (0.84, 2.25)
Ren *et al.*, 2010 (18)	1,845/2,275	Case-control	China	Between October 2005 and October 2007	Sal-preserved fish consumption; ever *vs.* never or rarely	Age, gender, education, smoking, consumption of alcohol, salted fish consumption, number of siblings, and number of children	2.62 (2.24, 3.07)
Turkoz *et al.*, 2011 (32)	183/183	Case-control	Turkey	NR	Processed meat; >4 *vs.* never (servings/week) 1–2 *vs.* never	Age, sex, lifestyles, smoking habits, alcohol consumption, household type, occupation, and socioeconomic status	1.83 (1.16, 2.87); 1.05 (0.57, 1.93)
Polesel *et al.*, 2011 (31)	198/594	Case-control	Italy	NR	Processed meat; third *vs.* first quartile (servings/week); fourth *vs.* first quartile	Age, sex, place of living, year of interview, education, tobacco smoking, alcohol drinking, and nonalcohol energy	1.28 (0.74, 2.23); 1.40 (0.85, 2.29)
Hsu *et al.*, 2012 (30)	375/327	Case-control	Taiwan, China	Between July 1991 and December 1994	Salted, smoked, and barbecued meat; >0.7 *vs.* ≤0.25	Age, gender, ethnicity, educational level, NPC family history, total calories intake, years of cigarette smoking, and exposures to formaldehyde and wood dust	0.89 (0.59, 1.35)
Fachiroh *et al.*, 2012 (28)	681/1,078	Case-control	Indonesia	NR	Salted fish; weekly or more *vs.* never to rarely	Gender and age	0.92 (0.68, 1.25)
Ruan *et al.*, 2013 (19)	1,387/1,459	Case-control	China	Between October 2005 and October 2007	Salted fish; ≥ weekly *vs.* < monthly	Age, sex, education level, dialect, rural or urban household type, and all other variables	1.55 (1.25, 1.92)
Lourembam *et al.*, 2015 (20)	105/115	Case-control	India	NR	Processed meat; ever *vs.* never <1 *vs.* never; >1 *vs.* never (servings/month)	Age, sex, and ethnicity matched	7.95 (4.31, 14.66)
Barrett *et al.*, 2019 (26)	2,554/2,648	Case-control	China	Between 2010 and 2013	Total Chinese-style salted fish; >1.64 in male and ≥1.36 in female *vs.* 0	Sex, age, residential area, education level, current housing type, current occupation, first-degree family history of NPC, cigarette smoking, adult daily energy intake (log transformed), energy-adjusted intake of other foods, and childhood frequency of intake of total preserved foods	0.93 (0.78, 1.10)

CI, confidence intervals; NPC, nasopharyngeal carcinoma; NR, not reported; OR, odds ratio; Q, quartile; RR, relative risk.

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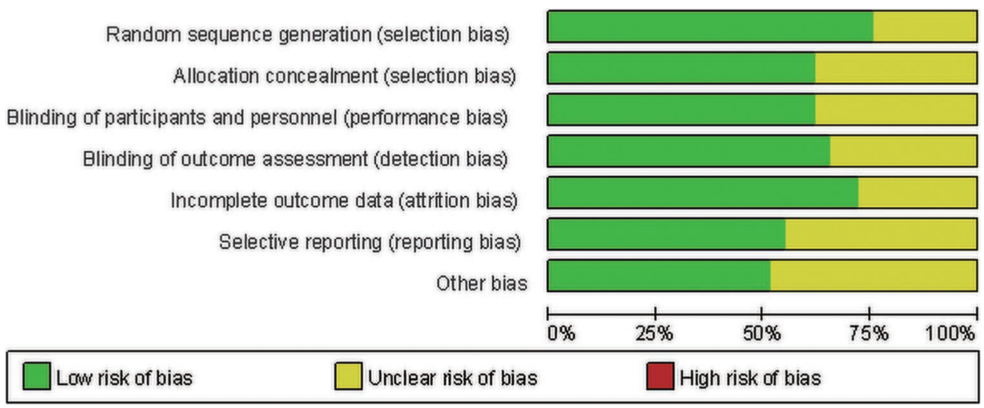

Figure S1 Risk of bias graph.

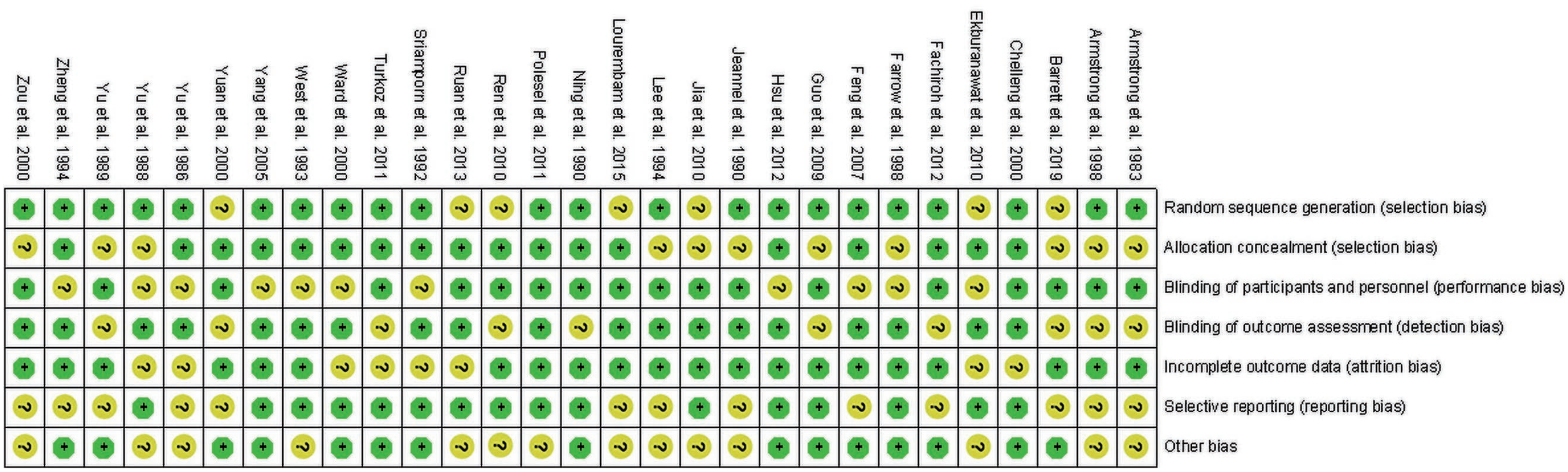

Figure S2 Details of the risk of bias summary.

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