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Fish consumption and risk of depression: a meta-analysis

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ABSTRACT

Background The association between fish consumption and risk of depression is controversial. We performed a meta-analysis to evaluate the association.

Methods A literature search was performed in PubMed, EMBASE and Web of Science database for all relevant studies up to March 2015. We pooled the relative risks (RRs) with 95% CIs from individual studies with random effects model, and conducted meta-regression to explore potential sources of heterogeneity. Publication bias was estimated by Egger's test and the funnel plot.

Results A total of 26 studies involving 150 278 participants were included in the present meta-analysis. The pooled RR of depression for the highest versus lowest consumption of fish was 0.83 (95% CI 0.74 to 0.93). The findings remained significant in the cohort studies (RR=0.84, 95% CI 0.75 to 0.94, n=10) as well as in the cross-sectional studies (RR=0.82, 95% CI 0.68 to 1.00, n=16). When men and women were analysed separately, a significant inverse association was also observed. There was no evidence of publication bias.

Conclusions This meta-analysis indicates that high-fish consumption can reduce the risk of depression.

INTRODUCTION

Depression is a common mental health disorder, with an estimated 350 million people affected.[1] According to the WHO, depression is now the leading cause of disability worldwide.[2] It is projected to be the world's second leading cause of disease burden by the year 2020.[2] In addition, depression is also an important risk factor for lifetime suicide attempt, with a population attributable risk proportion of about 28%.[3] However, the current treatment for depression is not satisfactory, because of the poor compliance, side effects and high recurrence rate with antidepressant medications.[4] Considering its public health impacts, there is increasing interest in exploring modifiable lifestyle factors to prevent depression.

In 1998, Hibbeln[5] suggested that dietary factors may account for the variation in depression prevalence between countries. Much studies have investigated the associations between food consumption and depression risk.[6 7] Furthermore, a meta-analysis published recently indicated that a healthy dietary pattern, characterised by a high intake of fruits, vegetables, fish and whole grains, was significantly associated with a reduced risk of depression.[8] However, it is not yet clear which component of the dietary pattern would be responsible for the protective effect. Fish, as an important source of n-3 polyunsaturated fatty acids (n-3 PUFAs), which may play important roles in neural structure and function,[9 10] has been reported to be associated with depression in several studies.[11–14] However, others did not find an association between fish consumption and depression risk.[15–19]

Considering the inconsistent and inconclusive findings of the epidemiology studies, we conducted a meta-analysis to summarise the results of observational studies on the association between fish consumption and depression risk.

MATERIALS AND METHODS

We consulted Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines for reporting of meta-analyses in this analysis.[20]

Search strategy

We performed a literature search up to March 2015 in the databases of PubMed, EMBASE and Web of Science, with the following search terms, 'depression' or 'depressive disorder' or 'depressive symptoms' and 'fish'. All searches were limited to studies conducted in humans and published in English. Furthermore, the reference lists of retrieved articles were reviewed for undetected relevant studies.

Inclusion criteria

The studies were included if they met the following criteria: (1) they followed an observational study design, including cross-sectional, case–control and cohort studies; (2) the participants of interest were from the general population (ie, excluding the studies in disease-specific populations, such as in patients with cardiovascular disease and cancer); (3) the exposure of interest was fish consumption; (4) the outcome was depression, excluding postpartum depression and depression in pregnancy. Depression was defined as reporting a doctor's diagnosis of depression, beginning regular use of antidepressant medication or identified by interview or depression rating scales; and (5) the multivariate adjusted OR or relative risk (RR) with 95% CI of depression for the highest versus lowest consumption of fish was provided (we presented all results with RR for simplicity). If data were duplicated in more than one study, the most recent and complete article was included.

All studies were carefully reviewed independently by two investigators to identify and determine whether an individual study was eligible for inclusion criteria in this meta-analysis. If the two reviewers could not reach a consensus about the eligibility of an article, it was resolved by dialogue with a third investigator.

