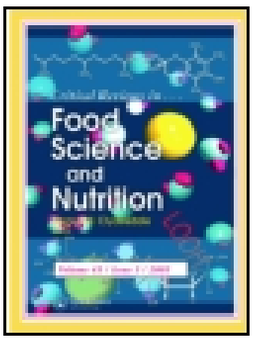

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Dietary fiber intake reduces risk for Barrett's esophagus and esophageal cancer

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Running head: Dietary fiber and Barrett's esophagus and esophageal cancer

Abstract

Background: Observational studies suggest an association between dietary fiber intake and risk of Barrett's esophagus and esophageal cancer. However, the results are inconsistent.

Objective: To conduct a meta-analysis of observational studies to assess this association.

Design: All eligible studies were identified by electronic searches in PubMed and Embase

through February 2015. Dose-response, subgroup, sensitivity and publication bias analyses were performed.

Results: A total of 15 studies involving 16,885 subjects were included in the meta-analysis. The pooled OR for the highest compared with the lowest dietary fiber intake was 0.52 (95% CI, 0.43-0.64). Stratified analyses for tumor subtype, study design, geographic location, fiber type, publication year, total sample size and quality score yielded consistent results. Dose-response analysis indicated that a 10 g/d increment in dietary fiber intake was associated with a 31% reduction in Barrett's esophagus and esophageal cancer risk. Sensitivity analysis restricted to studies with control for conventional risk factors produced similar results, and omission of any single study had little effect on the overall risk estimate. **Conclusions:** Our findings indicate that dietary fiber intake is inversely associated with risk of Barrett's esophagus and esophageal cancer. Further large prospective studies are warranted.

Keywords: Diet; Barrett's esophagus; Esophageal cancer; Epidemiology

Introduction

Esophageal cancer is the sixth most common cause of cancer-related deaths and the eighth most common cancer worldwide (Pennathur et al., 2013). More than 90% of esophageal cancers are esophageal adenocarcinoma or esophageal squamous cell carcinoma (ESCC) (Enzinger et al., 2003). Barrett's esophagus, the condition in which a metaplastic columnar mucosa replaces an esophageal squamous mucosa, is considered to be the only known precursor in esophageal adenocarcinoma (Maley et al., 2006, Hvid-Jensen et al., 2011, Spechler et al., 2014).

Dietary fiber plays an important role in the prevention of esophageal cancer. Recently, studies have shown that dietary fiber could remove damaged cells and carcinogens from the esophageal epithelium (Slavin, 2000). Moreover, fiber-rich foods are also known to be associated with lower concentrations of inflammation biomarkers, such as interleukin-6, which play important roles in carcinogenesis (Ma et al., 2008).

A previous meta-analysis (Coleman et al., 2013) of dietary fiber intake and risk of esophageal cancer reported a pooled risk estimate of 0.66 (95% confidence interval [CI], 0.44-0.98) for esophageal adenocarcinoma and 0.61(95% confidence interval [CI], 0.31-1.20) for esophageal squamous cell carcinoma (ESCC) for the highest versus lowest category of dietary fiber intake. However, the study had significant unexplained heterogeneity across studies. Moreover, dietary fiber intake in the highest and lowest categories differed substantially between studies, which made it difficult to interpret the summary estimate based on results from study populations with

different ranges of dietary fiber intake. A more robust method to combine results from individual studies and to derive a summary relative risk for a standardized increase in dietary fiber intake is needed.

With newly published studies, we conducted the meta-analysis to analyze the effect of dietary fiber on the risk of Barrett's esophagus and esophageal cancer. In order to better quantify the potential association between dietary fiber intake and esophageal cancer risk, we conducted a dose–response meta-analysis, which provided a solution to the problem with different ranges of dietary fiber intake in different populations.

Methods

Search strategy and selection criteria

We conducted the literature search in PubMed and Embase for eligible studies through February 2015. The associated medical subject headings and terms were: (dietary fiber) AND (Barrett's Esophagus OR esophageal cancer). Moreover, we also reviewed the reference lists for potentially relevant studies. A standard guideline for designing, conducting and reporting meta-analysis of observational studies was followed (Stroup et al., 2000).

Eligible studies included in our meta-analysis had to meet the following criteria: (1) use a case-control or cohort design; (2) the exposure of interest was dietary fiber intake; (3) the outcome of interest was Barrett's esophagus or esophageal cancer; (4) reported the odds ratio (OR), and the corresponding 95% confidence interval (CI) for the association. Abstracts,

reviews and editorials were excluded. As for the duplicates, the most recent and complete studies were included. Two authors (LS and ZZ) independently evaluated the retrieved studies according to the selection criteria and reached a consensus on all the items by discussion.

Data extraction and quality assessment

The following information was collected from each eligible study: the first author's last name, publication year, study design, geographic location, age, sex, study period, sample size, fiber intake assessment and comparison method, OR value from the most fully adjusted model for the highest compared with the lowest dietary fiber intake and the corresponding 95% CI, and confounders adjusted for in the multivariate analysis. Two authors (LS and ZZ) independently extracted the data and then cross-checked it.

