Meta-Analysis

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Association between fish intake and glioma risk: a systematic review and meta-analysis

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Abstract

Objectives: We investigated the association between the consumption of fresh and processed fish and glioma risk using a meta-analysis approach.

Methods: We selected and analyzed observational studies that discussed the relationships between fresh and processed fish intake on glioma risk from PubMed, Web of Science, Embase, and the SinoMed and Wanfang databases from inception to 31 March 2020. Studies were selected according to pre-established eligibility criteria and data were extracted separately by two researchers. A meta-analysis was conducted based on a random-effects model to provide pooled odds ratios (OR) and 95% confidence intervals (CIs).

Results: Eight studies considered the relationship between fish intake (seven fresh and seven processed fish) and glioma risk and were included in this meta-analysis. The OR effect size for fresh fish intake and glioma risk was 0.72 (95%CI 0.53–0.97) and the overall OR effect size for processed fish intake and glioma risk was 1.88 (95%CI 1.06–3.34).

Conclusion: Dietary intake of fresh fish may reduce the risk of glioma, but consumption of processed fish may increase the risk of glioma. This study had some limitations, and further studies are therefore required to clarify the associations between fish intake and glioma risk.

Keywords

Fish, dietary intake, glioma, meta-analysis, processed fish, risk

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Introduction

Gliomas originate from glial cells and are the most common type of brain cancer, accounting for nearly 80% of all malignant primary intracranial tumors.[1] The incidence of gliomas is relatively high at about 4–5/100,000 people per year, with the highest incidence in the sixth decade of life.[1,2] In addition to genetic factors, studies aimed at identifying lifestyle factors that may affect the risk of glioma have suggested that dietary intake, such as intakes of fruit and vegetables,[3] vitamins,[4–6] tea and coffee,[7] and poultry and eggs,[8] may influence the development of glioma. Mozaffari et al.[9] recently reviewed the association between dietary fish intake and the risk of inflammatory bowel disease. However, the role of fish consumption on the risk of glioma is unclear. Fish are rich in polyunsaturated fatty acids (PUFAs), which can reduce the production of free radicals and carcinogens, suggesting that fish intake may reduce the risk of glioma. Although previous studies have examined the effects of fish intake on glioma risk, the results have been inconsistent. For example, Boeing et al.[10] indicated that fresh fish consumption reduced the risk of glioma, but the results were not significant, while Giles et al.[11] found an increased, but also non-significant, association between glioma risk and fresh fish intake in men. Although Hu et al.[12] showed that eating processed fish significantly increased the risk of glioma, other studies have failed to find any positive results. We therefore conducted a meta-analysis to evaluate the effects of eating fresh and processed fish on the risk of glioma.

Methods

The current meta-analysis was performed according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Figure 1).[13]

Data sources and search strategies

We conducted an extensive search of PubMed, Web of Science, Embase, the SinoMed database, and the Wanfang database (from inception to 31 March 2020) using the following keywords: ("fish" OR "seafood") combined with ("glioma" OR "brain cancer" OR "brain tumors") with no restrictions. If the reported data were ambiguous, we contacted the original authors. The search was carried out by two authors independently, and any disagreements between these two authors were resolved by a third author. This study was a meta-analysis and was therefore exempt from approval by an ethics review committee.

Eligibility criteria

Eligible studies were selected in accordance with the following inclusion criteria: (a) observational studies, including cohort and case control studies; (b) observational studies of patients with glioma aged $\geq$18 years; and (c) studies that reported the association between fish intake and glioma risk and provided enough data on odds ratios (OR) and 95% confidence intervals (CIs). Case reports, review articles, preclinical studies, and other non-relevant studies, and studies with inadequate information on ORs were excluded.