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Data extraction

The data were extracted from each study by two independent investigators. Discrepancies in data extraction were discussed and resolved by consensus. The following information was extracted : (1) the first author's last name; (2) publication year; (3) country where the study was performed; (4) study design; (5) age range of participants; (6) sex; (7) sample size; (8) the number of depression cases; (9) fish consumption assessment; (10) depression diagnosis method; (11) variables adjusted for in the analysis; (12) the comparison of fish consumption; and (13) the most adjusted RR with 95% CI of depression for the highest versus lowest consumption of fish. The study quality was assessed using the Newcastle-Ottawa quality assessment scale (http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp).

Statistical analysis

We weighted the study-specific log RRs by the inverse of their variance, to calculate pooled RRs with corresponding 95% CIs of the association between fish consumption and risk of depression. Furthermore, we also evaluated the association separately in men and women. Heterogeneity among studies was assessed using the Q test and I^2 statistic. I^2 values of 0%, 25%, 50% and 75% represent no, low, moderate and high heterogeneity, respectively.[21] The DerSimonian and Laird random effects model (REM) was selected as the pooling method.[22] Meta-regression with restricted maximum likelihood estimation was used to explore potential sources of heterogeneity,[23] including covariates: publication year, continent (Europe, Asia, North America, South America and Oceania), sex (men and women), study design (cohort study and cross-sectional study), sample size, the number of depression cases, Newcastle-Ottawa score, dietary intake assessment and depression diagnosis method. Subgroup analysis by the continent and study design was conducted. If the heterogeneity could not be explained by the meta-regression and subgroup analysis, a leave-one-out sensitivity analysis would be carried out to evaluate the key studies that have substantial impact on between-study heterogeneity.[24] The influence analysis was performed with one study removed at a time to assess whether the results could have been affected markedly by a single study. Publication bias was evaluated with visual inspection of the funnel plot and Egger's test because the adjusted RR was used in our meta-analysis.[25] All statistical analyses were performed with Stata V.12.0 (Stata Corp, College Station, Texas, USA). All reported probabilities (p values) were two-sided with $p<0.05$ considered statistically significant.

RESULTS

Search results and study characteristics

The search strategy identified 744 articles from PubMed, 1561 articles from Web of Science and 1859 articles from EMBASE. Five additional articles were found in reference lists. After reviewing the title or abstract, 101 articles were retrieved. Eighty-five articles were subsequently excluded for various reasons after reviewing the full text. As a result, 16 articles including 26 studies met the inclusion criteria and were included in the meta-analysis.[11–19 26–32] The flow diagram of the literature search is shown in figure1.

The characteristics of the studies included in this meta-analysis are present in online supplementary file 1. The 26