Study quality was assessed by an evaluation system based on the Newcastle-Ottawa Scale (NOS) (Stang, 2010). The NOS is judged on 3 aspects: the selection of study populations, the comparability of the populations and elucidation of exposure or the outcomes of interest for case-control or cohort studies respectively.

Statistical analysis

We extracted ORs from the included studies, and calculated the standard errors from the corresponding 95% CIs. A random-effects model was used to evaluate the pooled OR for the association between dietary fiber intake and risk of Barrett's esophagus and esophageal cancer. The heterogeneity among studies was assessed with the χ^2 test and I^2 statistics (Higgins et al.,

2003).

A cumulative meta-analysis was adopted to update an accumulated effect from all studies, and to demonstrate the trend of risk effect regarding dietary fiber intake on Barrett's esophagus and esophageal cancer as new evidence accumulated. (Lau et al., 1992) Moreover, stratification analyses were performed by subtypes of esophageal cancer, study design, geographic location, fiber source, fiber type and quality score to evaluate the potential effect modification of these variables on the results. We also conducted a sensitivity analysis to explore the influence of a single study on the entire outcome by removing each study in sequence.

For the dose-response meta-analysis, we used the estimation method proposed by Greenland and Longnecker (Greenland et al., 1992) to assess the trend from the correlated log OR estimates according to categories of fiber intake. Among all the included studies, only that reported the number of case and control subjects and the OR and corresponding 95% CI for at least 3 quantitative exposure categories were included. For those included studies, the mean or median fiber intake for each category was used for the estimation.

To evaluate the potential publication bias, we used funnel plots (Begg et al., 1994) and the Egger linear regression test (Egger et al., 1997). All the statistical analyses were performed using STATA version 12.0 (StataCorp LP, College Station, TX, USA).

Results

Search results, study characteristics and quality assessment

Total searches yielded 51 entries, of which 25 were considered to be possibly relevant after title and abstract review. Among the 25 studies, 10 were excluded after detailed assessment for the following reasons: review or editorial (n = 4); no OR or 95% CI reported (n = 2); association not evaluated (n = 4). As a result, 15 studies (21 results) (Kabat et al., 1993, Tzonou et al., 1996, Zhang et al., 1997, De Stefani et al., 1999, Mayne et al., 2001, Soler et al., 2001, Terry et al., 2001, Chen et al., 2002, Wu et al., 2007, Kubo et al., 2009, Mulholland et al., 2009, Jessri et al., 2011, Jiao et al., 2013, Tang et al., 2013, Lahmann et al., 2014) that contained 16,885 subjects were included in our meta-analysis (Fig. 1).

These 15 included studies were published between 1993 and 2014. Of the 15 studies, 7 were population-based case-control studies, and 8 were hospital-based case-control studies (Table 1). The sample size of the included studies ranged from 143 to 4740. The quality scores of each individual study were summarized in Table 2. The quality scores ranged from 6 to 8, and the median score was 7.

Fiber intake and the risk of Barrett's esophagus and esophageal cancer

The multivariable-adjusted ORs for each study and the pooled OR for the highest compared with the lowest categories of dietary fiber intake are shown in Fig. 2. For the 21 results, 19 showed that dietary fiber intake was associated with a decreased risk of Barrett's esophagus and esophageal cancer, 15 of which were statistically significant. Overall, the pooled OR was 0.52 (95% CI, 0.43-0.64) with significant heterogeneity ($P < 0.001$, $I^2 = 71.6\%$; Fig. 2). In the

cumulative meta-analysis, the combined OR achieved significance beginning in 1996 and displayed a trend of association as published studies accumulated (Fig. 3).

Dose-response meta-analysis

We next evaluated the dose-response relationship between dietary fiber intake and risk of Barrett's esophagus and esophageal cancer. Four case-control studies (Terry et al., 2001, Kubo et al., 2009, Jiao et al., 2013, Lahmann et al., 2014) were included in the dose-response meta-analysis. The dose-response analysis indicated that the risk of Barrett's esophagus and esophageal cancer decreased by 31% (OR: 0.69, 95% CI 0.61-0.79) for a 10 g/d increase in dietary fiber intake.

Stratification analyses

Stratifying by subtypes, the ORs were 0.50 (95% CI, 0.37-0.67) for esophageal adenocarcinoma, 0.42 (95% CI, 0.29-0.61) for Barrett's esophagus, and 0.53 (95% CI, 0.31-0.90) for ESCC (Fig 4). Stratifying by study design, significant inverse associations were observed both in population based case-control studies (OR, 0.47; 95% CI, 0.35-0.62) and hospital based case-control studies (OR, 0.62; 95% CI, 0.49-0.79; Table 3). Stratified by geographic region, the ORs were 0.36 (95% CI, 0.28-0.45) for studies in US, and 0.76 (95% CI, 0.64-0.90) for studies in Europe. In the subgroup analyses by fiber source and fiber type, the ORs were 0.81 (95% CI, 0.61-1.07) for cereal fiber, 0.61 (95% CI, 0.45-0.83) for vegetable fiber, 0.73 (95% CI, 0.48-1.12) for fruit fiber, 0.85 (95% CI, 0.65-1.11) for grain fiber, 0.40 (95% CI, 0.20-0.78) for

soluble fiber and 0.37 (95% CI, 0.18-0.75) for insoluble fiber. Furthermore, significant inverse associations were also observed in the stratified analyses by publication year, sample size and quality score.