Data extraction and quality assessment

Two reviewers evaluated the observational studies using the same eligibility evaluation form. Conflicting evaluations were discussed with a third investigator until the reviewers reached consensus. The detailed information listed in Table 1 was extracted by one reviewer and verified by another. The quality of each study was evaluated according to the Newcastle-Ottawa-Scale (NOS).[14]

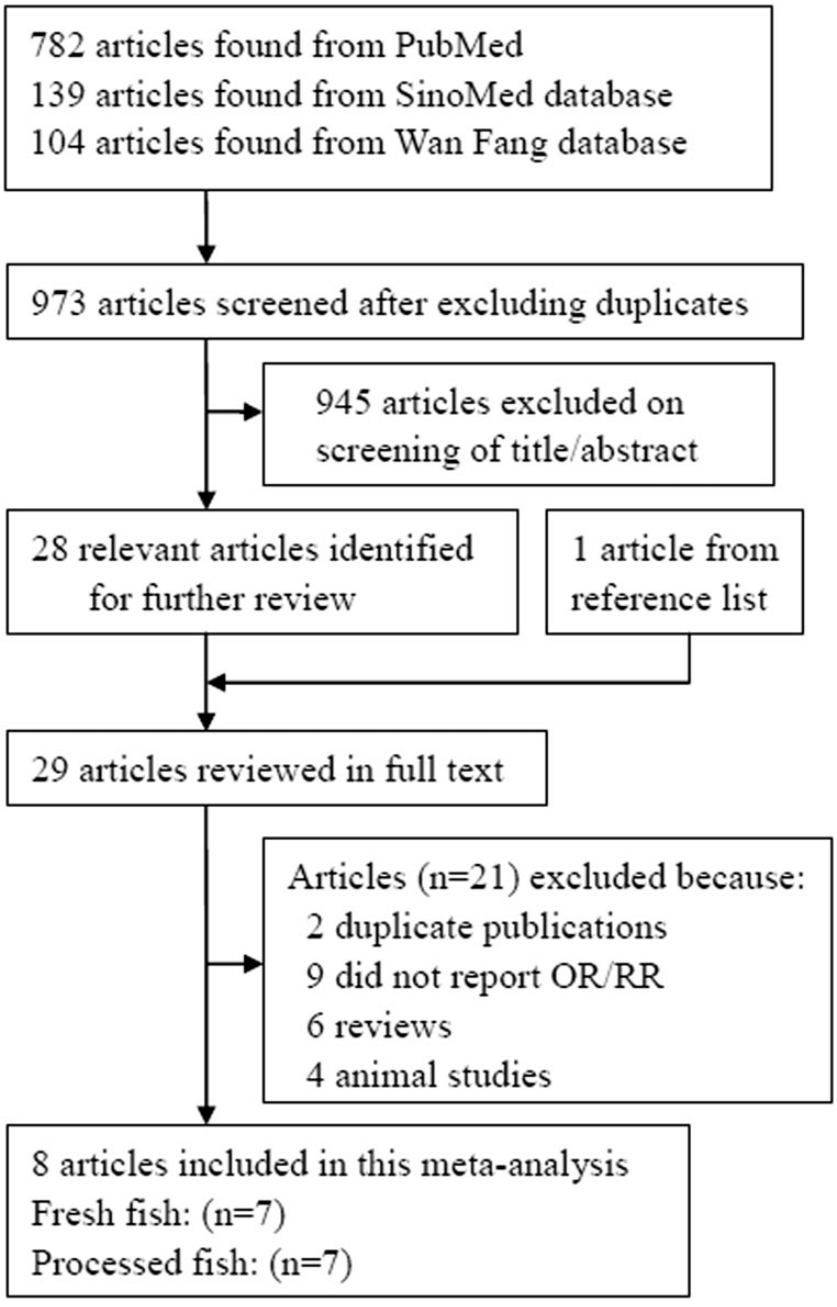

Figure 1. Flow chart of meta-analysis for exclusion/inclusion of studies.
OR, odds ratio; RR, relative risk.

Table 1. Characteristics of all studies.