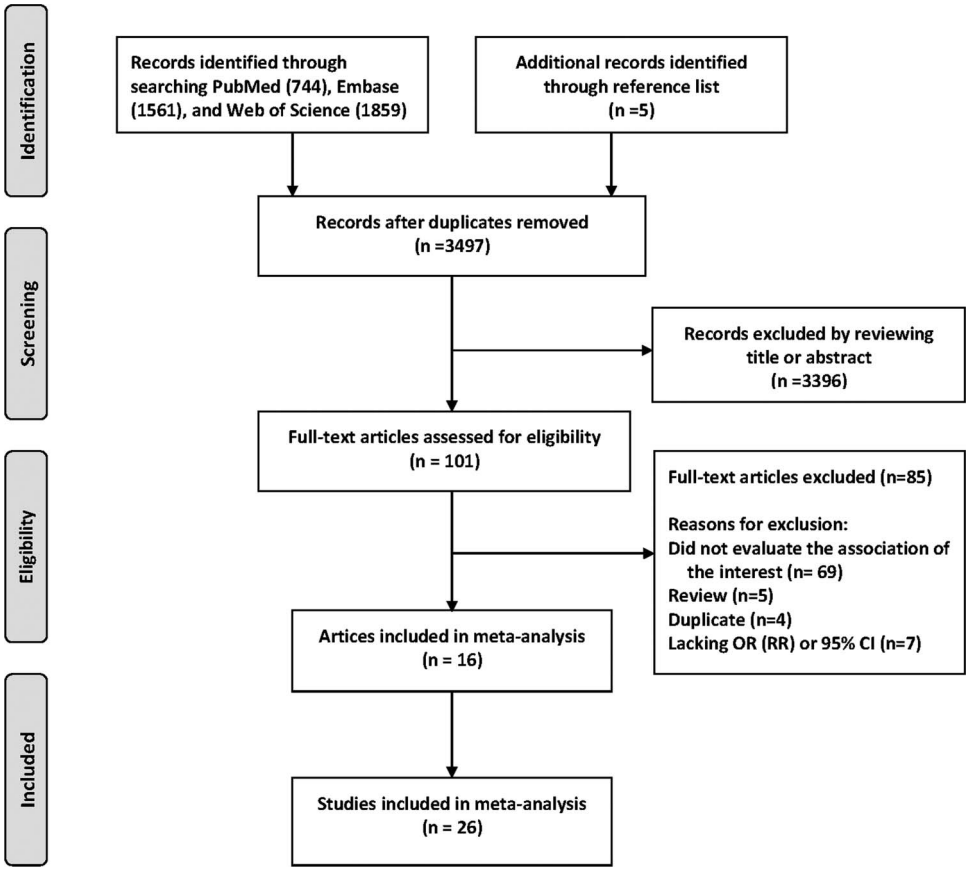

Figure 1 Flow diagram of the literature search.

studies were published between years 2001 and 2014, and involved a total of 150 278 participants. Of these studies, 10 were cohort studies[12 13 16–19 26 28] and 16 were cross-sectional studies.[11 14 15 27 29–32] With regard to the study continent, 10 studies were conducted in Europe,[11–15 29 31 32] 7 in North America,[16 17 27 28] 4 in Asia,[18 27 30] 3 in Oceania[19 26] and 2 in South America.[27] Nine studies evaluated the association between fish consumption and depression in men,[12 15 16 26 28–30 32] and 10 studies did so in women.[11 12 15–17 19 26 28 30 32] One study[30] was conducted among adolescents and the rest were conducted among adults. The major adjustment confounding factors included age, gender, marital status, education, smoking, alcohol use and body mass index. Quality assessment showed that the Newcastle-Ottawa score of 14 articles was not less than 7, indicating that the methodological quality was generally good (see online supplementary file 2).

Quantitative synthesis

Among the 26 studies, 12 studies showed a significant association between fish consumption and depression; while the other 14 studies indicated no relation between them. The pooled RR of depression for the highest versus lowest consumption of fish was 0.83 (95% CI 0.74 to 0.93, I^2=64.5%, P_Q<0.001, figure 2). After excluding the single study[30] conducted among adolescents, the findings remained significant (RR=0.83, 95% CI 0.73 to 0.94) for the studies conducted among adults.

Subgroup analysis by continent and study design was performed. The findings showed a significant inverse association both in cohort studies (RR=0.84, 95% CI 0.75 to 0.94) and cross-sectional studies (RR=0.82, 95% CI 0.68 to 1.00). Moreover, higher fish intake was associated with reduced risk of depression for studies conducted in Europe (RR=0.72, 95% CI 0.63 to 0.82), but not in those conducted in the other continents. The detailed results are presented in table 1.

When men and women were analysed separately, the pooled RR of depression was 0.80 (95% CI 0.65 to 0.99, I^2=50%, P_Q=0.042, figure 3) in men and 0.84 (95% CI 0.77 to 0.92, I^2=5.7%, P_Q=0.389, figure 4) in women.