Sensitivity analyses

Exclusion of 1 study (Jessri et al., 2011) that did not adjust for dietary factors or energy intake yielded an OR of 0.53 (95% CI: 0.43-0.66), with substantial evidence of heterogeneity ($P < 0.001$, $I^2 = 73.0\%$). Restricting analysis to studies that were adjusted for smoking yielded similar results (OR: 0.53, 95% CI: 0.43-0.66; n = 14), yet heterogeneity was still present ($P < 0.001$, $I^2 = 72.4\%$). Further exclusion of any single study did not materially change the overall result, with a range from 0.49 (95% CI, 0.40-0.61) to 0.58 (95% CI, 0.49-0.70).

Publication bias

The funnel plot did not show any substantial asymmetry. Egger's test also showed no evidence of significant publication bias ($P > 0.05$).

Discussion

Our meta-analysis containing 16,885 participants provides evidence that dietary fiber intake is significantly and independently associated with a decreased risk of Barrett's esophagus and esophageal cancer. Stratified analyses for tumor subtype, study design, geographic location, type of fiber, publication year, sample size and quality score of the study yielded similar results. Moreover, the dose-response analysis indicated that an increase in dietary fiber intake of 10

g/day was associated with a statistically significant 31% decreased risk of Barrett's esophagus and esophageal cancer.

The previous meta-analysis (Coleman et al., 2013) didn't show a strong association between dietary fiber intake and a decreased risk of ESCC (OR = 0.61, 95% confidence interval [CI], 0.31-1.20). However, adding newly published studies, dietary fiber intake significantly reduced ESCC risk with the pooled estimates of 0.53 (95% CI, 0.31-0.90) in our meta-analysis. Thus, further evidence is warranted to verify our findings.

Many studies have investigated the possible mechanisms underlying the anticancer effect of a high dietary fiber intake. High dietary fiber intake indicates a diet rich in fruits and vegetables or micronutrients, some of which have been proven to prevent esophageal cancer (Gonzalez et al., 2006, Jessri et al., 2011). Inositol hexaphosphate, one component in food sources high in dietary fiber, has been demonstrated in vitro experiment to inhibit the growth rate of Barrett's-associated esophageal adenocarcinoma cells by reducing cellular proliferation and stimulating apoptosis (McFadden et al., 2008). Dietary fiber phenolic compounds ferulic acid and p-coumaric acid may have an anti-proliferative effect on cell cycle (Janicke et al., 2011). In addition, a high dietary fiber diet is associated with lower plasma levels of systematic inflammation biomarkers such as tumor necrosis factor-α receptor-2 (TNF-α-R2) and interleukin-6 (IL-6), which may influence the process of carcinogenesis (Ma et al., 2008). These studies support our finding that moderate dietary fiber intake is associated with a decreased risk

of Barrett's esophagus and esophageal cancer.

Study strengths and limitations

Because a single study may be underpowered to evaluate the overall effects, a quantitative synthesis of the accumulated data from all eligible studies is an important method to provide evidence on the association of dietary fiber intake with Barrett's esophagus and esophageal cancer risk. We also conducted subgroup analyses to evaluate the effect modifications on results and explore potential sources of heterogeneity. Moreover, the presence of dose-response relationship further strengthened the association of dietary fiber intake with the risk of Barrett's esophagus and esophageal cancer.

This meta-analysis also had several limitations. First, due to the observational design, the possibility that other factors may account for the observed association could not be excluded. However, most studies in this meta-analysis adjusted for potential confounders, including age, sex, education, smoking, alcohol consumption and total energy intake. The association persisted when we restricted the analysis to studies that adjusted for all these factors. Further study with a prospective design is warranted to verify the findings. Second, we combined the data of Barrett's esophagus, esophageal adenocarcinoma and ESCC for the analyses considering the limited studies. In order to observe the effect of dietary fiber intake on Barrett's esophagus, esophageal adenocarcinoma and ESCC separately, stratified analysis by subtype was conducted. Moreover, there was substantial heterogeneity among included studies, which was not

surprising given the differences in population characteristics, sample sizes, adjustments for risk factors and dietary fiber intake assessment methods. Our stratified analyses showed that the heterogeneity was not significant in US and Europe subgroups separately, which indicated that population differences might potentially account for the heterogeneity.

Conclusions

Our meta-analysis suggests that dietary fiber intake is significant associated with a reduced risk of Barrett's esophagus and esophageal cancer. However, the results should be treated with caution given the limited number of studies, the influence of other potential confounders and substantial heterogeneity among the studies. Well-designed large prospective studies for dietary fiber supplementation are warranted to confirm this association and to better establish the potential dose-response relationship, which may play an important role for the prevention of esophageal cancer in the future.

Acknowledgments

Authors' responsibilities: LS and ZZ conducted the literature search and extracted the data. LS and ZZ conducted the statistical analysis. LS prepared the first draft of the article. LS, ZZ, JX, GX and XL contributed to the writing, editing and proof reading of the final version of the article. We thank Benjamin Kidder for editing for English grammar. No conflicts of interest were declared.