Study	Year	Country	Study type	Cases	Controls	Age (years)	Quality score	Categories	OR (95%CI)
Burch et al.[19]	1987	United States	Case–control	215	215	25–80	6	Salted fish: 1/month vs. <1/month Smoked fish: ≥1/month vs. <1/month	Salted fish: 1.40 (0.44–4.41) Smoked fish: 1.67 (0.61–4.59)
Boeing et al.[10]	1993	Germany	Case–control	115	418	25–75	7	Fish: T3 vs. T1 Processed fish: T3 vs. T1	Fish: 0.7 (0.4–1.4) Processed fish: 1.4 (0.8–2.4)
Giles et al.[11]	1994	Australia	Case–control	409	409	20–70	7	Fresh fish: men: T3 vs. T1; women: T3 vs. T1 Processed fish: men: T3 vs. T1; women: T3 vs. T1	Fresh fish: men: 1.29 (0.79–2.12); women: 0.63 (0.32–1.26) Processed fish: men: 1.19 (0.62–2.26); women: 1.44 (0.77–2.66)
Blowers et al.[20]	1997	United States	Case–control	94	94	25–74	7	Fresh fish: T3 vs. T1	Fresh fish: 0.4 (0.2–1.1)
Hu et al.[12]	1999	China	Case–control	73	258	20–74	6	Fresh fish: Q4 vs. Q1 Processed fish: Q4 vs. Q1	Fresh fish: 0.38 (0.20–0.90) Processed fish: 50.83 (11.2–230.9)
Chen et al.[21]	2002	United States	Case–control	236	449	≥21	7	Fish: Q4 vs. Q1	Fish: 0.6 (0.3–1.2)
Bunin et al.[22]	2006	United States and Canada	Case–control	315	315	NA	8	Smoked fish: ≥1/month vs. <1/month	Smoked fish: 1.3 (0.6–2.6)
Terry et al.[23]	2009	Caucasian	Case–control	1185	2486	20–80	8	Fresh fish: Q4 vs. Q1	Fresh fish: 0.9 (0.7–1.1)

OR, odds ratio; CI, confidence interval; NA, not available; Q4, quartile 4; Q1, quartile 1; T3, tertile 3; T1, tertile 1 (quartiles defined according to original studies).

Data synthesis and analysis

This meta-analysis was based on a random-effects model and conducted using RevMan version 5.3.[15,16] Outcomes were pooled with ORs and 95%CIs. Egger's test[17] and funnel plots[18] were carried out to assess publication bias, using R 3.5.2. The I^2 statistic, which describes variations across trials rather than sampling errors, was calculated to assess heterogeneity, and I^2 values >50% indicated significant heterogeneity.[16] Statistical significance was set at $P<0.05$ for all analyses. The robustness of the results was evaluated by sensitivity analysis by excluding each study sequentially. The results were considered robust or reliable if the pooled OR of the sensitivity analysis did not differ significantly from the overall results.

Results

Study selection

A total of 782 citations from PubMed, 139 from the SinoMed database, and 104 from the Wanfang database were retrieved during the first search (Figure 1). After screening the titles/abstracts, the full texts of 29 relevant articles were reviewed, and eight articles,[10–12,19–23] including 2674 glioma cases and 7350 participants, were finally subjected to quantitative synthesis and meta-analysis.

Study characteristics

Fish consumption was categorized as indicated in Table 1. Among the included studies, Boeing et al.,[10] Giles et al.,[11] and Hu et al.[12] reported on both fresh and processed fish intake and glioma risk. Giles et al.[11] reported the risks for men and women, respectively, and Burch et al.[19] reported risks for salt fish and smoked fish, respectively. Seven studies thus analyzed the relationship between fresh fish intake and glioma risk and seven studies analyzed the effect of processed fish intake on glioma risk. Seven of the included studies were conducted in Caucasians and the remaining one was conducted in Asians. All eight studies showed relatively high quality (>6 stars), with an average NOS score of 7. Detailed information is shown in Table 1.

Relationships between fish intake and glioma risk

The relationships between fish intake and risk of glioma stratified according to fresh and processed fish was shown in a forest plot (Figure 2). The OR effect size for fresh fish and glioma risk was 0.72 (95% CI (0.53–0.97, $P=0.032$), and the overall OR effect size for processed fish intake and glioma risk was 1.88 (95%CI 1.06–3.34, $P=0.032$). Subgroup analysis by quality assessment (quality score <7 or ≥7) was performed. Six of the seven included studies had quality scores ≥7 for the association between fresh fish and glioma risk, and the association was similar to the overall result (OR 0.79, 95%CI 0.60–0.98, $P=0.049$). Three studies had quality scores <7 and four studies had quality scores ≥7 for the association between processed fish intake and glioma risk. The association was significant in the studies with a quality score ≥7 (OR 1.34, 95%CI 1.01–1.83, $P=0.041$), but not in the studies with a quality score <7 (OR 4.59, 95%CI 0.62–33.78, $P=0.135$).