Meta-regression and sensitive analysis

As shown in figure 1, moderate heterogeneity (I^2=64.5%, P_Q<0.001) was observed in the analysis. Univariate meta-regression analysis was conducted with the covariates of publication year, continent, sex, study design, sample size, the

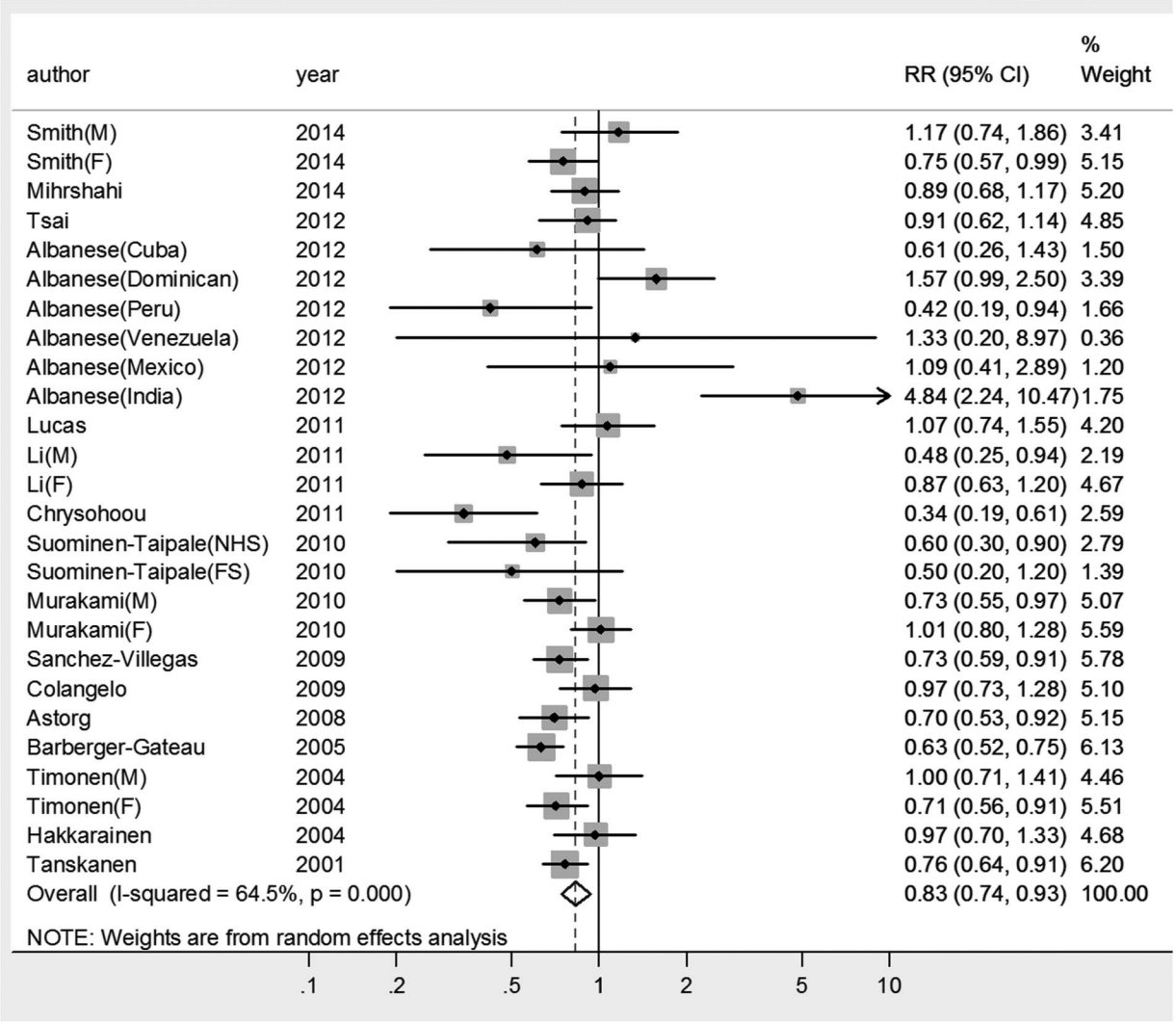

Figure 2 Forest plot of the relative risks (RRs) with corresponding 95% CIs of studies on fish consumption and depression. The size of the grey box is positively proportional to the weight assigned to each study, and horizontal lines represent the 95% s. FS, Fishermen Study; NHS, Nationwide Health 2000 Survey.