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Table 1. Characteristics of the included studies

Study/ Year	Design	Country	Age, sex	Study period	Case/ Control	Assessment of intake/ food item number/ fiber intake calculation/ nutrient database	Comparison	OR (95% CI)	Adjusted or matched variables
Esophageal Adenocarcinoma									
Kabat et al. 1993	HCC	US	-,M	1981-1990	121/4544	FFQ/30/-/ USDA's food	Quartiles	0.31(0.14-0.67)	Age, smoking, alcohol,
Tzono et al. 1996	HCC	Greece	-,M/F	1989-1991	56/200	FFQ/115/nutrient content × frequency/a nutrient database in Greece	Quintiles	0.74(0.55-0.99)	Age, sex, birthplace, schooling, height, analgesics, coffee drinking, alcohol intake, tobacco smoking and energy intake
Zhang et al. 1997	HCC	US	-,M/F	1992-1994	90/124	NCI's HHHQ/-/(food frequency portion size × nutrient content × seasonality factor)/100/ USDA's food composition data	Quartiles	0.3(0.1-0.8)	Age, sex, race, education, smoking, alcohol intake, BMI, and total dietary intake of calories
Mayne et al. 2001	PCC	US	30-79, M/F	1993-1995	282/687	FFQ/104/portion size × frequency /US nutrition coding center nutrient	Quartiles	0.28(0.19-0.40)	Age, site, sex, race, proxy status, BMI, income, education, smoked,

						data system			and alcohol consumption
Terry et al. 2001	PCC	Sweden	67, 68 M/F	1995-1997	185/815	FFQ/63/nutrient content × frequency/-	Quartiles	0.8(0.5-1.3)	Age, sex, BMI, smoking, alcohol consumption, antioxidant intake, total energy consumption, socioeconomic status and reflux
Chen et al. 2002	PCC	US	62.3/59.8 M/F	1988-1993	124/449	HHHQ/60/portion size × frequency/US DIETSYS database	Quartiles	0.5(0.3-0.9)	Age, age squared, sex, respondent type, BMI, alcohol use, tobacco use, education, family history of cancers, and vitamin supplement use
Wu et al. 2007	PCC	US	30-74 M/F	1992-1997	206/1308	FFQ/124/portion size × frequency/USDA's nutrient database	Quartiles	0.40(0.2-0.7)	Age, sex, race, birthplace, education, smoking, BMI, reflux, use of vitamins, total

									calories, and fat
Mulholland et al. 2009	PCC	Ireland	64/63 M/F	2002-2005	224/256	EPIC's FFQ/101/ Englyst method, Southgate method/-	Tertiles	0.79(0.43-1.44)	Age, sex, energy intake, smoking, BMI, education, occupation, alcohol, regular NSAID use, location, and H. pylori
Lahmann et al. 2014	PCC	Australia	18-79 M/F	2002-2005	288/1490	FFQ/135-item/-/-	Quartiles	0.49(0.31-0.77)	Age, sex, education, BMI, smoking, physical activity, alcohol intake, NSAID, diabetes, total fruit intake (except for fiber), red meat, processed meat, and total energy
Barrett's Esophagus									
Kubo et al. 2009	PCC	US	62.3, M/F	2002-2005	296/309	FFQ/110/portion size × frequency/ Dietary Data Systems	Quartiles	0.34(0.15-0.76)	Age, sex, race, long-term vitamin use (>2 years), and energy
Mulholland et al. 2009	PCC	Ireland	64/63, M/F	2002-2005	220/256	EPIC's FFQ/101/Englyst method,	Tertiles	0.40(0.22-0.73)	Age, sex, energy intake, smoking,

						Southgate method/-			BMI, education, occupation, alcohol, regular NSAID use, location, and H. pylori
Jiao et al. 2013	HCC	US	40-80, M/F	2008-2011	41/259	FFQ/110/portion size × frequency/ USDA My-Pyramid Equivalents Database	Tertiles	0.50(0.28-0.90)	Age, sex, energy intake, ethnicity, smoking, alcohol consumption, waist-to-hip ratio, recent use of aspirin, use of proton pump inhibitor, reflux, and physical activity
Esophageal Squamous Cell Carcinoma									
Kabat et al. 1993	HCC	US	-,M	1981-1990	75/4544	FFQ/30/-/ USDA's food composition tables	Quartiles	0.77(0.32-2.00)	Age, smoking, alcohol, education, hospital, and remaining dietary factors
Tzono et al. 1996	HCC	Greece	-,M/F	1989-1991	43/200	FFQ/115/nutrient content × frequency/a nutrient database in Greece	Quintiles	0.88(0.64-1.21)	Age, sex, birthplace, schooling, height, analgesics, coffee