Heterogeneity

Although we found significant associations between both fresh and processed fish intakes on glioma risk, high heterogeneity existed in both groups. We therefore conducted sensitivity analysis to assess the stability of the results. We excluded one study of fresh fish intake and glioma risk (Giles

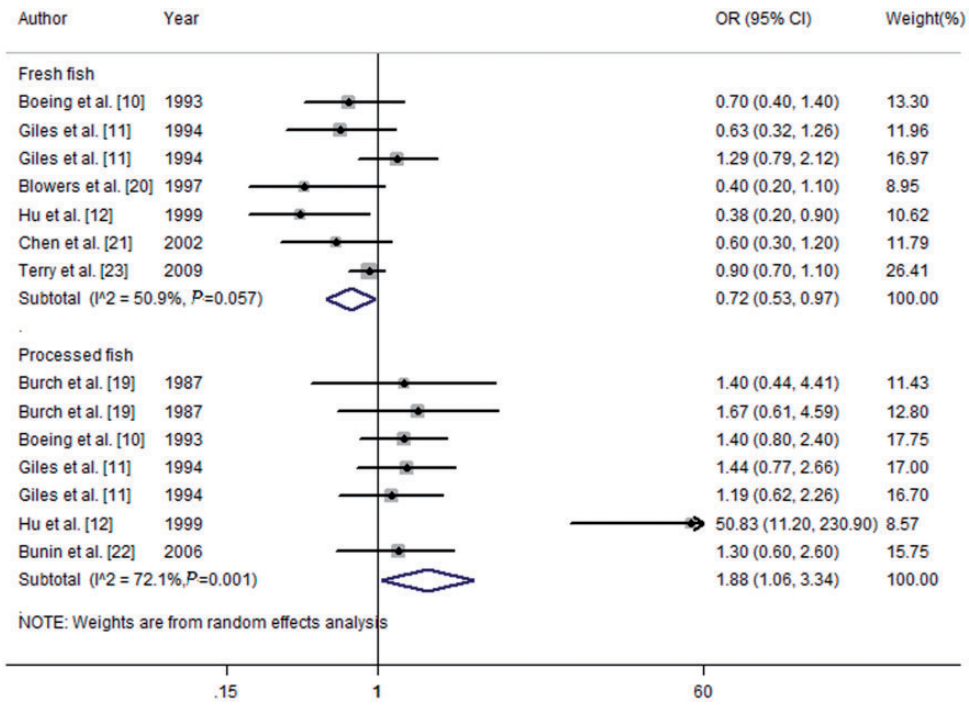

Figure 2. Forest plot of association between fish intake and risk of glioma stratified according to fresh and processed fish.

et al.[11]), which might have influenced the substantive results. The OR effect size for the association between fresh fish and glioma risk was lower than the overall result (OR 0.65, 95%CI 0.48–0.88), and the heterogeneity was reduced to 40.4% ($P = 0.136$). Similarly, exclusion of one study of processed fish intake and glioma risk (Hu et al.[12]) that carried a high risk of bias resulted in an overall OR of 1.37 (95%CI 1.02–1.83) and reduced the heterogeneity to 0.0% ($P = 0.996$).

Risk of bias across studies

We used funnel plots to check for possible publication bias for fresh fish (Figure 3a) and processed fish (Figure 3b). Egger's tests for publication bias were negative for both fresh fish ($P = 0.102$) and processed fish ($P = 0.081$).

Sensitivity analysis

Sensitivity analysis was conducted by excluding each study sequentially to identify their respective influence on the pooled OR. The results showed that removal of any study had no significant effect on the combined OR.