Table 1 Pooled RRs and 95% CI of depression for the highest versus lowest consumption of fish

	Number of studies	RR (95% CI)	Heterogeneity		Articles included
			I^2 (%)	P_Q Value	
All studies	26	0.83 (0.74 to 0.93)	64.5	<0.001	11–19, 26–32
Studies in adults	25	0.83 (0.73 to 0.94)	65.3	<0.001	11–19,26–29,31,32
Sex					
Men	9	0.80 (0.65 to 0.99)	50.0	0.042	12, 15, 16, 26, 28–30, 32
Women	10	0.84 (0.77 to 0.92)	5.7	0.389	11, 12, 15–17, 19, 26, 28, 30, 32
Study design					
Cohort	10	0.84 (0.75 to 0.94)	23.6	0.226	12, 13, 16–19, 26, 28
Cross-sectional	16	0.82 (0.68 to 1.00)	74.0	<0.001	11, 14, 15, 27, 29–32
Continent					
Europe	10	0.72 (0.63 to 0.82)	46.2	0.053	11–15, 29, 31, 32
North America	7	0.95 (0.75 to 1.20)	42.2	0.109	16, 17, 27, 28
South America	2	0.53 (0.21 to 1.34)	16.6	0.273	27
Asia	4	1.15 (0.74 to 1.79)	85.6	<0.001	18, 27, 30
Oceania	3	0.87 (0.71 to 1.08)	26.4	0.257	19, 26

RR, relative risk.

number of depression cases, the Newcastle-Ottawa score, dietary intake assessment and depression diagnosis method. However, the findings showed no covariates having a significant impact on between-study heterogeneity (p>0.05). Next we conducted the leave-one-out sensitivity analysis. Three studies[14 27] were found to contribute to between-study heterogeneity. After further excluding these studies, the heterogeneity (I^2=33%, P_Q=0.06) was decreased and the result remained significant (RR=0.81, 95% CI 0.74 to 0.87).

Influence analysis and publication bias

Influence analysis showed that no individual study had excessive influence on the pooled RR. The funnel plot and Egger's test showed no evidence of significant publication bias (p=0.419; figure 5).

DISCUSSION

This meta-analysis provides a comprehensive evaluation of the association between fish intake and the risk of depression. The study included 150 278 participants and the findings showed a significant inverse association between fish consumption and depression overall. Furthermore, the association remained significant when men and women were analysed separately. We also conducted subgroup analysis by study design. A significant association was observed in cohort studies as well as in cross-sectional studies. High-fish consumption was significantly