									drinking, alcohol intake, tobacco smoking and energy intake
Mayne et al. 2001	PCC	US	30-79, M/F	1993-1995	206/687	FFQ/104/portion size × frequency /US nutrition coding center nutrient data system	Quartiles	0.24(0.14-0.38)	Age, sex, site, race, proxy status, BMI, income, education, smoked, and alcohol consumption
Terry et al. 2001	PCC	Sweden	67/68, M/F	1995-1997	165/815	FFQ/63/nutrient content × frequency/-	Quartiles	1.1(0.6-1.9)	Age, sex, BMI, smoking, alcohol consumption, antioxidant intake, total energy consumption, socioeconomic status and reflux
Jessri et al. 2011	HCC	Iran	40-75, M/F	—	47/96	semi-quantitative FFQ/125//USDA's food composition table	Tertiles	0.29(0.13-0.76)	Age, sex, reflux[a], BMI, smoking, physical activity, and education
Lahmann et al. 2014	PCC	Australia	18-79 M/F	2002-2005	227/1490	FFQ/135-item/-/-	Quartiles	0.38(0.23-0.63)	Age, sex, education, BMI, smoking, physical activity,

									alcohol intake, NSAID, diabetes, total fruit intake (except for fiber), red meat, processed meat, and total energy
Esophageal Cancer									
De Stefani et al. 1999	HCC	Uruguay	-, M/F	1996-1997	66/393	FFQ/-/-/food composition tables	Tertiles	1.0(0.7-1.4)	Age, sex, residence, urban/rural status, education, BMI, tobacco smoking, total alcohol intake and total energy intake
Soler et al. 2001	HCC	Italy	<79, M/F	1992-1997	304/1950	FFQ/78/-/Italian food composition databases	Quintiles	0.7(0.51-0.96)	Age, sex, center, education, alcohol and tobacco consumption and non-alcohol energy intake
Tang et al. 2013	HCC	China	61.4/60.6, M/F	2008-2009	359/380	FFQ/137 item/-/Chinese food composition tables	Tertiles	0.47(0.32-0.69)	Age, sex, education, BMI, total energy intake, smoking, alcohol drinking

									and family history of cancer in first-degree relatives

HCC: hospital-based case-control; PCC: population-based case-control; FFQ: Food Frequency Questionnaire; USDA: United States Department of Agriculture; NCI: National Cancer Institute; HHHQ: Health Habits and History Questionnaire; EPIC: European Prospective Investigation into Cancer and Nutrition NSAID: non-steroidal anti-inflammatory drug; BMI: body mass index.

Table 2. Methodologic quality of case-control studies included in the meta-analysis

Study	Adequate definition of cases	Representativeness of cases	Selection of controls	Definition of controls	Control for important factors[a]	Exposure ascertainment	Same method of ascertainment for all subjects	Nonresponse rate[b]	Total quality scores
Kabat et al.(1993)	☆	☆	–	☆	☆☆	–	☆	–	6
Tzono et al.(1996)	☆	☆	–	–	☆☆	☆	☆	–	6
Zhang et al.(1997)	☆	☆	–	☆	☆☆	☆	☆	–	7
Stefani et al. (1999)	☆	☆	–	☆	☆☆	–	☆	–	6
Mayne et al.(2001)	☆	☆	☆	–	☆	☆	☆	–	6
Soler et al.(2001)	☆	☆	–	☆	☆☆	☆	☆	–	7
Terry et al.(2001)	☆	☆	☆	–	☆☆	☆	☆	–	7
Chen et al.(2002)	☆	☆	☆	–	☆☆	☆	☆	☆	8
Wu et al.(2007)	☆	☆	☆	–	☆☆	☆	☆	–	7
Mulholland et al.(2009)	☆	☆	☆	☆	☆☆	☆	☆	–	8
Kubo et	☆	☆	☆	–	☆☆	☆	☆	–	7

al.(2009)									
Jessri et al.(2011)	☆	☆	–	☆	☆	☆	☆	–	6
Jiao et al.(2013)	☆	☆	–	–	☆☆	☆	☆	–	6
Tang et al.(2013)	☆	☆	–	☆	☆☆	☆	☆	–	7
Lahmann et al. (2014)	☆	☆	☆	–	☆☆	☆	☆	–	7

[a]A maximum of 2 stars could be awarded for this item. Studies controlled for age received 1 star, and studies controlled for intake of other nutrients received an additional star.

[b]One star was assigned if there was no significant difference in the response rate between case and control subjects by using the chi-square test ($P > 0.05$).

Table 3. Stratified analyses of dietary fiber intake and Barrett's esophagus and esophageal cancer risk

			Heterogeneity		
Group	Studies, *N*	OR (95% CI)	χ^2	*P*	I^2 (%)
Total	15	0.52 (0.43-0.64)	70.35	<0.001	71.6
Subtypes					
Esophageal adenocarcinoma	9	0.50 (0.37-0.67)	24.63	0.002	67.5
Barrett's esophagus	3	0.42 (0.29-0.61)	0.63	0.731	0.0
ESCC	6	0.53 (0.31-0.90)	28.75	<0.001	82.6
Design					
HCC	8	0.62 (0.49-0.79)	22.11	0.009	59.3
PCC	7	0.47 (0.35-0.62)	31.92	<0.001	68.7
Geographic location					
US	7	0.36 (0.28-0.45)	9.83	0.277	18.6
Europe	4	0.76 (0.64-0.90)	7.15	0.307	16.0
Fiber source					
Cereal fiber	3	0.81 (0.61-1.07)	3.97	0.264	24.5
Vegetable fiber	4	0.61 (0.45-0.83)	9.22	0.056	56.6
Fruit fiber	4	0.73 (0.48-1.12)	20.59	<0.001	80.6
Grain fiber	2	0.85 (0.65-1.11)	0.21	0.644	0.0
Fiber type					
Soluble fiber	2	0.40 (0.20-0.78)	18.71	<0.001	89.3
Insoluble fiber	2	0.37 (0.18-0.75)	21.10	<0.001	90.5
Publication year					
Before 2000	4	0.72 (0.53-0.97)	11.22	0.047	55.5
2000 or later	11	0.48 (0.38-0.59)	39.39	<0.001	64.5
Sample size (total)					
< 1000	8	0.55 (0.43-0.70)	18.58	0.029	51.6
≥ 1000	6	0.48 (0.35-0.67)	36.64	<0.001	75.4
Quality score					
< 7	6	0.50 (0.34-0.74)	50.83	<0.001	84.3
≥ 7	9	0.54 (0.44-0.67)	19.29	0.056	43.0