Discussion

Numerous studies have examined the relationship between dietary fish intake and glioma risk, with conflicting results. We therefore conducted a meta-analysis to clarify if higher intakes of fresh and processed fish affected the risk of developing glioma. Eight publications, involving 2674 glioma cases and 7350 participants, were included in the meta-analysis. The pooled results suggested that the highest category of fresh fish intake was significantly associated

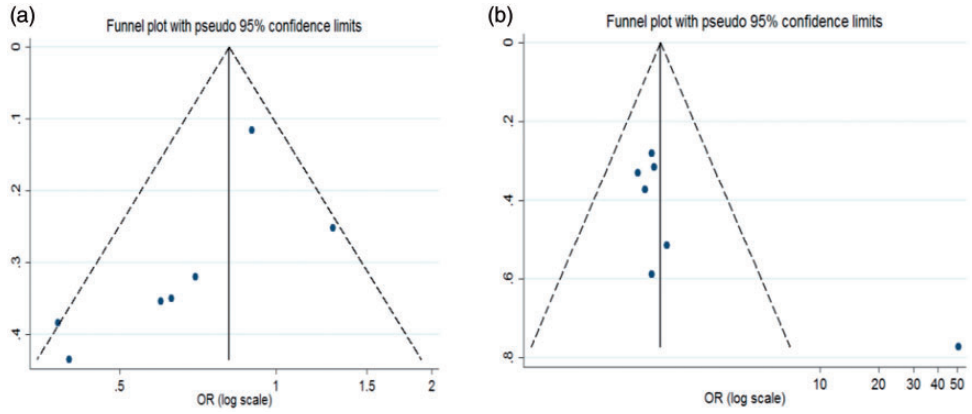

Figure 3. Funnel plot for the analysis of publication bias in studies analyzing effects of intake of (a) fresh fish and (b) processed fish on glioma risk.
OR, odds ratio.

with a lower risk of glioma, compared with the lowest category of fresh fish intake. In contrast, however, processed fish intake could increase the risk of glioma.

A previous meta-analysis indicated that fish intake and n-3 polyunsaturated acids (PUFAs) could reduce the risk of inflammatory bowel disease.[9] Moreover, a meta-analysis by Sepidarkish et al.[24] suggested that PUFAs and vitamin E supplementation could affect oxidative stress. Fresh fish is rich in PUFAs, and may thus have anti-inflammatory effects, as well as reducing the production of free radicals and carcinogens.[25,26] This could explain why increased consumption of fresh fish reduces the risk of glioma. However, processed fish may contain nitrates and nitrites, which could conversely increase the risk of glioma.[27] The current study accordingly distinguished between fresh and processed fish because of their potentially different roles in terms of glioma risk.

Seven of the eight included studies involved Caucasians and the remaining one involved Asians. The associations in the Caucasian subgroup were all consistent with the overall results. However, more studies in other ethnicities are warranted to further explore the related association.

This meta-analysis had some limitations, which should be considered when designing future studies. First, the small number of included studies might have led us to overestimate the effects of fresh fish and processed fish on the risk of glioma. Second, all the included studies were case-control studies, which may be subject to some bias. Further prospective studies are therefore needed to confirm the relationships between fish intake and glioma risk. Third, we only searched for published papers and may therefore have missed some unpublished and meeting papers, which might have influenced the results of our study. Fourth, we did not conduct subgroup analyses by age, sex, and other related factors. The included studies did not involve any subjects younger than 20 years, and there was no detailed age-stratified information in any study. Furthermore, no sex-related data were reported in any study. We aim to update this meta-analysis with additional relevant studies with fewer potential biases one age- and sex-related information becomes available.

In conclusion, dietary intake of fresh fish may decrease the risk of developing glioma, but intake of processed fish intake may increase the risk of glioma. More studies are required to explore these associations

and to overcome the limitations of the current study.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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References