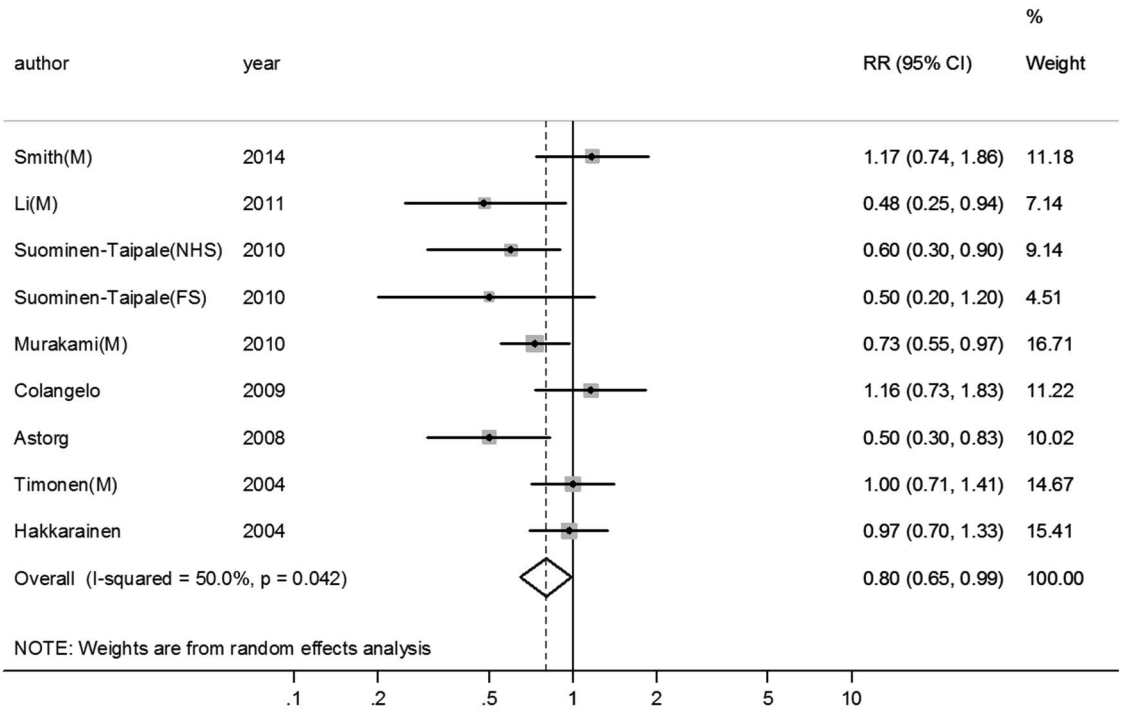

Figure 3 Forest plot of the relative risks (RRs) with corresponding 95% CIs of studies on fish consumption and depression mellitus in men. The size of the grey box is positively proportional to the weight assigned to each study, and horizontal lines represent the 95% s. NHS, Nationwide Health 2000 Survey.

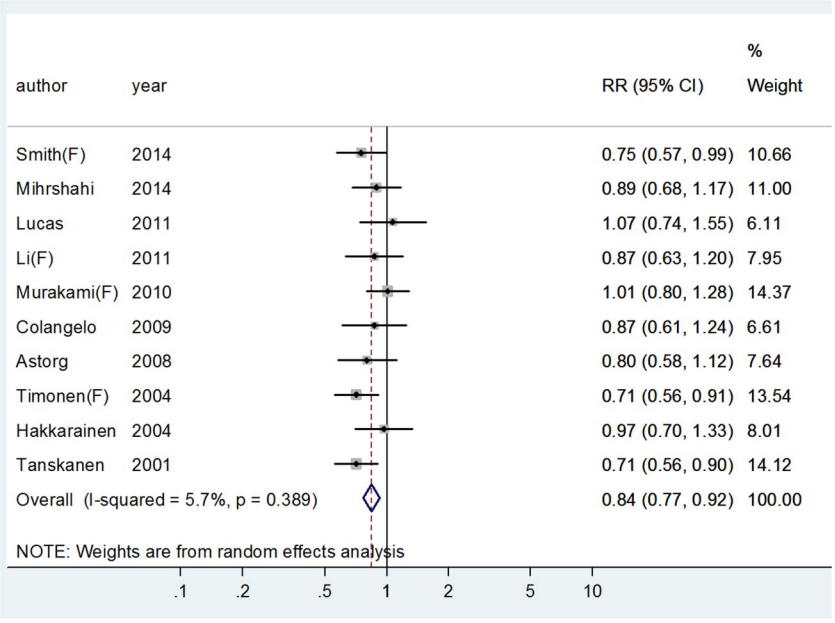

Figure 4 Forest plot of the relative risks (RRs) with corresponding 95% CIs of studies on fish consumption and depression mellitus in women. The size of the grey box is positively proportional to the weight assigned to each study, and horizontal lines represent the 95% s. FS, Fishermen Study; NHS, Nationwide Health 2000 Survey.

associated with reduced risk of depression only among studies conducted in Europe, and not in those conducted in North America, South America, Asia and Oceania.

The exact biological mechanisms whereby high-fish intake reduce risk of depression are not well established. It has been proposed that n-3 PUFAs are the beneficial component of fish for the inverse association by changing membrane microstructure and modifying serotonergic and dopaminergic neurotransmission.[33–35] In addition, high-quality protein, vitamins and minerals may have a protective effect on depression.[36 37] Finally, high-fish consumption may also be related to a healthier diet and better nutritional status, which could contribute to the lower risk of depression. The specific mechanisms require large experimental studies to confirm.

Between-study heterogeneity is common in meta-analysis because of diversity in population stratification, characteristics of the sample, different methodology issues, variation of covariates, etc. In this meta-analysis, moderate heterogeneity was found. However, the between-study heterogeneity was not successfully explained by subgroup analysis and meta-regression.