ESCC: Esophageal squamous cell carcinoma.

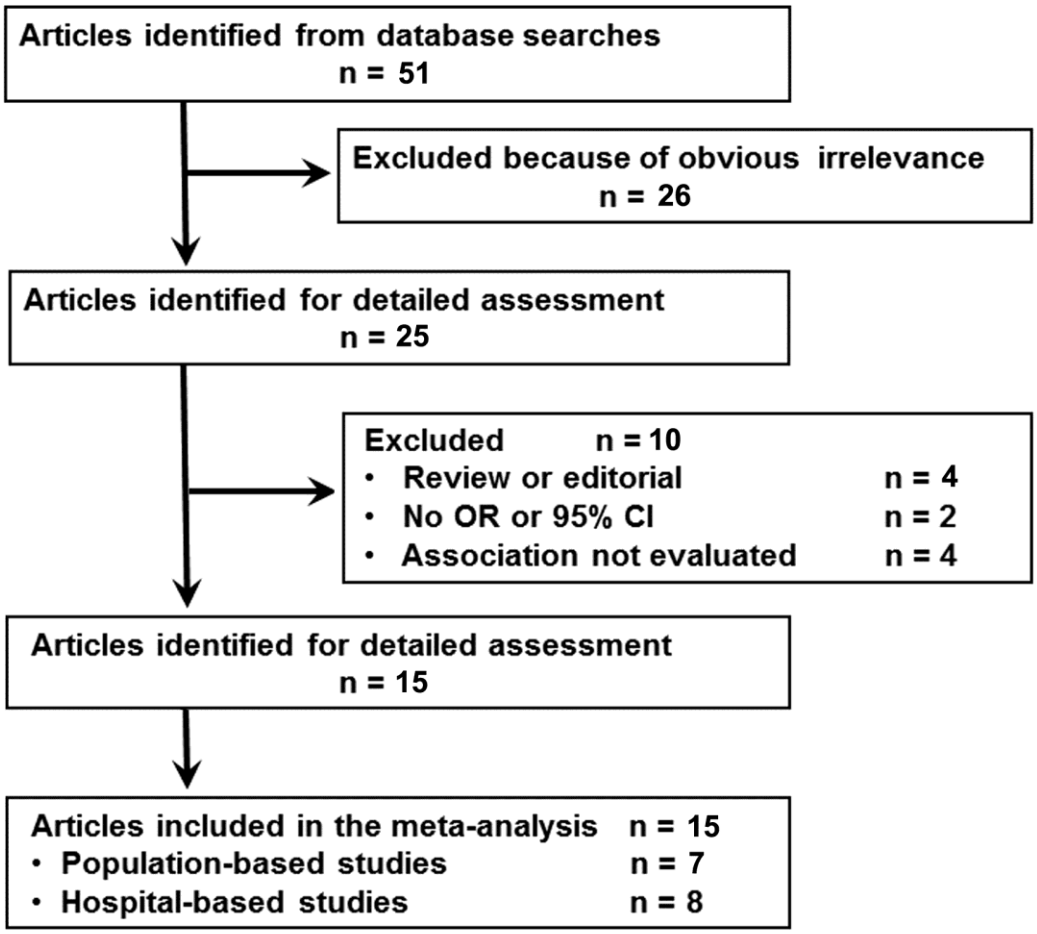

Figure 1

Figure 1. Flow diagram of study selection.