1. Stupp R, Brada M, Van Den Bent MJ, et al. High-grade glioma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2014; 25: iii93–iii101.
2. Porter KR, McCarthy BJ, Freels S, et al. Prevalence estimates for primary brain tumors in the United States by age, gender, behavior, and histology. *Neuro Oncol* 2010; 12: 520–527.
3. Li Y. Association between fruit and vegetable intake and risk for glioma: a meta-analysis. *Nutrition* 2014; 30: 1272–1278.
4. Lv W, Zhong X, Xu L, et al. Association between dietary vitamin A intake and the risk of glioma: evidence from a meta-analysis. *Nutrients* 2015; 7: 8897–8904.
5. Zhou S, Wang X, Tan Y, et al. Association between vitamin C intake and glioma risk: evidence from a meta-analysis. *Neuroepidemiology* 2015; 44: 39–44.
6. Qin S, Wang M, Zhang T, et al. Vitamin E intake is not associated with glioma risk: evidence from a meta-analysis. *Neuroepidemiology* 2014; 43: 253–258.
7. Song Y, Wang Z, Jin Y, et al. Association between tea and coffee consumption and brain cancer risk: an updated meta-analysis. *World J Surg Oncol* 2019; 17: 51.
8. Luo H, Sun P, He S, et al. A meta-analysis of the association between poultry and egg consumption and the risk of brain cancer. *Cell Mol Biol (Noisy-le-grand)* 2019; 65: 14–18.
9. Mozaffari H, Daneshzad E, Larijani B, et al. Dietary intake of fish, n-3 polyunsaturated fatty acids, and risk of inflammatory bowel disease: a systematic review and meta-analysis of observational studies. *Eur J Nutr* 2020; 59: 1–17.
10. Boeing H, Schlehofer B, Blettner M, et al. Dietary carcinogens and the risk for glioma and meningioma in Germany. *Int J Cancer* 1993; 53: 561–565.
11. Giles GG, McNeil JJ, Donnan G, et al. Dietary factors and the risk of glioma in adults: results of a case-control study in Melbourne, Australia. *Int J Cancer* 1994; 59: 357–362.
12. Hu J, La Vecchia C, Negri E, et al. Diet and brain cancer in adults: a case-control study in northeast China. *Int J Cancer* 1999; 81: 20–23.
13. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Ann Intern Med* 2009; 151: 264–269, W64.
14. Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. *Eur J Epidemiol* 2010; 25: 603–605.
15. DerSimonian R and Laird N. Meta-analysis in clinical trials. *Control Clin Trials* 1986; 7: 177–188.
16. Higgins JP, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analyses. *BMJ* 2003; 327: 557–560.
17. Egger M, Davey Smith G, Schneider M, et al. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997; 315: 629–634.
18. Begg CB and Mazumdar M. Operating characteristics of a rank correlation test for publication bias. *Biometrics* 1994; 50: 1088–1101.
19. Burch JD, Craib KJ, Choi BC, et al. An exploratory case-control study of brain tumors in adults. *J Natl Cancer Inst* 1987; 78: 601–609.
20. Blowers L, Preston-Martin S and Mack WJ. Dietary and other lifestyle factors of women

with brain gliomas in Los Angeles County (California, USA). *Cancer Causes Control* 1997; 8: 5–12.
21. Chen H, Ward MH, Tucker KL, et al. Diet and risk of adult glioma in eastern Nebraska, United States. *Cancer Causes Control* 2002; 13: 647–655.
22. Bunin GR, Gallagher PR, Rorke-Adams LB, et al. Maternal supplement, micronutrient, and cured meat intake during pregnancy and risk of medulloblastoma during childhood: a children's oncology group study. *Cancer Epidemiol Biomarkers Prev* 2006; 15: 1660–1667.
23. Terry MB, Howe G, Pogoda JM, et al. An international case-control study of adult diet and brain tumor risk: a histology-specific analysis by food group. *Ann Epidemiol* 2009; 19: 161–171.
24. Sepidarkish M, Akbari-Fakhrabadi M, Daneshzad E, et al. Effect of omega-3 fatty acid plus vitamin E Co-Supplementation on oxidative stress parameters: a systematic review and meta-analysis. *Clin Nutr* 2020; 39: 1019–1025.
25. Daniel CR, Cross AJ, Graubard BI, et al. Prospective investigation of poultry and fish intake in relation to cancer risk. *Cancer Prev Res (Phila)* 2011; 4: 1903–1911.
26. MacLean CH, Newberry SJ, Mojica WA, et al. Effects of omega-3 fatty acids on cancer risk: a systematic review. *JAMA* 2006; 295: 403–415.
27. Xie L, Mo M, Jia HX, et al. Association between dietary nitrate and nitrite intake and site-specific cancer risk: evidence from observational studies. *Oncotarget* 2016; 7: 56915–56932.