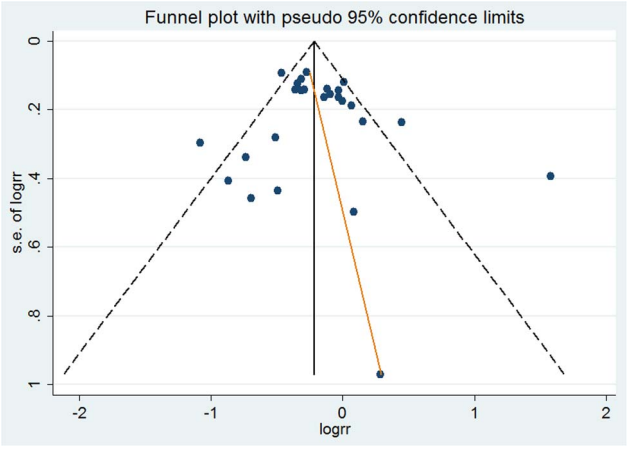

Figure 5 Funnel plot of the relative risks of 26 studies on fish consumption and depression. Each dot represents a different study.

Presumably, differences in fish type, fish preservation and cooking styles, may be an important determinant in the heterogeneity. Furthermore, many different measurement units of fish intake were reported, such as grams, servings, times per day, etc, which may have contributed to the heterogeneity. We also conducted a leave-one-out sensitivity analysis to reduce the heterogeneity. After excluding three studies, the heterogeneity decreased and the results remained significant.

To the best of our knowledge, this is the first meta-analysis to explore the association between fish consumption and risk of depression. There are some advantages in our study. First, a significant inverse association was evaluated from cohort studies in subgroup analysis, indicating a potential causal relationship between fish consumption and depression. Second, the large number of participants, reducing sampling error to a great extent, allowed a much greater possibility of reaching reasonable conclusions. Third, we extracted RRs that reflected the greatest degree of control for potential confounders, increasing the credibility of the results. Fourth, we found no evidence of publication bias in this meta-analysis.

However, several limitations should be acknowledged in our meta-analysis. First, although we extracted the most adjusted RRs from the original studies, the extent to which they were adjusted and residual confounding by other unmeasured factors should also be of concern. Second, fish consumption was measured using different dietary assessment methods and not all the methods were validated, including food frequency questionnaire, diet history questionnaire, diet history interview and dietary records, which led to incomparability of results to some extent. Third, depression diagnosis was largely inconsistent. Most studies relied on rating scales, such as the Center for Epidemiological Studies Depression (CES-D) Scale, the Beck Depression Inventory (BDI), the Hopkins Symptom Checklist (HSCL) depression subscale and the Geriatric Depression Scale (GDS); Some diagnoses were based on diagnostic interview schedules, including Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV), the Munich version of the Composite International Diagnostic Interview (M-CIDI) and International Classification of Diseases, Tenth Revision, (ICD-10); and others were (self-reported) physician diagnosis or

based on regular antidepressant medication use. Fourth, two articles[26 31] included seafood in the fish category and we did not differentiate fish type because of the limited available studies.

In conclusion, higher fish consumption may be beneficial in the primary prevention of depression. Future studies are needed to further investigate whether this association varies according to the type of fish.

What is already known on this subject

- A meta-analysis published recently indicated that a healthy dietary pattern, characterised by high intake of fruits, vegetables, fish and whole grains, was significantly associated with a reduced risk of depression
- Many studies have been conducted to assess the association of fish consumption with depression risk and the results remain controversial.

What this study adds

- This is the first meta-analysis to evaluate the association between fish consumption and depression risk.
- This meta-analysis shows that higher fish consumption is significantly associated with reduced risk of depression.

Contributors FL and DZ conceived the study, participated in its design and coordination and were involved in drafting the manuscript. FL and XL carried out the literature search, data extraction and interpretation of the data. FL, XL and DZ reviewed and revised the manuscript critically for important intellectual content and approved the final manuscript as submitted.

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