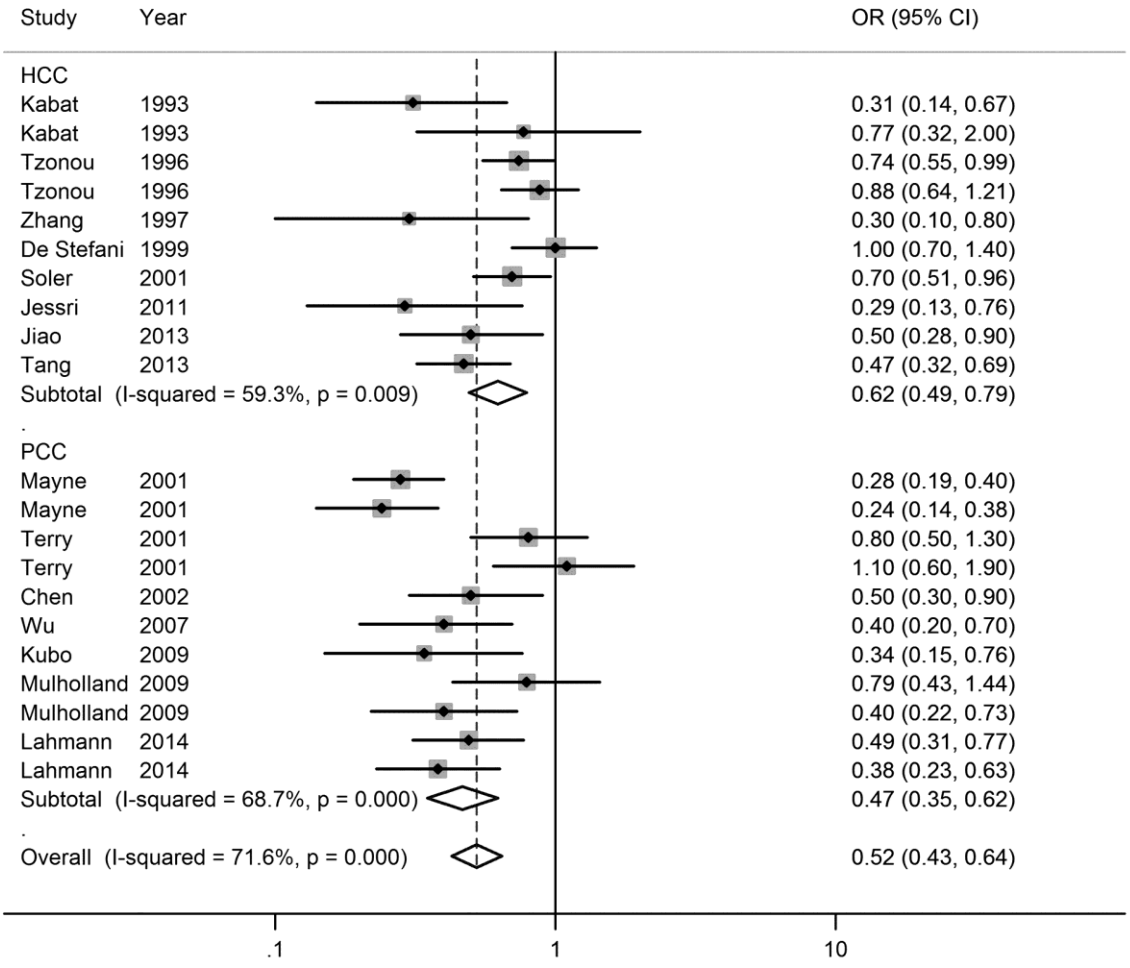

Figure 2. Forest plot of dietary fiber intake and the risk of Barrett's esophagus and esophageal cancer. HCC, hospital-based case-control; PCC, population-based case-control.

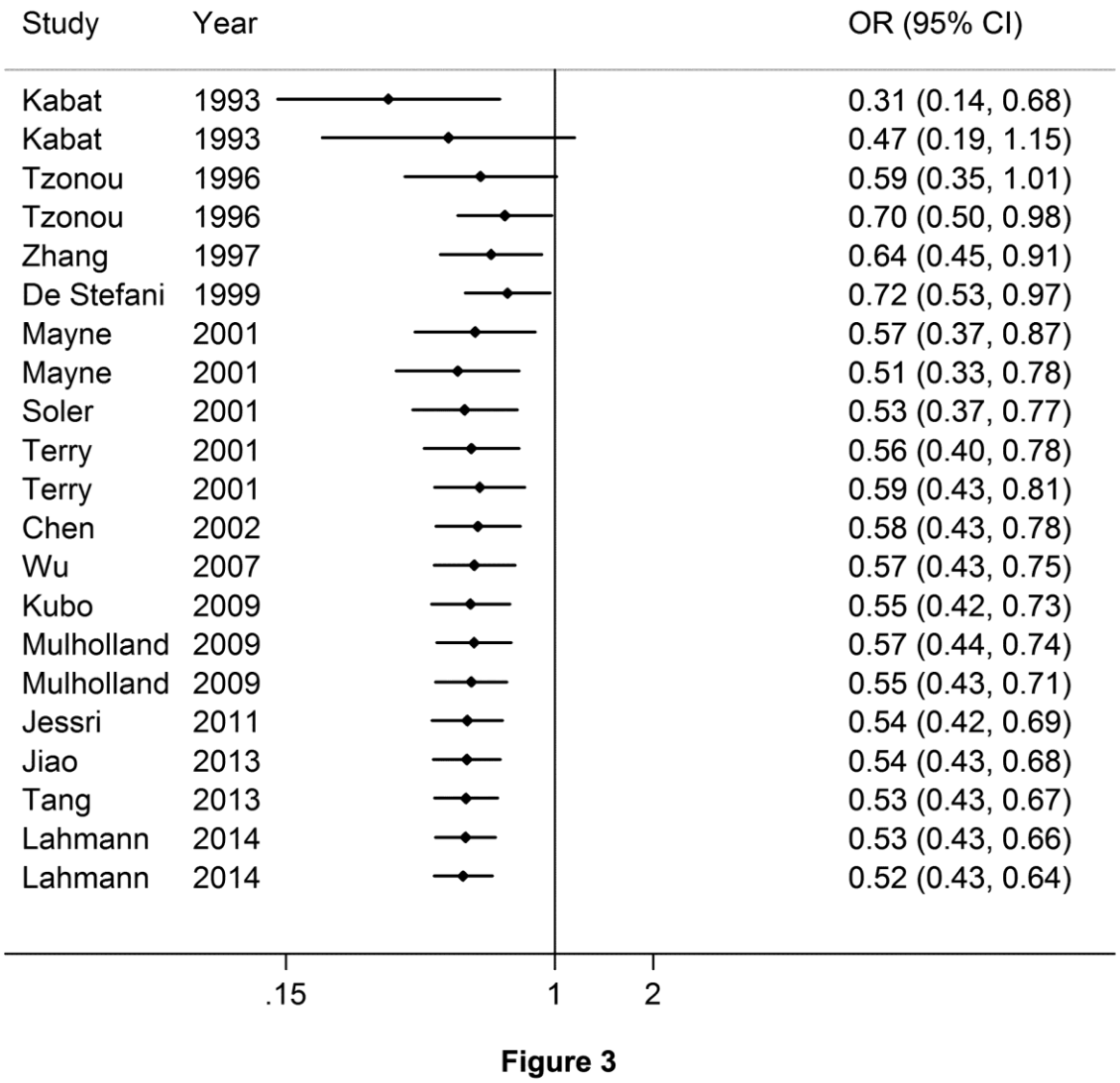

Figure 3. Cumulative meta-analysis.

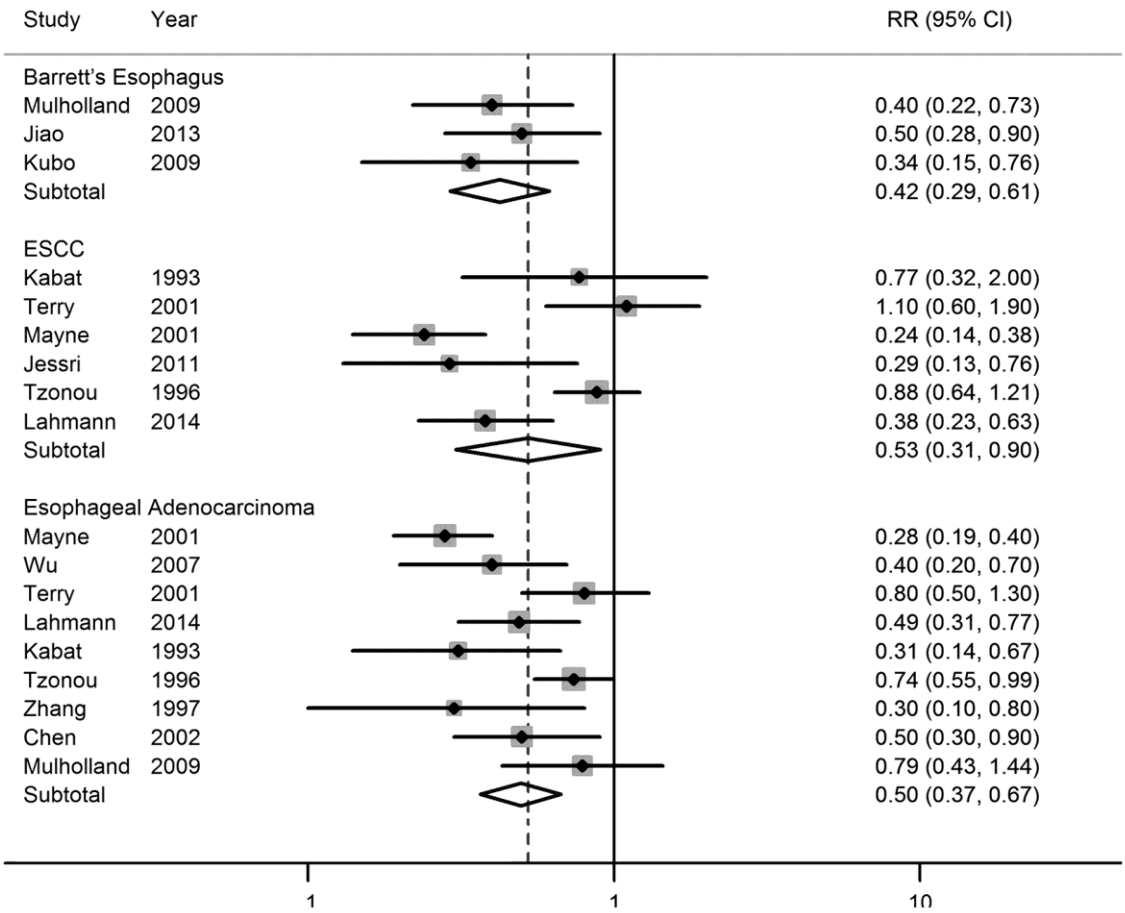

Figure 4. Forest plot of dietary fiber intake and the risk of Barrett's esophagus and esophageal cancer separately.